Irish Medical Journal
Established 1867

February 2021 Vol. 114 No. 2

COMMENTARY

EDITORIALS

INTERVIEW

ORIGINAL PAPERS

Paluck et al found that the group of cystic fibrosis children on these therapies had a reduction in ALT, ALP, GGT, and bilirubin levels. An initial rise in AST in two children settled over time.

Kelly et al found that among 156 women with breast cancer, an NLR >2.5 and PLR>150 were adverse prognostic factors.

Ward et al carried out an 8-week exercise program on 6 haemodialysis patients. Their sitto-stand performance increased from 21.1 in one minute to 27.3 in one minute.

ORIGINAL PAPERS (Continued)

AN AUDIT OF PATIENT SATISFACTION IN AN OUTPATIENT HYSTEROSCOPY CLINIC SETTING

Roseingrave and Lalchandani report their experiences with an outpatient hysteroscopy service. Among 60 women surveyed, there was a high level of satisfaction.

FATTY LIVER INFILTRATION ON EXECUTIVE HEALTH SCREEN

Frengopoulos et al found moderate fatty liver infiltration in half of 36 individuals presenting for an executive health screen.

NEONATAL THERAPEUTIC HYPOTHERMIA FOR NEONATAL ENCEPHALOPATHY - MORTALITY AND NEURODEVELOPMENTAL OUTCOME

Power et al report the outcome for 127 infants with neonatal encephalopathy treated with therapeutic hypothermia. 12 infants died. Among the survivors, 81% had a normal brain MRI. The neurodevelopmental outcomes at two years are documented.

IRISH MATERNITY - A CHANGING ETHNIC LANDSCAPE

Rowland report that in their hospital there was 62,259 Irish mothers, and 28, 456 non-Irish mothers. The number of non-Irish mothers increased from 1453 in 2001 to 3136 in 2012.

SCREWING OUR ENVIRONMENT - AN ANALYSIS OF ORTHOPAEDIC IMPLANT RELATED WASTE

Hennessy et al document the large amount of packaging associated with orthopaedic fixation devices.

ENDOSCOPIC EAR SURGERY (EES) A NEW VISTA IN OTOLOGY

Keogh et al describe their experience with Endoscopic Ear Surgery procedures.

TRAINEES' PERCEPTION OF MEDICOLEGAL PRACTICE IN SURGERY

Mohan et al report on 135 trainees and their perceptions about litigation. 33% have already received medicolegal correspondence. 96% expect to be sued into the future. Two thirds state that the issue makes them more risk adverse.

THE IMPACT OF THE COVID-19 PANDEMIC ON THE UPTAKE OF THE SEASONAL INFLUENZA VACCINE

O'Sullivan et al report that there has been a 27.4% increase in 'flu vaccine uptake' in 2020 compared with 2019.

SHORT REPORTS

EVALUATION OF A POLYSACCHARIDE HAEMOSTATIC SYSTEM IN OBSTETRICS AND GYNAECOLOGY

Nolan et al report on 50 surgeries where HaemoCer Plus was employed. It was easy to use and was an effective haemostatic agent.

COHORT OF HAEMODIALYSIS PATIENTS WITH COVID-19 IN AN IRISH NEPHROLOGY CENTRE

Herbert et al report that 20 patients on haemodialysis contracted Covid-19. Ten of the patients subsequently died.

THE PYJAMA SESSIONS - TRANSITION TO ONLINE EDUCATION DURING A PANDEMIC

Cassidy et al describe their experience with on-line education sessions. 95% found the sessions useful. 83% attended when not scheduled to work.

HOSPITALISED OLDER PEOPLE WITH COVID-19 - ONE MONTH OUTCOMES

Fallon et al report 86 hospitalised patients over 65 years with Covid-19. One month after contracting the virus, 33% had died, 14% were waiting rehabilitation, and 44% had been discharged.

OCCASIONAL PIECES

ADVANCING PROFESSIONAL HEALTHCARE BY THE USE OF MENTORSHIP

CASE REPORTS

BEDSIDE ULTRASOUND IN THE EMERGENCY DEPARTMENT ENABLES RAPID DIAGNOSIS OF PUJ OBSTRUCTION SYNDROME

Fitzpatrick et al describe the value of rapid ultrasound in a case of PUJ obstruction in a male presenting to ED with severe left flank pain.

ENDOPHTHALMITIS, CLOSTRIDIUM SEPTICUM BACTERAEMIA AND THE SEARCH FOR COLONIC MALIGNANCY

Quill et al describe an 86-year-old man with endophthalmitis due to Clostridium Septicum. Subsequent investigations identified a right sided colonic malignancy.

CASE REPORTS (Continued)

SPONTANEOUS ESCHERICHIA COLI MENINGITIS AND PYOGENIC VENTRICULITIS IN AN ADULT RECEIVING ANTI-TUMOUR NECROSIS FACTOR ALPHA THERAPY

Hare et al report a 60-year-old male receiving Etanercept for ankylosing spondylitis, who developed E Coli meningitis and ventriculitis.

PROTRACTED BACTERIAL BRONCHITIS RELATED TO BAGPIPE PLAYING IN A TEENAGER

Stephens and Ni Chroinin describe a 14-year-old girl who developed chronic bronchitis with Pseudomonas Aeruginosa secondary to bagpipe playing. She responded to IV antibiotics and nebulised Tobramycin.

A CHILD PRESENTING WITH RESPIRATORY AND CIRCULATORY COMPROMISE SECONDARY TO GROSS CONSTIPATION

Mohamed et al describe a 14-year-old boy with marked abdominal distension due to constipation. Initial pallor and tachycardia was treated with IV saline and oxygen. He responded well to laxatives.

CASE SERIES

ADVANCED MERKEL CELL CARCINOMA IN THE ERA OF IMMUNOTHERAPY

O'Brien and Power describe 3 patients with Merkel cell carcinoma. Two of the patients responded to immunotherapy.

POEMS

COVID-19-WELCOME TO THE VACCINE

LETTERS TO THE EDITOR

OBSTETRICS AND GYNAECOLOGY CORE ROTATION INDUCTION - STUDENT EXPERIENCE

VARIANT OF GUILLAIN-BARRÉ SYNDROME

TRENDS IN ANTIMICROBIAL RESISTANCE IN CHILDREN ADMITTED WITH ESCHERICHIA COLI URINARY TRACT INFECTIONS

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RESPONSE LETTERS

LETTER IN RESPONSE TO ARTICLE “COVID-19 THE FIRST 100 DAYS IN THE SOUTH OF IRELAND”

Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P256

The Covid-19 Pandemic: The Outlook for Year Two

J.F.A. Murphy - Editor of the Irish Medical Journal

It is almost one year since the first cases of Covid-19 were reported in Ireland and the UK. It has been a tumultuous period for us all. Richard Horton[1] in this week's Lancet states that the measures needed to control the pandemic have led to 'the greatest imposition of restricted civil liberties ever seen in peacetime. Indeed, during world war II, cinemas, theatres, cafes, restaurants, and pubs all remained open'. As commentators sift through the events of the past 12 months, thoughts turn to the best strategies on the path to normal living. This first anniversary of Covid-19 is an opportune time to recalibrate. We are now clearer about what is promising and what does not appear to work. An apt description[2] is the distinction between 'green apples and useless therapies'. The ultimate destination is a safe return to normal living. The timing around when this will be achieved, will vary from country to country depending on a number of critical factors.

Covid-19 vaccination is the key to our emergence from the pandemic. It has surpassed expectations with a 90-95% efficacy. This represents a 20-fold risk reduction in contracting the disease[3]. Israel reports only a 0.04% rate of infection after two doses of the Pfizer vaccine. Currently, they have vaccinated a significant proportion of their population, and plan to complete their vaccination programme by the end of March 2021. The UK have administered the Covid-19 vaccine to 14 million people. The vaccination status of various countries as of February 12th,2021 is as follows; Israel 71.2 per 100 people, United Arab Emirates 48.5 per 100, UK 21 per 100, US 21 per 100, Ireland 4.6 per 100, Germany 4.4 per 100.

The current pressing concerns in Ireland are vaccine availability and the administration logistics. The involvement of GPs is a very welcome development. They are the medical group with a long and successful record in the delivery of vaccines. Dr Ray Walley, GP and former IMO president, points out that each year, 'Irish GPs administer the flu vaccine to 750,000 patients in a 7-week timeframe'.

As the vaccination roll-out gathers pace, the issues around vaccine hesitancy will emerge. A US survey carried out from November 30th to December 8th, 2020 found that 34% would take it, 39% would wait, 9% would take it if required by the employer, and 15% would definitely not take it. A corresponding Irish survey conducted on January 25th, 2021 was much more positive. It found that 75% will take the vaccine, 18% are unsure, and 7% will not. Among the over 65s, the acceptance rate is 86%.

Discussions have begun in some countries around the issue of vaccine mandates[4]. Up to now mandates have been rare in adults, while being more common for schoolchildren in some countries. The World Health Organisation (WHO) is opposed to mandates based on previous experiences. It is generally felt that compulsion can backfire and that it may galvanise the anti-vaccine campaign. The main reservation is that a mandate over-rides personal autonomy. On a practical note, there is no clear mechanism on how to enforce a mandate. The objective must be to convince and persuade. It remains very important that there is a high uptake among healthcare workers and those in the service industries.

Another issue is the future behaviour of vaccinated people. The advice is that they should behave as before in relation to mask wearing. This sends the message that we are protecting each other. In addition, there is insufficient data about asymptomatic carriage after vaccination. Another concern is that the efficacy of the vaccine could decline over time.

Masking has emerged as an important tool in the prevention of Covid-19 spread. The Centre for Disease Control and Prevention (CDC) have performed a series of laboratory experiments in relation double masking[5]. Double masking is where a cloth mask is worn over the surgical mask. The findings were as follows; a surgical mask blocked 56% of particles from a simulated cough, a cloth mask blocked 51% of particles, a cloth mask worn over a surgical mask blocked 85% of particles.

When both the source and the receiver are wearing double masks, the receiver's exposure is reduced by 96%. In a separate experiment it was found that by simply knotting the ear loops together where they are attached to the mask, a tighter fit to the face can be achieved. This knotted modification to the surgical mask increased the particle block from 51% to 77%.

The social distancing recommendation is two metres. There are good scientific reasons for this. While Covid-19 is mostly spread by respiratory droplets, there may also be aerosol transmission. Respiratory droplets (> 5 microns) fall to the ground within three feet of the source. The smaller aerosol particles dry quickly, remain suspended in the air, and travel further.

The gold standard RT-PCR test is undertaken at the National Virus Reference Laboratory (NVRL) and at least 42 hospital locations. The mean turn round time in the community is 29 hours and 16 hours for hospital patients[6].

There is an important distinction between diagnosis and random testing. RT-PCR testing is needed for the former but rapid tests may have a role for the latter. Different levels of sensitivities are required in different situations. Rapid, easily accessible tests would help in opening up institutions including universities. The development of this type of testing is an engineering challenge rather than a biological problem. The WHO states that rapid antigen detection tests (RADTs) performance should be sensitivity >90% and specificity >99%. A systematic review of RADT diagnostic accuracy reported a mean sensitivity 56% and specificity 99%. Antigen tests are now being undertaken on Irish truck drivers travelling to France, following a French government directive.

The challenges posed by the Covid-19 pandemic are constantly changing. The hope is that the vaccination programme will provide effective societal immunity leading to a return to normal activities.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P257

Atrial Fibrillation and Anticoagulation in the Nursing Home Setting

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Atrial fibrillation (AF) is an important predisposing risk factor for stroke. Its prevalence increases with age and the majority of those affected are over 75. Based on the CHA_2DS_2-VASc risk score, anticoagulation is indicated in all those over the age of 75 before additional risk factors are even considered. The BAFTA study in 2007[1] was the first randomised controlled trial demonstrating safety and efficacy of anticoagulation in this age group, with earlier studies excluding older patients. Despite further research supporting its use in this population, the medical community has been slow to implement anticoagulation, possibly due to misconceptions around life expectancy and bleeding risk.

Nursing home residents with AF are at high risk of thromboembolic stroke based on the range of vascular comorbidities commonly encountered in this setting[2], but also challenges to anticoagulation related to limitation of physical mobility, falls and cognitive and sensory impairment[3]. Nonetheless there are concerns that many older nursing home residents are not anticoagulated for AF where this strategy might be appropriate[4]. This problem is akin to prevention and treatment strategies for other conditions in nursing homes, reflective of a lack of a professional focus on nursing home medicine[5] and represents an opportunity for reflection and action to tailor care appropriately to this group.

At the time of writing, a literature search on the topic of anticoagulation for AF generated 7,596 articles in the preceding 10 years: combining the search with the term "nursing homes" yielded only 11 publications. These document a unifying theme of heterogeneity in physicians' attitudes, as well as their decisions to anticoagulate or not. This is in part due to the application of clinical reasoning and consideration for issues such as quality of life, pill burden and falls risk: however, the variability in prescribing patterns goes beyond these important considerations. One multivariate analysis of AF patient characteristics found that history of prior stroke was the only factor positively associated with anticoagulant use. This may be attributable to changes in patient outlook or to physician bias, but it is indicative of a need for a more nuanced and pro-active approach to clinical decision making in the nursing home setting, symptomatic of this group's underrepresentation in the literature.

A patient-centred approach to clinical decision making is needed in those who are particularly vulnerable to falls: while nursing home residents are especially at risk, this care setting offers a unique opportunity to implement strategies to prevent falls or to reduce their severity. Measures such as pressure-activated alarms, low level beds and shock absorbing mats have been successful to varying degrees. Given the correlation between severity of falls and risk of intracranial haemorrhage, the application of these measures may facilitate less risky anticoagulation thereby reducing the risk of disabling ischaemic stroke.

The proportion of patients in Ireland with AF treated with anticoagulation has risen steadily over the last two decades with the introduction of non-vitamin K antagonist oral anticoagulants (NOACs), and their reimbursement under the various repayment schemes. Less necessity for monitoring with blood tests, fewer dietary interactions and reduced medication incompatibilities are some of the factors attributable to the more widespread use of NOACs compared to warfarin. Beyond these, quality of life and ease of access issues influencing patient and physician choice, the safety and efficacy of NOACs in aging populations is well described in the literature and unlike warfarin, the seminal clinical trials for NOACs benefit from inclusion of older people. A meta-analysis of 26 randomised controlled trials favoured anticoagulation of patients over 65 years of age, with NOACs achieving superior safety and efficacy over warfarin. Coupled with the option for validated dose reduction in certain circumstances, this likely plays an important role in physician confidence when engaging in the shared decision to anticoagulate their older patient.

Screening for AF remains controversial, with no randomised trial affirming a net benefit of anticoagulation in screening-detected AF: however opportunistic screening and prophylactic anticoagulation is a continually evolving area of research[6], and new wearable device technology is already increasing detection independently of structured screening programmes. The absolute risk of stroke increases significantly with age after adjustment for other risk factors, resulting in a much lower number needed to treat which persists despite competing risk for death in all but the most advanced frailty. Despite this, observational data frequently demonstrate an association between advancing age and non-utilisation of preventative anticoagulation[7].

The net benefit of anticoagulation must be balanced with risk, and the established tools for calculation of bleeding risk are crude in their utility in the context of advanced frailty[8]; nonetheless frailty per se should not be considered a contraindication to anticoagulation[9]. Current guidelines emphasise remediation of modifiable risk factors such as hypertension, falls and medication interactions in preference to withholding anticoagulation. Similarly, in patients with cognitive impairment the benefit of anticoagulation is preserved despite the increased risk of mortality. There remains a need for clinical judgement as well as further research in this area to abstract a more discerning clinical decision tool for nursing home patients.

In light of the current aging population it is predictable that the prevalence of AF will continue to rise[10]. As technology advances this may be compounded by improved detection. A comprehensive strategy to manage the associated risk of stroke and systemic embolism is needed, particularly in higher risk groups such as those with previous cardiovascular events, diabetes and advanced age.

Nursing home residents are particularly vulnerable to the complications of both AF and its treatments, however the evidence discussed above favours greater use of anticoagulation. Mitigation of bleeding risk by methods such as the adjunctive therapies outlined is preferable to omission of treatment. Consequently, further work is needed to examine outcomes with anticoagulation in nursing homes and to promote a better understanding of the treatment options, and their merits and pitfalls, amongst physicians attending to the unique challenges and needs of this vulnerable cohort of patients, which remains an underdeveloped area in terms of literature and professional competence.

Keywords (MeSH): Atrial Fibrillation; Aging; Nursing Homes; Prevention; Anticoagulants

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P258

Covid-19 and General Practice: Part 5

Interview with Dr. Ray Walley MRCGP FRCGP,
Member of the National Covid-19 GP Liaison Committee

General Practice is represented by high level members of the Irish Medical Organisation (IMO) and Irish College of General Practice (ICGP) in liaison with the HSE and Department of Health in response to the COVID-19 pandemic.

This briefing covers the period 21/11/20 to 15/02/21.

The National GP / HSE Liaison Committee teleconference on a formal weekly basis at 7.30am Fridays with further engagement continuing between the secretariats/practitioners of IMO / ICGP / HSE / Dept. of Health where appropriate.

How has General Practice continued to respond to Covid-19:

1. In this period Ireland progressed to a third wave lockdown on December 30th with more than 1000 deaths and 100,000 cases recorded in January. Positivity rates reached 20-30% with significant staffing capacity issues for healthcare settings forcing the invoking of 'the derogation work policy'. By January 22nd the UK variant was identified in >50% of cases and recognised as more infectious. General Practice continued to be first point of call for the majority of acute/new Covid-19 consultations and referrals for Covid-19 testing in this period.

2. Recognising the danger of the potential for exacerbation of the pandemic by a seasonal outbreak of Influenza, 'Flu' vaccination of all patients over 65 years old was prioritised. By 16th of December 900,000 adult vaccines were administered, 75% by GPs and 25% by pharmacists. The target of >70% of over 65s coverage was achieved. Equally 230,000 children were flu vaccinated by same date.

3. Covid-19 mass vaccination clinics of GPs and Practice Nurses were organised with cooperation from the National Ambulance Service / HSE / Irish Defence Forces with the IMO and ICGP playing a significant management component. 1900 GPs and Practice Nurses were done at 3 venues on the 17th of January with a further 5000 practice staff at 4 venues on the weekend of the 13th of February. Talks are ongoing to ensure all remaining practice staff will be vaccinated.

Contractual changes:

Covid-19 prevalence has required that GMS contract changes be prompt, dynamic and fluid. Recent GMS contract changes negotiated by the IMO includes:

1. Provision of the chronic care contractual services is ongoing having been expanded from 1st of January to GMS patients >65 years old with co-morbidities including A Fib / IHD / CCF / COPD / Asthma and Diabetes Mellitus.

2. The IMO secretariat supported by the GP committee have organised continued contractual arrangements for Covid-19 telemedicine. Consultation/test referral/results advice and respiratory assessments for both public and private patients.

3. Contractual arrangements negotiated by the IMO continue in place for out of hours GP care provision.

4. The IMO were successful in ensuring that appropriate indemnity was put in place for the Covid-19 Vaccination Programme.

Covid-19 Vaccinations:

The National Immunisation Advisory Committee (NIAC) provided evidence-based advice to the Chief Medical Officer to inform policies on vaccines and immunisation in Ireland. On this basis a Covid-19 rolling programme starting with vaccination of the most vulnerable has been set in train. In recognition of the success of General Practice in significantly improving vaccine rates of children since transfer of the primary Child immunisations to General Practice in 1996 with similar success in the recent Flu vaccine programme it was decided to focus vaccinations of the over 70s in the community in General Practice. GPs have a unique continuity of care relationship with their patients allowing them to identify accurately and quickly patient cohorts as specified by the National Covid-19 vaccination programme. Vaccinations will occur in well ventilated rooms with appropriate social distancing in the GP recovery facility. The following ages are the order in which patients will be initially invited 85+, 80 – 84, 75 – 79 & 70 – 74.

900 practices have been identified as having over 200 >70 years old patients and will receive a delivery of vaccines to their designated centres based on their registered patient populations. Smaller practices are allowed buddy-up with larger surgeries whilst facilities are being arranged to allow mass vaccination of smaller practice lists utilising the economies of scale of existing General Practice staff.

First deliveries of vaccines to general Practitioners commenced on the 15th of February starting with Practices with larger cohorts of over 85s.

The IMO secretariat and committee members have played a significant role in the facilitation of this roll out.

Education and the Media:

The IMO and ICGP have recognised the importance of continued education of all Medical Practitioners and have organised on a weekly/monthly basis webinars. Most recent webinars have included the planned rollout of the Pandemic vaccine.

1. GP Media expert opinion placement has been a priority for both IMO and ICGP to ensure knowledgeable commentary from General Practice. Important Media messages have been.
2. The IMO and ICGP have ensured that timely opinion is accessible through their respective public relations units.
3. The ICGP continues to update its excellent website daily and is the most up to date information point for GP educational issues.

Covid-19 GP Hubs:

Covid-19 Hubs are for Covid-19 + / or Presumed Covid-19 + patients and GP referral only.

Exclusion criteria includes: -

1. Acutely unwell patients who require AMAU/ Emergency Dept. referral
2. Non Covid-19 patients
3. Maternity patients
4. Children under 16 years of age

Hubs in the third wave have either had to expand service hours with many being re-opened. These hubs have proved to be an asset to GP practices over-burdened with Covid-19 preventing the need for Emergency Department immediate referral allowing safe community assessment for patients and staff. By 9th of February 2021 there were 17 hubs in operation.

Ongoing challenges for General Practice include (in no particular order):

Representations were made to the HSE on the following issues with an abridged status included:

- Direct referral Access to all diagnostics incl. Xray, Ultrasound, CT, and MRI imaging – operational nationally.
- Covid-19 testing for children with imminent procedural appointments via GP – operational
- Deficiencies with contact tracing system – ongoing employment of new staff
- Reversal of redeployment to allow re opening of allied community service provision. – ongoing discussion
- Ensuring continued access to PPE – operational with plans to revert to Monthly order system with a back-up system for emergency orders - ongoing
- Recognition of need for Isolation / quarantine arrangements for foreign travellers – ongoing
- Nursing home test access for new staff - operational
- Consideration of expanding Children's flu access up to and including 17 years old if surplus supply available – completed
- Mental Health prevalence and service access – ongoing
- General Practitioner health matters – ongoing

Consultations having previously returned to >70% face to face reverted to a more pronounced triage with greatly reduced in person attendance at surgeries due to the significant prevalence of Covid-19 Nationally. Workloads are prioritised on clinical basis with 'urgents' taking precedence over 'routines', with the administrative task list lengthening.

Personal Healthcare of both GPs and their staff is emphasised to ensure maintenance of good physical and mental health.

Irish Medical Journal
Established 1867
Issue: Ir Med J; Vol 114; No. 2; P259

Liver Function Tests in F508del Homozygous Paediatric Patients with Cystic Fibrosis Taking Lumacaftor/Ivacaftor Combination Therapy

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Abstract

Aims

In clinical trials, elevated liver transaminase levels in patients taking lumacaftor/ivacaftor therapy were reported. Our aim was to assess in clinical practice, whether F508del homozygous paediatric CF patients had a derangement of liver functions tests (LFTs) while on lumacaftor/ivacaftor therapy.

Methods

A retrospective chart review audit in a single CF centre.

Results

Thirty-nine (43%) patients out of 91 CF clinic patients met criteria to start treatment. We observed a statistically significant decrease in ALT, ALP, GGT and total bilirubin levels, and no change in AST levels during first 3 months of treatment. In two patients (5%) AST levels rose to greater than three times the upper limit of normal (ULN) during treatment, however, these levels then decreased with continued use. A similar trend of improved LFTs was seen in a subgroup of patients with pre-existing liver disease (6/15.4% of patients). No patients died or experienced hepatic encephalopathy.

Conclusion

Our results were unexpected and encouraging. They suggest that, although the clinical trials report a risk of derangement of LFTs, the risk appears to be low.

Keywords
Cystic fibrosis, liver disease, CFTR modulators, adverse events, therapy

Introduction

Cystic Fibrosis (CF) is a genetic, multi-system condition, with progressive lung disease resulting in early death[1]. Ireland has the highest incidence of CF in the world and one in 19 people carry a defective gene[2]. The most common Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) variant is F508del and in Ireland 55% of patients are F508del homozygous[2].

The combination of lumacaftor (a CFTR corrector) and ivacaftor (a CFTR potentiator) is licensed for the treatment of patients with CF who are homozygous for the F508del mutation. It became available in Ireland to patients 12 years and older in 2017, and to patients aged 6-11 years in early 2018. Prior to this, select patients, with advanced disease, were able to receive the drug on a "managed access programme" (MAP). In clinical trials, serious adverse reactions related to elevated liver transaminase levels were reported [3-5]. Consequently, it is recommended that serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and bilirubin are monitored prior to initiating the drug, and every three months for the first year of treatment, then annually. In patients with raised LFTs at baseline, more frequent monitoring is recommended, but not defined. Patients with significant liver disease were excluded from the original clinical trials[3-5]**.** The aim of this study was to ascertain if F508del homozygous paediatric CF patients had a derangement of LFTs while on lumacaftor/ivacaftor therapy in the first year after treatment, in the "real world" setting of a paediatric CF clinic.

Methods

This study was conducted at the University Hospital Limerick (UHL) Paediatric CF unit. This is a retrospective chart review performed as an audit process in July 2018. Homozygous F508del patients attending the unit, who fulfilled the criteria to start lumacaftor/ivacaftor combination therapy, were identified from the clinic patient database, and their medical notes were reviewed.

The following variables were extracted from the medical records for each patient: date of birth, gender, date and age at initiation of treatment, cohort (12 years and older, 6-11 years old), dose cohort. Patients aged 12 years and older started on the higher dose (lumacaftor 200mg/ ivacaftor 125mg, two tablets twice daily) and patients aged 6-11 years started on the lower dose (lumacaftor 100mg/ivacaftor 125mg two tablets twice daily). In an effort to reduce the risk of chest discomfort and transient decrease in lung function at the initiation of treatment, we instigated a local policy of starting with one tablet twice daily for the first week, increasing to two tablets in the morning, and one in the evening for the second week, before increasing to the final, steady state dosing of two tablets twice daily from the third week onwards. The LFTs included: AST, ALT, alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) and bilirubin. Results at

baseline, three, six, nine and 12 months of treatment were extracted. At the time of our study, none of our patients had been on treatment for longer than a year. To aid comparisons across time, blood levels taken within six weeks of a set time point were included in that time point (ie. three months +/- six weeks). Patients with pre-existing CF liver disease (CFLD) were also identified. These patients had been assessed for, and diagnosed with, CFLD at the national CFLD specialist centre, at Our Lady's Children's Hospital Crumlin (OLCHC), Dublin. This sub-group had more frequent monitoring in the initial weeks after initiation of treatment. As the medication product leaflet does not describe a monitoring system for patients with CFLD, a local protocol was devised with the following time intervals: at baseline, then at the two, four, six and 12 weeks, and, if stable, patients were followed as per the standard recommendations of every third month, until 12 months and then annually.

Data was analyzed using SPSS. Excel was used to graph the data. Distribution was determined using a combination of histogram and box-plot analysis and the Shapiro-Wilk test for normality (p-value <0.05). If the data had a skewed distribution, then it was compared using the Wilcoxon signed-rank non-parametric test for related data, with each patient compared to their previous level. If the data were normally distributed, then a paired samples t-test was used to compare the data. A p-value <0.05 was deemed statistically significant. The UHL Audit Office reviewed the protocol and endorsed the study.

Results

From a total clinic of 91 paediatric patients with CF we identified 42 (46%) who were F508del homozygous and over six years of age. Three children did not start treatment (7%); one (2%) was post lung transplant, one was listed for liver transplant (2%), and one was recruited into a tezacaftor/ivacaftor clinical trial (2%).

There were 39 patients who fulfilled the criteria to start treatment at time of study in July 2018. See Table 1 for patient demographics. All 39 initiated, and continued, treatment during the study period. No patients died, and none experienced liver failure, hepatic encephalopathy or jaundice during the study. Two patients received treatment as part of the MAP (5%). The patients aged 12 years and older were started on the higher dose (lumacaftor 200mg/ ivacaftor 125mg) and the patients aged 6-11 years were started on the lower dose (lumacaftor 100mg/ivacaftor 125mg). Prior to initiation of treatment, all patients had LFTS checked, however, two patients (5%) had no AST level reported due to lab error. There were 34 patients (87%) who had completed three months of treatment, 18 (46%) completed six months, 16 (41%) completed nine months and 13 (33%) completed 12 months at data collection.

Table 1: Demographics of CF patients at UHL Paediatric CF clinic. CFLD: Cystic Fibrosis Liver disease.

	All patients (n=39)	CFLD (n=6)
Average age (years)	11.1	12.3

Male sex	21 (54%)	4 (67%)
>12yo	18 (46%)	4
6-11yo	20 (51%)	2

Figure 1 displays the median levels for AST, ALT, ALP, GGT at each timepoint. AST, ALT, GGT all remained steady and within the normal reference range, with ALP having an overall graphical trend towards normalization of values.

Figure 1: AST, ALT, ALP, GGT median levels graphed at each time point. Median was used due to skewed distributions. Normal values: AST (5-34 IU/L), ALT (10-55 IU/L), ALP (47-175 IU/L), GGT (9-36 IU/L).

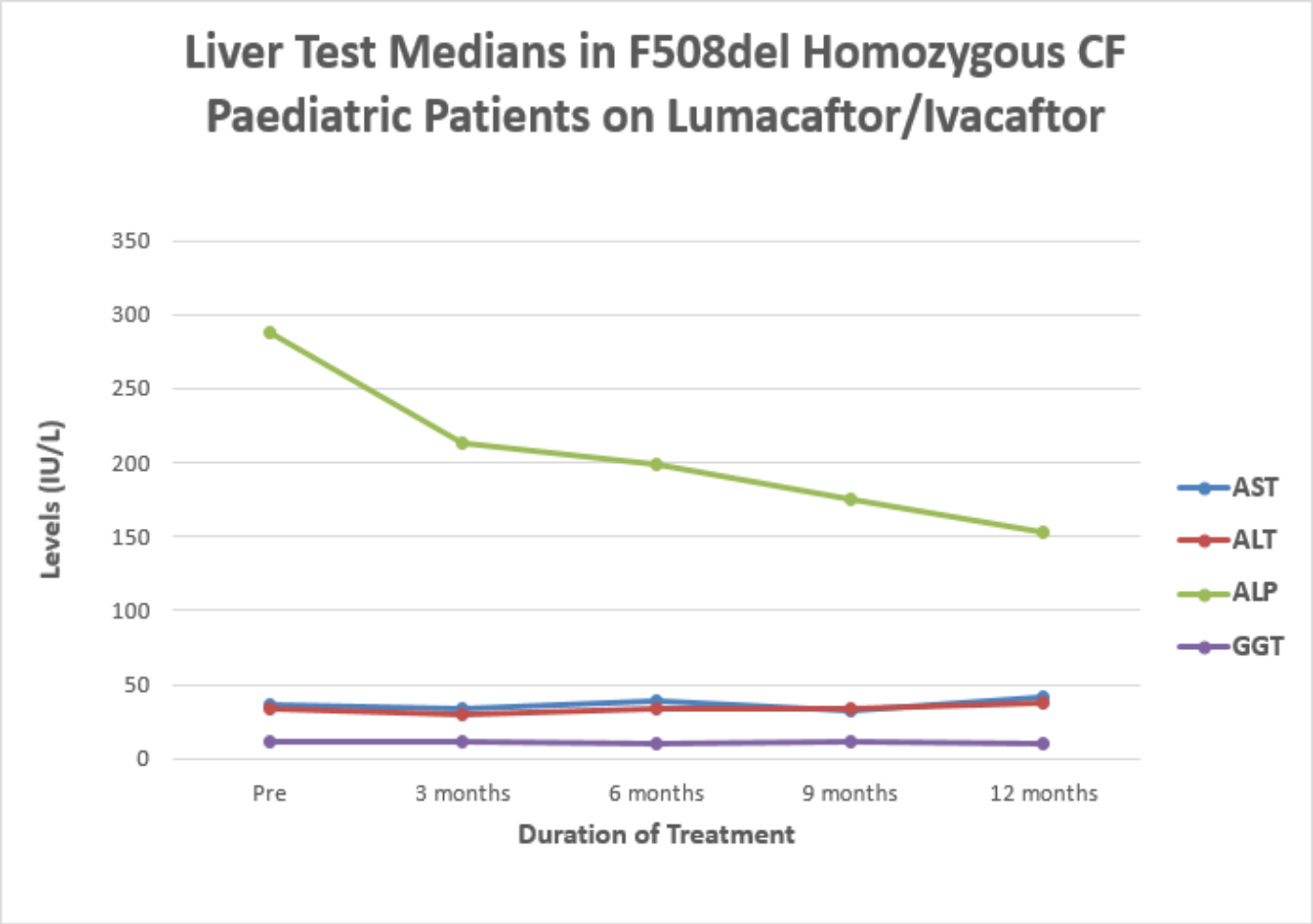
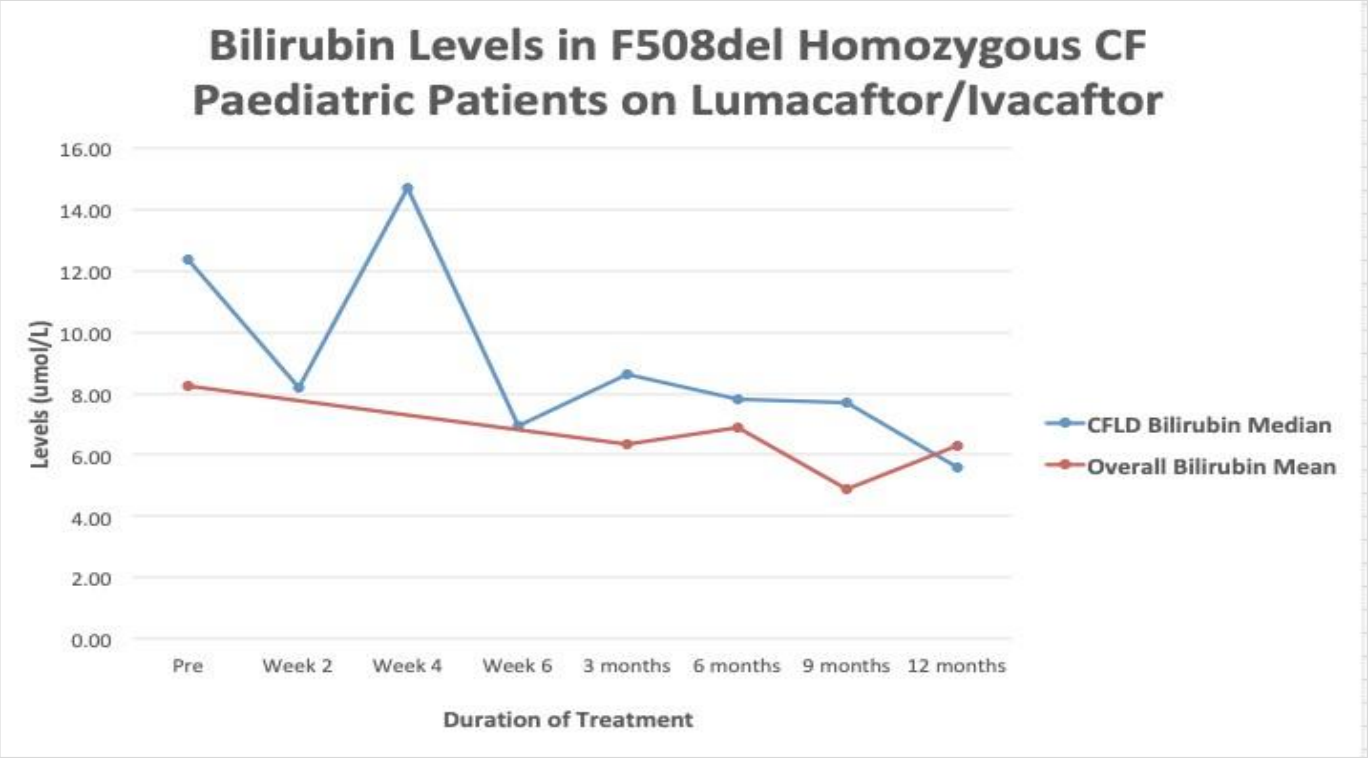


Figure 2 displays the total bilirubin levels for all patients and those specifically with CFLD. Overall, the bilirubin levels remained within normal range throughout treatment.

Figure 2: Bilirubin levels graphed at each timepoint. CFLD patients had closer LFT monitoring during the first 6 weeks of treatment. The remaining patients did not have levels checked during this time. Bilirubin levels from all patients had a normal distribution, thus the mean was used for analysis. The data for the 6 patients with CFLD was skewed, thus, the median was used. Bilirubin normal values: 3-21 umol/L.

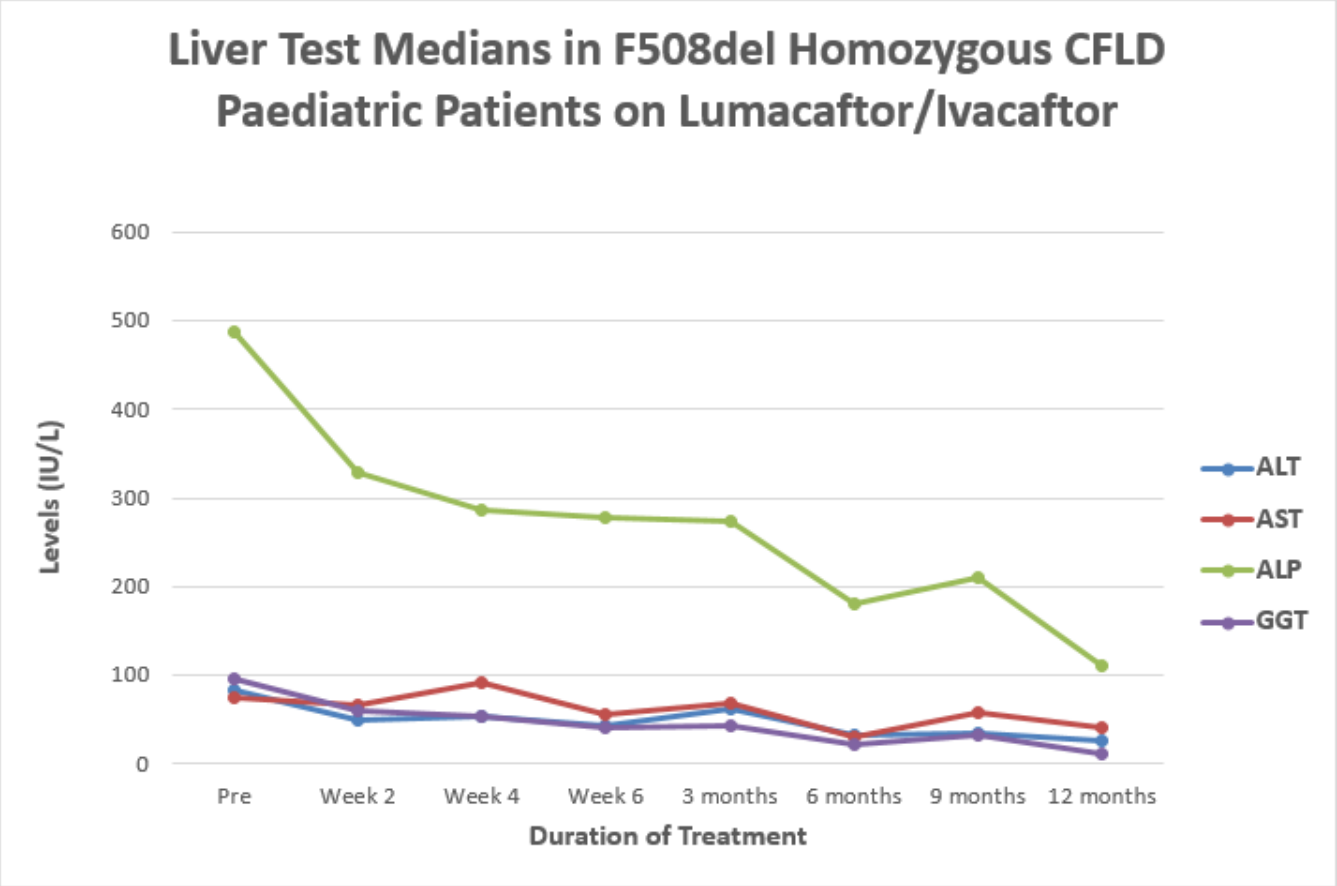


We had adequate numbers of test results only at baseline and at three months for all patients to perform a statistical analysis. The ALT, AST, ALP and GGT data were determined to have a skewed distribution based on histogram and boxplot distributions and the Shapiro-Wilk test for normality. Thus, the data were compared using the Wilcoxon Signed Rank Test. The total bilirubin levels were determined to have a normal distribution, thus a paired samples t-test was applied. Overall, we found our patients had a statistically significant decrease in ALT, ALP, GGT and total bilirubin levels, and no statistically significant change in AST levels as follows; the median LFT values (IU/L) at baseline (pre-treatment) and at three months, respectively, were : ALT 34 and 30 (p-value 0.016), ALP 288 and 213.5 (p-value 0.001), GGT 12 and 12 (p-value 0.002), and AST 37 and 33.5 (p-value 0.076). The mean bilirubin levels (umol/L) at baseline (pre-treatment) and at three months on treatment for all patients was 8.26 and 6.36 respectively, (p value:

0.002). Two patients (5%) had increased AST levels during treatment > 3 x ULN, however, these levels then decreased with continued use. None of our patients had LFTs > 8 x ULN, or > 5 x ULN during treatment, and none had ALT, ALP or total Bilirubin levels > 3 x ULN during treatment.

The data for six patients with pre-existing CFLD were extracted and were also analyzed separately. See table 1 for demographic details. Results were similar to those without established CFLD. The median levels at each time point for bilirubin and AST, ALT, ALP, GGT are graphically depicted in Figures 2 and 3, respectively and demonstrate a clear graphical trend of improving LFTs across all parameters. We could not determine statistical significance in CFLD population due to the limited number of patients.

Figure 3: AST, ALT, ALP, GGT median levels graphed at each time point for CFLD patients only (n=6). Median was used due to skewed distributions. Normal values: AST (5-34 IU/L), ALT (10-55 IU/L), ALP (47175 IU/L), GGT (9-36 IU/L)



Discussion

We present the first "real world" study of the short-term effect of lumacaftor / ivacaftor combination therapy on the liver function status of children with CF. Our results were unexpected and encouraging. They suggest that, although the clinical trials raised a concern that commencing a child on this new CFTR modulator therapy came with a significant risk of derangement of LFTs, the risk appears to be low and therapy may actually help improve LFTs.

CFLD is a significant complication of CF primarily evolving in the school age years and can have a detrimental effect on morbidity and mortality [6, 7]. To date there has been no intervention which has demonstrated efficacy in altering the course of CFLD [6, 7]. Pre-existing CFLD was an exclusion criteria for the clinical trials, however it is not a contra-indication to prescribing lumacaftor / ivacaftor combination therapy. Although our numbers are small, with just six patients (15%) with significant CFLD, the trends observed are encouraging. Dempsey *et al*, found similar improvements in LFTs in a small number (n=7) of patients with CFLD, but did not assess the effect of lumacaftor / ivacaftor on those without CFLD[8]. Firstly, it appears these patients can tolerate the treatment safely. Secondly, and perhaps more encouragingly; this may represent the first evidence of an intervention that can improve LFTs in patients with CFLD. Further observation is required to ascertain if this is translated into improvements in liver synthetic function and the manifestations of portal hypertension, such as splenomegaly and oesophageal varices.

Similar to many other medications lumacaftor / ivacaftor combination therapy may indeed come with a risk of liver injury. Drug induced liver injury (DILI) is the most common reason for withdrawing an agent from the market, and / or issuing warnings and modifications for their use[9-11]. RUCAM (Roussel Uclaf Causality Assessment Method) is a well-established methodology to assess causality in suspected DILI[9, 12, 13]. DILI is defined as, the now familiar, ALT levels above 5 × ULN and/or ALP levels greater than 2 × the ULN[9, 12, 13]. In addition the Hy's law predicts a 10% mortality (range 5-50%) when hepatocellular DILI is associated with a serum bilirubin level of ≥ 3 ULN[14]. However, determining causality of DILI remains complex and challenging with the majority of cases classed as "idiosyncratic" – essentially unexpected and unexplained[10]. Relevant to this discussion is the fact that, in the liver, CFTR is not expressed in hepatocytes, but exclusively in cholangiocytes[15, 16]. Defective chloride channel function can result in inspissated secretions that obstruct biliary flow, peri-biliary fibrosis, and for some patients progression from focal to multilobular biliary cirrhosis[16-20]. Onset of clinically significant disease is typically during the first decade of childhood[21, 22]. One might speculate that there are two separate processes at play here. The medication may come with a risk of liver injury, by a mechanism yet to be clearly defined, but may also come with a marginal, but potentially important, improvement in CFLD by improving CFTR functioning at the apex of cholangiocytes lining the bile ducts. Consistent with this theory, Kutney *et al*, demonstrated, using magnetic resonance imaging proton density fat fraction analysis, that lumacaftor / ivacaftor therapy was associated with reduced hepatic steatosis. Interestingly, the study excluded patients with CFLD or persistently elevated liver enzymes[23].

Our study has several limitations. It is a single centre study, with a small sample size. We had adequate numbers to perform a statistically valid comparison of baseline and three-month data, however the ability

of this dataset to make inferences about the wider CF population is limited, and the findings should be viewed with caution. Also, many of the time points have missing data. This illustrates the challenges of applying a stringent surveillance system for adverse events requiring frequent blood draws in a paediatric CF clinic. We continue to explore local policies to improve adherence to the surveillance policy.

Although the results of our study are encouraging, continued vigilance is required. On the basis of these findings we plan to expand our study to involve greater numbers, across multiple sites, and to include both adult and paediatric subjects.

Acknowledgements:
We would like to thank the children with CF and their parents/guardians that contributed to this study.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P260

Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) as Prognostic Markers in HER2-Positive Early Stage Breast Cancer

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Abstract

Background

The objectives of our study were to evaluate the neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) in patients with locally advanced Her-2 breast cancer treated with neoadjuvant chemotherapy and to correlate NLR and PLR with disease free survival (DFS) and overall survival (OS).

Methods

This was a retrospective, single centre study of locally advanced Her 2+ breast cancer who received neo-adjuvant chemotherapy. The survival benefit of NLR and PLR at baseline with respect to OS and PFS were examined with kaplen-meier curves with log-rank testing. The prognostic value of NLR and PLR were examined with univariate analyses using the cox proportional hazard regression model for hazard ratio (HR) with respect to OS and DFS.

Results

Among 156 women, patients with an NLR <2.5 at baseline had significantly improved DFS (p=0.02) and OS (p=0.04) compared to those who had a baseline NLR >2.5. Patients with a PLR <150 at baseline had significantly improved OS (p=0.04) compared to those who had a PLR>150 at baseline, however, there was no statistically significant improvement in DFS in the PLR >150 group.

Conclusion

Baseline NLR >2.5 and PLR >150 are adverse prognostic features in locally advanced Her-2 breast cancer patients receiving neoadjuvant chemotherapy.

Introduction

HER2 amplified breast cancers have traditionally exhibited aggressive biological behaviour. However, the advent of HER2 directed therapies have dramatically altered survival outcomes for patients treated in the neoadjuvant and adjuvant setting[1,2]. Preoperative chemotherapy has been typically used for locally advanced breast cancers with the aim of treating micrometastases early and downstaging tumours to permit breast conservation surgery. Its role in patients with HER2 positive breast cancer has been substantiated in several clinical trials.

A large amount of pre-clinical and clinical data produced over the last decade have made it evident that immune biology associated with solid tumours, as well as individual immune genetic traits, contributes to survival. An increasing emphasis has been out on the importance of tumour microenvironment and the complex interplay between neoplastic cells and the host's immune system. Cancer-associated inflammation produces myeloid-derived suppressor cells. Inflammatory cells have been shown to promote tumour cell proliferation, angiogenesis, invasion and metastatic dissemination. Host systemic markers of inflammation, including C-reactive protein (CRP) and the neutrophil to lymphocyte ratio (NLR) are associated with a poor prognosis in solid tumours.

NLR reflects the myeloid and lymphocytic lineages in peripheral blood and is a sensitive marker of altered myelopoiesis arising in cancer. Lymphocytes suppress cancer progression and lymphopenia is an independent predictor of inferior survival. Studies show that the presence of tumour-infiltrating lymphocytes are associated with better responses to therapy[3,4]. NLR plays an important prognostic role in solid tumours. Higher NLR is significantly associated with reduced overall survival, reduced cancerspecific survival, and reduced progression-free and disease-free survival in a variety of cancers and stages of disease It has also been shown to be predictive the neoadjuvant setting, as well as amongst phase 1 clinical trial patients [5].

Pre-operative NLR significant is associated with recurrence-free survival[5]. Chemotherapy can normalize elevated NLR early after the introduction of treatment and early changes in NLR are associated with response to therapies [6,7]. NLR represents a potential area for tailoring of therapy in patients with advanced cancer. It could allow early adaptation and discontinuation of ineffective treatment which would minimise toxicity and may improve the quality of life of cancer patients [8].

PLR is calculated as platelet counts divided by lymphocyte counts. Increasing evidence shows that PLR can be used as a prognostic and predictive biomarker in patients with breast cancer and may be helpful in-patient selection. Meta-analysis has now confirmed that high baseline PLR is indicative r of poor prognosis in patients with breast cancer [9].

Methods

We conducted a retrospective analysis on a prospectively maintained database – called the *One Thousand HER2 Patients Project* – of all patients with HER2-positive breast cancer treated with

trastuzumab at the Department of Medical Oncology of St Vincent's University and St Vincent's Private Hospitals in Dublin, Ireland.
This database was established in 2010 with the aim to create a clinical resource for translational studies across all the different stages of HER2-positive breast cancer.

To be included in the present study, patients must have Stage I to III invasive breast cancer which was HER2-positive in accordance to the international guidelines (i.e. ASCO/CAP guidelines) in use at the time of diagnosis, must have received at least one dose of trastuzumab-containing therapy, and have adequate follow up information. Also, full details on tumour biology (i.e. tumour grade, oestrogen [ER] and/or progesterone receptors [PgR]), as well as information on all pharmacological therapies administered (i.e. dates, schedules and doses of all cycles of treatments) had to be available for review. Patients diagnosed and followed up at our Institution but who received treatments, even only in part, elsewhere were excluded.

For all patients, we recorded the dates of initial diagnosis of breast cancer (based on the first Pathology report showing invasive carcinoma), of definitive breast surgery, of the first and last administration of trastuzumab, and last follow up at our Institution or death. Most patients had a fine-needle aspiration (FNA) for cytological examination in case of abnormal axillary lymph nodes on imaging. Patients with unequivocal metastatic involvement of supraclavicular or internal mammary lymph nodes (Stage N3b and N3c) – confirmed by either FNA/core biopsy or PET-CT – and those who had inoperable locally advanced breast cancer were excluded from this study. The clinical and pathological data of all patients deemed eligible for the study were individually reviewed and verified against the patients' hospital medical records as the main source document. In order to ensure that most patients had a minimum of three years of follow up, we included in the study only patients who were receiving neo-adjuvant chemotherapy and were treated in St Vincent's University Hospital between March 2006 –July 2016. For those patients who relapsed after curative therapy, we recorded the date and the site of relapse (loco-regional or distant). The database was locked for outcome analyses on March 31st, 2017.

The primary objective of this study was to analyse the possible correlation between NLR and PLR with disease free survival (DFS) and overall survival (OS) in patients with locally advanced operable HER2positive breast cancer treated with neo-adjuvant chemotherapy. Patients were eligible if they had locally advanced HER-2 positive breast cancer, were receiving neo-adjuvant chemotherapy and were treated in St Vincent's University Hospital between March 2006 –July 2016 Retrospective data collection captured NLR and PLR at baseline, defined as the closest full blood cell count (FBC) available to the date of the initiation of neo-adjuvant chemotherapy. The survival benefit of NLR and PLR at baseline with respect to overall survival (OS) and progression free survival (PFS) were examined with Kaplan Meier curves with log-rank testing. The prognostic value of NLR and PLR were examined with univariate analyses using the cox proportional hazard regression model for hazard ratio (HR) with respect to OS and DFS.

Results

One-hundred-fifty-six patients were identified in the database who met all the pre-defined inclusion/exclusion criteria outlined above. Patients had a median age of 55.6 years (range: 27-78 years). Median time from initial diagnosis to HER-2 therapy was 4 weeks (range: 1-18 weeks).

In terms of tumour characteristics; majority of patients (99 pts, 63%) had grade 3 histology, were oestrogen receptor (ER) positive 93 (60%) patients and were lymph node negative in 111 (71%) patients. TCH chemotherapy was administered to 116(74%) patients, while 20 (13%) patients received ACTH/FEC and TH. Full patients' characteristics are detailed in Table 1. Median follow up was 4.3 years (1.2-10.9 years)

In terms of peri-operative characteristics, the median time from diagnosis to surgery was 24 weeks. The rate of pathological complete response was 64 (41%). Median DFS and OS were not reached for all analyses. DFS rate 92% and OS rate is 96%. Baseline NLR < 2.5 was significantly associated with improved DFS (p= 0.02) and OS (p=0.04) (Figure 1 and Figure2). Baseline PLR <150 showed a statistically insignificant trend towards improved DFS (p= 0.61) (Figure3), however baseline PLR<150 demonstrated a statistically significant improvement in OS (p= 0.04) (Figure4). On univariate analyses for OS showed HR 0.13 (p=0.06) and HR 0.14 (p=0.07) for NLR<2.5 and PLR<150 respectively, and for DFS showed HR 0.34 (p=0.05) and HR 0.30 (p=0.04) for NLR<2.5 and PLR<150 respectively.

Figure 1: Baseline NLR and Disease-Free Survival.

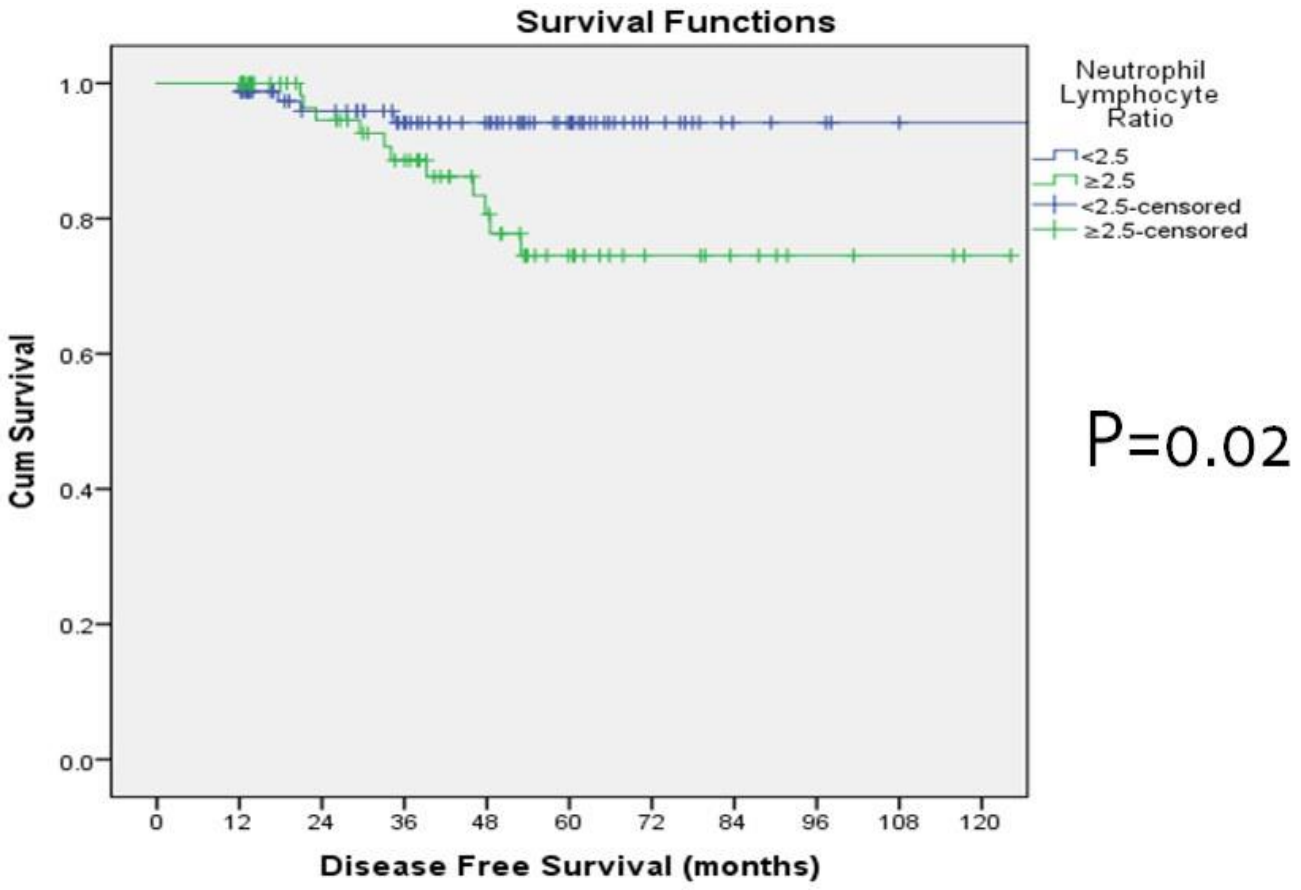


Figure 2: Baseline NLR and Overall Survival.

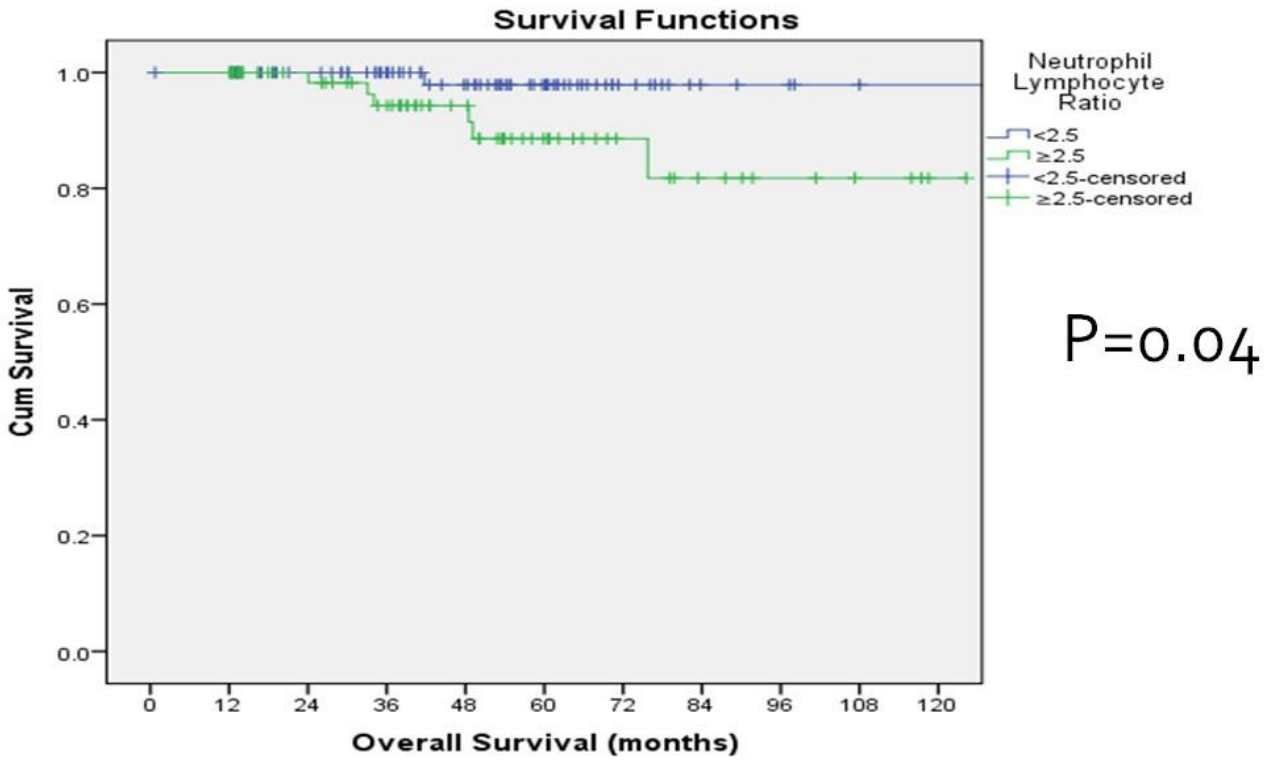


Figure 3: Baseline PLR and Disease-Free Survival.

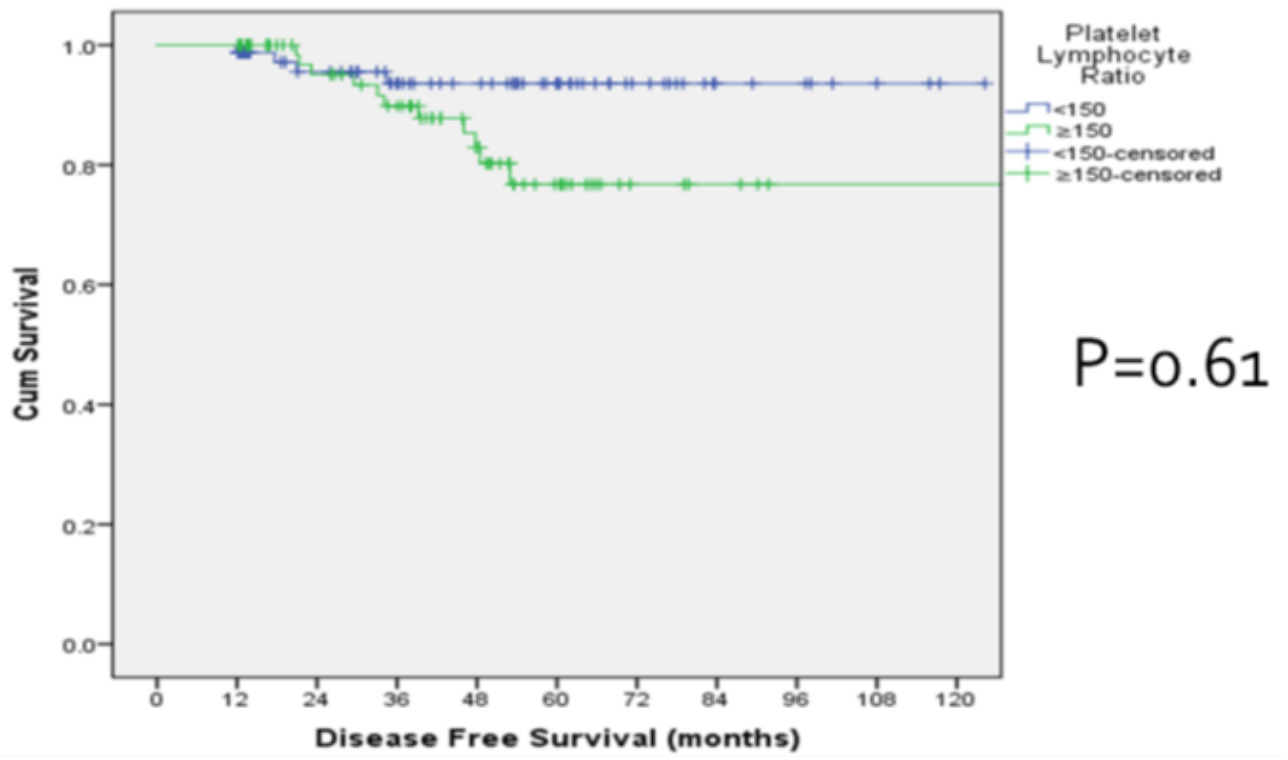
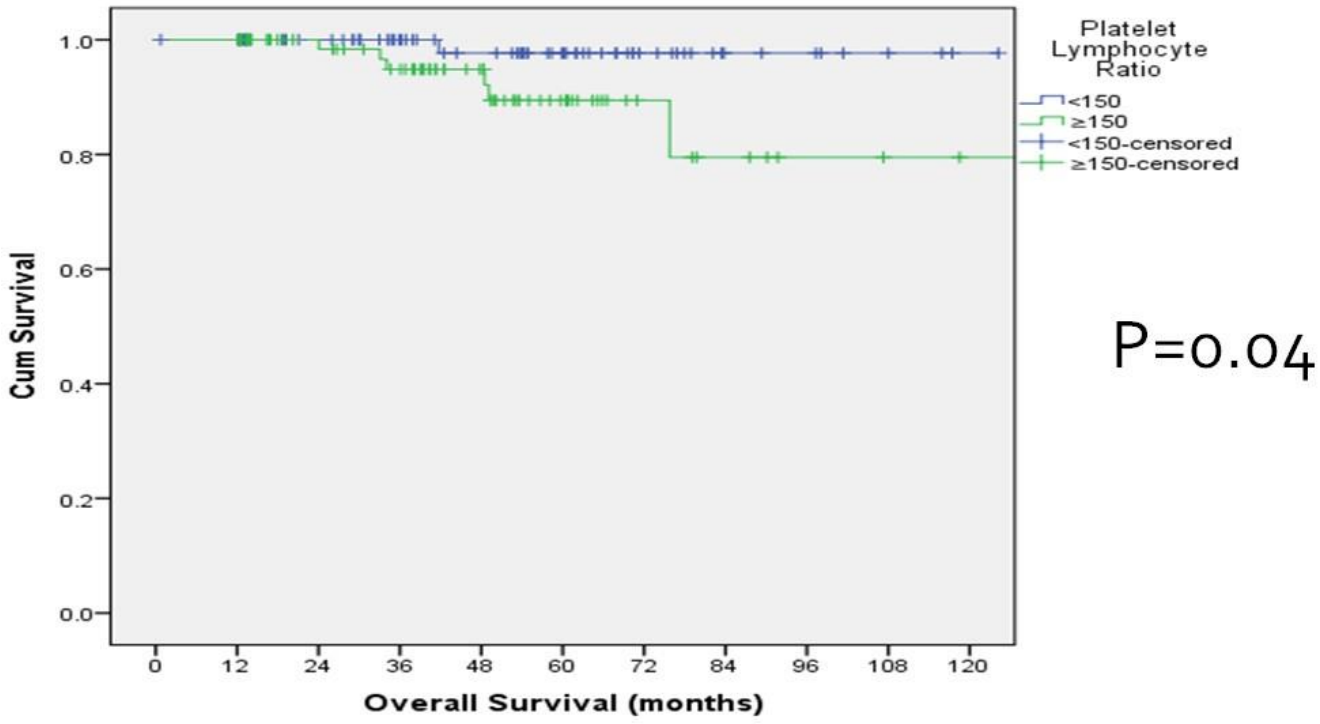


Figure 4: Baseline PLR and Overall Survival.



Discussion

Several studies have shown that elevated NLR is associated with worse survival in patients with various metastatic solid tumours, irrespective of the primary tumour site, line of chemotherapy, age, gender and ECOG [8]. NLR has prognostic value as a continuous variable with research showing that an increase in NLR of 1 standard deviation (SD) increased the risk of death by 35% ($p<0.0001$) in solid tumours [10].

Pre-operative NLR is significantly associated with recurrence-free survival in solid tumours[11]. Chemotherapy can normalize elevated NLR early after the introduction of treatment and early changes in NLR are associated with response to therapies[4,11]. NLR represents a potential area for tailoring of therapy in patients with advanced cancer. It could allow early adaptation and discontinuation of ineffective treatment which would minimise toxicity and may improve the quality of life of cancer patients [8].

NLR appears to be a useful tool in patients receiving immunotherapy. High NLR at baseline and during treatment is adversely prognostic in patients with advanced solid tumours receiving PD-1/PD-L1 inhibitors whilst decreasing NLR over time is associated with response to immunotherapy. NLR and PLR may be useful in for selection of patients and could be considered in the baseline evaluation of candidates for immunotherapy. NLR is not helpful in predicting risk of immune toxicity. However, as immune related adverse events (irAEs) can be life-threatening and treatment-limiting, appropriate and timely identification of patients not responding to treatment would avoid toxicity and minimise unnecessary exposure to therapy unlikely to be effective [12, 13]. All prospective studies of immunotherapy in solid tumours could consider the inclusion of baseline and serial NLR data.
Our results show that a pre-treatment NLR >2.5 and PLR > 150 are adverse prognostic factors in locally advanced, operable HER2-positive breast cancer patients receiving anti-HER2 containing neoadjuvant chemotherapy. Previous studies of NLR in breast cancer demonstrate that NLR has a significant prognostic effect on OS and DFS both in early and advanced disease. The magnitude of effect on DFS is highest in ER-negative, HER2-negative subtypes. It is clear that different clinical outcomes are seen amongst patients with similar classical prognostic factors and the role of inflammatory cells and mediators in the tumour microenvironment in cancer progression may account for some of this variability.

In the future improvement in technology could allow improved understanding of this area. Immunomethylomics is a technique that allows complete characterization of patient immune profiles, using DNA from archival peripheral blood after application of methylation profiling. This technique could explore aberrant immune profiles in the context of cancer-associated inflammation, potentially adding significantly to prognostic and mechanistic information for solid tumours [14].

NLR and PLR are inexpensive and readily available prognostic markers that could be incorporated into clinical tools to prognosticate patient outcomes after systemic therapy. Serial NLR and PLR may be useful for early tailored treatment adjustments as well for treatment selection and de-escalation.

In conclusion, our single-institution study in a homogenous cohort of patients with HER2-positive operable breast cancer treated with neo-adjuvant anti-HER2-containing chemotherapy demonstrates that NLR and PLR at baseline can be a useful predictor of long-term prognosis. This study represents one of the largest real-world datasets looking at NLR and PLR within this patient cohort. NLR and PLR

may have a helpful role to play in the refinement of risk estimates within disease stages and subgroups, treatment de-escalation and for clinical trial stratification.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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Issue: Ir Med J; Vol 114; No. 2; P261

Intra-dialytic Exercise for Haemodialysis Patients: A Pilot Program

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Abstract

Aim

Intra-dialytic exercise is associated with many clinical benefits but has not been widely adopted in routine practice. An intra-dialytic exercise program was piloted to investigate patient adherence and early clinical benefits in an Irish haemodialysis cohort.

Methods
An 8-week exercise program was conducted in six patients. The primary outcome was patient adherence. Secondary outcomes included physical functionality, quality of life and dialysis adequacy. Physical functionality was assessed by hand-grip strength, the sit-to-stand test and the Duke Activity Status Index (DASI). Patients partook in 45-minute exercise classes twice-weekly, which included resistance training and aerobic training.

Results
The mean age of the patients was 58.2years (SD 18.2), with a mean dialysis vintage of 24.3 months (SD 30.8). Adherence was high, with 5 of 6 patients completing >75% of sessions. There was a significant increase in physical functionality, as measured by the sit-to-stand test, from a mean of 21.1 (in 1 minute) to 27.3 (in 1 minute) following the program (Z=-3.29, p=0.001). There was no significant change noted in the other secondary outcomes. No safety concerns were encountered.

Conclusion
Structured, physiotherapy-led, intra-dialytic exercise can be safely and effectively introduced to Irish haemodialysis units, associated with a high level of adherence and early physical gains.

Introduction

Exercise training is known to be beneficial for adult patients with chronic kidney disease.[1] There is a growing body of evidence that providing a structured exercise programme to haemodialysis patients during their routine dialysis treatment has significant benefits, including increased exercise tolerance, improved mobility and functional status, improved muscle strength and improved quality of life.[2-6] These programmes are also associated with improvement in other clinical parameters such as blood pressure control, arterial stiffness and small solute clearance.[2,4,7] Exercise programmes typically combine aerobic (endurance) and resistance training and are carried out under the supervision of exercise specialists or physiotherapists, while the patients are undergoing their routine haemodialysis session.[8] These programmes are reportedly well tolerated by the participants, with no significant patient safety concerns evident.[8-10]

Unlike successful cardiac and pulmonary exercise programs established throughout the Irish healthcare system, exercise programs for haemodialysis patients have not become established routine practice and may represent a missed opportunity to improve outcomes for both patients and healthcare economics. Adjusted for co-morbidities and socio-economic confounders, data from the DOPPS cohort demonstrate reduced mortality risk among patients who exercised regularly and also at facilities that provide exercise programs.[11] A reduced inpatient length of stay has also been reported in haemodialysis patients undertaking an exercise program, which could have major cost-saving implications in this cohort of patients with frequent, and often prolonged, hospitalisations.[12]

Here, we report the first pilot study of patient adherence and early clinical benefits in an exercise program for chronic haemodialysis patients in an Irish setting.

Methods

Participants were recruited from a single-centre haemodialysis cohort, being eligible for inclusion if they were chronically undergoing haemodialysis (for at least 3 months) and were in a stable medical condition. Patient selection was opportunistic to coincide with limited physiotherapy availability and a logistical requirement that participants be suitable to dialyse in a single 6-patient bay without need for isolation precautions. Patients suffering from advanced cognitive impairment, symptomatic ischemic heart disease, orthopaedic or musculoskeletal problems interfering with exercise training or those who could not give informed consent were ineligible.

The pilot cohort consisted of 6 patients, who underwent intra-dialytic exercise sessions twice weekly for an 8-week period. Each exercise session consisted of approximately 45 minutes exercise, under the direct supervision of a physiotherapist, to include aerobic exercise (stationary cycle ergometer for 1015minutes, at low to moderate intensity based on the patient's ability) and resistance training with weights and elastic bands, focusing on 10 specific exercises (2 sets of 8 repetitions for each exercise). The exercises included were the shoulder press, shoulder abduction, external shoulder rotation, biceps curls, triceps extension, hip flexion, hip abduction, straight leg raise, hamstring curl and inner-range quadriceps exercise.
Our study protocol allowed for inclusion of participants who were undergoing dialysis via an upper limb AV fistula, with the fistula arm not being exercised during dialysis in those patients.

The primary outcome measure was individual patient participation in each exercise session and the proportion of training sessions completed in the 8-week programme. The supervising physiotherapist adjudicated whether an individual session was completed satisfactorily. For the secondary outcome measures, subjective physical functionality was measured by Duke's Activity Stats Index (DASI), a 12item questionnaire used to assess functional capacity.[13] Objective physical functionality was measured by a timed sit-to-stand test (for 1 minute) and hand-grip strength dynamometer. Patient quality of life (QOL) was measured by the SF-36 survey. Dialysis clearance was measured by the urea reduction ratio (URR). Outcome measures were assessed at baseline and after completion of the 8-week programme.

Study participants' demographic and clinical data were gathered from medical and/or electronic charts, including age, gender, aetiology of endstage kidney disease, diabetes status, cardiovascular comorbidity and dialysis vintage. Biochemical parameters were collected from the patient's routine monthly bloodwork before and after the programme was been completed. Participant clinical and demographic details were reported using descriptive statistics. The number of successfully completed exercise sessions for each patient was reported as a percentage of the total scheduled sessions. Continuous outcome variables measured before and after the exercise programme were compared by the Wilcoxon rank test. The alpha level of significance was set at <0.05. All participants provided written consent prior to commencement of the exercise program. The pilot study was approved by the local ethics review committee.

Results

The mean age of the six patients was 58.2years (SD 18.2), with a mean dialysis vintage of 24.3 months (SD 30.8) and most of the participants were male (n=5). All patients were undergoing dialysis via a tunnelled central venous catheter. The aetiology of end-stage kidney disease was ischaemic nephropathy (n=2), chronic glomerulonephritis (n=1) and unknown aetiology (n=3) in the included patients.

Exercise Adherence

The observed adherence with scheduled intra-dialytic exercise sessions was perceived to be high in 5 out of the six patients, who completed more than 75% of sessions (Fig 1). One patient had low adherence with the program due to an unanticipated departure from the dialysis centre for personal reasons during the program, although the patient had completed all scheduled sessions prior to departure and following return to the unit. Reasons cited for incomplete sessions in the remaining patients included intra-dialytic hypotension (n=2), patient fatigue (n=7) and an intercurrent viral illness (n=2).

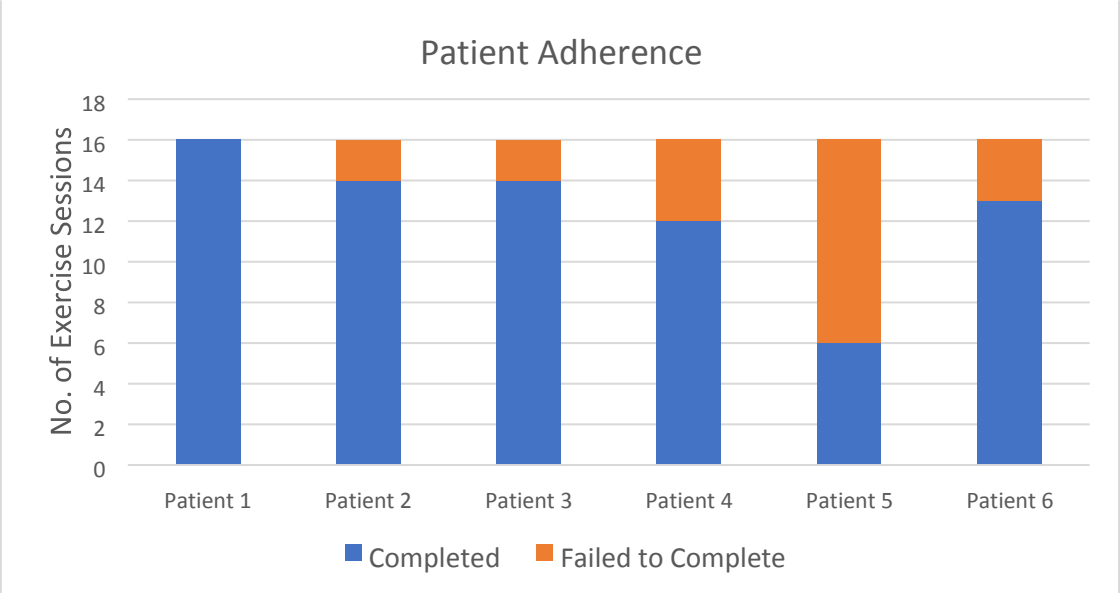

Figure 1. Patient Adherence with scheduled intra-dialytic exercise sessions.

Physical/Functional Gains

Subjective physical functional status, as measured by the DASI questionnaire, remained unchanged at the pre- and post-program assessments, with a mean score of 31 (SD=16.5) vs 32.1 (SD=12.8), respectively (z=-0.2, p=0.8). Objective physical functionality based on the timed sit-to-stand test improved significantly from a mean of 22.1 repetitions (SD=6.5) in 1 minute to 27.3 (SD=10.9) repetitions following completion of the program (z=-3.29, p=0.001), with all patients showing a nominal improvement (Fig. 2). There was non-significant trend towards improvement in mean hand grip strength, 24.8kg (SD=10.9) versus 27.5kg (SD=7.4), equating to a mean increase in grip strength of 2.6kg

(95% CI -2.1 – 7.5, p=0.2). Of note, different participants demonstrated the most improvement in the sit-to-stand test and hand grip strength outcomes, suggesting a possible differential benefit for individual patients.

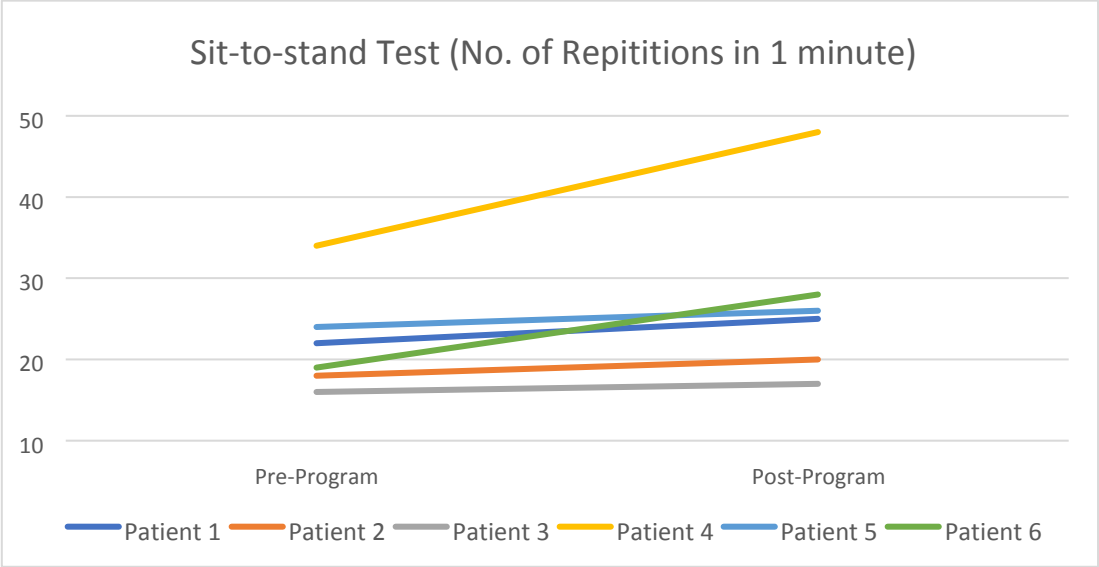

Figure 2. Sit-to-stand Test Outcomes pre- and post-program (Number of Repetitions in 1 minute).

Other Outcomes

There was no significant change in self-reported QoL as assessed by the SF-36 questionnaire when compared pre- and post-program, with mean scores of 2194 (SD=309) versus 2180 (SD=619), respectively (z=0.08, p=0.9). There was also no significant change noted in dialysis adequacy over the 8-week program in terms of the recorded mean urea reduction ratio, 65% versus 68.2% (z=-1.64, p=0.1).

Discussion

We present the first report of a structured, intra-dialytic, physiotherapy-supervised exercise program in an Irish haemodialysis unit. The pilot program was well-adhered to and well-tolerated, with no negative impact on quality of life or dialysis adequacy noted. After a relatively short 8-week program, an early and significant improvement in physical functionality, as measured by the sit-to-stand test, was recorded. Although it is possible that results may be skewed by individual performance in such a small cohort, all participants showed some degree of measured improvement and the overall finding is consistent with previous reports of the benefits of exercise therapy in this cohort.[8] A trend towards improved hand-grip strength was also noted, although it is likely that insufficient study power excluded the possibility of demonstrating a more robust outcome response after exercise training, as has been demonstrated in previous controlled clinical trials.[14]

Physical frailty and reduced functional status are common in haemodialysis cohorts, and are associated with reduced quality of life, increased risk of hospitalization and increased mortality. Current guidelines recommend regular exercise for patients with CKD, although evidence suggests that <50% of dialysis patients exercise at least once per week. Observational evidence from the Dialysis Morbidity and Mortality Study demonstrated an association between more regular exercise and reduced mortality.[15,16] Our findings are consistent with previously reported systematic reviews regarding

haemodialysis patients and exercise therapy, with multiple studies reporting high adherence rates and improvement in physical fitness and muscle strength. Unfortunately, the literature to date is of mostly low to moderate quality RCTs with a high risk of bias.[17, 18]

Despite reports published over the last three decades supporting the benefits of exercise therapy in dialysis patients, the nephrology community has been slow to actively endorse the practice, with only a small minority of dialysis units internationally routinely providing this service. Other medical specialities in Ireland have successfully introduced exercise programs, such as cardiac rehabilitation, which is backed at a national policy-level and based on reported clinical benefits for patients and favourable cost-effectiveness for healthcare providers.[19, 20] We believe that there is currently a missed opportunity in this regard in the haemodialysis cohort, at whom a very significant proportion of the annual healthcare budgets are directed. March et al. reported on a subset of patients enrolled in the CYCLE-HD study, demonstrating a 3-day reduction in hospital length of stay in dialysis patients enrolled on an exercise program compared to controls, which would equate to an estimated annual cost saving of £25.7million related to inpatient stays.[12] This is consistent with other reports of reducing inpatient hospital length of stay through structured exercise therapy.[21, 22]

The reasons for inertia in the field of nephrology are not clear but are likely influenced by cost and resource issues surrounding physiotherapy personnel and equipment.
Jhamb et al. described barriers to intra-dialytic exercise including patient concerns over the safety and type of exercise and staff concerns over the impact on workload and resistance to changing dialysis routine.[23] Our data, in conjunction with other reports, indicates that it is safe and feasible to introduce exercise programs in this setting of the dialysis unit and can be used to reassure potential participants. Regarding participation in exercise therapy while dialysing via an AV fistula, the majority of previous trials have focused resistance training on lower limbs only to avoid any interference with the fistula arm.[24] However, there is evidence available that the non-fistula arm can be included in exercise without any significant safety concerns.[4] A lack of high-quality clinical trial evidence is also a barrier to more widespread use of intra-dialytic exercise programs, which may be soon addressed by CYCLE-HD (ISRCTN11299707) and PEDAL (NCT02222402) clinical trials. A lack of clarity on the best modality in which to implement exercise therapy (daily, intra-dialytic, non-dialysis day, home or in-centre) also acts as a barrier, with most literature focusing on supervised, intra-dialytic programs. The EXCITE study reported improved physical performance and quality of life with a personalized, low-intensity, homebased exercise program managed by dialysis staff.[25]

The limitations of the current pilot study are linked primarily to available resources which allowed for a single iteration of the program for 6 patients over an 8-week period, due to limited physiotherapy personnel. The small cohort size precludes any definitive statement regarding the potential benefit in terms of the study's clinical outcomes. A 6-minute walk tests was considered as another physical performance outcome but was not possible due to the logistical need to conduct the test on a nondialysis day which would have required additional visits to the dialysis unit for participants. The program duration was relatively short, and we hypothesis that significant improvement in secondary outcomes would be encountered in a more prolonged program. Through a more sustained introduction and expansion of this program, the available evidence suggests that significant cost savings could be made into the future through reduction of inpatient length of stays, which provides a business case for resource allocation at individual centres.

The introduction of an intra-dialytic, physiotherapy-supervised, structured exercise program is a feasible undertaking in an Irish haemodialysis unit, is well-tolerated and adhered to, and is associated with early physical gains. The findings of this pilot study are consistent with international findings. More widespread introduction and expansion of such programs across the national chain of dialysis units would be expected to result in significant clinical benefits for patients and potentially significant costsavings for healthcare providers.

Declaration of Conflicts of Interest:
None to declare.

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Established 1867

Issue: Ir Med J; Vol 114; No. 2; P262

An Audit of Patient Satisfaction in an Outpatient Hysteroscopy Clinic Setting

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Abstract

Aims
We aimed to review experiences of women attending the outpatient hysteroscopy clinic (OHC) in University Hospital Kerry across five months in 2017.

Methods
Data collection was prospective and on-site. Green-top Guideline No. 59: Best Practice in Outpatient Hysteroscopy, published by the Royal College of Obstetricians and Gynaecologists (RCOG), was the standard used for comparison.

Results
There was a one hundred percent response rate (100%; 60/60). Six aspects of the service met the required standards, and five failed to meet the standards. Aspects that met the standards included convenience of service and staff assessment. Those that fell below the standards included ease of locating the clinic and comfort while waiting.

Conclusion
Despite the majority reporting mild to moderate pain, almost all the women (93.5%; 56/60) would recommend the clinic to a friend. Changes have been instituted since the audit, including installation of new signage to direct women to the clinic. A re-audit questionnaire has been developed to review the service. Outpatient hysteroscopy is a convenient and acceptable experience for women attending our gynaecology services.

Introduction

Outpatient hysteroscopy is carried out primarily for investigation of abnormal uterine bleeding[1-3]. It can also be used for office procedures such as guided endometrial biopsy, endometrial polypectomy, treatment of small submucous leiomyomas and retrieval of intrauterine devices[4-7]. It is safe, well tolerated, and obviates the need for general anaesthesia[8]. The Royal College of Physicians Ireland (RCPI) recommend that this service should be the standard of care for women accessing hysteroscopy services, as it has significant patient benefits and cost savings[9]. Benefits for women include reduced recovery time and faster return to work, as well as engagement with care. The RCOG recommends that all gynaecology units should be equipped with a dedicated outpatient hysteroscopy service[8].

However, outpatient hysteroscopy can also be associated with pain, embarrassment and anxiety[10-12]. Due to the clinical and economic advantages of outpatient hysteroscopy, it is important to ensure that women have a positive

experience and are satisfied with this valuable service. Clinicians must ensure that discomfort is minimised through means such as operator expertise, the use of appropriate equipment, hysteroscopy patient information leaflets, appropriate techniques and pharmacological agents, pre-procedure counselling, and the use of the 'vocal local'.

Cill Ide is University Hospital Kerry's (UHK) dedicated consultant-led outpatient hysteroscopy clinic (OHC). It opened in 2009 and treats more than 150 women per year. It offers diagnostic as well as operative procedures. Equipment includes five 30-degree three-millimetre diagnostic hysteroscopes, and two 30-degree three-millimetre operative alphascopes. A bipolar Gynecare Versapoint Bipolar Electrosurgery system is also used for operative procedures including treatment of endometrial polyps and submucous leiomyomas. Local anaesthetic is used for selected cases. Cill Ide is equipped with a waiting room, clinic room, doctor's office, and toilet facilities. It is staffed by a clinical nurse specialist or nurse and a secretary, and procedures are performed by either the consultant or a non-consultant hospital doctor under direct consultant supervision. Women are provided with written information pre- and post-procedure. Informal feedback to date has generally been positive, and in 2017 an audit was conducted to formally evaluate satisfaction with the service. The outcomes and implications of the audit are outlined below.

Methods

Data was collected over five months from July to December 2017. The target population was women attending the OHC during the specified time period. Data was collected prospectively and on-site, with a written questionnaire offered to women following their hysteroscopy and consultation. The questionnaire centred on the following themes: ease of getting to clinic; attendance at clinic; written information; recommendation to a friend or relative; pain; staff assessment and facility. Questions were either multiple choice, with the options of 'very good', 'good', 'fair' or 'poor', or yes/no. There was a visual analogue score for pain, and a space left for comments.

The RCOG Green-top Guideline No. 59, 'Best practice in outpatient hysteroscopy' was used as the standard for auditing the service. Standards were set at 80%. Consequently, for questions with a graded response choice, 80% of women were expected to respond with 'very good'. For yes/no questions, 80% of women were expected to respond with 'yes'. Data was collated in an Excel spreadsheet. Results were subsequently analysed by the chief researcher and reviewed by the supervising consultant.

Results

Sixty women were offered the questionnaire. There was a response rate of 100% (60/60), likely due to the on-site nature of data collection. Figures one to three represent patient responses to nine of the eleven aspects (two aspects not included: hysteroscopy information read prior to the procedure; would recommend to a friend or relative). Figure four represents pain assessment as measured by the women on a visual analogue scale (VAS).

Figure 1: Ease of getting to clinic.

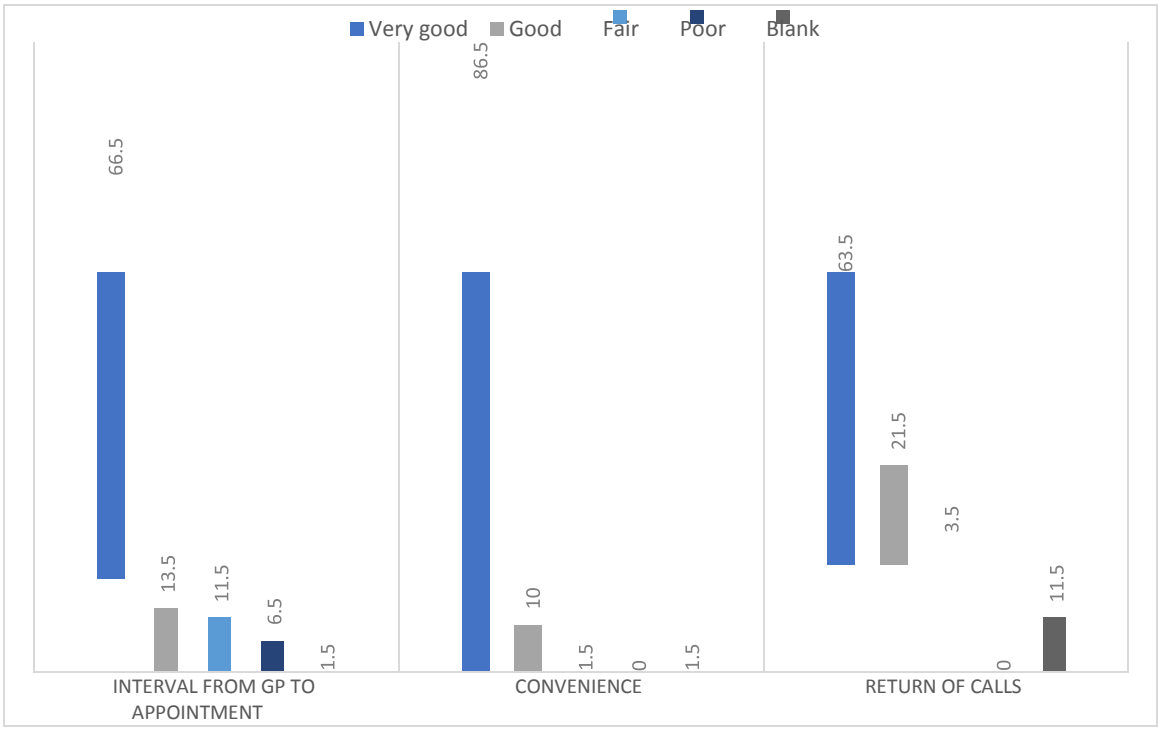


Figure 2: Facility.

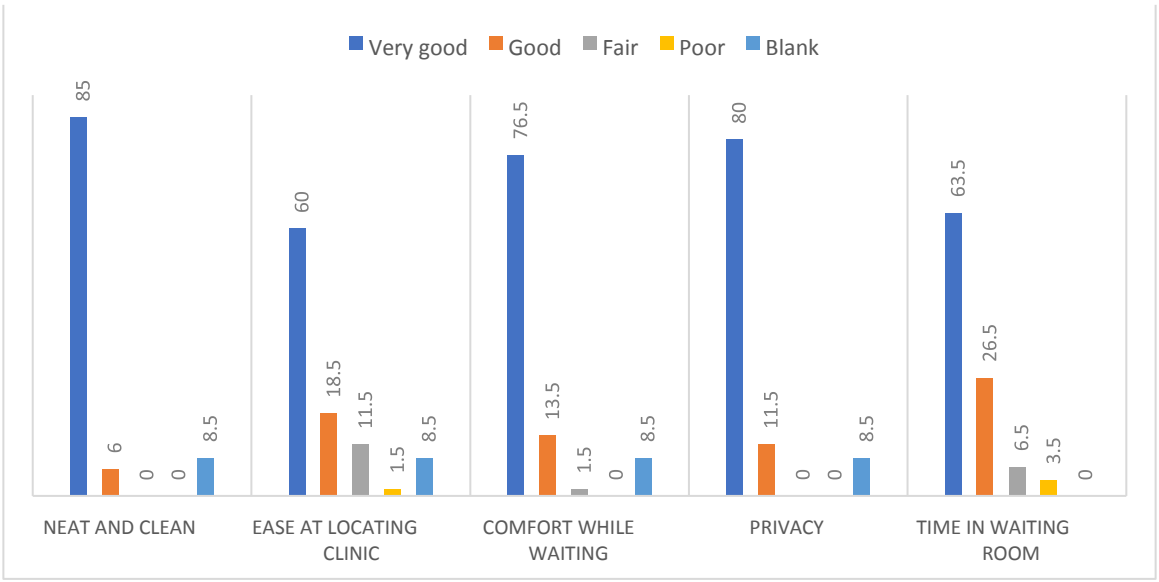


Figure 3: Staff assessment.

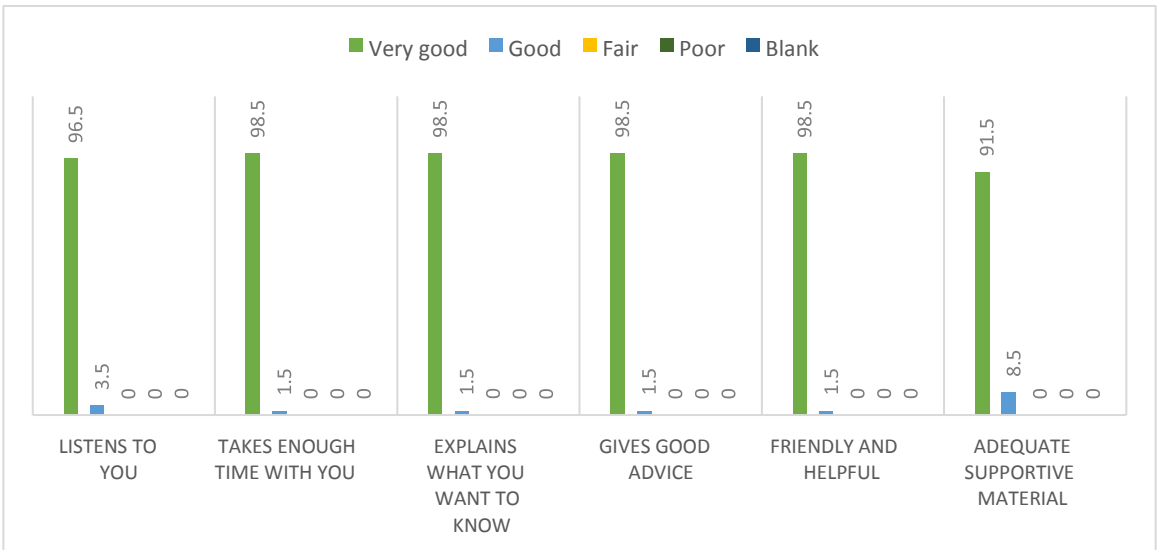
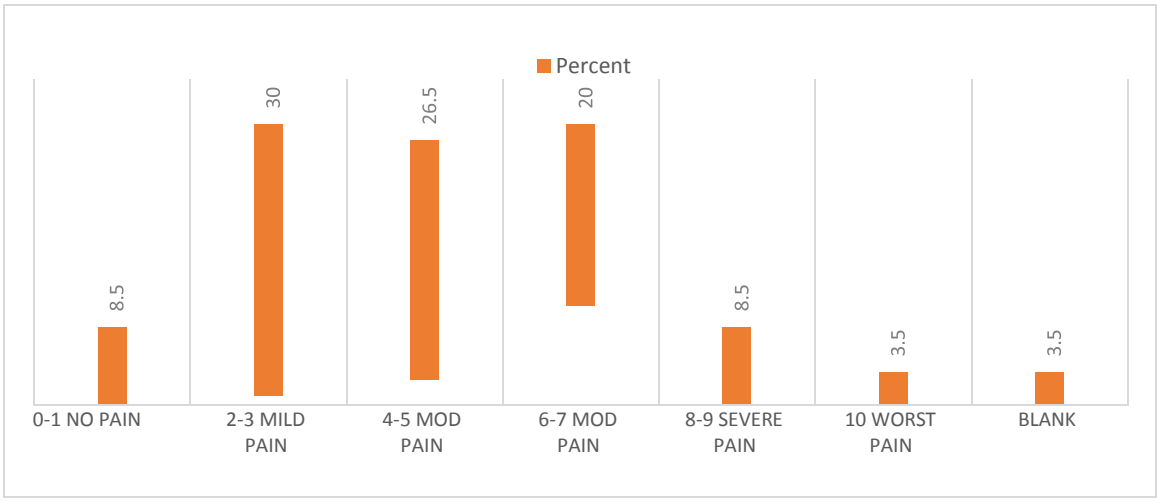


Figure 4: Overall experience by VAS (visual analogue scale).



Six aspects of the service met the expected standards, and five fell short of the standards. The majority of the women (86.5%; 52/60) felt that the service was convenient, and almost all of the women (93.5%; 56/60) would recommend the service to a friend. Most of the women (86.5%; 52/60) read the information leaflet in advance of their procedure. The staff met or excelled beyond the set standards on all aspects of care. Almost all of the women felt that the staff listened to them (96.5%; 58/60) and took enough time with them (98.5%; 59/60). Almost all of the women (98.5%; 59/60) felt that the staff explained what they wanted to know, gave good advice and were friendly and helpful. Most of the women (91.5%; 55/60) felt that the supportive material provided was adequate. The majority of women rated the facilities as neat and clean (85%; 51/60) and were satisfied with the level of privacy afforded (80%; 48/60).

Regarding the aspects of the service that fell short of the standards, only 40 women (66.5%; 40/60) were satisfied with the time interval between GP referral and appointment. Thirty-six women (60%; 36/60) felt that the clinic was easy to locate, and 38 (63.5%; 38/60) rated their time in the waiting room as satisfactory. Forty-six women (76.5%; 46/60) felt comfortable while waiting for their procedure.

The majority of women also experienced mild to moderate pain during the procedure (mild pain: 30%, 18/60; moderate pain: 46.5%, 28/60).

Eighteen women left comments on their questionnaire. Nine of these were comments expressing satisfaction with the service, with one suggesting that the option of 'excellent' should be added to the questionnaire. Two comments suggested better signage to locate the clinic. Two felt the waiting times were too long. Two women made comments about the information leaflet – one felt it was unclear and one suggested informing women of the need to provide a urine sample prior to the procedure. Two women provided suggestions for improving the waiting room by adding a TV, more magazines or a radio.

Discussion

The OHC reached audit targets in six out of eleven areas. Overall, patient satisfaction was very high, however areas for improvement were highlighted.

Regarding the interval between GP and appointment time, there may be a number of logistical barriers to a timely appointment. Ultrasound scan of pelvis (US pelvis) is booked for all women with abnormal uterine bleeding prior to OHC appointment. Due to radiology waiting lists, the time interval between GP referral and OHC appointment may be prolonged.

Regarding prompt return of calls, this relies on administration staff who are available only during working hours. To counter this issue, the telephone number of the gynaecology ward will be included in the new OHC patient information leaflet. This will provide women with access to the service out of hours.

Only 36 women (60%; 36/60) felt the ease of locating the clinic was 'very good'. One comment suggested improved signage, and following this finding, the team has installed a large sign outside the main hospital entrance to direct women to the clinic.

With respect to time spent in the waiting room, some suggestions in the comments section included requests for a television, magazines or a radio. During the audit period the TV in the waiting room was not working, but staff have since resolved this issue. Unfortunately, the magazines previously present have now been removed during the COVID19 pandemic as per national guidelines for health and safety reasons. The women are asked to bring their own reading material while waiting.

Regarding pain during the procedure, the majority of women reported mild to moderate pain. However, most women (93.5%; 56/60) would still recommend the clinic to a friend or relative. This finding is in line with previous outpatient hysteroscopy satisfaction studies. Downes and Al-Azzawi[13] found that despite a six percent failure rate and a mean visual analogue score of 3.25/10 for pain, patient satisfaction was still 97%. Reflecting on this result, Kremer, Duffy and Moroney[14] commented that "patients still tolerate acceptable failure and discomfort and still remain satisfied" (p.281). Our study supports this theory. The RCOG recommends the use of non-steroidal anti-inflammatories routinely for women prior to outpatient hysteroscopy[8] and this advice is contained in our pre-procedure information leaflet. Routine cervical preparation is not used in our clinic as it has not been shown to reduce pain and is not recommended by the RCOG[8]. Of note, there is no dedicated recovery area in the clinic post-procedure for the women, but there is a side room with a clinic bed if further recovery is required. This aspect of the service could be investigated in a future audit.

In conclusion, women reported high levels of satisfaction with the outpatient hysteroscopy service in UHK. Our audit also highlights areas for improvement. These areas include reduced time between GP referral and appointment, prompt return of calls, improved signage, and improved waiting room facilities. Some changes have already been made to improve the service, and other changes are in progress.

Our re-audit questionnaire has been designed to include an option of 'excellent' as recommended by one woman in the comments. Our re-audit will also include demographics such as age, parity and menopausal status to allow more in-depth analysis of experiences across groups.

Declaration of Conflicts of Interest:
No conflicts of interest.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P263

Fatty Liver Infiltration on Executive Health Screen

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Abstract

Aim

To describe the relationship between level of fatty infiltration in non-alcoholic fatty liver disease (NAFLD) and known risk factors in a population with incidentally discovered findings.

Methods

This was a retrospective cohort study through chart audit of asymptomatic patients attending an executive health screen. Pearson correlation coefficients (r) were calculated between degree of fatty liver infiltration and known risk factors of fatty liver disease.

Results

Thirty-six individuals were included. Participants tended to be male (n=27,75.0%) with high BMI (30.59±3.66 kg/m^2). Nearly half of patients (n=15, 41.7%) had a moderate degree of fatty infiltration. The degree of infiltration was positively correlated with BMI, total cholesterol, LDL and triglycerides and negatively correlated with weekly alcohol consumption and presence of metabolic syndrome. None of these relationships were statistically significant.

Discussion

The current study investigates the relationship between level of fatty liver infiltration and known pathogenic risk factors previously described in the literature. No relationship was found between level of fatty liver infiltration and metabolic syndrome, BMI, lipid levels, or alcohol consumption in our population of asymptomatic individuals. This study further highlights the need to better identification and management of NAFLD to optimize risk factors and decrease risk of complications.

Introduction

The histological representation of hepatic steatosis has been known for centuries. Initial descriptions were used in the setting of alcoholic liver disease, however in 1980, a non-alcoholic steatosis was described.[1] This Non-Alcoholic Fatty Liver Disease (NAFLD) was noted in biopsy samples of patients without a history of alcohol abuse or a significant history of alcohol intake.[1]

Other distinguishing features are the biochemical patterns: NAFLD is described as having alanine aminotransferase (ALT) levels exceeding those of aspartate aminotransferase (AST), while alcoholic liver injury is characterized by a high AST:ALT ratio.[2]

NAFLD is currently defined as macrovesicular steatosis in ≥5% hepatocytes, with the absence of secondary causes, such as alcohol or drugs.[3,4] It refers to a spectrum of disease from non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH) to fibrosis and cirrhosis.[2–4] The global prevalence is estimated to be around 25%, with a rising incidence due to increasing levels of obesity, Type 2 Diabetes Mellitus (T2DM) and metabolic syndrome.[2,3,5,6] This prevalence may be underestimated due to the asymptomatic nature and prolonged period before progression. NAFLD may be initially identified due to derangement of liver function tests or evidence of hepatic steatosis on abdominal ultrasound, with the gold standard for diagnosis being liver biopsy.[2,4,7]

The pathogenesis of NAFLD is related to a decrease in insulin sensitivity and hyperinsulinemia.[8] This insensitivity results in decreased effects of insulin on the metabolism of both lipids and glucose.[9] The literature indicates that this effect is not only found in patients with abnormal glucose regulation or obesity, but is also observed in some individuals with normal weight and normal glucose tolerance.[8,9] Research supports the connection between metabolic syndrome and NAFLD, with some suggesting that the two are merely different facets of the same pathophysiologic mechanism.[5] Other proposed risk factors for the development of NAFLD include diet high in fats and cigarette smoking.[10] However, there are still gaps in the literature with regards to the lifestyle factors that predispose individuals to developing NAFLD, especially in asymptomatic patients.

The objective of the current study is to describe the relationship between level of fatty infiltration in hepatic steatosis and known risk factors in a population with incidentally discovered fatty liver disease.

Methods

This was a retrospective cohort study through chart audit on individuals attending Bon Secours Hospital in Limerick, Ireland for Executive Health Screen between 2011-2018. Data were abstracted for individuals with incidental findings of fatty liver on abdominal ultrasound.

The following information was collected from patient charts: age, sex, height, weight, blood pressure, total cholesterol, HDL, LDL, triglycerides, fasting glucose, ALT, GGT, smoking status, alcohol consumption, and extent of fatty liver infiltration.
Presence of metabolic syndrome was identified by the presence of three or more of the following: abdominal obesity (waist circumference >102 cm in men, >88 cm in women), elevated triglycerides (>150 mg/dl or on drug treatment for elevated triglycerides), reduced HDL-C level (<40 mg/dl in men, <50 mg/ dl in women or on drug treatment for reduced HDL-C), hypertension (systolic blood pressure >130 mmHg or diastolic blood pressure >85 mm Hg or on antihypertensive drug treatment) and impaired fasting glucose (100 - 125 mg/dl or on antidiabetic drug treatment).[5]

Level of fatty infiltration was graded as mild, moderate or severe. Above information was collected as part of the Executive Health Screen. Individuals were asymptomatic at the time of screening.

Pearson correlation coefficients (r) were calculated between degree of fatty liver infiltration and the following: BMI, presence of metabolic syndrome, total cholesterol, LDL, triglycerides, alcohol consumption per week. No patients in the current study met criteria for alcoholic fatty liver disease. We hypothesized that level of fatty liver infiltration would be positively correlated with all abovementioned variables.

Variables were calculated as means and SDs or frequencies and percentages as appropriate. Significance level was set to $p<0.05$. Statistical analysis was performed using the IBM SPSS Statistics version 24.0 (IBM Corporation, Armonk, NY).

Results

Demographic data are summarized in Table 1. Thirty-six participants were included in the study. Participants in the analysis tended to be male (n=27, 75.0%) with BMI in the class I obesity range (BMI=30.59±3.66). A number of participants reported having comorbid conditions (n=19, 52.8%). The most commonly reported conditions were dyslipidemia (n=6, 16.7%), hypertension (n=6, 16.7%), respiratory conditions (n=3, 8.3%) and thyroid conditions (n=3, 8.3%). Just under half of participants (n=17, 47.2%) were not taking any medication. Of participants taking medications, four (11.1%) were taking lipid lowering medications, four (11.1%) were on antihypertensive medications and two (5.5%) were taking both lipid lowering medications and antihypertensives. Nearly half of patients (n=15, 41.7%) had a moderate degree of fatty liver infiltration based on ultrasound reports.

Table 1. Descriptive statistics for n=36 patients included in study.

Characteristic	**Values**
Age (years)	59.89 ± 10.29
Sex (n, % males)	27 (75.0%)
Body Mass Index (kg/m^2)	30.59 ± 3.66
Blood Pressure (mmHg)	135.31 ± 12.13 / 73.17 ± 6.91
Alcohol Consumption (units/week)	6.77 ± 8.53
Metabolic Syndrome (n, % yes)	7 (19.4%)
Number of Medications	1.89 ± 2.63
Total Cholesterol	5.19 ± 1.19
HDL	1.26 ± 0.32
LDL	3.15 ± 1.06

Triglycerides	1.68 ± 0.83
Glucose	5.52 ± 0.54
ALT	40.72 ± 17.45
GGT	44.72 ± 55.50
Level of Fatty Infiltration Minor Minor to moderate Moderate Moderate to severe Severe	 9 (25.0%) 3 (8.3%) 15 (41.7%) 1 (2.7%) 8 (22.2%)

Note: Values are mean ± SD, n (%), or as otherwise indicated

Level of fatty liver infiltration was negatively correlated with weekly alcohol consumption and presence of metabolic syndrome, but positively correlated with BMI, total cholesterol, LDL and triglycerides. None of these relationships were statistically significant. Unsurprisingly, presence of metabolic syndrome was positively correlated with BMI, $r(36)=0.432$, $p=0.015$ and total cholesterol was correlated with LDL $r(36)=0.797$, $p<0.001$. Complete results for the correlation analysis are found in Table 2.

Table 2. Correlation analysis of relationships between fatty liver infiltration and other variables.

	Fatty Liver Infiltration	Body Mass Index	Metabolic Syndrome	Total Cholesterol	LDL	Triglycerides	Alcohol Consumption per week
Fatty Liver Infiltration		0.213 0.250 36	-0.065 0.728 36	0.142 0.447 36	0.280 0.127 36	0.339 0.062 36	-0.084 0.654 36
Body Mass Index			**0.432*** **0.015** **36**	-0.158 0.397 36	-0.044 0.815 36	0.067 0.721 36	0.077 0.682 36
Metabolic Syndrome				0.020 0.916 36	-0.110 0.557 36	0.182 0.328 36	0.090 0.630 36
Total Cholesterol					**0.797**** **0.000** **36**	0.300 0.101 36	-0.112 0.547 36
LDL		Pearson *r* Sig (2 tailed) N				0.004 0.984 36	-0.192 0.302 36
Triglycerides							0.075 0.688 36
Alcohol Consumption per week							

*Note: *Correlation significant at p<0.05; **Correlation significant at p<0.001*

Discussion

The current study was a retrospective chart audit of patients with incidental finding of fatty liver disease on Executive Health Screen. It demonstrates that level of fatty liver infiltration is not related to metabolic syndrome, BMI, lipid levels, or alcohol consumption.

Participants in the current study were demonstrated to have significant levels of fatty liver infiltration while being asymptomatic for any liver pathology. This is similar to reports in the literature, where hepatic steatosis was detected incidentally during investigation of other complaints.[2,3] While in NAFLD there are described patterns of liver biochemical tests,[2] there is also evidence that many patients will have normal liver function tests.[3] This has been a limitation with regards to screening for NAFLD in the general population.[5] Other limitations have include the low accuracy of non-invasive tools and inconsistency of self-reported ethanol ingestion histories.[2,5,8]

Interestingly, level of fatty liver infiltration in the current study was not found to be related to metabolic syndrome. However, these results may be limited by the small sample size of the current study. Metabolic syndrome refers to a cluster of risk factors that lead to an increased risk for atherosclerotic cardiovascular disease, type 2 diabetes mellitus and chronic kidney disease.[5,11] The etiology of both metabolic syndrome and NAFLD have been linked to insulin resistance and compensatory hyperinsulinemia in patients with obesity and normal body weight.[5,8,9,11,12]

The results from this study demonstrate a relatively healthy overweight population, with many reporting one or no comorbidities. The BMI of the participants reported in the current study is similar to the average BMI of those presenting for Executive Health Screen at this institution over the study period. The high BMI found in study participants is not surprising as the prevalence of obesity has been increasing in Ireland over the last two decades.[13] The 2017 Healthy Ireland Survey reported that 39% of Irish adults were overweight and 23% were obese.[14] These numbers increase to 44% in the overweight category and 32% in the obese category for adults between the ages of 55-64 years, which is the age group captured by the current study.[14] Therefore, the population captured by the current study may be comparable to the larger population, although further research is needed to confirm whether the findings of the current study are generalizable. Other considerations when interpreting the results from the current study are recall bias and possible under-reporting of alcohol consumption.

Although the initial stages NAFLD are asymptomatic, there are several serious complications that must be considered. In some patients with NAFLD, isolated steatosis can progress to advanced stages with non-alcoholic steatohepatitis (NASH) and fibrosis, increasing the risk of cirrhosis and hepatocellular carcinoma,[12] although only a minority of patients will develop these complications of chronic liver disease.[3] The most commonly described complications and cause of death in patients with NAFLD is cardiovascular disease.[5,9,15] A large cohort trial has demonstrated a higher 5-year health care cost in individuals with NAFLD due to the cardiovascular burden in these individuals.[16]

Management of NAFLD is crucial in order to minimize complications. Current options depend on severity of disease but includes lifestyle modifications and pharmacological treatment.
Drug treatments assessed in NAFLD seem to differ with respect to cardiometabolic and antifibrotic efficacy, suggesting the need to better identify and tailor the most appropriate treatment approach, or to use a combination of approaches.[12] The assessment and management of blood pressure, lipids, weight, smoking status and diabetes control are therefore the basis of management in NAFLD, especially in the early stages.[3,6] Further longitudinal research is required to better characterize the risk profile and impact of treatment in individuals with NAFLD.

To conclude, the current study investigates the relationship between level of fatty liver infiltration and known pathogenic risk factors previously described in the literature. No relationship was found between level of fatty liver infiltration and metabolic syndrome, BMI, lipid levels, or alcohol consumption in our population of asymptomatic individuals. This study further highlights the need to better identification and management of NAFLD.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P264

Neonatal Therapeutic Hypothermia for Neonatal Encephalopathy: Mortality and Neurodevelopmental Outcome

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Abstract

Aim

To study the mortality and neurodevelopmental outcome of infants with neonatal encephalopathy (NE) who required therapeutic hypothermia (TH).

Methods

All infants requiring TH between Jan 2009 – Dec 2016 at a single NICU were included. Data was obtained from clinical notes, MRI brain reports, The Bayley Scales of infant and toddler development-III (BSIDIII).

Results

127 infants received TH. 12 infants died. Of the 115 surviving infants, 75 (65%) were male with a median birthweight of 3.54 kg and median gestation of 40 weeks. Brain MRIs of the surviving cohort were normal in 91 (81%) infants. The Bayley's score showed that the number (%) of infants below the normal range (≤

89) was: Motor:15/112 (13.9%), Cognitive: 17/112 (15.7%), Speech & Language: 33/112 (33.3%). When the babies are subdivided into those with normal and abnormal brain MRIs the proportion with scores ≤89 are:

Normal MRI: Motor - 8.9%, Cognitive - 8.9%, Speech & Language - 26.9%. Abnormal MRI: Motor - 30.4%, Cognitive – 39.1%, Speech & Lang – 47.8%.

Conclusion

In this series of infants with NE requiring TH there was a preponderence of male infants: 78 vs 49. Among those who died there was a preponderence of females: 9 vs 3. The neonatal mortality rate in our series (9.4%) is similar to the Irish national data. The majority of infants had a satisfactory BSID-III score and a normal MRI brain report. The brain MRI is predictive of neurodevelopmental outcome.

Introduction

Hypoxic-ischaemic encephalopathy (HIE) is one of the most common neurological disorders of the perinatal period, and a major cause of significant morbidity and mortality in childhood.[1,] It has an incidence of 1.5 to 2.5 per 1000 live births in developed countries.[2] HIE, can, if significant, trigger a cascade of neuronal injury, leading to neonatal encephalopathy (NE) with resultant long-term neurological sequelae.

Therapeutic hypothermia (TH) has emerged as the international gold standard of care for neonates with moderate or severe encephalopathy.[3,] A Cochrane Systematic Review (2013) concluded that TH in term and late preterm infants with HIE resulted in a statistically significant and clinically important reduction in mortality and neuro-disability at 18 months of age.[4]

The Bayley Scales of Infant and Toddler Development [5] (Bayley-lll) and brain Magnetic Resonance Imaging (MRI), have predominantly been used to assess, predict and counsel about neurodevelopmental outcomes in these newborns.[6]

We have reviewed all neonates requiring TH in our unit over an eight-year period. Our primary outcome was to describe the short-term and medium-term neurodevelopmental outcomes [using the Bayley Scales of Infant and Toddler Development (Bayley-lll) [7]] and neuro-radiological findings (using the Barkovich MR Scoring System [8]) of the surviving neonates.

Methods

This was a retrospective descriptive study of all neonates who received TH for neonatal encephalopathy at a single, level 3 NICU over an eight-year period (January 2009 – December 2016).

Infants received TH according to the established hospital TH Protocol. The National Neonatal TH Candidacy Checklist outlines the criteria for initiation of TH used at this neonatal unit.[9]

Clinical psychology, medical and nursing databases were used to identify all infants who received TH at this centre over the study period. Medical charts were reviewed to provide clinical and demographic data. Infants were classified in the medical notes as having a mild, moderate or severe encephalopathy based on clinical Sarnat assessment. This data was extracted and recorded. Bayley-lll scores for the study population were retrieved from clinical psychology records. The Bayley Assessment Scores were performed by a clinical psychologist (MS) at 2 years corrected gestational age. The MRI brain reports of

this infant cohort were sourced from a combination of medical charts and electronic radiology records. These were reviewed and classified using the validated Barkovich MR Scoring System by a Consultant Paediatric Radiologist (VD).

The collected data was anonymised and entered on a Microsoft Excel spreadsheet. The data was analysed using descriptive statistics.

Results

A total of 127 neonates received therapeutic hypothermia over the eight-year study period. Twelve neonates (9.4%) died shortly after birth.

Characteristics of infants who died

Twelve infants died in the neonatal period., at a median of 5.5 days. Of these, 3 infants (25%) were male. The median birth weight was 3545g (IQR 767). The median gestation was 40 weeks (IQR 2). Median apgar scores at 5, 10, 15 and 20 minutes were 0 (IQR 2), 2 (IQR 3.25), 3 (IQR 5.25) and 5 (IQR 2.5) respectively. Mean cord gases were pH 6.8, BE -18, pH 7.0, BE -15. Nine infants (75%) required inotropic support. Eight infants (67%) had clinical and electrographically detected seizures. All infants had a severe encephalopathy based on Sarnat examination. Six infants (50%) had an MRI brain at a median of 2.5 days. All had extensive basal ganglia and watershed injuries.

The characteristics of the surviving infants is shown in Table 1.

Table 1. Neonatal Encephalopathy requiring Therapeutic Hypothermia - Characteristics of Surviving Infants [Number of patients (%)]

Total number of surviving infants	115
Male gender	75 (65.2)
Birth weight (median), (Interquartile range)	3540g (820)
Gestation (median), (Interquartile range)	40 weeks (2) N=1 received therapeutic hypothermia at 33 weeks gestation, n=114 were ≥ 35 weeks
Apgar scores (median), (Interquartile range) At 1 minute At 5 minutes At 10 minutes At 20 minutes	 2 (2.25) 4 (4) 5(4) 5 (2)
Cord gases (mean)(SD)	Arterial: pH 7.06 (0.17), BE -11 (5.01), Venous: pH 7.12 (0.15), BE -10 (4.31)
Inotropic support	22 (19.1)
Clinical seizures	54 (46.9)
Electrographically detected seizures	53 (46.1)

Grade of Encephalopathy (based on clinical examination)	
Mild	15 (13.0)
Moderate	88 (76.5)
Severe	9 (7.8)
Not recorded	3 (2.6)

The Bayley Scales of Infant and Toddler Development

All surviving neonates (n=115) were referred for a Bayley-lll (See table 2). A Bayley-lll score was available for 108 infants (93.9%). Of the remaining 7 patients, 5 patients were lost to follow up and 2 patients were unsuitable for assessment due to uncooperative behaviour. The Bayley-lll was performed at 2 years corrected gestational age by a clinical psychologist.

Table 2. Bayley III Scales of Infant and Toddler Development of Neonates with encephalopathy requiring Therapeutic Hypothermia [Number of patients (%)]

Total no. of patients, n=108

Composite Score	**Cognition**	**Language**	**Motor**	**Motor Scaled Score**	**Gross Motor**	**Fine Motor**	
Above Average Range (≥110)				the mean	(11.1)		
Normal Range	52 (48.1)	38 (35.2)	47 (43.5)	Normal	79	56 (51.9)	
39 (36.1)		33 (30.5)	46 (42.6)	≥1 SD above	12		43 (39.8)
(90-109)				range (8-12)	(73.1)		
Below Average Range (≤89)				the mean	(14.8)		
Not recorded				*Not recorded*	1 (0.9)	1 (0.9)	
	17 (15.7)	36(33.3)	15 (13.9)	≤1 SD below	16	8 (7.4)	
		1 (0.9)					

Of the 15 infants with a mild encephalopathy, 93% (n=14), 80% (n=12) and 86% (n=13) had ≥ average scores for cognitive, language and motor scores respectively. One infant did not have a Bayley-lll score recorded. Regarding the 88 infants with a moderate encephalopathy, 80% (n=70), 61% (n=54) and 83% (n=73) had ≥ average cognitive, language and motor scores respectively. One infant did not have a Bayley-lll score performed. One infant only had cognitive and motor scores recorded.

With regards to those neonates described as having severe encephalopathy (n=9, 7.82%), median Apgar scores of 0 at 1 minute, 1 at 5 minutes, 6 at 10 minutes and 3.5 at 20 minutes were recorded. Mean cord

gases (arterial pH 6.9 (SD 0.21), Base Excess -14 (SD 6.77), venous pH 7.1 (SD 0.24), Base Excess 12 (SD 8.24)) were noted. Seven infants (78%) required inotropic support. Seven infants (78%) had clinical and electrographically detected seizures.

BSID-III scores were available for the nine infants with severe encephalopathy (100%). Four patients (44%) had below average composite cognitive scores, three of which had scores in the 'Extremely low' range. The remainder (n=5) had scores in the 'Average' (n=3), 'High Average'(n=1) or 'Very Superior' range (n=1). Six patients (n=6, 66.7%) had Below Average composite language scores, four of which had scores in the 'Extremely Low' range. The remainder, (n=3) had scores in the 'High Average' range. Regarding assessment of motor skills, four patients (44%) had Below Average composite scores, three of which had scores in the 'Extremely Low' range. The remainder (n=5) had scores in the 'Average' (n=3), 'High Average' (n=1) and 'Very Superior' (n=1) range.

Barkovich Scoring System of MRI Brain Reports

MRI reports were obtained for 112 of 115 surviving patients (97.4%). Three reports (2.6%) were unable to be retrieved. MRI Brain imaging was carried out at median of 6.5 days. (See table 3)(Next Page)

Table 3. Barkovich Scoring System of MRI Brain reports [Number of patients (%)]	
Basal ganglia	
Normal	99 (88.4)
Mild abnormality (Abnormal signal in the thalamus / Abnormal signal in thalamus and lentiform nucleus)	9 (8)
Severe abnormality (Abnormal signal in thalamus, lentiform nucleus, and perirolandic cortex / More extensive involvement	4 (3.6)
Watershed	
Normal	95 (84.8)
Mild Abnormality (Single focal infarction / Abnormal signal in anterior or posterior watershed white matter	5 (4.5)
Severe Abnormality (Abnormal signal in anterior or posterior watershed cortex and white matter / Abnormal signal in both anterior and posterior watershed zones / More extensive cortical involvement	12 (10.7)
Basal ganglia/Watershed	
Normal	91 (81.2)

Mild Abnormality **(**Abnormal signal in basal ganglia or thalamus / Abnormal signal in cortex	14 (12.5)
Severe Abnormality Abnormal signal in cortex and basal nuclei (basal ganglia or thalami) / Abnormal signal in entire cortex and basal nuclei	7 (6.3)

In total, 89 infants (79.5%) had normal MRI brain reports. Thirteen out of 15 infants with mild encephalopathy had an available MRI brain report, all of which were normal. An MRI brain report was available for 87 out of 88 infants with moderate encephalopathy. Of these, 82% (n=72) were normal. An MRI report was available for all infants (n=9) with a severe encephalopathy. Four out of 9 infants (44.4%) with severe neonatal encephalopathy had a normal MRI brain.

A Bayley-lll score was available for 84 out of 89 neonates with normal MRI brain reports (94.3%) (See table 4)(Next Page). Of the remainder (n=5), one patient was uncooperative for assessment, 4 patients were lost to follow up. Regarding the neonates with abnormal MRI findings (n=23, 20.5%), Bayley Assessment Scores were available for 21 patients (91.3%). One infant was uncooperative for developmental assessment. One patient was lost to follow up.

Table 4. BSID-III Score of Infants stratified according to MRI Brain results [Number of patients (%)]

Composite Score	**Cognition**		**Language**		**Motor**	
MRI Brain Result	**Normal**	**Abnormal**	**Normal**	**Abnormal**	**Normal**	**Abnormal**
	(n=89)	**(n=23)**	**(n=89)**	**(n=23)**	**(n=89)**	**(n=23)**
Above Average Range (≥110)	(37)	(21.7)	(33.7)	(13)	(43.8)	(21.7)
Normal Range (90-109)	43 (48.3)	7 (30.4)	30 (33.7)	6 (26)	37 (41.6)	9 (39.1)
Below Average Range (≤89)	(8.9)	(39.1)	(26.9)	(47.8)	(8.9)	(30.43)
Not recorded	5 (5.6)	2 (8.7)	5 (5.6)	3 (13)	5 (5.6)	2 (8.7)
	33	5	30	3	39	5
	8	9	24	11	8	7

Discussion

In the 115 surviving infants requiring TH, the majority had a normal MRI brain and a satisfactory neurodevelopmental outcome. The diffusion-weighted MRI was predictive of a normal Bayley-lll assessment at 2 years of age. A sub-cohort of neonates who had normal MRI brain reports had isolated Speech and Language issues in the infantile period. Subtle changes in the language centres are perhaps not identifiable by MR imaging. Early referral to Speech and Language therapy should be considered for neonates requiring TH. This is supported by previous studies.[10,11]

Our study is strengthened by the large patient cohort that was reviewed. Furthermore, two reliable and validated assessment tools were used for analysis – the Bayley-lll, and the Barkovich MRI Scoring System. All but 7 infants had a Bayley-lll assessment. MRI reports were available for 112 surviving infants (97.4%). A single clinical psychologist and consultant radiologist carried out the Bayley-lll assessments and Barkovich scoring respectively, thus eliminating the risk of inter-observer variability.

Noteworthy, the majority of infants requiring TH were male (n=75, 65.2%). This was also reflected in the Irish National Report on neonatal TH (2018).[12] In 2018, two-thirds of the infants who received TH in Ireland were male (76.8%; n=53). Male sex has previously been identified as a risk factor for NE in the literature.[13] The mechanisms underlying this sex difference are poorly understood.[14,15] Although the majority of infants requiring TH in our study were male, only 25% (n=3) of the neonatal deaths were male. A higher mortality rate for female infants requiring TH was also reported nationally. Between 2016-2018 in Ireland, 14.5% of females requiring TH died (n=11) versus 9.8% of males (n=13).

The neonatal mortality rate in our series of 127 infants was 9.4%. This is similar to the Irish national data from 2018 (mortality rate 6.1%). In contrast, the mortality rates for the control group in the TOBY study[7], the NICHD[16] study and ICE study[17] were 25.7% 24%, and 25% respectively. Advances in NICU care over the last decade may account for these differences. The Bayley-lll scores were satisfactory in the overall patient cohort, in each of the core developmental domains. Eighty-four percent of neonates (n=91) had cognitive scores in the average or above average range.
The TOBY study reported that 70% (n=81) of their cohort undergoing TH had cognitive scores in the normal range. Of note, a cut-off composite score of ≥85 was used to define 'Average' in their study.

Chalak et al [18] conducted a prospective cohort study of infants requiring TH in Texas, U.S (2005-2011). Ninety neonates received TH. Similar to our study, moderate encephalopathy was described in 80 (89%) infants, while severe encephalopathy occurred in 10 infants (11%). Bayley-lll scores were available for 62 infants at a mean ± SD age of 20 ± 2.9 months. In comparison to our study, 53% (n=33) had average or above average cognitive scores versus 84% (n=91) in our study. Average or above average language scores were reported for 56% (n=35) versus 66% (n=71) in our cohort. Sixty-eight percent (n=42) had average or above average motor scores versus 86% (n=93) in our population. Of note, a cut-off composite score of ≥85 was used to define 'Average' in their study. We have described the 'Average' score as ≥90. As this study was conducted prior to our study (2005-2011), one could postulate that advancements in NICU care may potentially account for these differences.

MRI is widely used to predict outcomes in neonatal encephalopathy.[19,20,21] One can extrapolate from our data that if an infant has normal brain imaging, their chances of having normal cognitive, language and

motor outcomes at 2 years corrected gestational age are 85%, 67% and 85% respectively. This data provides useful prognostic information. It also emphasises the importance of Speech and Language Therapy in the management of these neonates.

In conclusion, we have described the neurodevelopmental outcomes and neuro-radiological findings of infants with NE requiring TH in a single, Level 3 NICU over an eight-year period. This study will enable more accurate prognostication of neuro-developmental outcomes and correlation with MRI Brain findings for health-care professionals, patients and their families.

List of Abbreviations used:

HIE - Hypoxic Ischaemic Encephalopathy
MRI - Magnetic Resonance Imaging
TH – Therapeutic Hypothermia
Bayley-lll - Bayley Scales of Infant and Toddler Development – 3rd edition NICU – Neonatal Intensive Care Unit

Declaration of Conflicts of Interest:

The authors have no conflicts of interest to declare.

Ethical Approval:

Ethical approval was obtained from the National Maternity Hospital Ethics Committee.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P265

Irish Maternity: A Changing Ethnic Landscape

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Abstract

Aim

We have experienced an increase in non-Irish women booking at the Rotunda Hospital. The aim of this study was to identify changing trends in ethnicity in women booking for prenatal care at the Rotunda Hospital.

Methods

A retrospective review of hospital data on ethnicity of 90,715 mothers booking over an 11-year period (2001-2012) was undertaken. Trends in numbers of Irish vs. non-Irish women were compared. A Linear regression model was used to analyse if these trends reached statistical significance.

Results

A total of 62,259 Irish and 28,456 non-Irish women booked over the study period. The number of Non-Irish women booking each year significantly increased over the study timeframe, from 1453 women in 2001 to 3136 women in 2012 ($p<0.0001$). Regarding non-national women, a significant increasing trend in bookers from South Asia ($p<0.0001$), South East Asia ($p=0.005$), East Asia ($p=0.008$) and Eastern Europe (p values < 0.05) was observed.

Conclusion

In a single large tertiary referral maternity hospital, we witnessed a significant increase in the number of women booking of non-Irish ethnicity over the past decade. Barriers to language, as well as cultural differences, will be encountered, and will require attention to improve clinical outcomes, and maternal well-being.

Introduction

Over the past 20 years, Ireland has seen significant changes in its population. Immigration is increasing, and our population is becoming more ethnically diverse every year. There has been an overall increasing trend in numbers of non-Irish nationals immigrating to Ireland. Over the years examined in this study (2001-2012), there was a positive overall net migration into Ireland almost every year, with 2007 seeing the highest levels of immigration of the previous ten years [1].

Immigrant mothers have been shown to be at increased obstetric risk. Many studies have identified that, compared with women from the host country, immigrant women are at an increased risk of a number of poor maternal and fetal outcomes including low birth weight infants [2], poor mental health [3], gestational diabetes [4], and late pregnancy stillbirth [5]. As well as this, communication and language barriers can impede doctor-patient interactions.

In the Rotunda Hospital, an increase in women booking for prenatal care from non-Irish backgrounds has been observed over recent years. We sought to examine how trends in ethnicities have changed over the past decade, in order to assess how our patient population, and women's needs, may be changing.

Methods

A retrospective review of prospectively collected hospital data on ethnicity over an 11-year period, from 2001-2012, was carried out. Ethnicity is recorded for all women at their first booking visit. Ethnicity was determined from the woman's self reported country of birth. This data was extracted from electronic records in the form of anonymised reports, which were then used for analysis. Over this time, 92,580 mothers delivered at our institution. We compared the number of women of Irish ethnicity vs. all other non-Irish ethnicities booking for prenatal care over this time period. Trends in ethnicities of non-Irish women were sought. A linear regression model was used to analyse if these trends reached statistical significance.

Results

A total of 62,259 Irish and 28,456 non-Irish women booked in our institution over the study period. There were 1865 women over this timeframe for whom nationality was not listed at booking. Women's countries of origin were grouped into geographical regions for analysis (see table 1 for examples). Trends in ethnicities of women from each geographical region were analysed.

Geographical Region	Countries

EU European	Spain France Lithuania Poland Latvia	Romania Slovakia Estonia Slovenia
Non-EU European	Moldova Ukraine Kosovo Bosnia & Herzegovina	Kosovo Belarus Chechnya Serbia Albania
Central Asia	Kyrgyzstan Kazakhstan Afghanistan	Uzbekistan Azerbaijan
South Asia	Bangladesh India Pakistan	Sri Lanka Nepal
East Asia	China Japan	Korea (North & South) Mongolia
South-East Asia	Malaysia Thailand	Vietnam Philippians
Middle East	Turkey Iran Iraq Saudi Arabia Syria	Israel Palestine Jordan Qatar Oman

***Table 1*:** Examples of countries included in each geographical region for analysis.

Both the number of Irish and Non-Irish women booking each year significantly increased ($p<0.0001$, Figure 1). The overall number of Non-Irish women booking increased from 1453 in 2001 to 3136 women in 2012 (22.5% of total bookings to 35.4% of total bookings).

***Figure 1*:** Graph showing number of Irish and non- Irish women booking per year over the study period.

Asia

A significant increasing trend in bookers from Asia was observed over the study timeframe, from 101 women in 2001 to 521 women in 2012. This geographical region was further subdivided into three areas for analysis – South Asia, South East Asia and East Asia. There was a statistically significant increase in women booking from each of these three regions- South Asia ($p<0.0001$), South East Asia ($p=0.005$) and East Asia ($p=0.008$). (Figure 2)

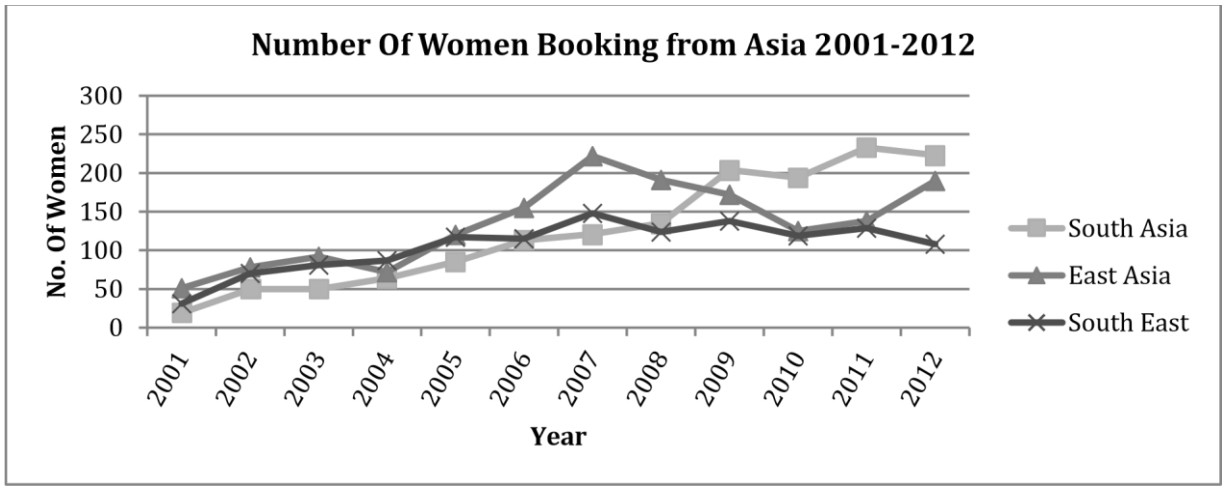

Figure 2: Graph showing the increasing number of women booking from South, East and South East Asia.

Europe

We examined the numbers of women booking from both European Union (EU) and non-EU European countries. An overall increase in women booking from EU European countries was observed, increasing from 454 women in 2001 to 1873 women in 2012. In particular, a significant increase in women booking from Poland, Latvia and Lithuania was seen (p values all < 0.05). (Figure 3)

The number of women booking from non-EU European countries did not vary significantly over the study period ($p=0.11$)

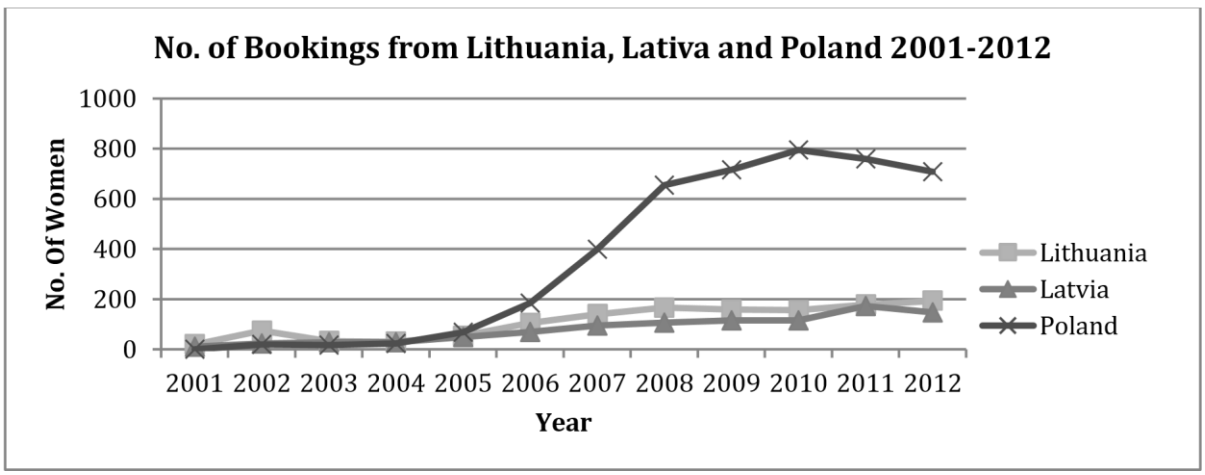

***Figure 3*:** Graph showing the increase in the numbers of women booking from Lithuania, Latvia and Poland from 2001- 2012.

North and South America

A modest increase in bookings of women from North America was observed over the study period, rising from 16 women to 36 women in 2012. Although overall numbers remain small, this increase was found to be statistically significant (p=0.001). An increase in the number of women booking from Brazil mainly accounts for the increase in bookings seen from South American women, which rose from one woman in 2001, up to 36 women in 2012 (p<0.0001).

Africa

The numbers of women booking from the African continent varied greatly over the study period, with booking numbers peaking in 2003 at 931 women, before steadily and significantly falling again in the following years, down to 400 women in 2012. Overall, this increase was found to be statistically significant (p=0.009)

Middle East and Central Asia

Overall, the numbers of women booking from these regions were small. The number of women booking from central Asia did not vary greatly over the 12 years (p=0.19). The numbers of women booking from the Middle East increased from 18 to 58 over the study period, and this increase was statistically significant (p=0.0001)

Discussion

In the Rotunda hospital, one of the largest tertiary referral centres in the world, we witnessed significant changes in the number of women attending for prenatal care who represent non-Irish ethnicities over the past decade. We observed an increase in numbers of women from Asia, Eastern Europe, in particular Poland, Lithuania and Latvia, the Middle East and South America, particularly Brazil.

Studies have identified immigrant mothers are at increased obstetric risk. In a systematic review by the International Reproductive Outcomes and Migration collaboration, Asian and African women had greater perinatal health risks than women from the receiving country [6]. A study conducted in Norway identified that, compared with Norwegians, women from East, Southeast, and Central Asia had increased risk for operative vaginal delivery, postpartum bleeding, and low Apgar score. Women from South and Western Asia were also show to have an increased risk for low birth weight[2, 7]. A study from the UK indicated 74% of Chinese immigrants had little or no English. For this study, compared with their British counterparts, Chinese women's pre-defined risk, gestation at delivery, birth weight, duration of labour, estimated blood loss and mean 5-min Apgar scores were comparable, however Chinese mothers were more likely to have a perineal tear (p<0.005) [8]. Furthermore, research into the mental health of Chinese immigrants in the UK indicates a higher risk of poor mental health [3]. Higher rates of gestational diabetes are also seen in women of Asian and middle-eastern descent, and consequently increased rates of the associated adverse maternal and fetal outcomes [4]. Another study,

carried out in Australia, showed a difference in rates of stillbirth according to nationality. Women of Asian descent, specifically south Asian, were found to have significantly higher rates of late pregnancy (after 37 weeks) stillbirths [5].
This has implications for the way in which we deliver care to women of Asian descent and calls into question the actions required to address these disparities.

Ethnic diversity is over-represented in maternal mortality. According to the latest MBRRACE-UK report, there remains a five-fold difference in maternal mortality rates amongst women from Black ethnic backgrounds and an almost two-fold difference amongst women from Asian ethnic backgrounds compared to white women. In terms of the proportion of women who died during this triennium, 16% (13/100,000) and 4% (9/100,000) were of Asian and Chinese/other descent respectively [9]. Although we identified a decrease in women delivering in our institution who are of Black ethnic descent, our data regarding increasing numbers of Asian, Chinese and mixed ethnicity mothers requires attention in light of this report. Asian mothers also appear to be at increased risk of obstetric anal sphincter injury [10], suggesting the need for increased vigilance and preventative strategies to be implemented during all vaginal deliveries.

The increase in numbers of women from non-Irish backgrounds being cared for at our institution will highlight the increasing need for efficient interpreting services. Language barriers have been shown to significantly increase the risk of serious adverse events due to inability to adequately communicate [11] and are also associated with less frequent visits, less follow-up and less satisfaction with health services [12]. Use of interpreting services improves delivery of health care to patients with limited English[13]. Unfortunately, these services are not always easy to access, particularly afterhours, or in the emergency setting. It is not uncommon for patients with limited English to experience difficulty accessing interpreting services when seeking medical care [14]. A study looking at immigrant women's experience with Maternity services found that women's satisfaction levels and quality of care are affected by communication difficulty, lack of information and lack of understanding of the consent process, as well as perceived discrimination or stereotyping [15]. The Rotunda Hospital in Dublin has been one of the first institutions in the country to successfully implement the electronic health care record (Maternal, Neonatal Clinical Monitoring System, MNCMS). With advances in digital platforms, ease of access to interpreting services by means of hospital electronic devices and smart phone applications is a further step in improving delivery of care.

Given the link between some adverse obstetric outcomes and ethnicity, streamlined obstetric care pathways are required. Attention should also be given to the 'healthy immigration' effect and how this can, unfortunately, be mitigated by length of time since immigration. This may be relevant with respect to breastfeeding rates in Ireland, whereby immigrant rates are reported as high as 84% compared with native Irish of 46%. Studies indicate patterns of breastfeeding in immigrant populations converge to native levels as length of time in host country increases [16]. There may be learning opportunity to understand the breastfeeding successes for immigrant mothers and how these can be relevant to Irish mothers. Furthermore, preventing the loss of the 'healthy immigrant effect' over time, not only in relation to obstetric outcome, but for general health, is an important public health challenge in Ireland.

The inequalities in maternal mortality in relation to ethnic diversity emphasize the need for continued focus on actions to address these disparities.

The first step in addressing this is in understanding the reasons for inequality and identifying actions to reduce the disparity, with the aim of improving maternal and perinatal health. A greater awareness and questioning of the way we deliver care, and whether this involves unconsciously disadvantaging different groups of women based on ethnicity and socio-economic status is called into question. A next-steps approach is determining whether the current methods of identifying higher risk groups of women and current provision of interpreting services at our institution is adequate. Implicit bias amongst healthcare professionals can affect both the patient-doctor interaction, and how we deliver care [17.] Challenging our unconscious bias and drawing attention to our knowledge of how diverse cultural backgrounds may impact on maternal health will identify gaps and areas for individual and institutional improvement. Consideration needs to be given to ways in which we can address these biases going forward. Specific training and workshops for healthcare professionals may go some way to addressing this issue.

We have seen an increase in numbers of non-Irish patients booking at our hospital. This accurately reflects the multicultural nature of our society in Ireland today. We can expect to encounter language and cultural barriers on a more frequent basis. Inequalities in maternal mortality and morbidity are evident in relation to ethnic background. Pathways to aid communication between healthcare staff and patients are needed in order to improve the experience, and obstetric outcomes, of non-Irish mothers and their infants. Establishing streamlined obstetric care pathways is an increasingly important national maternity strategy. One of the first steps in improving outcomes is an awareness of our own unconscious biases.

Declaration of Conflicts of Interest:

The authors declare no conflicts of interest.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P266

Screwing Our Environment: An Analysis of Orthopaedic Implant Related Waste

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Abstract

Introduction

Medical waste contributes a significant burden to our environment and operating theatres have been shown to disproportionately contribute to healthcare associated waste. In orthopaedics and trauma, a portion of this comes from packaging surrounding implants.

Methods

During a standard open reduction internal fixation of a single malleolus ankle fracture all implant related waste was collected. We recorded the amount of implant related waste associated with each case by weight in grams, and also recorded what proportion of the waste was cardboard vs plastic and what proportion was recycled. A retrospective audit of theatre books was carried out to establish to number of ankle open reduction internal fixations in our unit over the course of one year.

Results

209 patients underwent open reduction internal fixation of an ankle fracture in Galway university hospital between July 2018 and July 2019. In the case studied 144 grams (68%) was cardboard, 42 grams (20%) was hard plastic and 25 grams (12%) was soft plastic. 110 (52%), was from screws alone. In one year, this would account for over 44 kilograms of waste from one type of procedure alone. Of this waste only the hard plastic was recyclable. No theatres contained recycling bins.

Conclusion

Orthopaedic implants contribute a significant amount of operative waste, which could be reduced by decreasing the volume and layers of packaging and encouraging recycling.

Keywords environment; waste; trauma; theatre; implant; packaging; recycling

Introduction

According to the Lancet and University College London Institute for Global Health Commission report released in 2009 "Climate change is the biggest global health threat of the 21st century"[1]. Paradoxically, as healthcare remains one of the largest industries globally, it contributes a significant burden to what remains one of the "hottest" topics of the century. Within healthcare, surgical departments in particular have a sizeable impact on the environment[2,3]. While the carbon footprint of our operating theatres is multifactorial, including excess energy usage and greenhouse gas production[4], waste equates to a significant component of this.

Medical waste contributes a significant burden to our environment. In a recent report published by the Environmental Protection Agency in Ireland, our acute hospitals contribute over 10'000 tonnes of waste per annum, much of it high risk medical waste which requires incineration or sterilisation prior to disposal[5]. In this report, 17% of high-risk healthcare waste was attributed to our operating theatres, and operating theatres have been shown to disproportionately contribute to healthcare associated waste[6]. Indeed, studies carried out in other centres worldwide have quoted the burden of operative waste to range from 30%[7] to as high as high as 70%[8]. This waste carries a significant economic and environmental burden, as medical waste costs over 1800 euros to dispose of per tonne, and often requires additional steps in disposal including incineration and chemical sterilisation.

In orthopaedics and trauma, a portion of this waste comes from packaging surrounding implants, including screws and plates, which often consists of non-recyclable cardboard and single use plastics. While some of this packaging is necessary for sterility, this is not always the case, and alternatives to this system are possible. For example, some manufacturers provide implant sets which are not supplied in single use packaging and are re-sterilised following each case in a similar fashion to surgical implement sets. This naturally contributes overall to less waste.

In this study we aim to assess the burden of waste associated with implant packaging in our operating theatres. For this, we decided to focus on ankle open reduction internal fixation (ORIF), due to its requirement for multiple individually packaged screw and plates to be opened. However, many procedures require a similar implant burden.

Methods

We conducted an in-theatre study of a standard open reduction internal fixation of a single malleolus ankle fracture. During the case, all implant related waste including instructional material, was collected. We recorded the amount of implant related waste associated with each case by weight in grams, and also recorded what proportion of the waste was cardboard vs plastic. We then conducted a retrospective audit of theatre books to establish to number of ankle open reduction internal fixations carried out in out unit over the course of one year.

Following this, for comparison, implant related packaging was collected from a range of common trauma procedures including clavicle ORIF, humerus ORIF, hip hemi arthroplasty and kyphoplasty. This was to illustrate the extent of waste produced across a number of procedures.

Results

In total, 209 patients underwent open reduction internal fixation of an ankle fracture in Galway university hospital between July 2018 and July 2019. In the case studied 211 grams of implant related waste was produced. Of this, 144 grams (68%) was cardboard, 42 grams (20%) was hard plastic and 25 grams (12%) was soft plastic. Overall, 110 (52%), was from screws alone.

Over the course of one year, this would account for over 44 kilograms of waste from one type of procedure alone, excluding elective and revision ankle open reduction internal fixations. Of this waste only the hard plastic was recyclable. Soft plastic was not recyclable, and the type of cardboard used, known as "glossy cardboard" is not currently recyclable.

This also does not account for additional waste generated by more complex cases requiring the use of multiple plates and additional screws. Additionally, the amount of packaging produced will vary between different procedures, with some procedures contributing an even higher burden of waste as illustrated in table 1. Of particular note, each kyphoplasty procedure produces over 3kg of waste in packaging alone.

	Cardboard	Plastic	Total
Ankle ORIF	144	67	211
Humerus ORIF	142	52	194
Clavicle ORIF	222	282	504
Hip Hemiarthroplasty	460	322	782
Kyphoplasty	1800	1300	3100

Table 1. Illustrating the weight of packaging per procedure associated with a number of common orthopaedic procedures

Discussion

Overall, implant related packaging contributes a significant amount of waste in our operating theatres, and much of it is non-recyclable. In the case of recyclable materials, whether or not these are is recycled is dependent on the theatre nurse manager on a day to day basis, and how conscious they are in separating waste into recyclable and non-recyclable components. Currently none of our theatres contain recycling bins, and as a result all waste must be sorted through at a later stage to separate recyclable and non-recyclable elements. Based on our study, we would suggest the implementation of a separate recycle bin in theatres to encourage as much recycling as possible.

Another potential solution is the use of ORIF kits which come with a selection of plate sizes and numerous screws etc in sterile sets, which are then re-sterilised between procedures, resulting in minimal physical waste being produced. They also have the added advantage of the operating surgeon being able to see and trial plates while on table, which may contribute to less overall wastage of implants and require less packaging to be opened.

In conclusion, orthopaedic implants contribute a significant amount of operative waste, much of which may be potentially avoidable by reducing volume and layers of packaging. In addition, the use of implant kits which are re-sterilised between procedures is associated with significantly less waste. Given the current appetite for environmentally friendly practices, the onus is now on surgeons to demand more green solutions from implant producing companies, and to encourage increased recycling within our operating theatres.

Declaration of Conflicts of Interest:
The authors have no conflict of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P267

Endoscopic Ear Surgery (EES): A New Vista in Otology

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Abstract

Aim

Endoscopic Ear Surgery (EES) is increasingly being used both as an adjunct to surgery with a microscope and as a standalone procedure. Technological advancements such as high definition cameras and small diameter fibreoptics, allow superior quality images with a wider field of view. As with all new surgical procedures, there are advantages and disadvantages. We aim to share our experience of EES.

Methods

Following institutional ethical approval. We undertook a retrospective review of a consecutive cohort of patients (children and adults) who, between 2008-2019, underwent otologic surgery in our centre. Data was collected using theatre records and clinical notes.

Results

2,062 procedures were included, 1,703 with binocular microscope and 359 EES procedures. The first EES procedures in our centre were carried out in 2013. Numbers and complexity have increased year on year; 2013 (3), 2019 (118). All EES were day case procedures and there were no major complications associated with the introduction of EES. EES procedures ranged from examination under anaesthesia to tympanoplasty, middle ear exploration and ossicular chain reconstruction.

Conclusion

EES uses the ear canal as an access port to the middle ear. With practice, more complex, totally endoscopic otologic surgeries may be carried out, targeting dysventilation, the fundamental cause of chronic ear disease and cholesteatoma. EES has proven to be a safe and valuable otologic procedure, facilitating high definition views of areas otherwise unseen.

Introduction

The middle ear is a complex structure wrapped in dense bone and surrounded by very important structures [1]. The brain, carotid artery, jugular vein and facial nerve are intimately associated and only millimetres away (figure 1). In the pre antibiotic era chronic infective and inflammatory diseases of the middle ear or mastoid frequently spread to the meninges and brain [2]. Otogenic intracranial complications were associated with mortality rates as high as 80% [3]. Acute otitis media and otitis media with effusion continue to be among the most common conditions affecting children worldwide [4].

The advent of antibiotics has significantly reduced the incidence of complications secondary to acute and chronic otologic disease [5]. The introduction of the binocular operating microscope in 1951 and the development of the high-speed drill were landmark events in modern otologic surgery [6]. Better, safer visualisation and more precise removal of chronic disease have resulted in significant improvements in surgical outcomes [7].

Until recently there has been little innovation or change in the surgical approach to chronic ear disease. However, a small but increasing number of otologists have championed the practice and development of minimally invasive ear surgery [8,9]. Using the external auditory canal as the access port and the Hopkins rod endoscope, a new vista has evolved, Endoscopic Ear Surgery (EES). Using the rigid endoscope as a primary tool for ear surgery allows the surgeon to target the birthplace of chronic ear disease and better manage the underlying cause, dysventilation (figure 2). When the complete surgery is performed endoscopically it is called Totally Endoscopic Ear Surgery (TEES).

Recent optical advancements such as small (2-3mm) diameter fibreoptics and HD monitors bring the otologist into a magnified world of superior images. (Figure 3)

Otoendoscopic procedures can range from tympanostomy tube insertion to middle ear exploration. EES is challenging with a steep learning curve, like all new surgical techniques there are advantages and disadvantages. Recently surgeries have been performed using the endoscope in the management of cerebellopontine angle tumours [10]. Literature has shown that endoscopic approaches are comparable to traditional microscopic surgeries [11,12]. The aim of this study is to share our experiences introducing EES into our otology practice.

Methods

Local institutional ethical approval was obtained. We undertook a retrospective review of a consecutive cohort of patients, children and adults, who underwent otologic surgery in our centre. Cases were included from 2009 to 2019 under the care of the senior author (I.K). Data was compiled using theatre records and clinical notes. We examined how EES has changed our practice over the past 10 years. Descriptive data analysis was conducted using Microsoft® Excel (Microsoft® Corp., Redmond, WA).

Results

Two thousand and sixty-two Otologic surgeries were carried out over a 10-year period under the care of a single consultant surgeon. Patients ages ranged from 9 months to 86 years old. Microscope was used for 1703 otologic cases. Three hundred and fifty-nine EES procedures were carried out. Our first EES procedures were carried out in 2013, three cases of otoendoscopy using a 4mm rigid Hopkins rod endoscope and standard middle ear instruments.

All EES were day case procedures and there were no complications associated with the introduction. The number of EES at our centre has risen on an annual basis since its introduction with 95 cases completed using otoendoscopy in 2018 and 118 cases in 2019. There has been an increase in case complexity and variation year on year with no increase in complications or operating times. In 2019 approximately 80% of otologic surgeries were carried out by TEES alone. A significant advantage has been the ability to perform all these surgeries as day cases. Many of these patients would have required overnight admission, particularly if there was a post auricular or endaural approach. Apart from the obvious financial advantages, patients do not require head bandage dressings, wound management, and importantly have no scars. Procedures varied from assessment and photography using the endoscope to endoscopic middle ear exploration and mastoid debridement (Table 1).

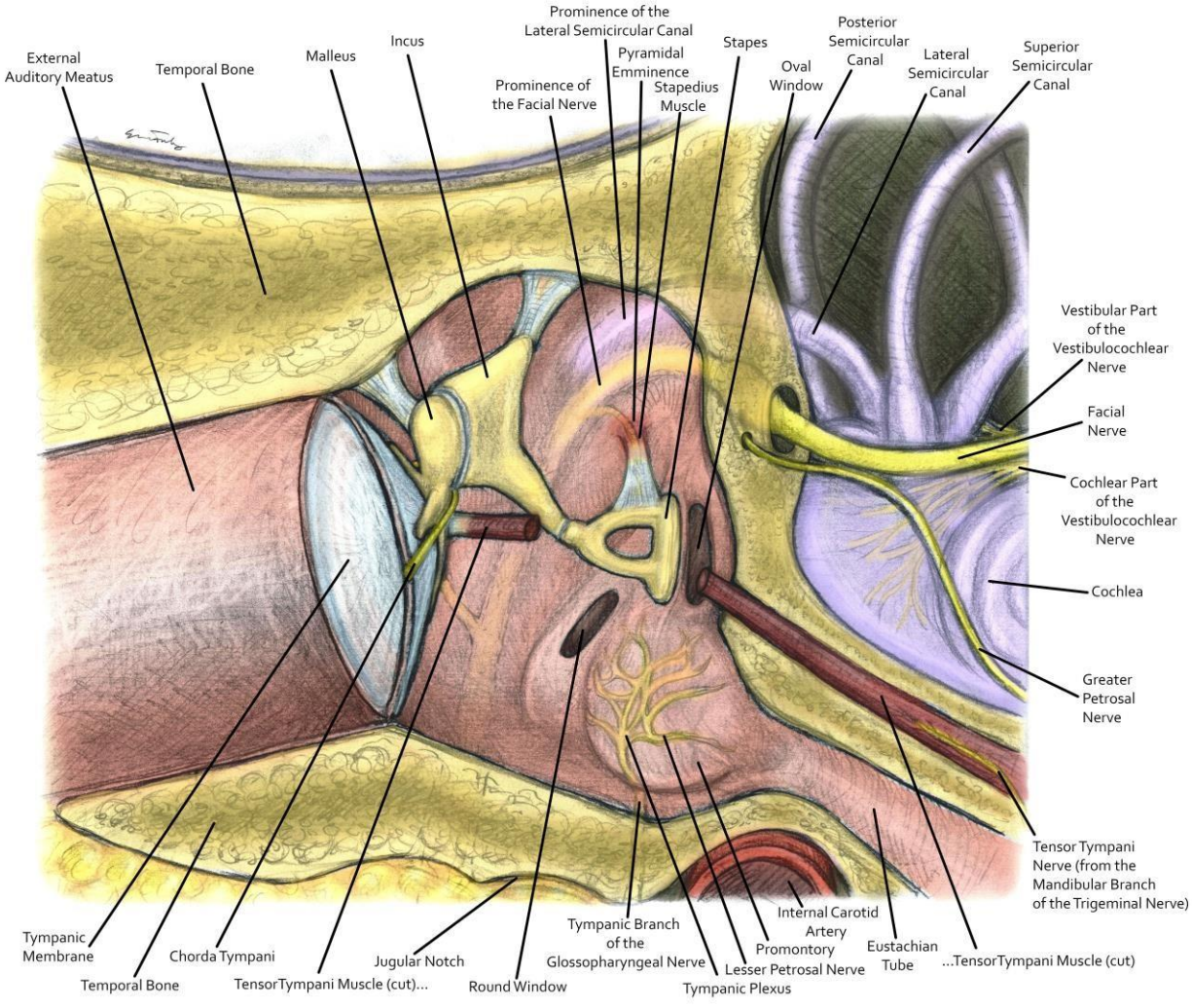

Figure 1: Relations of the middle ear.

Table 1. Endoscopic Ear Surgery by Procedure.

Endoscopic Ear Surgery by Procedure	
Otoendoscopy	135
Ventilation tube insertion	97
Middle ear exploration +/- Ossicular Chain Reconstruction	19
Debulk Attic/cholesteatoma	72
Transcanal tragal cartilage tympanoplasty	28
Mastoid debridement / excision of cholesteatoma	8

Figure 2: Endoscopic Ear Surgery set up.

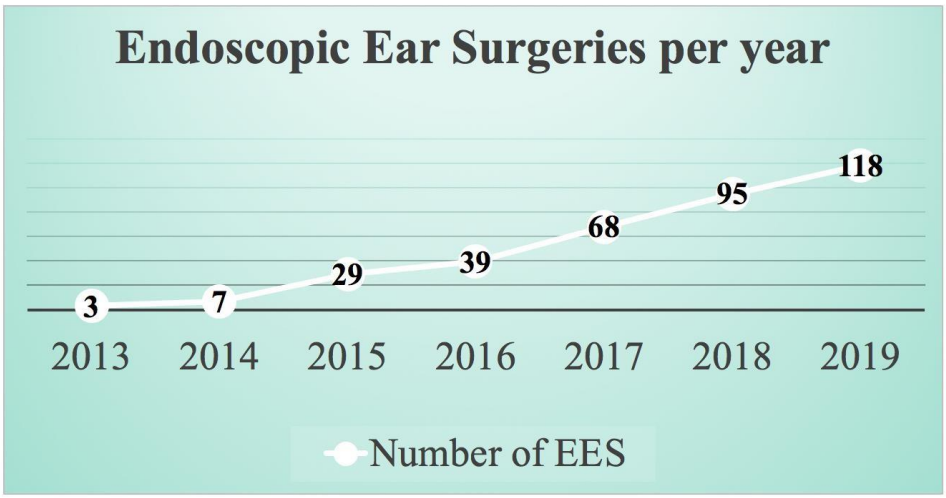

Figure 3: Annual Endoscopic Ear Surgeries.

Discussion

Otoendoscopy is a useful, minimally invasive diagnostic tool. Excellent visualization is afforded of diseased tympanic membranes, mastoid cavities and middle ears. Procedures are less invasive than traditional microscopic surgery. High quality images can be captured, printed and recorded. This gives an objective visual aid to the surgeon for future operative planning. Furthermore, these images can be used for comparative purposes following therapeutic interventions or to monitor disease progression. Images taken at time of surgery can later be shown to the patient to facilitate better patient understanding. Microscopic ear surgery relies very much on the line of sight. The narrowest segment of the ear canal and bony "overhangs" limit visualisation. Traditionally this limitation resulted in the necessity of a parallel port through the mastoid bone and a post auricular approach. This allowed parallel access to the attic and facial recess. Fundamental optical limitations have not improved until recently.

The main advantage of EES over microscopic ear surgery is the image quality produced. Not only is the endoscope capable of getting closer to structures within the ear and providing a higher quality image. The endoscope has a wider angle of view and is able to visualize areas of the middle ear otherwise unseen under a microscope. This allows a greater field of vision and allows the user to 'look around corners' using angled lenses. The detail seen using the endoscope is particularly useful in locating residual cholesteatoma when compared to a microscope [(13)].

EES offers non-invasive methods that reduce the need for a post auricular approach to the middle ear. In the case of choleasteatoma removal a post-auricular mastoidectomy via microscope is often necessary to provide adequate visualization on the middle ear and to evaluate disease. Due to the non-invasive approach afforded by EES patients may have a shorter recovery time and may avoid external scars [(14)].

There is a learning curve associated with EES. Endoscopic dissection requires a single-handed approach as the surgeon is also required to hold the endoscope. Depth perception can be more challenging as microscopic surgery allows binocular vision. Microscopes are more easily available and accessible to trainees so can be easier for practicing and developing skills. Care must be taken when performing EES as imprecise movements can result in trauma to the ossicular chain and external auditory canal or thermal injury from the light source. Overall complication rates are comparable between microscopic and endoscopic surgery [(15,16)]. Once external canal diameter is suitable to admit an endoscope and instrumentation there is no absolute contraindication to EES.

A variety of specialized endoscopic otology instrument sets are now available. Finer instruments with a range of angled "heads" and some with suction ports improve technical challenges. Zero-degree 3mm (11cm) Hopkins rod endoscopes are now standard for EES. Minor ergonomic changes need to be made in theatre, with the huge advantage that EES forces the surgeon into a heads up and straight back position, potentially avoiding the frequent neck and back musculoskeletal issues suffered by many otologists, who are often "bent under" a microscope for hours at a time.

Not only is it useful for the surgeon to have the ability to compare 'before and after' images of the tympanic membrane and other structures, it is also a valuable learning resource for trainee's and medical students alike. With more procedures and an increased endoscopic caseload, trainees can progress with index procedures and can be directed and supervised safely using the monitor. In an outpatient setting, having the opportunity to review images of a previously diseased ear and to then compare it to a current situation is an effective tool both clinically and for teaching purposes. Anecdotally, trainee registrars and more junior staff alike find it to be a useful resource and aid in picking up on subtle findings on ear examination that may otherwise go unnoticed.

The use of EES is increasing. Otoendoscopy provides high quality images with a wide angled view for optimal visualization of anatomy of the ear. Its use exclusively or as an adjunct in procedures reduces the need for invasive techniques and improves patient recovery times. With better understanding of the equipment more extensive surgeries can be performed using a totally endoscopic approach. This minimally invasive technique has the potential to improve patient care and significantly reduce the need for overnight admissions. EES has proven to be a valuable safe, patient focussed tool in an ENT surgeon's arsenal giving an eye to areas otherwise unseen.

Declaration of Conflicts of Interest:
The authors report no conflicts of interest in this work.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P268

Trainees' Perception of Medicolegal Practice in Surgery

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Abstract

Aim

Successful patient outcomes remain at the forefront of surgical practice. A perceived increase in surgical medicolegal cases has heightened awareness of risk management and safety. This study's objective was to assess surgical trainees' perception of medicolegal surgical practice.

Methods

A survey of Irish surgical trainees across all levels and subspecialties evaluating aspects of medicolegal practice was conducted.

Results

Three hundred and eighty-five trainees were invited to participate with a response rate of 35.3% (136). Clinical experience ranged from 3.4 to 11.6 years following qualification. Forty-six (33%) of those surveyed have received medicolegal correspondence, with 90% (123) of trainees maintaining supplementary personal medical indemnity. While only 0.74% (1) of trainees have attended judicial court for medicolegal investigation, 96% (131) of trainees foresee future involvement in a medicolegal case, with 61.8% (84) anticipating this to occur between one and five times. While 70.6% (96) of trainees feel medicolegal concerns have made their practice more risk adverse, only 37.5% (51) reported having received medicolegal training.

Conclusion

Most surgical trainees across all levels and subspecialties anticipate medicolegal involvement during their careers. Enhanced medicolegal understanding through dedicated training may aid in the minimisation of risk, enhancement of patient safety and a positive resolution for all parties.

Introduction

Successful patient outcomes and minimisation of clinical risk remains at the forefront of modern medical practice. While innovations in healthcare safety and open disclosure have improved patients' experiences[1, 2], patient satisfaction remains a complex measure of the healthcare journey[3]. Accordingly, medical litigation remains a reality, with up to 7.4% of physicians subject to a malpractice claim each year[4]. Historically, surgical specialties have tended to attract a higher rate of claims, with up to 98% of surgeons projected to have been subject to a malpractice claim by the age of 65[4]. While the incidence of litigation within surgical subspecialties varies[4, 5], increases of up to 66% have been observed across surgery[5].

Multiple potential sequelae have arisen from increased medicolegal surgical practice. It has been suggested that analysis of claims can help improve clinical care[6], and the widespread adoption of surgical risk management improvements in safe practice[7]. While this aspect of medicolegal practice may confer benefit it has also been suggested that the increasing medicolegal presence can adversely affect care, with up to 75% of healthcare professionals more defensive in their own practice due to medicolegal concerns[8]. Additionally, there is a potential cost associated with recent medicolegal trends, with an 11.5% yearly increased reported in medicolegal claims in the UK causing burden on already finite financial resources[8]. Surgical claims make up a significant proportion of medicolegal payments[5], and this coupled with the potential cost of defensive medicine may impact surgical resources and care[9].

With medicolegal claims becoming an increasing reality in surgery[10], there is now an onus on minimising its potential impact through education and risk management[8]. In modern surgical practice, expectation lies upon surgical trainees to help support and deliver care of the highest standard, both as trainees as well as future consultants[11], with patient satisfaction a vital component[12]. Developing an understanding of medicolegal practice in surgical trainees is thus of particular relevance[13]. To do so, strategies including postgraduate training[14] with regular review[15] is gaining prominence across all medical subspecialties. This could apply seamlessly to the structured surgical training programmes that today's trainees undertake[11]. Establishing the medicolegal baseline of surgical trainees may therefore potentially help guide future development of such strategies.

The objective of this study was therefore to evaluate both current perception and understanding of surgical trainees towards medicolegal issues as well as whether there is a perceived deficit in medicolegal training.

Methods

A national cross-sectional online survey of Irish surgical trainees was undertaken. Doctors registered to National Surgical Training Programme (NSTP) were identified and invited to participate. All invited trainees are undertaking an 8-year training cycle based upon a standardised intercollegiate training pathway between the four Royal Colleges of Surgeons in the UK and Ireland[11].

An online electronic 11-item survey was developed by the authors to ascertain general perception of respondents towards medicolegal aspects of surgical practice. This survey was disseminated using SurveyPlanet™ (www.surveyplanet.com) and SurveyMonkey™ (www.surveymonkey.com), both anonymised, confidential online survey platforms. The survey was circulated on a single occasion with an accompanying email invitation. This email highlighted the survey's purpose as well as its confidential and voluntary nature. No participation honorarium was offered. The survey could only be opened once by a single IP address, allowing for minimisation of repeat participant responses. A follow-up email was circulated and access to the survey was closed at one and four weeks following initial circulation respectively.

Data collection was recorded by a single assimilator. Surgical trainees in the NSTP are subdivided into Core Surgical Training (CST), an exposure to a variety of subspecialties in the first two years of training (ST1-ST2) and Higher Surgical Training (HST) which involves training in a single subspecialty for the remaining six years of training (ST3-ST8). This classification formed a subdivision of the participants, with those undertaking HST further categorised by their chosen subspecialty.

Analysis of the recorded responses included both a descriptive analysis and statistical assessment of difference between training groups. Statistical analysis of the recorded data was undertaken utilising SPSS Version 26 for Windows®, assessing for potentially significant association between training group (CST versus HST) and between subspecialties within the HST group. This was assessed using either a chi-squared test or Fisher's exact test where appropriate, with a p value <0.05 considered statistically significant. Where a statistically significant association was detected, a Cramer's V test was used to demonstrate the strength of association.

Results

A total of 385 surgical trainees were invited to participate. Of those invited, 136 responses were obtained, yielding a 35.3% response rate. Mean time of survey completion was 102.5 seconds.

Forty (29%) of responses were furnished by CST trainees and ninety-six (71%) of responses by HST trainees. Of the HST trainees, the most frequently encountered subspecialties were Trauma & Orthopaedic Surgery (41%) and General Surgery (18%), with responses obtained from trainees in each of the 11 surgical subspecialty HST training programmes. The most frequently encountered training grades were ST3 (19%) and ST1 (18%), with representation from each of the 8 training years (ST1-ST8). The mean number of years that trainees had been practicing medicine at time of survey was 6.5 years, ranging from 3.4 years in ST1 and ST2 to 11.6 years in ST8. Descriptive statistics for the included trainees are further described in Table 1.

One hundred and twenty-three (90%) of all trainees maintained supplementary personal medical indemnity (Table 1). There was no significant difference between training grade (CST vs HST) in the proportion of those who maintained personal medical indemnity ($p=0.329$) nor was there a significant difference between subspecialties within the HST group ($p=0.970$).

Forty-six (33%) of trainees had received medicolegal correspondence, ranging from 8% of ST1 trainees to 73% of ST8 trainees (Table 1). There was a statistically significant moderate association between training group (CST vs HST) and the frequency of those who received correspondence (p=0.003, Cramer's V=0.257), with CST trainees less likely to receive medical indemnity correspondence (OR 0.247, 95% CI 0.95-0.644). There was no significant difference between subspecialties within the HST group (p=0.837). Only 0.74% (1) of trainees attended judicial court in respect of a medicolegal case, with 0.74% (1) declining to comment. There was no statistical difference detected between CST & HST groups in this parameter (p=0.655) (Table 1).

One hundred and thirty-one (96%) of trainees felt that they would likely be sued during their future medical practice (Table 2), with 46.3% of trainees feeling the likelihood of this being 100% (Table 3) and 61.8% of trainees anticipating being sued between one and 5 times during their careers (Table 4). There was no statistically significant difference in perceived likelihood of being sued (p=0.638) between training groups (CST vs HST). Additionally, there was no significant difference in perception between the most highly represented surgical subspecialties when compared to the cumulative HST group, namely Trauma & Orthopaedic Surgery (p=0.615) and General Surgery (p=0.547).

Ninety-six (70.6%) of trainees felt that medicolegal concerns made them more risk-adverse in their daily practice (Table 2), with no statistically significant difference in behaviour found between CST and HST trainees (p=0.107) or between HST subspecialties (p=0.082). Only 37.5% of trainees were certain they had received dedicated medicolegal education during their training (Table 2), with 5.9% unsure as to whether they had received medicolegal education. There was no statistically significant difference in the level of medicolegal education between CST and HST groups (p=0.273) or within HST subspecialties (p=0.549).

Table 1: Included Trainees Medicolegal Experiences to Date.

Group	No. of Participants	Mean No. of Years Practicing Medicine (+/-SD)	% Maintain Personal Medical Indemnity		% Received Medicolegal Correspondence		% Attended Judicial Court for a Medicolegal Case	
			% Yes	%No	% Yes	% No	% Yes	% No
Total	136	6.5 Years (+/- 3.0)	90% (123/136)	10% (13/136)	33% (46/136)	67% (90/136)	0.74% (1/136)	98.5% (134/136)
Core Surgical Training (CST)	40	3.4 Years (+/-1.1)	85% (34/40)	15% (6/40)	15% (6/40)	85% (34/40)	0% (40/40)	100% (40/40)
Higher Surgical Training (HST: All Specialties)	96	7.5 Years (+/-2.8)	93% (89/96)	7% (7/96)	42% (40/96)	58% (56/96)	1.0% (1/96)	97.9% (94/96)

Trauma & Orthopaedic Surgery (HST)	39	7.4 Years (+/-2.2)	92% (36/39)	8% (3/39)	44% (17/39)	56% (22/39)	
Group	**No. of Participants**	**Mean No. of Years Practicing Medicine (+/-SD)**	**% Maintain Personal Medical Indemnity**		**% Received Medicolegal Correspondence**		**% Attended Judicial Court for a Medicolegal Case**
General Surgery (HST)	17	8.6 Years (+/-3.3)	94% (16/17)	6% (1/17)	35% (6/17)	65% (11/17)	
Cardiothoracic Surgery (HST)	3	5 Years (+/-2.9)	100% (3/3)	0% (0/3)	33% (1/3)	67% (2/3)	
Neurosurgery (HST)	1	9 Years	100% (1/1)	0% (0/1)	100% (1/1)	0% (0/1)	
Ophthalmic Surgery (HST)	7	6.5 Years (+/- 2.8)	100% (7/7)	0% (0/7)	57% (4/7)	43% (3/7)	
Oral & Maxillofacial Surgery (HST)	2	7 Years (+/- 5.7)	100% (2/2)	0% (0/2)	0% (0/2)	100% (2/2)	
Otolaryngology, Head & Neck Surgery (HST)	8	5.7 Years (+/- 3.2)	100% (8/8)	0% (0/8)	13% (1/8)	87% (7/8)	
Paediatric Surgery (HST)	3	11 Years (+/- 4.6)	67% (2/3)	33% (1/3)	67% (2/3)	33% (1/3)	
Plastics, Reconstructive & Aesthetic Surgery (HST)	4	6.7 Years (+/- 3.8)	100% (4/4)	0% (0/4)	50% (2/4)	50% (2/4)	
Urology (HST)	6	7.2 Years (+/- 1.9)	83% (5/6)	17% (1/6)	33% (2/6)	67% (4/6)	
Vascular Surgery (HST)	6	9.0 Years (+/- 3.7)	83% (5/6)	17% (1/6)	67% (4/6)	33% (2/6)	
ST1	25	3.4 Years (+/-1.1)	92% (23/25)	8% (2/25)	8% (2/25)	92% (23/25)	
ST2	15	3.4 Years (+/-1.0)	73% (11/15)	27% (4/15)	27% (4/15)	73% (11/15)	
ST3	26	5.0 Years (+/- 1.6)	92% (24/26)	8% (2/26)	15% (4/26)	75% (22/26)	
ST4	14	6.1 Years (+/- 1.6)	93% (13/14)	7% (1/14)	21% (3/14)	79% (11/14)	
ST5	18	7.4 Years (+/-1.9)	100% (18/18)	0% (0/18)	44% (8/18)	56% (10/18)	
ST6	10	9.3 Years (+/-2.1)	100% (10/10)	0% (0/10)	50% (5/10)	50% (5/10)	

ST7	17	9.2 Years (+/- 1.4)	94% (16/17)	6% (1/17)	71% (12/17)	29% (5/17)
ST8	11	11.6 Years (+/-1.5)	73% (8/11)	17% (3/11)	73% (8/11)	17% (3/11)

Table 2: Medicolegal Perception, Behaviour & Training.

Group	**Sued in Future Medical Practice?**		**Medicolegal Concerns Make You More Risk Adverse?**			**Received Medicolegal Education?**		
	% Yes	**% No**	**% Yes**	**% No**	**% Maybe**	**% Yes**	**% No**	**%Not Sure**
Total	96% (131/136)	4% (5/136)	70.6% (96/136)	11.0% (15/136)	18.4% (25/136)	37.5% (51/136)	56.6% (77/136)	5.9% (8/136)
Core Surgical Training (CST)	98% (39/40)	2% (1/40)	80% (32/40)	2.5% (1/40)	17.5% (7/40)	30% (12/40)	60% (24/40)	10% (4/40)
Higher Surgical Training (HST: All Specialties)	96% (92/96)	4% (4/96)	66.6% (64/96)	14.6% (14/96)	18.8% (18/96)	40.6% (39/96)	55.2% (53/96)	4.2% (4/96)
Trauma & Orthopaedic Surgery (HST)	97% (38/39)	3% (1/39)	82.0% (32/39)	7.7% (3/39)	10.3% (4/39)	46.2% (18/39)	51.3% (20/39)	2.7% (1/39)
General Surgery (HST)	100% (17/17)	0% (0/17)	58.8% (10/17)	11.8% (2/17)	29.4% (5/17)	29.4% (5/17)	64.7% (11/17)	5.9% (1/17)
Cardiothoracic Surgery (HST)	100% (3/3)	0% (0/3)	66/7% (2/3)	33.3% (1/3)	0% (0/3)	33.3% (1/3)	33.3% (1/3)	33.3% (1/3)
Neurosurgery (HST)	100% (1/1)	0% (0/1)	0% (0/1)	100% (1/1)	0% (0/1)	100% (1/1)	0% (0/1)	0% (0/1)
Ophthalmic Surgery (HST)	86% (6/7)	14% (1/7)	100% (7/7)	0% (0/7)	0% (0/7)	57% (4/7)	43% (3/7)	0% (0/7)
Oral & Maxillofacial Surgery (HST)	100% (2/2)	0% (0/2)	50% (1/2)	50% (1/2)	0% (0/2)	0% (0/2)	100% (2/2)	0% (0/2)
Otolaryngology, Head & Neck Surgery (HST)	75% (6/8)	25% (2/8)	37.5% (3/8)	12.5% (1/8)	50% (4/8)	25% (2/8)	75% (6/8)	0% (0/8)
Paediatric Surgery (HST)	100% (3/3)	0% (0/3)	33.3% (1/3)	66.7% (2/3)	0% (0/3)	33.3% (1/3)	66.7% (2/3)	0% (0/3)
Plastics, Reconstructive & Aesthetic Surgery (HST)	100% (4/4)	0% (0/4)	50% (2/4)	25% (1/4)	25% (1/4)	50% (2/4)	50% (2/4)	0% (0/4)
Urology (HST)	100% (6/6)	0% (0/6)	50% (3/6)	16.7% (1/6)	33.3% (2/6)	16.7% (1/6)	66.7% (4/6)	16.7% (1/6)
Vascular Surgery (HST)	100% (6/6)	0% (0/6)	50% (3/6)	16.7% (1/6)	33.3% (2/6)	66.7% (4/6)	33.3% (2/6)	0% (0/6)
ST1	96% (24/25)	4% (1/25)	88% (22/25)	4% (1/25)	8% (2/25)	44% (11/25)	44% (11/25)	12% (3/25)
ST2	100% (15/15)	0% (0/15)	66.7% (10/15)	33.3% (5/15)	0% (0/15)	6.7% (1/15)	86.7% (13/15)	6.7% (1/15)

ST3	92% (24/26)	8% (2/26)	65.4% (17/26)	7.7% (2/26)	26.9% (7/26)	19.2% (5/26)	76.9% (20/26)	3.9% (1/26)
ST4	93% (13/14)	7% (1/14)	71.4% (10/14)	14.3% (2/14)	14.3% (2/14)	42.9% (6/14)	35.7% (5/14)	21.4% (3/14)
ST5	100% (18/18)	0% (0/18)	77.8% (14/18)	5.6% (1/18)	16.7% (3/18)	72.2% (13/18)	27.8% (5/18)	0% (0/18)
ST6	90% (9/10)	10% (1/10)	60% (6/10)	20% (2/10)	20% (2/10)	30% (3/10)	70% (7/10)	0% (0/10)
ST7	100% (17/17)	0% (0/17)	64.7% (11/17)	17.7% (3/17)	17.7% (3/17)	35.3% (6/17)	64.7% (11/17)	0% (0/17)
ST8	100% (11/11)	0% (0/11)	54.6% (6/11)	36.4% (4/11)	9.1% (1/11)	54.6% (6/11)	45.5% (5/11)	0% (0/11)

Table 3: Surgical Trainees' Perceived Likelihood of Being Sued During Future Clinical Career.

Group	**0%**	**0-24%**	**25-49%**	**50-74%**	**75-99%**	**100%**
Total	3.7% (5/136)	3.7% (5/136)	6.6% (9/136)	13.2% (18/136)	26.6% (36/136)	46.3% (63/136)
Core Surgical Training	2.5% (1/40)	5% (2/40)	7.5% (3/40)	22.5% (9/40)	20% (8/40)	42.5% (17/40)
Higher Surgical Training (HST: All Specialties)	4.2% (4/96)	3.1% (3/96)	6.3% (6/96)	9.4% (9/96)	29.2% (28/96)	47.9% (46/96)
Trauma & Orthopaedic Surgery (HST)	2.6% (1/39)	2.6% (1/39)	2.6% (1/39)	7.7% (3/39)	25.6% (10/39)	59.0% (23/39)
General Surgery (HST)	0% (0/17)	0% (0/17)	0% (0/17)	5.9% (1/17)	41.2% (7/17)	52.9% (9/17)
Cardiothoracic Surgery (HST)	0% (0/3)	0% (0/3)	0% (0/3)	33% (1/3)	33% (1/3)	33% (1/3)
Neurosurgery (HST)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	0% (0/1)	100% (1/1)
Ophthalmic Surgery (HST)	14.3% (1/7)	28.6% (2/7)	14.3% (1/7)	0% (0/7)	28.6% (2/7)	14.3% (1/7)
Oral & Maxillofacial Surgery (HST)	0% (0/2)	0% (0/2)	50% (1/2)	0% (0/2)	0% (0/2)	50% (1/2)
Otolaryngology, Head & Neck Surgery (HST)	25% (2/8)	0% (0/8)	12.5% (1/8)	0% (0/8)	37.5% (3/8)	25% (2/8)
Paediatric Surgery (HST)	0% (0/3)	0% (0/3)	0% (0/3)	67% (2/3)	0% (0/3)	33% (1/3)
Plastics, Reconstructive & Aesthetic Surgery (HST)	0% (0/4)	0% (0/4)	50% (2/4)	25% (1/4)	0% (0/4)	25% (1/4)
Urology (HST)	0% (0/6)	0% (0/6)	0% (0/6)	16.7% (1/6)	33.3% (2/6)	50% (3/6)
Vascular Surgery (HST)	0% (0/6)	0% (0/6)	0% (0/6)	0% (0/6)	50% (3/6)	50% (3/6)

ST1	4% (1/25)	8% (2/25)	4% (1/25)	20% (5/25)	20% (5/25)	44% (11/25)
ST2	0% (0/15)	0% (0/15)	13.3% (2/15)	26.7% (4/15)	20% (3/15)	40% (6/15)
ST3	7.7% (2/26)	7.7% (2/26)	3.8% (1/26)	15.4% (4/26)	34.6% (9/26)	30.8% (8/26)
ST4	7.1% (1/14)	0% (0/14)	0% (0/14)	14.3% (2/14)	21.4% (3/14)	57.1% (8/14)
ST5	0% (0/18)	5,6% (1/18)	11.1% (2/18)	0% (0/18)	50% (9/18)	33.3% (6/18)
ST6	10% (1/10)	0% (0/10)	10% (1/10)	0% (0/10)	10% (1/10)	70% (7/10)
ST7	0% (0/17)	0% (0/17)	11.8% (2/17)	11.8% (2/17)	17.6% (3/17)	58.8% (10/17)
ST8	0% (0/11)	0% (0/11)	0% (0/11)	9.1% (1/11)	27.3% (3/11)	63.6% (7/11)

Table 4: Surgical Trainees' Perceived Frequency of Being Sued During Future Clinical Career.

Group	**0**	**1**	**1-5**	**5-10**	**>10**
Total	3.7% (5/136)	8.1% (11/136)	61.8% (84/136)	19.1% (26/136)	7.4% (10/136)
Core Surgical Training	2.5% (1/40)	7.5% (3/40)	70% (28/40)	17.5% (7/40)	2.5% (1/40)
Higher Surgical Training (HST: All Specialties)	4.2% (4/96)	8.3% (8/96)	58.3% (56/96)	19.8% (19/96)	9.4% (9/96)
Trauma & Orthopaedic Surgery (HST)	0% (0/39)	7.7% (3/39)	56.4% (22/39)	23.0% (9/39)	12.8% (5/39)
General Surgery (HST)	5.88% (1/17)	5.88% (1/17)	70.6% (12/17)	17.6% (3/17)	0% (0/17)
Cardiothoracic Surgery (HST)	0% (0/3)	33.3% (1/3)	33.3% (1/3)	33.3% (1/3)	0% (0/3)
Neurosurgery (HST)	0% (0/1)	0% (0/1)	0% (0/1)	100% (1/1)	0% (0/1)
Ophthalmic Surgery (HST)	14.3% (1/7)	28.6% (2/7)	57.1% (4/7)	14.3% (0/7)	14.3% (0/7)
Oral & Maxillofacial Surgery (HST)	0% (0/2)	0% (0/2)	50% (1/2)	50% (1/2)	0% (0/2)
Otolaryngology, Head & Neck Surgery (HST)	12.5% (1/8)	25% (2/8)	37.5% (3/8)	12.5% (1/8)	12.5% (1/8)
Paediatric Surgery (HST)	0% (0/3)	0% (0/3)	66.7% (2/3)	33.3% (1/3)	0% (0/3)
Plastics, Reconstructive & Aesthetic Surgery (HST)	0 (0/4)	0% (0/4)	50% (2/4)	50% (2/4)	0% (0/4)
Urology (HST)	0% (0/6)	0% (0/6)	0% (0/6)	100% (6/6)	0% (0/6)

Vascular Surgery (HST)	0% (0/6)	0% (0/6)	50% (3/6)	0% (0/6)	50% (3/6)
ST1	4% (1/25)	8% (2/25)	64% (16/25)	20% (5/25)	4% (1/25)
ST2	0% (0/15)	0% (0/15)	80% (12/15)	25.4% (2/15)	6.6% (1/15)
ST3	3.8% (1/26)	7.7% (2/26)	53.8% (14/26)	30.8% (8/26)	2.85% (1/26)
ST4	7.1% (1/14)	7.1% (1/14)	64.3% (9/14)	14.3% (2/14)	21.4% (3/14)
ST5	5.6% (1/18)	16.7% (3/18)	61.1% (11/18)	5.6% (1/18)	11.1% (2/18)
ST6	10 (1/10)	10% (1/10)	60% (6/10)	20 (2/10)	0% (0/10)
ST7	0% (0/17)	5.9% (1/17)	58.8% (10/17)	17.7% (3/17)	17.7% (3/17)
ST8	0% (0/11)	0% (0/11)	54.6% (6/11)	27.7% (3/11)	18.2% (2/11)

Discussion

The frequency of medicolegal litigation is growing[4, 5]. A corresponding rise in medicolegal complaints involving trainee doctors of up to 94% per annum has been witnessed, most frequently observed in surgical trainees[16]. These increases precipitate the need for understanding surgical trainees' perceptions and background in medicolegal practice[13, 16].

The trainees surveyed in this study broadly represented all grades and subspecialties. Awareness of medicolegal practice within the broader surgical trainee group appeared to be high, with the vast majority across all subgroups maintaining their own personal medical indemnity, which allows for increased safeguarding of the trainee when involved with specific claims and costs incurred by medicolegal matters[17]. This demonstrates an appreciation amongst trainees of the need to prepare for potential medicolegal involvement.

Surgical trainees' perception is further indicated in their anticipation of medicolegal involvement. A vast majority felt their chances of being sued during their careers is high, with most feeling this would happen more than once. This belief appeared consistent across all training grades and subspecialties. A number of factors may potentially contribute to this. Current healthcare constraints can create challenges with regards to optimisation of the patient-physician relationship, particularly in terms of the time available for direct contact[18]. While patient satisfaction is multifactorial[3], the physicianpatient interaction has been shown to be of particular importance[19], and allowing for conditions to optimise this within surgical practice may ameliorate trainees' perceived risk of medicolegal involvement.

Surgical trainees' concerns of medicolegal involvement appear to have translated into their clinical practice, with a majority of trainees feeling they have become more risk adverse as a result. This trend appears consistent across training grades and subspecialties, indicating that this is due to perception rather than accumulated through experience. While surgeons adopting a strategy of risk reduction is

vital in establishing patient safety[20], the practice of "defensive" medicine in an attempt to minimise potential medicolegal risk can also cause negative associations such as surplus investigations, prolonged hospitalisations, higher costs and delayed healthcare access[18, 21]. Establishing an appreciation of these negative sequelae in trainees is hence of paramount importance in reducing its potential occurrence.

While trainees' perceived risk of medicolegal involvement appears high, the reality to date appeared to be less severe, with only a small percentage of trainees involved in formal legal proceedings to date. While an argument that the risk of medicolegal involvement increases with growing clinical responsibilities exists, as evidenced in the proportionally higher rate of medicolegal correspondence in HST trainees when compared to CST trainees, the disparity between perceived and experienced medicolegal exposure emphasises the negative connotations of medicolegal proceedings in practice. Doctors who have been subject to medicolegal claims have been shown to be more likely to have negative attitudes to work, feel more distant from patients and consider either reducing or giving up their medical careers [22], and these fears may result in increased concerns within surgical trainees.

Strategies to improve surgical trainees' medicolegal understanding and perception would likely confer benefit to patients, trainees and healthcare systems alike. Education of healthcare practitioners in medicolegal practice has been suggested to help achieve this[8]. The majority of trainees in this study felt they had not received medicolegal training. Furthermore, a small proportion of trainees were unsure as to whether they had undertaken medicolegal training, further indicating uncertainty as to what this training involves.
Dedicated medicolegal physician training has been shown to be effective in improving knowledge in both prevention and management of claims[14], and adopting uniform medicolegal training across all surgical trainees may confer similar benefits.

Limitations to this study exist in regards the overall sample size of those surveyed, particularly in surgical subspecialties with fewer trainees, limiting the ability to compare subspecialties. The overall response rate of 35.3%, while relatively favourable when compared to other surveys of medical practicioners[22, 23], further contributed to this potential limitation. Nevertheless, the authors believe this study to be of importance as it offers insight into trainees' understanding of an increasingly prominent aspect of surgical practice. It also allows for a broad representation of the medicolegal perception of surgical trainees across all levels and subspecialties within a national system, which to the authors' knowledge has not been reported to date.

To conclude, a significant proportion of surgical trainees across all grades and subspecialties anticipate involvement in medicolegal claims during their careers. While a majority of trainees have yet to be involved in claims, a high percentage of trainees both maintain personal medical indemnity and feel medicolegal concerns have made them more risk adverse in their practice. Most trainees have yet to receive dedicated medicolegal training during their training, and strategies to address this within the context of surgical training programmes should be considered.

Declaration of Conflicts of Interest:

The authors have no conflicts of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P269

The Impact of the COVID-19 Pandemic on the Uptake of the Seasonal Influenza Vaccine

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Abstract

Aims

We sought to determine whether the COVID-19 pandemic has impacted the uptake of, and changed attitudes towards, the seasonal influenza vaccine.

Methods

A 12 item cross sectional survey was designed and distributed to 465 patients in an urban GP practice over a two-week period in October 2020.

Results

There was a 27.4% increase in uptake of the seasonal influenza vaccine in 2020 relative to 2019. Two hundred and thirty-three patients (76%) were more likely to take the vaccine this year due to the COVID-19 pandemic. This was dependant on age (p=0.001). The 13-30yrs group were 3.2 times less inclined to take the vaccine due to COVID-19 (95%CI: 1.71-6.01) than the other age groups. One hundred and forty-nine patients (48.9%) felt the vaccine is more important than they previously appreciated. One hundred and thirty-six (58.4%) of patients who were more inclined to receive the vaccine cited wanting to 'avoid seeing a doctor/needing to go to hospital this year in particular'). Fifty-two patients (22.3%) took the seasonal influenza vaccine in the belief it would 'offer some protection against COVID-19'.

Discussion

The COVID-19 pandemic has contributed to an increased uptake and increased appreciation of the importance of the seasonal influenza vaccine. Further research will be required to determine whether this will be sustained in the years to come.

Introduction

Influenza (flu) is a contagious viral disease that results in up to five million cases of severe illness and 650,000 deaths worldwide each year.[1] Influenza season in the Northern Hemisphere lasts from October until May. Influenza outbreaks usually last from 6 to 8 weeks and can impact people of all ages, especially the very young and the very elderly.[2] In Ireland the 2018/19 flu season resulted in high levels of hospitalisations for confirmed influenza cases resulting in a significant impact on the health system with sentinel GP consultation rates for influenza like illness of 53/100,000 at peak, 7,943 influenza cases notified to the Health Protection Surveillance Centre, 3,244 confirmed influenza cases hospitalised, 159 confirmed influenza cases admitted to ICU, and 97 deaths in notified influenza cases.[3]

The seasonal influenza vaccine (SIV) remains the best tool available to reduce influenza-associated morbidity and mortality.[4] In Ireland, the SIV is made available free of charge to all adults aged 65 and over, pregnant women, children and adults over 6 months of age with certain chronic medical conditions, those with Downs Syndrome, those living in a nursing home or long-term care facility, carers, healthcare workers, those who work with pigs, poultry or waterfowl.[5]

There are many factors which impact vaccine acceptance. The World Health Organisation published a document in 2013 which highlighted the broad spectrum of factors which may impact vaccine uptake. They grouped these factors into contextual, individual and group influences. Examples include economic and political factors, the pharmaceutical industry, anti- or pro-vaccination lobbies, experience with past vaccinations, attitudes towards health and prevention, perceived risk/benefit and vaccination as a social norm.[6]

In 2020 the government of Ireland introduced changes to allow all of those in the HSE-defined at-risk groups, aged from 6 months to 69 years inclusive, to access the vaccine without charge. The quadrivalent live attenuated nasal flu vaccination was also made available to all children in Ireland aged from 2 to 12 years inclusive, free of charge for the first time in 2020.[7] This policy change was introduced as Ireland was facing a major public health challenge in the form of the novel coronavirus – SARS CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), resulting in the clinical condition COVID 19.[8] Having originated in the Wuhan province of China in late 2019,[8] the virus rapidly spread worldwide with 84 532 824 confirmed cases of COVID-19, including 1 845 597 deaths, as of week 53 2020.[9]

The SARS-CoV-2 virus and resultant COVID-19 pandemic has brought the threat posed to society from infectious disease into sharp focus. SARS-CoV-2 and seasonal influenza are completely separate entities. However, the two viruses have regularly been referenced together during the COVID-19 pandemic with the infectivity, mortality and morbidity of the novel SARS-CoV-2 regularly compared to seasonal influenza.[10,11,12]

While there are similarities in terms of the symptomatology, one major difference between the viruses is that there are established safe and effective vaccines for seasonal influenza,[1] while up until late December 2020 there was no licenced COVID 19 vaccine available in Ireland.[13]

It is as of yet unclear whether this increased attention on infectious respiratory disease, and on vaccination as a public health measure, will have an impact on SIV uptake this year and in years to come.

Early evidence in the UK suggests the COVID-19 pandemic has positively influenced SIV uptake.[14] However, our literature review did not find any published studies on this issue in an Irish population to date.

The aim of this study was to determine whether the COVID-19 pandemic has impacted the uptake of, and attitudes towards, the seasonal influenza vaccine.

Methods

This was a qualitative original questionnaire-based study conducted in a four doctor, urban, GP practice in the south of Ireland during the 2020 'flu season'. The questionnaire was distributed to 465 patients who attended during a two-week period in October 2020, after the SIV had been made available. Patients were invited to partake in the study by completing an anonymised questionnaire. Three hundred and seven patients completed the questionnaire. A parent or guardian was asked to complete the questionnaire for children or for adults with cognitive impairment.

The questionnaire contained questions on demographics in addition to factors influencing previous and current uptake of the SIV. Exclusion criteria included age under two years, lack of fluency in English (and no translator present), and patients requiring emergency treatment. Initial analysis of anonymised data was performed in Microsoft Excel.

Exploring associations of interest between predictor variables and dependent ones was carried out using SPSSv26. Chi-square statistics were calculated as is appropriate for comparison of categorical variables. Odds ratios were computed for statistically significant associations. The significance level chosen below which p-values would be considered statistically significant was $p < 0.05$.

Ethical approval was received from the Irish College of General Practitioners Research and Ethics Committee.

Results

Table 1. Characteristics and opinions of the study population.

		Number	Percentage
Age	2-12 years	40	13.0
	13-18 years	12	3.9
	19-30 years	40	13.0
	31-50 years	93	30.3
	51-70 years	90	29.3
	>70 years	30	9.8
	Missing	2	
Gender	Male	130	42.3
	Female	177	57.7
'At risk' group	Yes	122	39.7

	No	184	59.9
	Missing	1	
Previous COVID-19 test	Yes	64	20.9
	No	243	79.1
Consider the flu a threat	Yes	115	37.5
	No	191	62.2
	Missing	1	
Perception of flu vaccine safety	Very safe	143	46.6
	Safe	102	33.2
	Unsafe	8	2.6
	Very unsafe	3	1.0
	Don't know	48	15.6
	Missing	3	
Have gotten/will get flu vaccine this year	Yes	223	73.0
	No	83	27.0
	Missing	1	
Got the flu vaccine last year	Yes	140	45.6
	No	166	54.0
	Missing	1	
If no, what was the reason? (participants had the option of choosing more than one option)	Not advised	79	47.6
	Too expensive	1	0.6
	Not enough time	9	5.4
	Worried they would get flu	19	11
	Worried about side effects	27	16.3
	Didn't believe at risk of contracting flu	49	30
Has COVID-19 made you more inclined to take the flu vaccine?	Yes	233	76
	No	73	24
	Missing	1	
If yes, which is applicable to you? (participants had the option of choosing more than one option)	Reduce the risk of needing to see a doctor/go to hospital	136	58.4
	I feel the flu vaccine will give me some protection against COVID-19	52	22.3
	Reduce the chances to undergo COVID-19 testing and isolation	60	25.9
	Protect family/friends	104	44.6
	Advised to get the flu vaccine this year for the first time	24	10.3

	Available to me free of charge this year for the first time	23	9.9
Has your perception of the flu vaccine changed following the outbreak of COVID-19?	No	142	46.6
	Yes – flu vaccine is more important	149	48.9
	Yes – flu vaccine is less important	0	0%
	Don't know	14	4.6
	Missing	2	0.6%

Population characteristics

Three hundred and seven patients completed the questionnaire during the two-week study period. This represented 66% of all patients who attended the surgery in this period.

The 31-50-year-old age category was the largest group in the study 30.3% (n=93), see Table 1. Children under 12 and the over 70s accounted for 13% (n=40) and 9.8% (n=30) respectively. Males represented 42.3% (n=130) of the study participants.

One hundred and twenty-two patients (39.7%) self-identified as being in the 'at risk' group for influenza (i.e. pregnancy, co-morbidities). Sixty-four patients (20.9%) had been tested for COVID-19.

Attitudes towards flu virus and flu vaccine

One hundred and fifteen patients (37.5%) in the study considered the influenza virus a threat to their health. Two hundred and forty-five patients (79.8%) felt that the influenza vaccine was safe or very safe. Forty-eight patients (15.6%) answered "don't know" regarding safety.

Two hundred and thirty-three patients (73.0%) had already received or were planning to get the SIV for the 2020/2021 influenza season. In comparison, approximately 45.6% (n=140) of the study participants had gotten the SIV in the 2019/2020 influenza season.

Impact of COVID-19

Two hundred and thirty-three patients (76.0%) felt that the COVID-19 pandemic had made them more likely to take the SIV this year. This result was dependent on age (p-value=0.001). When the 13-18yrs and 19-30yrs groups were combined, the 13-30yrs group were 3.2 times less inclined to take the SIV due to COVID-19 (95%CI: 1.71-6.01) than the other age groups.

Being more inclined to get SIV this year due to COVID-19 was associated with whether they intended to get/or got the SIV this year ($p < 0.05$, OR= 8.55 (4.74-15.43)), but not associated with whether they received their 2019 SIV ($p = 0.116$).

The inclination to take the SIV this year due to COVID-19 was not associated with gender (pvalue=0.091), underlying medical conditions (p-value=0.174), and of having had a COVID-19 test (pvalue=0.454).

The reasons listed by those more inclined to take the flu vaccine due to the COVID-19 pandemic crosstabulated with age is displayed below in Table 2 (note patients had the option of choosing more than one option).

One hundred and forty-nine patients (48.9%) stated they now felt the flu vaccine was more important than they had thought prior to the outbreak of COVID-19. This was independent of age group when all groups were considered (p=0.889).

Table 2. Factors associated with increased tendency to take the SIV in the wake of the COVID-19 pandemic>

Age	**Don't want to see a doctor/go to hospital this year**	**Want to protect friends and family from illness**	**Want to avoid COVID-19 test/selfisolating**	**Feel the SIV will protect against COVID - 19**	**Advised to get the SIV for the first time this year**	**SIV free of charge for the first time this year**
2-12yrs (n=35)	20 (57.1%)	21 (60.0%)	7 (20.5%)	10 (28.6%)	7 (20.0%)	5 (14.3%)
13-18yrs (n=7)	4 (57.1%)	2 (28.6%)	2 (33.3%)	1 (14.3%)	2 (28.6%)	1 (14.3%)
19-30yrs (n=2)	10 (45.5%)	9 (40.9%)	3 (13.6%)	5 (22.7%)	1 (4.5%)	2 (9.1%)
31-50yrs (n=67)	43 (64.2%)	25 (37.3%)	24 (35.8%)	15 (22.4%)	5 (7.5%)	4 (6.0%)
51-70yrs (n=90)	40 (53.3%)	32 (42.7%)	15 (20.0%)	16 (21.3%)	7 (9.3%)	7 (9.3%)
71yrs & older (n=75)	17 (68.0%)	13 (52.0%)	9 (36.0%)	5 (20.0%)	2(8.0%)	4 (16.0%)
Total ticked YES	134 (58.0%)	102 (44.2%)	60 (26.1%)	52 (22.5%)	24 (10.4%)	23 (10.0%)
Chi-square statistic	4.181*	6.310*	8.612*	1.160*	7.624*	3.135*
p-value	0.524	0.277	0.126	0.949	0.178	0.679

*tabs with less than five answers – interpret with caution

Discussion

This study demonstrated increased uptake in the SIV in the study population in 2020. Two hundred and thirty-three patients (73.0%) had already received (or planned to get) the SIV in 2020, which was an increase from 2019 (45.6%). This increase was shown to be influenced by the COVID-19 pandemic with 76% of patients stating they were more inclined to accept the flu vaccine in 2020 due to the COVID-19 pandemic.

Considering the poorer clinical outcomes in elderly COVID-19 patients, compared to younger patients;[15] it is unsurprising that age had a strong influence on whether the COVID-19 pandemic had made patients more inclined to take the SIV. With regards SIV uptake, the 13-30 year-old age group was 3.2 times less likely than the other age groupings to have been positively influenced by the COVID19 pandemic. This suggests that those who deemed themselves to be less at risk from COVID-19 were less likely to be influenced by the COVID-19 pandemic with regards to SIV uptake, notwithstanding the fact that the SIV is not routinely recommended in this age group.[5]

Offering the SIV free of charge had only a modest impact on SIV vaccine uptake. Only 14% of those more inclined to take the SIV in 2020 due to COVID-19 listed the SIV being available to them free of charge for the first time as a reason for this. Furthermore, only 0.6% of participants refused the SIV in 2019 due to cost.
Not being advised by their doctor to get the SIV was a much more important factor for not taking the SIV in 2019 (47.6%). Of those who felt the flu vaccine was unsafe, only 18% were more inclined to get the SIV due to the COVID-19 pandemic and only 9% now felt the SIV was more important than they had previously believed. This suggests that those who had safety concerns had a more fixed mindset in relation to the SIV.

A desire to 'protect friends and family from illness' was listed by 44.6% of patients more inclined to take the SIV this year (and 60% of the 2-12 year-old age group in this category), which is largely consistent with previous studies in the area.[16,17] However, nearly half of the patients now felt the SIV is more important than they had previously thought. This indicates that the COVID-19 pandemic has highlighted the importance of SIV but has not caused a paradigm shift in the factors influencing vaccine acceptance or refusal.

Wanting to avoid engaging with the acute services this year in particular, (58.4%), and a belief that the SIV would offer protection against COVID-19 (22.4%) were two common reasons participants were more inclined to take the SIV this year. It remains to be seen whether these factors will positively influence SIV uptake in the post-pandemic era.

The limitations of this study include being a single site study. It is possible local factors such as the incidence of COVID-19 in the locality, local economic factors and the degree in which SIV was encouraged within the practice, could have influenced the findings making them less generalisable to the population as a whole. As we used an original questionnaire, our study tool was not validated. There is a potential selection bias related to the timing of the study. As the two-week period in which the questionnaires were distributed coincided with the first two weeks in which the SIV was available, it is possible that there was an over-representation of patients who were positively disposed towards getting the SIV as they would have attended during this period with the express purpose of getting the SIV. As the survey was anonymous, we do not have data on non-responders. As such, we cannot rule out demographic differences between responders and non-responders which could equate to a selection bias.

The authors are unaware at this time of any other studies which investigate the impact of COVID-19 on the uptake of, and attitudes towards the SIV in Ireland. In the respondents of our survey, 76% of patients had become more inclined to take the SIV due to the COVID-19 pandemic. This pattern was also seen globally following the 2009 H1N1 pandemic but increases in SIV uptake were not maintained

in the years following.[17] While general public health concerns were a factor in the increased uptake (44.2% wanted to protect friends and family from illness), it cannot be assumed that the increased uptake of SIV this year will be sustained in the years coming. 22.4% received the SIV this year in the belief that it would offer some protection against COVID-19. With a COVID-19 vaccine now available[13] we cannot say this factor will be relevant in years to come. Further research is required to determine whether the increased uptake of SIV is sustained in future years.

Declaration of Conflicts of Interest:
No author has any conflict of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P270

Evaluation of a Polysaccharide Haemostatic System in Obstetrics and Gynaecology

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Abstract

Introduction

Adjuvant haemostatic agents are useful in surgery over broad areas of diffuse ooze, or where there is a risk of thermal injury from electrocautery. Repetitive strain injuries amongst surgeons are increasing, highlighting the importance of ergonomics. This study evaluated the ease of use and efficacy of an absorbable polysaccharide haemostat powder in obstetric and gynaecological surgery.

Methods

Prospective cohort study of 50 surgeries where HaemoCer Plus was used. The surgeon recorded their ease of use of the product and its efficacy.

Results

Caesarean section represented 84% of the procedures performed (42/50). The haemostatic powder was reported as 'easy' or 'very easy' to use by 98% of participants (49/50). It was reported as 'effective' by 82% (41/50), and 'very effective' by a further 16% (8/50).

Conclusions

HaemoCer Plus was easy to use and was considered an effective haemostatic agent by obstetricians and gynaecologists. This was consistent across both obstetric and gynaecological procedures.

Keywords

Topical haemostatic agents, obstetrics, gynaecology, surgery, ergonomics

Introduction

Intraoperative bleeding is associated with prolonged operative times, blood transfusion, and protracted hospital admission. Topical haemostatic agents are used in over 30% of surgeries[1] as an

adjunct to promote clotting and stop bleeding. Their use has increased from 10 – 21% in obstetrics and gynaecology[2].

The rate of caesarean section continues to rise[3], causing increased intra-abdominal adhesions. Topical haemostats are useful over broad areas of diffuse ooze where suturing may be impractical, or when there is a risk of thermal injury to adjacent structures from electrocautery[2,4]. Moreover they may have a beneficial effect on wound healing; animal models suggest a reduction in postoperative adhesions[4].

We are increasingly aware of the prevalence of work-related injuries among surgeons with as much as 88% reporting injuries[5-7]. Instruments that are easy and comfortable to use reduce surgeon injury, and hopefully intraoperative complications for women. This study aims to evaluate the operating surgeon's ease of use and perceived effectiveness of an absorbable polysaccharide haemostat powder in obstetric and gynaecological surgeries.

Methods

HaemoCer Plus (BioCer, Germany) is a haemostatic powder made from inert polysaccharide material. It accelerates the formation of a haemostatic plug by rapidly dehydrating blood to increase the concentration of platelets, red blood cells and coagulation proteins. Additionally, it forms a gelled matrix that acts as a tamponade and as a barrier to postoperative adhesions. The powder is deployed using one hand to operate a squeeze-and-release chamber, dispelling the product through a nozzle. No adverse reactions have been reported and the product is licensed for use within the European Union.

This prospective cohort study examined 50 consecutive obstetric and gynaecological procedures where HaemoCer Plus was used. There were no exclusion criteria. The primary operating surgeon completed a questionnaire detailing the ease of use and perceived efficacy of the product. Data on the number of units used, whether additional haemostatic measures were required, type of surgery, grade of the operating surgeon, and patient age were recorded. The study was undertaken in a public university-affiliated regional hospital that delivers approximately 3,500 women per year.

Results

Between July 2017 – April 2018 there were fifty consecutive obstetrics and gynaecology cases where HaemoCer Plus was used. 84% (42/50) were lower segment caesarean sections, see Table 1. Nonconsultant hospital doctors were the primary operator in 70% (35/50) of cases, while the remaining 30% (15/50) were performed by consultants. The median age of women undergoing surgery was 33 (range 19 – 48 years).

Table 1. Procedures where *HaemoCer Plus* was used.

Procedure	**No**	**(%)**

Lower Segment Caesarean Section	42	84%
Laparoscopic Ovarian Cystectomy	3	6%
Total Abdominal Hysterectomy	2	4%
Laparoscopic Bilateral Salpingo-oophorectomy	1	2%
Myomectomy	1	2%
Laparoscopically assisted vaginal hysterectomy	1	2%

The haemostatic powder was reported as 'easy to use' by 76% (38/50) and 'very easy' by 22% (11/50) of participants. One participant did not report ease of use. Efficacy was reported as 'effective' by 82% (41/50), 16% (8/50) reported it as 'very effective', and one case did not document effectiveness.

A single unit of HaemoCer Plus was used in 94% cases (47/50), while two units were used in the remainder. Additional modes of haemostasis were recorded in 72% (36/50) of cases. Electrocautery was used in 67% (24/36) of cases where additional haemostatic support was required. No adverse reactions were recorded.

Discussion

This study found that HaemoCer Plus is easy to use and is considered an effective haemostatic agent by the operating surgeon. While most data regarding topical haemostatic agents is derived from other specialties, the findings support its use in obstetrics and gynaecology.

Caesarean Section made up 84% of the operations, while the remainder were gynaecological procedures. This case-mix is representative of the workload of general obstetrics and gynaecology practitioners[8].

Additional haemostatic manoeuvres were required in 72% cases, the most common being electrocautery (67%) and sutures (24%). Electrocautery is used in almost all modern operative procedures, so this result is not surprising. The use of sutures may reflect different sources of bleeding; sutures being effective for significant bleeds from an identifiable vessel, while haemostatic powder is useful across broader areas of ooze.

Between 44 – 88% of laparoscopic gynaecological surgeons experience physical discomfort, especially neck, shoulder, and back pain[6,7]. This emphasizes the importance of ergonomics and a need to identify solutions to minimize work-related injuries. Cumbersome instruments are linked to repetitive strain injury[9], so identifying techniques and products that are comfortable for its operators is important.
Topical haemostatic agents are an effective adjunct in surgery and their use is increasing across multiple disciplines. This study showed that it was considered effective and easy to use by obstetricians and gynaecologists.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P271

Cohort of Haemodialysis Patients with COVID-19 in an Irish Nephrology Centre

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Abstract

Aims

COVID-19 has a mortality of 29-41% in haemodialysis (HD) patients, compared to 2% in the general population. In our HD centre, the largest nationally, we report a higher mortality rate of 50%, and aimed to determine underlying factors driving this.

Methods

In this retrospective observational study, we collected demographic and clinical data on our HD patients infected with COVID-19.

Results

20/296 HD patients were infected with sudden acute respiratory syndrome coronavirus 2 (SARS-CoV2), 10 of whom died. These cases represent 20/87 (23%) of COVID-19 positive HD patients nationally and 37% of deaths (10/27). Non-survivors were more likely to present with upper respiratory tract symptoms. Underlying frailty was associated with increased mortality (RR=2, CI 0.57,7.03).

Discussion

Dialysis patients remain susceptible to fatal COVID-19 illness, so efforts need to be made to reduce its spread, including isolation measures, and separate COVID-19 teams.

Keywords

COVID-19; SARS-CoV-2; Haemodialysis; End-stage renal disease; Frailty

Introduction

SARS-CoV-2 was first identified in Wuhan, China in January 2020 and has spread globally, with a mortality of 2%[1]. Patients with end stage kidney disease (ESKD) on haemodialysis (HD) are particularly

vulnerable for critical COVID-19 infections due to frequent attendances to medical facilities, dysregulated immune systems[2], and multiple comorbidities[3], in particular vascular risk factors[4].
To limit the spread of COVID-19 in HD patients, the Irish National Renal Office (NRO) published guidelines to control the outbreak on the 16/03/20[5]. As cases continued to rise, the NRO made further recommendations from the 07/04/20, including obtaining surgical masks for all HD patients[6].

Reported mortality rates among outpatient HD units internationally range from 29-41%[7-9]. We report a high mortality rate in our single centre experience, driven by an early nosocomial outbreak prior to implementing guidelines.

Methods

We conducted a retrospective observational study of all HD patients confirmed SARS-CoV-2 positive with a nasopharyngeal swab between the 18/03/20-15/05/20 in our HD centre and 2 satellite HD centres in Dublin, Ireland. Demographic and clinical characteristic data were collected. Descriptive statistics were conducted using Excel.

Patient characteristics were collected from the national renal database, eMed, and additional data was collected by review of the hospital online laboratory and chart system, PIPE.

Results

Between 18/03/20-15/05/20, 20/296 HD patients had symptoms suggestive of COVID-19 and were subsequently proven to be COVID-19 positive, of whom ten (50%) died. These numbers represent 20/87 (23%) of COVID-19 positive HD patients nationally and 37% of the deaths (10/27). Clinical characteristics are summarized in Table 1.

The nephrology ward suffered a COVID-19 outbreak in mid-March, which was responsible for ten of these twenty patients contracting COVID-19. An 11th patient contracted COVID-19 in another hospital. Amongst these eleven hospital-acquired cases, seven died and four recovered. One patient of the six community transmitted cases died. Two patients who contracted COVID-19 in a nursing home died.

Table 1: Clinical characteristics survivors vs. non-survivors of SARS-CoV-2 positive HD patients.

	Non-survivors (10 patients)	**Survivors** (10 patients)
Age (mean) *Standard Deviation (SD)* *Interquartile range (IQR)*	69.3 years [33-89] *16* *11*	68.6 years [42-91] *17.8* *29.5*

Gender		
Male	8 (40%)	9 (45%)
Female	2 (10%)	1 (5%)

Setting		
Inpatient	9 (45%)	5 (25%)
Outpatient	1 (5%)	5 (25%)
Symptoms at presentation		
Shortness of breath	10 (50%)	3 (15%)
Fever	9 (45%)	8 (40%)
Cough	8 (40%) 0	7 (35%)
GI Upset	(0%)	4 (20%) 0
Confusion/Agitation	3 (15%)	(0%)
Headache	0 (0%)	2 (10%)
Malaise/pre-syncope	1 (5%)	1 (5%)
Treatment		
CPAP	1 (5%)	1 (5%)
Antibiotics	5 (25%)	5 (25%)
Antivirals	0 (0%)	0 (0%)
Dexamethasone	0 (0%)	0 (0%)
ICU admission	0 (0%)	0 (0%)
Mode of transmission		
Hospital acquired	7 (35%) 1	4 (20%)
Home	(5%)	5 (25%)
Nursing Home	2 (10%)	0 (0%)
Rehabilitation centre	0 (0%)	1 (5%)
HD vintage (months)		
Mean	34.1	46.1
Median	20	21.5
SD	*39*	*81*
IQR	*36.75*	*28*
Cause HD		
Diabetes Mellitus	5 (25%) 1	4 (20%)
Hypertension	(5%)	2 (10%) 1
Acute Tubular Necrosis	2 (10%)	(5%)
AD PCKD	0 (0%)	2 (10%)
Cardiorenal syndrome	1 (5%)	0 (0%)
Thrombotic Microangiopathy	1 (5%)	0 (0%)
Vascular	0 (0%)	1 (5%)

Dialysis access *Line* *AV Fistula*	 10 (50%) 0 (0%)	 8 (40%) 2 (10%)
Comorbidities *Heart Failure* *Ischaemic heart disease* *Hypertension* *Diabetes Mellitus*	 7 (35%) 7 (35%) 6 (30%) 6 (30%)	 2 (10%) 4 (20%) 7 (35%) 5 (25%)
Atrial Fibrillation *Chronic lung pathology* *Stroke*	5 (25%) 3 (15%) 2 (10%)	1 (5%) 1 (5%) 1 (5%)
No. medications (mean) *SD* *IQR*	15.6 *5* *5.25*	11.8 *3* *3.5*
Clinical Frailty Score (CFS) (mean) *SD* *IQR*	6.2 [4-8] *1* *1*	5.7 [3-8] *1.6* *2*
Baseline mobility *Independent* *Wheelchair* *Zimmerframe* *Bedbound* *Assistance of 1*	 4 (20%) 2 (10%) 1 (5%) 2 (10%) 1 (5%)	 6 (30%) 3 (15%) 1 (5%) 0 (0%) 0 (0%)
No hospitalizations in last 12 months (mean) *SD* *IQR*	4 *1.8* *1.75*	2.2 *1.1* *2*

There was no difference in age between non-survivors and survivors (69.3 vs 68.6 years). Nonsurvivors were more likely to be have upper respiratory tract symptoms, including dyspnea (50% vs 15%) and cough (40% vs 35%), and had a shorter HD vintage (34.1 versus 46.1 months). The main predictor for mortality was underlying frailty, as indicated by the CFS (6.2 versus 5.7), number of hospitalizations in the preceding year (4 versus 2.2), baseline mobility, and number of medications (15.6 vs. 11.8). Seven patients had a CFS ≤5, two of whom died, and thirteen had a CFS>5, eight of whom died (relative risk (RR) 2, confidence interval (CI) 0.57,7.03)

Worse outcomes were associated with more profound lymphopenia ($0.7x10^9$/L versus $1.2x10^9$/L) and higher WCC ($7.4x10^9$/L versus $6.4x10^9$/L), and CRP (82 mg/L versus 53.4 mg/L) at presentation. Patients who died maintained a higher CRP at day 7 (200 mg/L versus 90.3 mg/L).

Prior to implementation of NRO-recommended guidelines on the 07/04/20, there were fifteen cases in our HD centre, compared to five after.

Discussion

In comparison to international data illustrating mortality rates between 29-41% in HD centres[7-9], we report a high mortality of 50%, largely driven by an early nosocomial outbreak and underlying frailty. COVID-19 HD cohorts with similar median ages[8,9] reported mortalities of 29-30.5%.

Changes made within our dialysis centre, guided by the NRO and previous recommendations[10], included temperature checks for patients and surgical masks for patients and health care workers; suspected cases received HD in isolated rooms, were swabbed for SARS-CoV-2 and reviewed by a renal physician; known SARS-CoV-2-positive patients were dialyzed in isolation rooms; all staff coming into contact with suspected or confirmed cases wore personal protective equipment; nephrology teams were divided into COVID-19 and non-COVID-19 teams; the nephrology ward was closed and decontaminated following the COVID-19 outbreak, then became a COVID-19 negative ward. Following implementation of these measures we observed a sustained decrease in the amount of new cases of COVID-19.

Interpretation of our data is limited by our small sample size, testing only symptomatic patients, meaning our numbers may not reflect the true incidence of COVID-19, and the likely natural decline in COVID-19 cases with national implementation of social distancing.

However, the significantly higher rate of mortality in our centre is difficult to ignore. Although guidelines exist for the prevention of COVID-19 in outpatient HD facilities, nosocomial transmission poses a serious potential risk for HD patients. We advocate early adoption of universal surgical mask protocols, isolation measures, separate inpatient COVID-19 teams and separate COVID-19 HD isolation facilities.

Declaration of Conflicts of Interest:
JH, VS and CM declare no financial or other conflicts of interest which may raise the question of bias in the work reported or conclusions, implications or opinions stated.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P272

The Pyjama Sessions: Transition to Online Education During a Pandemic

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Abstract

Aim
To gauge the successful transition to virtual learning during the Covid-19 pandemic.

Methods
Educational meetings in a tertiary neonatal intensive care unit were assessed over a two-week period in June 2020. Attending staff were sent an overall questionnaire and six meeting-specific questionnaires. 41 attendees (100%) responded to the overall questionnaire. We received 172 individual responses to the daily questionnaire (97%).

Results
164 respondents (95%) found virtual sessions useful. Attendance doubled compared to 2019 (mean 30 versus 15 attendees). 33 respondents (83%) attended when not scheduled to work. 38 attendees (97%) reported anxiety about their microphone or camera being on. 24 respondents (59%) attended online education sessions in their pyjamas.

Conclusion
Implementation of EWTD and a shift towards flexible working necessitates a creative approach to education. This pandemic has been a catalyst for moving towards virtual education, which our study showed can increase attendance whilst remaining useful to attendees.

Introduction

The COVID-19 pandemic necessitated immediate change worldwide in patterns of working, education and lifestyle[1]. The requirement for social distancing meant that long-established forms of medical education had to be cancelled or moved online[2]. In an effort to maintain continuing professional development (CPD) following public health restrictions on face-to-face meetings, we rapidly adapted to an online educational platform in April 2020. We aimed to gauge successful transition to virtual learning and identify how these changes in practice could be factored into future planning of educational programmes.

Methods

Three dedicated weekly educational meetings in our tertiary neonatal intensive care unit were assessed (Critical appraisal of literature, Peer-led teaching, Protocol development) over a two-week period in June 2020. We compared attendance with the same time period in 2019. We surveyed all medical, nursing and allied health care professionals (AHPs) participating in our educational programme. Participants were sent an overall (Lockdown) questionnaire and six additional meetingspecific questionnaires.

The questionnaires were designed to evaluate ease of attendance, educational value, participation, location at time of teaching and attendance outside of working hours. We aimed to capture changes in professional behaviour during an extraordinary time.

Results

41 staff members (100%) responded to the 'Lockdown' questionnaire (20% consultants, 58% nonconsultant hospital doctors (NCHDs), 12% nurses, 10% AHPs). 177 attendances were recorded at 6 meetings. We received 172 individual responses to the daily questionnaire (97%).

164 attendees (95%) indicated the individual educational sessions were useful. 82 attendees (47%) reported the sessions were interactive and 69 respondents (40%) found them to be enjoyable.

Attendance at teaching sessions doubled compared to 2019 (mean 30 versus 15 attendees per session). 33 respondents (83%) attended sessions when not scheduled to work. During a typical session, one quarter of those attending were not scheduled to work that day. On a daily basis, 50% were in work, 16% travelling, 20% in their kitchen or living room and 14% in their bedroom/bathroom.

31 respondents (78%) reported finding it easier to attend a virtual session late. 18 attendees (44%) found it more difficult to contribute. 35 attendees (88%) felt that they were more likely to multi-task. 28 of 32 responses (88%) felt that virtual sessions were more family friendly.

Five respondents (12%) reported virtual education sessions to be more anxiety-inducing, 24 attendees (59%) reported less anxiety. Ten presenters (28%) stated that a lack of visual or audio feedback and potential technical issues caused them anxiety. 38 attendees (97%) reported having anxiety about their microphone or camera being on, a feature locally described as 'Zoom anxiety', though several different online platforms were utilised.

Prior to the pandemic, attendees typically wore scrubs or workwear. From April 2020, 59% (n=24) had attended education sessions in their pyjamas.

Discussion

The aim of this study was to explore whether the recent transition to virtual learning in the setting of the Covid-19 pandemic was successful and how lessons learned from its implementation could be used for future planning of educational programmes[3].

We noted a dramatic increase in attendance with the majority reporting virtual education to be useful and more family friendly, a factor rarely assessed in teaching programmes[4].

Notably, one quarter of staff attended teaching when not scheduled to work. Implementation of the EWTD[5] and a cultural shift towards flexible working necessitates a creative approach to training and continuing professional development. Attendees chose a more informal approach to attending meetings, sometimes attending late, multitasking and dressing informally. Despite these potential educational drawbacks, our study showed that virtual learning increased accessibility in our cohort.

Presenters reported anxiety regarding technical issues and lack of audience feedback. Almost all attendees worried about unknowingly leaving their camera or microphone on. Over time, with continued virtual learning, we anticipate this anxiety will reduce.

Participants commented that they missed the collegiality that resulted from face-to-face teaching sessions and the requisite coffee afterwards. Due to the nature of virtual platforms, only one participant can communicate at a time and attendees often cannot see each other, leading to a sense of artificiality and a paucity of "catch-up chat". Initiatives that support morale and team-development are essential as virtual education becomes the norm.

Our study did not quantify the educational benefit of our programme and some of our questions are clearly tongue-in-cheek, but for our team this pandemic has been the catalyst necessary to advance virtual learning. Our findings can help future planning not just in this setting but also in the provision of the best, most accessible, educational platform for our staff. 'Zoom anxiety' is prevalent and we suggest that healthcare workers should invest in a good pair of pyjamas.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P273

Hospitalised Older People with Covid-19: One Month Outcomes

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Abstract

Aims

COVID-19 disproportionately affects older people, with those aged ≥65 years representing a significant proportion of hospital admissions and deaths. Our aim was to examine characteristics, inpatient course and one-month outcomes of older patients with COVID-19 managed in an Irish urban tertiary hospital.

Methods

A retrospective cohort study of patients aged ≥65 diagnosed with laboratory-confirmed-COVID-19 over one-month and managed as inpatients in an Irish tertiary referral hospital. Electronic and paper medical records were reviewed.

Results

Eighty-six inpatients aged ≥65 years (mean age 77) with laboratory-confirmed-COVID-19 were included. Participants were frail (Median Clinical Frailty Scale:5) with multiple comorbidities (Median Charlson Comorbidity Index:5). One month after diagnosis, 44.2% (38/86) were discharged, 33.7% (29/86) had died and 14.0% (12/86) were awaiting rehabilitation or long-term care(LTC). The remainder were medically recovering.

Discussion

COVID-19 had a significant impact on older people admitted to hospital with high case-fatality rates. The proportion awaiting rehabilitation or LTC at four weeks demonstrates a significant functional impact on this cohort.

Introduction

Since the emergence of COVID-19, it has become clear that older adults are more vulnerable to severe infection and death, with increasing prevalence of comorbidities with age compounding risk[1]. In Ireland, persons aged ≥65 years account for 24% of COVID-19 cases, but 54% of hospital admissions and over 92% of deaths[2,3].

Older adults are a heterogeneous group, with medical comorbidities often contributing to a complicated inpatient course. In patients with COVID-19, the Charlson Comorbidity Index (CCI) has been shown to predict mortality[4]. Higher Clinical Frailty Scale[5] (CFS) ratings have been associated with lower probability of discharge home[4]. Previous studies demonstrated that older patients with COVID-19 often present atypically. Delirium is a common presenting feature[6] and associated with poor four-week functional outcomes[7].

Our aim was to describe hospital inpatient course of older people diagnosed with COVID-19 over one month in an Irish, urban tertiary hospital and outcomes four weeks after diagnosis.

Methods

A retrospective cohort study of those aged ≥65 years with laboratory-confirmed COVID-19 diagnosed over a one-month period (25/03/2020-24/04/2020) and managed as inpatients. Medical records of included patients were accessed to review demographics, baseline function, CCI, inpatient course and outcomes four weeks post diagnosis. Delirium diagnosis and CFS were deduced through geriatrician review of multidisciplinary (MDT) medical records when not explicitly stated.

Results

Eighty-six older patients, aged ≥65 years, were diagnosed with laboratory-confirmed COVID-19 and managed as inpatients during the study period, compared to 79 patients aged <65 years. Only older patients were included in final analysis including 46 patients diagnosed with COVID-19 as a result of testing completed in the Emergency Department (ED) and a further 40 patients diagnosed through inpatient testing. Mean age was 77 years (range 65-93). Of those diagnosed with COVID-19 through ED testing, 37 patients (80%) had mild disease at presentation, eight (17%) moderate and one patient (2%) severe[8].

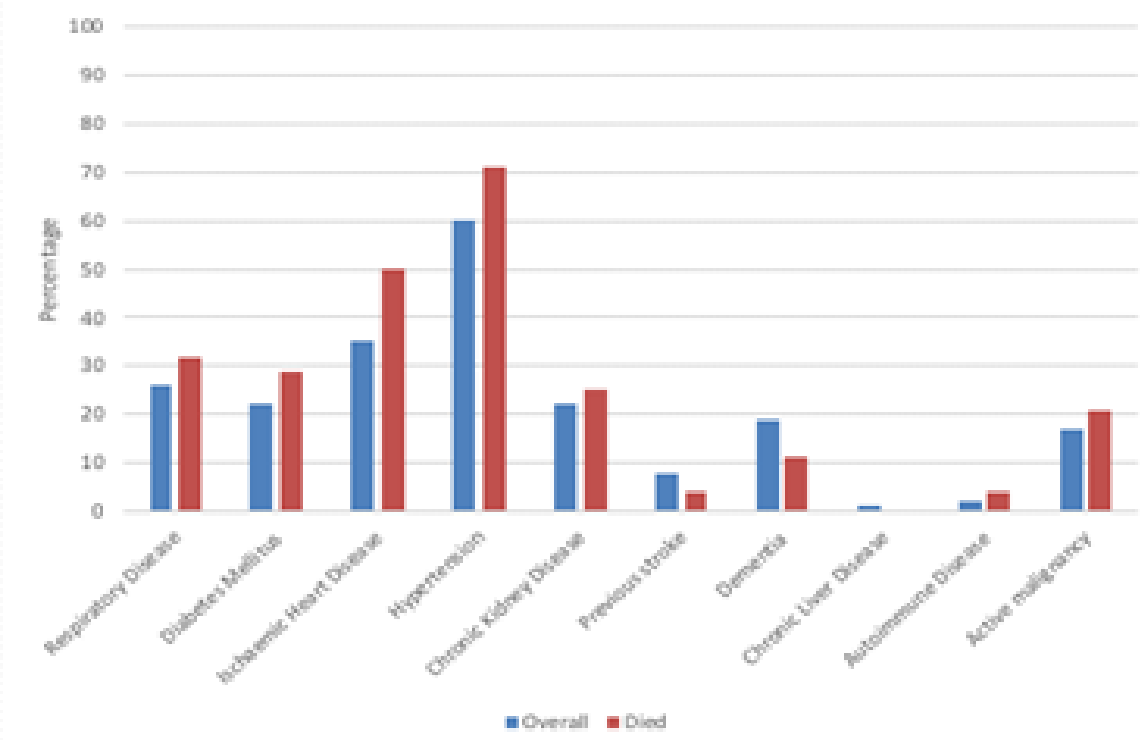
Twenty older patients (23%) were managed on specialist geriatric wards. Six (7%) were admitted to ICU during their admission, all of whom were intubated. Comorbidities were common [Table 1]. Median CCI was 5. Median pre-admission CFS was 5 (mildly frail). This was significantly higher in patients managed on geriatric wards compared to other wards (CFS: 6 vs 4, p=0.01). Delirium was present in 31 patients (36%).

At baseline, 46 patients (53%) were independently mobile without aids, 30 (35%) mobile with aids and 10 (12%) wheelchair-dependent or bedbound. Thirty-nine patients (45%) required assistance with

personal activities of daily living. Seven (8%) were nursing home residents. Ten (12%) experienced a fall during admission. During admission, 56 patients (65%) were reviewed by physiotherapy, 36 (42%) by occupational therapy, 52 (61%) by nutrition and dietetics and 37 (43%) by speech and language therapy. New dysphagia post COVID-19 diagnosis was noted in 16 patients (19%).

Four weeks after COVID-19 diagnosis, 38 patients (44.2%) were discharged, 29 (33.7%) had died, and 19 (22.1%) remained in hospital, of whom six (31.6%) remained medically unwell, four (21.1%) awaited rehabilitation and 8 (42.1%) awaited LTC. Mean age in those who had died was 79.7 years compared to 76.0 years for those still alive (p=0.07). Mean CCI was 5.8 and mean CFS 5.2 in those who had died compared to 5.0 and 4.1 respectively for those still alive.

Table 1: Comorbid illness in older patients with COVID-19 (n=86) vs patients who died (n=28).



Discussion

The inpatient population in this study had multiple comorbidities, with functional impairment and frailty common at baseline. They had a complex inpatient course, with delirium in over a third, a similar proportion to previously published studies[9]. Delirium diagnosis was ascertained from chart review, therefore likely an underestimate as delirium is frequently under-recognised. Inpatient falls and newly recognised dysphagia were prevalent. Many required MDT rehabilitation. One third of older patients had died at four weeks and co-morbidities in this group were similar to those previously reported[10].

Patients managed on specialist geriatric wards were significantly frailer, with a higher baseline CFS, and the majority of these remained inpatients four weeks following COVID-19 diagnosis. Nearly twothirds (63.2%) were awaiting off-site rehabilitation or LTC, reflecting the impact of COVID-19

hospitalisation on the functional status of older people with frailty. Rehabilitation facilities were closed or admitting smaller numbers, with further repercussions for those deconditioned following acute illness.

This study demonstrates the significant impact of COVID-19 on older people, particularly those with frailty, with a complex inpatient course and functional decline frequently experienced.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P274

Advancing Professional Healthcare by the Use of Mentorship

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Abstract

Mentorship is a method used to train healthcare professionals across a variety of disciplines. It comprises of a relationship between the 'mentor', or the trainer, and a 'mentee', or the learner. It is important to determine whether or not mentorship is a useful technique to increase the clinical competencies of healthcare professionals, to ascertain where further research should be directed. This paper explores the current knowledge on using mentorship to train new healthcare professionals and students in varying healthcare systems. It explores mentorship from both a clinical competency perspective, as well as a personal perspective.

Introduction

A variety of training techniques are used to ensure health-care providers meet their expected competencies, which is important for providing quality care to patients. One such technique is known as mentorship, also known as preceptorship. The usage of mentorship as a form of training less experienced health-care professionals has been applied in a variety of different health-care systems. It involves the expertise of a mentor, who is the trained individual, and a mentee, who is the individual being trained.[1] It is seen as a technique to offer personal support, alongside career growth. Mentorship can be described as a formal arrangement, where the mentor and mentee are generally assigned to one another. Formalized mentorship programmes can have more structure, whereas informal arrangements tend to involve relationships that develop naturally and are more relaxed.[2]

Structure of Mentorship Programmes

Naturally, mentorship is not limited to the health-care field, and can be found in a variety of professions, as well as personal life. However, within varying professional fields, there are specific quality characteristics found within a successful mentoring relationship, accordingly.[3]

Some programmes can be highly structured and pre-organized, whereas others can work to facilitate the individual needs of the mentee. Both mentors and mentees should exhibit specific characteristics in order to facilitate a successful mentoring relationship. The mentee should be aware of the time commitment the mentor has devoted to them, as well as consider any feedback provided by the mentor. Meanwhile, the successful mentor is found to act as a guide, monitor the progress of the mentee, and warn mentees of any potential risks. Successful mentorship programs found that mentors did not force their advice onto the mentee. Rather, they encouraged mentees to use any advice provided as a way to guide the mentee into the correct direction.[4]

As a whole, effective mentorship programmes are found to have certain characteristics. Primarily, it is important to have the programme targeted towards the mentee, establish clear identification of expectations, and be aware of the mentor's shortcomings.[3] Targeting the programme towards the mentee can help individualize needs, and identify what clinical competencies should be further improved upon. Identification of a mentee's skillset can be done by the mentor- training the mentor prior to holding a mentorship position can help to ensure that the competency expectations are met by the mentee. Effective mentoring requires mentors to remain up to date on current techniques and be experts in their field. However, it also requires mentors to act as educators, and teach such skills. Although health-care professionals may be highly skilled in their own work, they may lack the educational skills required to teach mentees.[5] Mentors may also be slowed down in the productivity of their own work when being placed with a mentee.[6]

Ineffective mentorship programmes were found to exhibit certain characteristics, which should be avoided when designing a mentorship programme. Some of the barriers towards the facilitation of effective mentorship within the health-care setting include unclear expectations, lack of mentors, and the lack of an appropriate time commitment. Increased distance between mentors and mentees were also factors visible in poor mentorship programme outcomes.[3] Furthermore, expectations of the learning outcomes should be made clear within the mentor-mentee relationship prior to the onset of a mentorship.

Mentors

Good mentors are found to have certain characteristics. Strong communicative skills, combined with guidance, feedback and respecting confidentiality were found to be some of the traits in favourable mentors.[7] For a successful mentorship to take place, a mentor should work to develop such character traits, and a mentee should acknowledge the difficulties their mentor may face, such as the workmentor balance. It is important to note that mentoring can be seen as difficult work with little rewards, offering less incentive for experienced health-care individuals to take part in a mentoring relationship.[2] Being a mentor is a committed task that requires extensive preparation and time dedication.

Healthcare Systems

Mentorship is a common form of training in regions with high-income health-care countries. Lowincome and middle-income health-care countries have also displayed an increased quality of care to patients when using mentorship as an interventional method.[8] On a global scale, low-income healthcare countries have a tendency to rely on didactic forms of training due to the effects of low levels of skilled professionals available.
However, this form of abstract training can poorly translate into real life clinical skills for health-care professionals. Addressing these issues through providing a mentorship programme in different regions of Africa was found to improve health outcomes, as well as staff satisfaction.[9] Such mentorship programmes were tailored to different regional needs and mentor availability, demonstrating the importance of flexibility within training programmes.

The successful development of mentorship programmes in low and middle income countries requires a combination of different factors. For one, the health-care institution should designate time for mentors to learn effective teaching skills. The mentorship relationship should benefit both parties, and the mentee should be encouraged to engage with the mentor. Institutions should ensure that there are adequate mentorship training opportunities available within the organization upon recognizing the importance of mentorship.[10]

Outcomes of Mentorship

The usage of mentorship has been found to improve attitudes towards the work environment. It can also enable co-workers to better engage with one another, which in turn can facilitate an environment that supports better communication and teamwork. Furthermore, mentorship creates a better mutual respect towards co-workers, and members of an interdisciplinary health team.[11] Good communication is very important within the functioning of a healthcare team and can help improve patient health outcomes. Failure to communicate between health-care professionals can create delay or error within patient diagnosis and/or treatment, which has the potential to have a profound impact on prognosis and quality of life.[12]

Although mentorship may commonly be seen within hospitals and other health-care organizations, it can also provide a variety of benefits towards health-care students who have yet to be qualified. For example, implementing mentorship programmes for medical students has a positive correlation with activity in research.[13] Students who have mentors have increased contact with individuals who work in their future job field, which may help nourish potential fields of interests.

High turnover rates of nurses in a variety of different countries are of particular concern to various health-care systems today. One study found working conditions, a lack of appreciation, and poor working environment to be common contributors for a high nursing turnover rate.[14] On the contrary, designing and using a preceptorship programme was determined to increase nursing retention rates.[15] There is potential for a conflict of roles between the mentor and mentee, due to the way a mentor is

placed in a position where it is easier for them to overuse their power, as the mentor may be considered to be superior within the mentor-mentee relationship. As such, it can be easier to take advantage of the mentee, who may consider themselves as having inadequate knowledge to know normal procedures.[6]

Conclusion

Closely observing mentorship connections can show benefits that last for a lifetime, both professionally, and for one's personal growth and development. The importance of strong, healthy mentorship relationships within the health-care field cannot be undervalued; it is a primary method of clinical training for recent health-care professional school graduates as well as medical students. Moving forward, mentorship programs should take into consideration personal factors when pairing a mentor and a mentee. Both the mentor's and mentee's perspectives should be considered. Prior to the initiation of a mentoring relationship, mentors should be provided proper training on acting as an educator, while mentees should note their personal learning outcomes.

Declaration of Conflicts of Interest:
The authors declare that there are no conflicts of interest.

Funding:
We acknowledge funding received by the Royal College of Surgeons in Ireland Research Summer School.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P275

Bedside Ultrasound in the Emergency Department Enables Rapid Diagnosis of PUJ Obstruction Syndrome

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Abstract

Presentation

A 27-year-old male presented to the Emergency Department with acute severe left flank pain following ingestion of 5 pints of beer. Approximately 20 bouts of similar episodes over the past year, in the setting of alcohol ingestion. Despite attending GP, no diagnosis reached yet.

Diagnosis

"Pelvo-ureteric junction (PUJ) obstruction Syndrome". Bedside ultrasound in the Emergency Department during the acute pain crisis: massive hydronephrosis left kidney. Finding confirmed on CT scan. Subsequent 99m-Tec renogram showed markedly decreased renal function on the left.

Treatment

Interval Pyeloplasty two months later.

Conclusion

Delayed recognition is the norm for PUJ obstruction syndrome, as CT/MRI/US studies often do not display hydronephrosis if the patient is asymptomatic. We could not find any reports in the literature of diagnosing PUJ obstruction syndrome using bedside ultrasound in the Emergency Department. We advise acquiring rapid bedside ultrasound imaging in suspected cases of PUJ obstruction syndrome, enabling earlier diagnosis.

Introduction

Pelvo-ureteric (PUJ) obstruction syndrome is a difficult diagnosis to make, as imaging studies are often normal by the time the pain has resolved. This can lead to delayed recognition. The key to timely diagnosis is obtaining appropriate imaging during an acute pain crisis.[1]

Case Report

A 27-year-old male presented to the Emergency Department with acute severe left flank pain following ingestion of 5 pints of beer. He reported approximately 20 bouts of similar painful episodes over the past year, in the setting of alcohol ingestion. These would usually resolve within a few hours. He had recently attended his GP, when not in acute pain; his GP was unable to find any abnormality on physical examination.

His medical history included an episode of left-sided epididymo-orchitis 2 months previously, which resolved with antibiotic treatment.

Clinical examination was unremarkable, as were renal function blood tests, inflammatory markers, and mid-stream urine analysis.

Point-of-care ultrasound (POCUS) performed in the Emergency Department revealed massive leftsided hydronephrosis (figure 1). This prompted a CT urogram to evaluate the level of ureteric obstruction. Hydronephrosis was confirmed on CT imaging (figure 2). The left renal pelvis was markedly dilated, while the ureter was decompressed. No obstructive stone or growth were seen to account for this; the diagnosis was pelvo-ureteric junction obstruction syndrome.

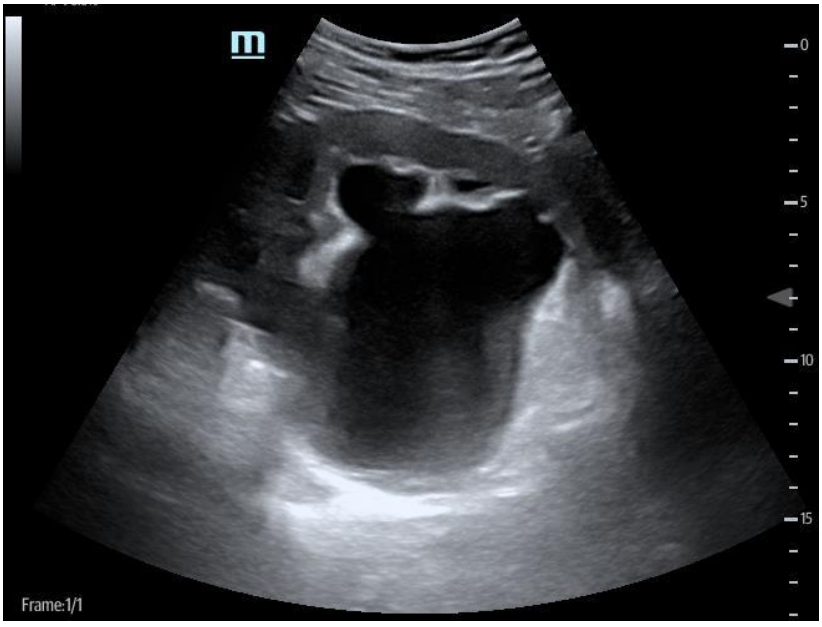

Figure 1: POCUS shows severe left hydronephrosis - hypoechoic area centrally in the renal pelvis with thinning of the renal cortex peripherally. There is no calculus seen.

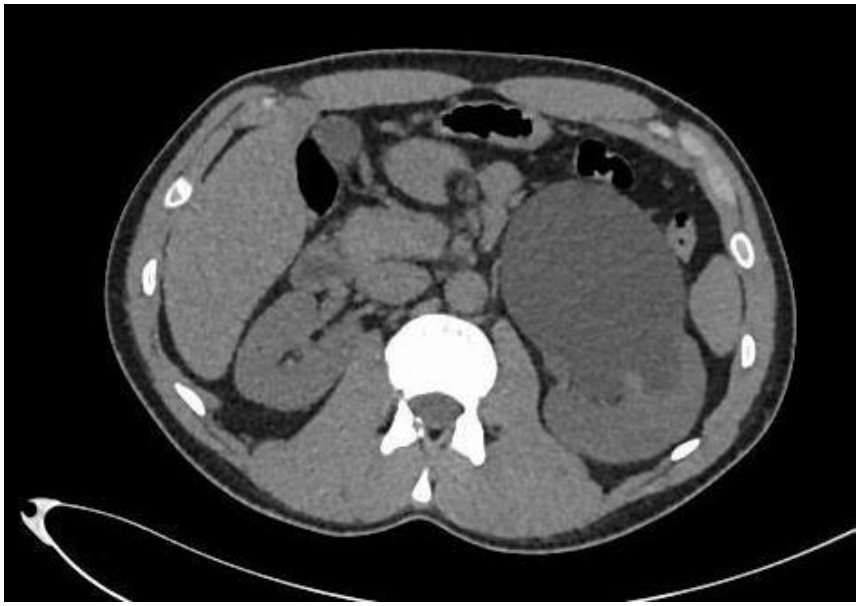

Figure 2: CT scan: renal pelvis hugely distended, no stone/growth seen: PUJ obstruction syndrome.

Discussion

Delayed recognition is the norm for PUJ obstruction syndrome, as CT/MRI/US studies often do not display hydronephrosis if the patient is asymptomatic[1]. A major benefit of bedside ultrasound performed in the Emergency Department is timeliness of the examination; a suggestive clinical examination and bedside ultrasound facilitated a more informed discussion with radiology and acquisition of rapid CT imaging while symptomatic.

Point-of-care ultrasound (POCUS) is becoming increasingly well-established in the Emergency Department. It is increasingly seen as a mandatory skill for Emergency Physicians and is compulsory in emergency medicine residency training programmes in the USA (2). POCUS has shown high sensitivity and specificity for the detection of hydronephrosis when compared with CT[3].

PUJ syndrome is defined as a partial or intermittent obstruction of the flow of urine from the renal pelvis to the proximal ureter, without an obvious causative lesion[4].

Common causes include an aberrant renal vessel causing external compression of the lower pole of the kidney ('Dietl's Crisis'), or intrinsic malformation of a segment of the proximal ureter. Less frequent aetiologies include higher insertion of the ureter or a polyp. Although more commonly discovered during childhood, some cases do not become symptomatic until adulthood and present with a classical history of alcohol-induced pain.

PUJ obstruction syndrome can be treated surgically with pyeloplasty, nephrectomy and percutaneous nephrostomy placement.[5]

Our patient proceeded to have a 99m-Tec renogram showing markedly decreased renal function on the left. Pyelopasty was performed.

In conclusion, in patients with a history of recurrent flank pain following fluid consumption, suggestive of PUJ obstruction, who present acutely to an ED with same, renal ultrasound should be considered on a rule-in basis if an appropriately trained EM physician is available. In the absence of such a physician or absence of hydronephrosis, further investigation is required as the diagnosis is not entirely excluded.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P276

Endophthalmitis, *Clostridium Septicum* Bacteraemia and the Search for Colonic Malignancy

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Abstract

Presentation
An 86-year-old man presented with a four-day history of subjective fevers and malaise. He developed a mucopurulent discharge from his right orbit, a corneal injection and a hypopyon shortly after admission.

Diagnosis
Endogenous endophthalmitis, secondary to *Clostridium septicum* bacteraemia.

Treatment
Topical, intravitreal and systemic antibiotics & right-sided tarsorrhaphy.

Discussion
This case highlights the ophthalmic complications of *Clostridium septicum* bacteraemia, as well as the rapidity of disease progression and the poor visual prognosis seen in *Clostridium septicum* endophthalmitis. It also reminds physicians of the association between *Clostridium septicum* bacteraemia and underlying malignancy, and with mycotic aortic aneurysms.

Introduction

Endogenous endophthalmitis is an intraocular infection caused by haematogenous seeding of microorganisms from a distant source[1]. Cases of endogenous endophthalmitis are most commonly described in association with infective endocarditis and liver abscesses[1].

Case Report

An 86-year-old man presented with a four day history of subjective fevers and malaise on a background of ischaemic heart disease, stage IV chronic kidney disease and intractable iron-deficiency anaemia. He was pyrexic (38.4^{o}C) and tachycardic (100 beats per minute) on admission. The rest of his vital signs were within normal limits.

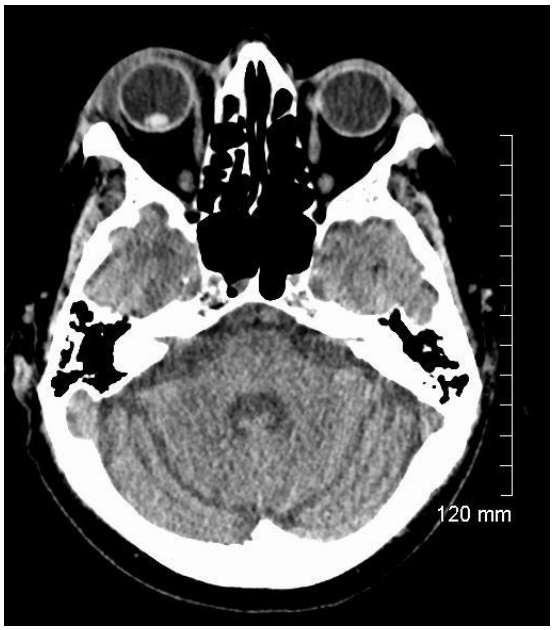
Preliminary laboratory investigations included; white cell count; 8.5 (3.5-10.5x10^{-9}/L), neutrophils 8.0 (1.70-7.00x10^{-9}/L) lymphocytes 0.1 (0.90-2.90x10^{-9}/L), C-Reactive Protein 220 (<3mg/L), haemoglobin

7.3 (14-18 mg/dL). Abdominal exam on admission was unremarkable.

In the first 12 hours of his hospital admission, the patient experienced a deterioration in visual acuity in his right eye from 6/6 vision to no light perception. Over the same time-period, the patient developed right periorbital swelling, right eye ophthalmoplegia and corneal injection with associated mucopurulent discharge**.** He denied right eye pain.

A single set of blood cultures was taken prior to commencing empiric antibiotic therapy with IV coamoxiclav and PO clarithromycin. The gram-positive bacillus, *Clostridium septicum*, was grown in the anaerobic blood culture bottle of this first set. No definite antimicrobial sensitivities were obtained in the laboratory. All other blood culture bottles displayed no growth. After discussion at the microbiology multidisciplinary team meeting, he was commenced on systemic metronidazole (500mg, IV, TDS), ceftriaxone (2g, IV, OD) & daptomycin (560mg (6mg/kg), IV, OD). Computed tomography (CT) of the orbits indicated right-sided periorbital oedema and posterior dislocation of the lens in the right eye (Fig. 1). Slit lamp examination of demonstrated a hypopyon of the right eye.

Fig. 1 CT Orbits: *CT orbits demonstrating right-sided periorbital oedema and posterior dislocation of the right lens.*

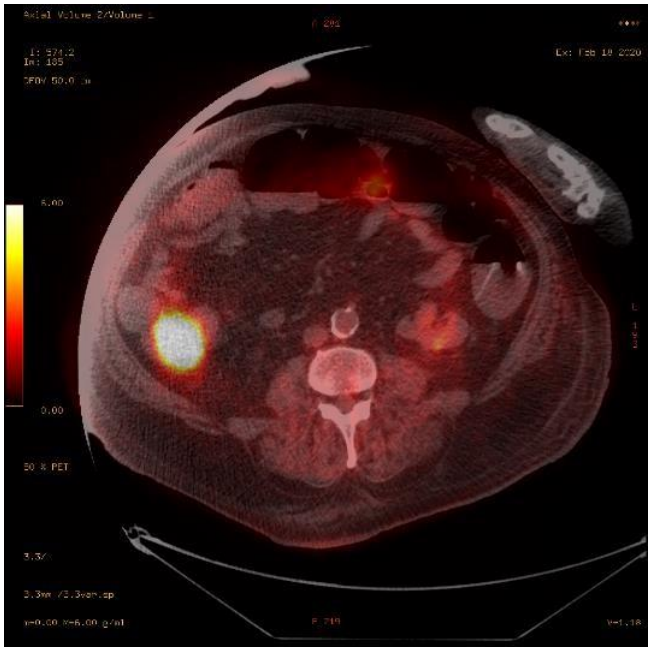


48 hours after initial presentation, a corneal abscess had developed and a new, right-sided relative afferent pupillary defect was noted. Intraocular pressures remained normal. The decision was made for referral to a specialist ophthalmology centre for urgent management of endophthalmitis.

Unfortunately, despite administration of topical (ceftazidime: 50mg/mL,1 drop, hourly; vancomycin: 50mg/mL,1 drop, hourly) & intravitreal (vancomycin 2mg, ceftazidime 2mg, dexamethasone 0.4mg) therapy, the patient developed an infected corneal-scleral ring, eventually precipitating a perforated right globe. He declined evisceration of the right eye and elected to undergo a total tarsorrhaphy. No growth was seen on vitreous culture.

The suspected source of the bacteraemia was eventually revealed by positron emission tomography (PET) CT imaging, which showed a likely new diagnosis of a right-sided colonic malignancy (Fig. 2) However, the patient declined biopsy of this colonic mass.

Fig. 2 PET CT abdomen: *PET CT showing intense 5-FDG avidity in the right colon.*



During the workup for malignancy as the source for bacteraemia, a CT thorax and subsequent CT angiogram revealed a distended, proximal descending aorta, likely indicating the development of a mycotic aneurysm. This CT angiogram finding was corroborated by the PET CT images, where high 5FDG avidity was seen in the vessel wall at the area of dilatation and in the surrounding soft tissue.

The patient initially responded to systemic antibiotic therapy but succumbed to a hospital acquired pneumonia 5 weeks after initial presentation. Autopsy was not performed, and no formal tissue diagnosis of malignancy was obtained.

Discussion

To the best of our knowledge, there have been 9 cases of endogenous *Clostridium septicum* endophthalmitis described to date[2,3-7].

In the case above, vitreous culture was negative. However, these can be negative in up to 25% of cases of bacterial endogenous endophthalmitis[8]. Furthermore, the patient had already received 3 days of topical and systemic antibiotics.

This case supports previous observations that *Clostridium septicum* endophthalmitis has a poor visual prognosis, typically exhibiting a rapid deterioration of visual acuity within 24 hours of onset of visual symptoms[2,4,6].

Clostridium septicum endophthalmitis may be a presenting feature of an underlying malignancy[2,3,5,6]. In a study carried out by Koranasky, Stargel and Dowell**,** colon cancer was the most common solid organ malignancy associated with *Clostridum septicum* bacteraemia[9].

Clostridium septicum bacteraemia appears to have a poor overall prognosis[2,4,5]. *Clostridium septicum* mycotic aneurysms have been described in the context of *Clostridium septicum* bacteraemia and colon cancer and contribute to the high mortality rate seen in this patient population. A systematic literature review by Ito et al. reported that the "6-month mortality rate was 100%" in patients with untreated *Clostridium septicum* mycotic aneurysms[10]. Considering the poor visual and overall prognosis of patients with endogenous *Clostridium septicum* endophthalmitis, it is crucial that prompt blood cultures are taken in the context of eye signs and pyrexia in order to prevent delayed diagnoses and potentially suboptimal outcomes.

Declaration of Conflicts of Interest:
The authors declare no conflicts of interest in preparing this article.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P277

Spontaneous *Escherichia coli* Meningitis and Pyogenic Ventriculitis in an Adult Receiving Anti-Tumour Necrosis Factor Alpha Therapy

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Abstract

Presentation

A 60-year-old male taking etanercept for ankylosing spondylitis was admitted to hospital with confusion and reduced level of consciousness over the preceding 24 hours.

Diagnosis

Magnetic Resonance Imaging (MRI) of his brain revealed pyogenic ventriculitis, and *Escherichia coli* was cultured from CSF.

Treatment

He required placement of an external ventricular drain and was treated with a prolonged course of intravenous ceftriaxone.

Conclusion

To our knowledge, this is the first reported case of spontaneous Gram-negative bacillary meningitis in a patient on anti-tumour necrosis factor (TNF)-alpha therapy, highlighting the risk of rare but serious infections associated with this class of medication.

Introduction

Gram-negative bacilli are an unusual cause of spontaneous meningitis in adults, which rarely presents as primary pyogenic ventriculitis. Herein we describe a case of spontaneous *E. coli* meningitis presenting with pyogenic ventriculitis, in a patient on anti-TNF-alpha therapy.

Case Report

A 60-year-old male was admitted to hospital with a 24-hour history of confusion and reduced levelof-consciousness, preceded by symptoms of a dry cough and abdominal discomfort for seven days. His medical history was significant only for a diagnosis of ankylosing spondylitis, and he had taken the anti-TNF-alpha inhibitor etanercept for 12 years. Of note, he had not experienced trauma or surgery in the recent past.

On presentation, he was afebrile, Glasgow Coma Scale (GCS) was 13/15 (verbal response 3/5) and physical examination revealed severe neck stiffness. White blood cell count was 22 $x10^9$/L (4-11 $x10^9$/L) (neutrophils 20.9$x10^9$/L) and C-reactive protein 404mg/L (0-5mg/L). The presumptive diagnosis was community-onset meningitis and he was commenced on intravenous (IV) ceftriaxone 2 grams 12-hourly, amoxicillin 2g 4-hourly, and vancomycin. Cerebrospinal fluid (CSF) revealed low glucose levels at 0.1mmol/L with significantly elevated protein at 10.34g/L, and microscopy showed numerous Gram-negative bacilli. Magnetic Resonance Imaging (MRI) of his brain revealed ventriculitis, with air-fluid levels in both lateral ventricles consistent with pus (figure 1). On day one, *Escherichia coli* susceptible to amoxicillin was cultured from CSF, and the isolate was subsequently genotyped as ST-144 by genome sequencing using the Illumina MiSeq platform. Cultures of blood and urine remained sterile. On day two, he was transferred to a neurosurgical unit for placement of an external ventricular drain (EVD) and his antibiotic regimen was rationalised to IV ceftriaxone, along with five days of intraventricular gentamicin, 5mg once daily. Serial CSF cultures had sterilised by day seven and the EVD was removed. Computerised Tomography (CT) of his abdomen was also performed; consistent with recent pyelonephritis. By day 27, repeat MRI showed an improvement in his ventriculitis, but an abscess in his left internal capsule (figure 2), not amenable to further drainage.

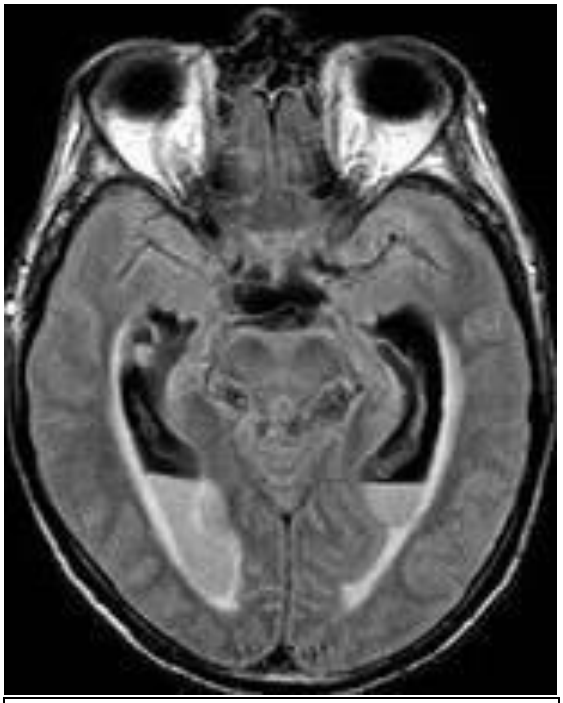

Figure 1. Axial FLAIR sequence MRI Brain, day 1: Fluid levels within both lateral ventricles likely representative of pus.

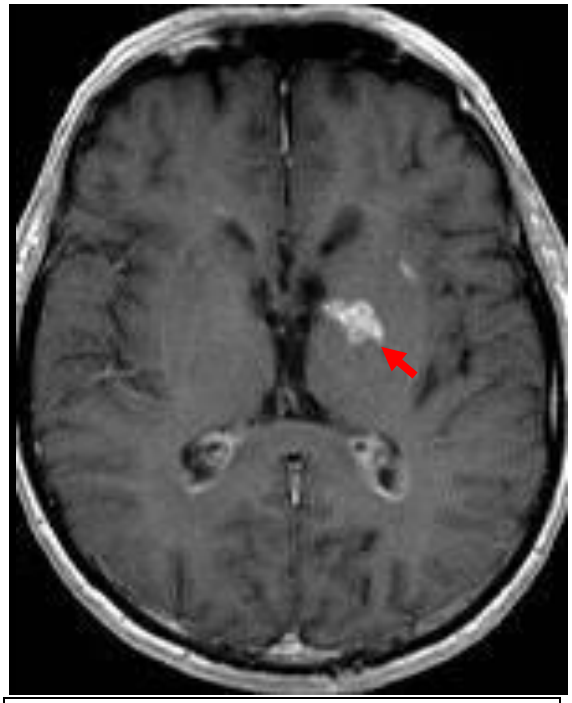

Figure 2. Axial MRI Brain –T1 post-gadolinium, day 27: Evidence of a localised cerebral abscess in the left internal capsule.

Currently, he remains an inpatient and has completed over 12 weeks of IV ceftriaxone. Serial imaging has noted a reduction in the size of the intracerebral abscess, and his GCS has recovered to 15/15 with multi-disciplinary rehabilitation.

Discussion

Gram-negative bacilli (other than *Haemophilus influenzae)* are a rare cause of community-acquired meningitis in adults, responsible for 0.7-7% of cases, and primary pyogenic ventriculitis has rarely been described in the literature[1-3]. According to the Health Protection Surveillance Centre (HPSC), *E. coli* was the pathogen identified in 7% of notified cases of bacterial meningitis in Ireland in 2018, with all cases involving infants aged between 1 and 5 months[4].

Gram-negative bacillary meningitis (GNBM) can be classified as traumatic or spontaneous in origin, with traumatic cases typically occurring in the aftermath of neurosurgery or head injury[5]. Spontaneous GNBM is usually described in patients with identified risk factors such as diabetes mellitus, alcoholism or liver cirrhosis[2,5], and most often arises as a consequence of haematogenous spread from foci such as the urinary tract[6]. Bacteraemia is believed to be a primary determinant for bacterial penetration into the CSF[7] and therefore it is interesting to note the absence of bacteraemia or bacteriuria in this case. Abdominal imaging, however, was suggestive of a urinary source and the *E. coli* was genotyped as ST-144 – a well-described uropathogenic strain[8].

Compared with other meningitides, patients with spontaneous GNBM tend to experience a fulminant clinical course with frequent neurological sequelae, and case fatality rates of 40-60%[2]. Diagnosis can be delayed because clinical features are often non-specific, although bacilli are visible by microscopy in up to 85%, underlining the importance of prompt CSF evaluation[2,6].

Our patient did not have established risk factors for spontaneous GNBM but was immunosuppressed based on taking etanercept – a recombinant receptor fusion protein that binds to TNF-alpha to reduce its bioavailability[9]. TNF-alpha is an important inflammatory cytokine responsible for numerous cellular signalling events, and blockade has been associated with serious bacterial infections, including meningitis caused by *Streptococcus pneumoniae*[9] and *Listeria monocytogenes*[10]. However, to our knowledge, this is the first reported association with spontaneous GNBM.

In conclusion, we describe the first case of spontaneous GNBM with ventriculitis in an adult without risk factors other than anti-TNF-alpha therapy. This serves as a reminder of the risk of rare but serious infections associated with these agents.

Acknowledgements:
The authors wish to acknowledge the help of Dr Niall Delappe and Mark Maguire, National CPE reference laboratory, Galway University Hospital, for their assistance sequencing the isolate.

Patient Consent:
Written consent for publication was obtained from the patient prior to submission.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P278

Protracted Bacterial Bronchitis Related to Bagpipe Playing in a Teenager

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Abstract

Presentation
A 15 -year- old girl presented with a progressive and productive cough and wheeze for four years unresponsive to bronchodilators, steroids, antimicrobials or physiotherapy.

Diagnosis
Sputum sample revealed Protracted Bacterial Bronchitis (PBB) secondary to Pseudomonas Aeruginosa in a champion bagpipe player.

Treatment
IV antibiotics and two cycles of nebulised tobramycin led to complete resolution of symptoms.

Discussion
Wind instruments can be associated with lung disease. Instruments must be correctly cleaned and stored and the importance of this to be made well known to all music players. A thorough social history must always be taken including past times. In particular, in those with recurrent pulmonary infections or conditions such as cystic fibrosis or primary ciliary dyskinesia a history of playing wind instruments should be sought and proactive advice given.

Introduction

Lung diseases have been reported in adults, with cases directly related to fungal contamination of wind instruments; bagpipes, saxophones and trombones. It is an avoidable disease with symptoms resolving when the causative pathogen is removed, and correct cleaning and maintenance of the instrument is practiced. There are similar reports in paediatrics.

Case Report

A fifteen- year- old girl presented with persistent productive cough and wheeze for four years, unresponsive to bronchodilators, high dose inhaled and steroids, oral antibiotics and physiotherapy.

She was born at 29½ weeks gestation, requiring brief intubation. She had resolved, mild eczema, but no food allergies. There was no family history of lung diseases.

She had marked inspiratory and expiratory wheeze and coarse crackles bilaterally. Other systemic examinations were normal.

Initial impression was that of bronchiectasis related to cystic fibrosis or primary ciliary dyskinesia. It later emerged that she was a champion bagpiper, practising regularly on a chanter and competing throughout the country. There was no cleaning routine for the instrument, which was often, heavily wet after being played.

Routine laboratory investigations were normal. Immunology work-up, CF genetics and nasal brushings were negative. Sputum sample was positive for pan- sensitive Pseudomonas Aeruginosa. High Resolution CT-Thorax showed no evidence of bronchiectasis. Initial spirometry revealed an FEV_1 81 % with no significant bronchodilator response.

Following a course of IV antibiotics and two cycles of nebulised tobramycin there was full resolution of symptoms. Spirometry improved; to FEV_1 108% and on later follow up to 122% predicted. Regular inhalers were no longer needed.

Discussion

We propose that our patient had chronic suppurative bronchitis, secondary to pseudomonas aeruginosa triggered or exacerbated by bagpipe playing. Cultures were not taken from the instrument. However, given previous reports in the literature, we suggest the strong likelihood that bagpipe playing in this teenager had a significant role in the pathogenesis of her disease.

Hypersensitivity Pneumonitis encompasses a range of inflammatory and allergic respiratory diseases triggered by the inhalation of fine particles; both organic and inorganic[1,2,3]. It has been described in association with prolonged bagpipe playing in adults with fungi being the causative organisms. Higher rates of chest infections have been reported in this cohort[4]. This phenomenon has loosely been coined ‘Bagpipe Lung’. The moist internal area of bagpipes creates an idyllic environment for bacteria and fungi to thrive in, though with simple cleaning, this can be reduced[5,6].

We suggest that a newer phenomenon termed ‘Protracted Bacterial Bronchitis’ may be responsible for our case. It describes respiratory conditions with clinical features of bronchiectasis in the absence of the associated radiographic features[7]. An important differentiating feature clinically between it and bronchiectasis is its higher incidence but less severe pathogenesis[8].

Multiple risk factors and aetiologies are associated with it, but to date, musical instrument use has not been cited. Pseudomonas Aeruginosa is a common pathogen in bronchiectasis and implicated in cases of chronic suppurative bronchitis[8]. In our case, cultures were not taken from the instrument. However, given the previous case reports we suggest the strong likelihood that the playing of the bagpipes in this teenager had a significant role in the pathogenesis of her disease.

Airway disease secondary to wind instruments is avoidable. The importance of correct cleaning and maintenance of these instruments is now being recognised and advocated for. Furthermore, an entrepreneurial Scottish teenager has developed a novel blowpipe that can minimise the accumulation of saliva in the bagpipe and ultimately reduce the growth of pathogenic organisms[9].

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P279

A Child Presenting with Respiratory and Circulatory Compromise Secondary to Gross Constipation

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Abstract

Presentation

We describe the unusual implications of long-standing constipation in a child presenting with respiratory and circulatory compromise.

Diagnosis

His abdominal and chest x-rays were very remarkable for gross constipation resulting in inadequate lung expansion.

Treatment

He initially received supplemental oxygen and an intravenous bolus of Normal saline for management of shock and was subsequently started on laxatives.

Conclusion

The respiratory and cardiovascular compromise occurred secondary to the progressive increase in intra-abdominal pressure.

Introduction

Children with long standing constipation can develop serious sequelae if left untreated. We discuss the case of a child presenting with respiratory and circulatory compromise secondary to long standing constipation.

Case Presentation

A 14 years old boy presented to our Emergency department with abdominal distension and shortness of breath. The abdominal distension was intermittently occurring for the previous 2 weeks. He was also complaining of abdominal pain and reduced appetite.

He had a past history of constipation not managed by any medications, occasionally associated with overflow soiling. He mentioned that lying down and passing flatus had given him some relief. He was passing urine normally.

On assessment he was alert but pale looking, he was distressed but able to talk. He was apyrexial, his heart rate was 136/min, blood pressure was 136/76, respiratory rate was 26/min, oxygen saturations were 98% in room air.

Abdominal exam showed a massively distended abdomen, tense on palpation. An abdominal mass was felt in the left lower quadrant that was non tender, there was no visceromegaly. Examination of the perianal area was difficult due to soiling, but no abnormalities were found on exam. The rest of his systemic examination was unremarkable.

His initial investigations including full blood count, renal and liver function tests were normal. Coeliac screen and thyroid function tests were also normal.

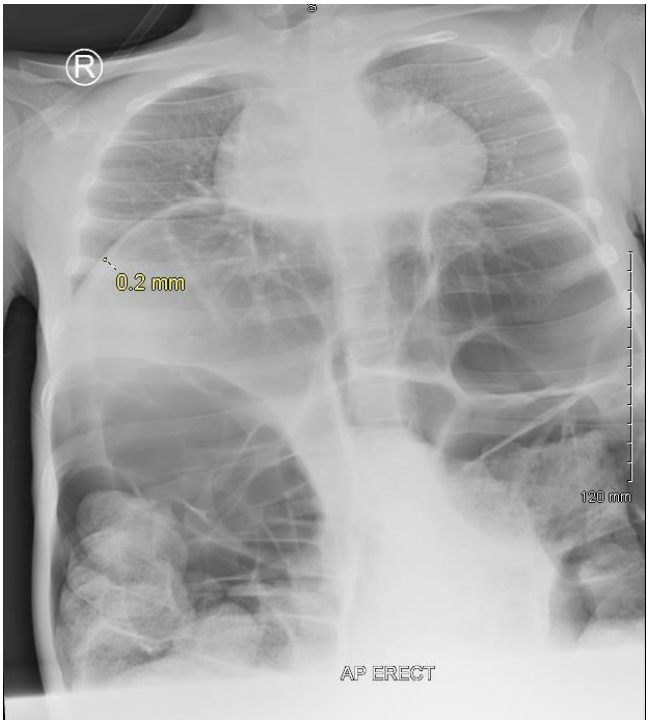

Figure 1: Chest and abdominal x-rays on day 1 of admission showing inadequate lung expansion. The distended loops of colon in the upper abdomen caused elevation of the diaphragm, consistent with splinting of the diaphragm.

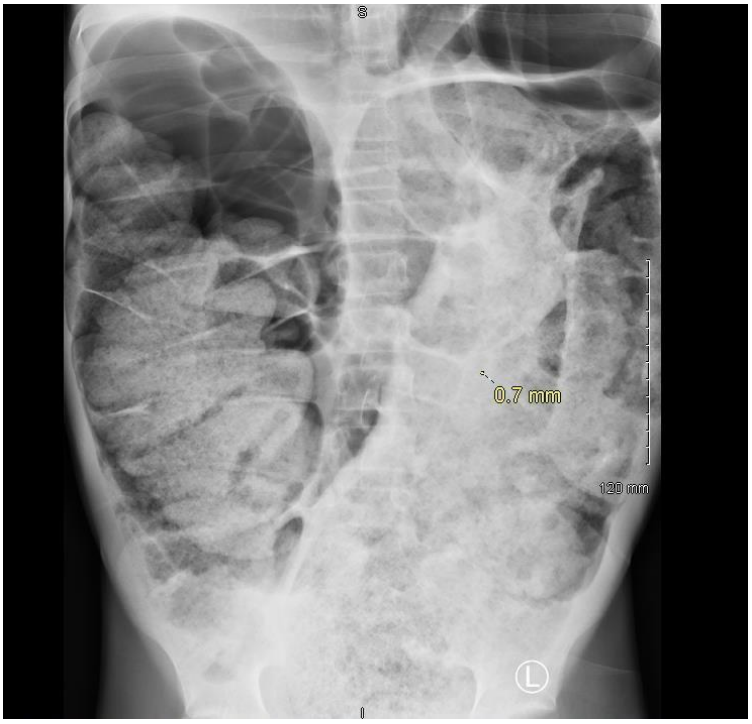

Figure 2: Abdominal x-ray on day 1 of admission showing marked faecal loading of the colon and rectum with marked dilatation of the large bowel.

His initial chest x-ray (Figure 1) and abdominal x-ray images (Figure 2) showed marked faecal loading of the colon and rectum with marked dilatation of the large bowel. The distended loops of colon in the upper abdomen caused elevation of the diaphragm, consistent with splinting of the diaphragm. The lungs showed inadequate expansion, however there was no major collapse or consolidation.

He initially received supplemental oxygen and an intravenous bolus of Normal saline for management of shock as he was pale and tachycardic then he was started on intravenous maintenance fluids. His heart rate started normalizing following the bolus.

He was appropriately started on laxatives.

He passed a large soft stool after which his abdominal girth was noted to decrease. He continued to pass semi solid stools during his admission with significant improvement of his symptoms.

Repeated x-ray images on day 3 of admission showed significant improvement in the aeration of the lung bases. There was marked interval reduction in the colonic dilatation in the upper abdomen since the previous x-ray despite the persistence of extensive faecal loading of the colon and rectum.

He was discharged home on day 6 of admission and advised to continue regular laxatives. He was reviewed 3 weeks later at the outpatient's department and had remained well, therefore the laxatives were weaned off gradually. His case was discussed with the social services due to his late presentation; the case was closed later on as there were no child protection or serious child welfare concerns.

Discussion

As depicted in our patient during his acute deterioration, the bowel dilation secondary to the faecal loading resulted in an increasing intra-abdominal pressure and compression of intra-abdominal vasculature. [1] [2]

Compression of the venous system leads to venous occlusion and a reduction in cardiac preload, while arterial compression leads to reduced arterial compliance and an increased afterload. The combined effects subsequently lead to a reduced cardiac output. The cardiac output may further be compromised by an increase in intra-thoracic pressure due to diaphragmatic splinting and elevation. This occurs through direct compression of the heart leading to reduction of the right and left ventricle end-diastolic volumes. [2]

Consequently, our patient presented as a case of shock, with pallor, tachycardia and respiratory distress. The child was initially appropriately treated as such with aggressive fluid resuscitation and oxygen supplementation.

The respiratory distress occurred secondary to the displacement of the hemi-diaphragms cephalad[3] , limiting alveolar gas filling and leading to a ventilation-perfusion mismatch. Radiologically, the colonic dilatation was appreciated, and the respiratory sequelae was recognized by his markedly elevated hemi-diaphragms [4] and inadequate lung expansion.

Despite extensive testing, a diagnosis of functional constipation still holds. Hirschsprung's disease was out ruled due to the age of presentation. [5] Furthermore, with close monitoring, the treating team was successful in reinstituting a healthy bowel regimen following his discharge. This rare case supports that aggressive treatment of constipation is imperative as neglecting long standing constipation can have serious implications. [6]

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to disclose.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P280

Advanced Merkel Cell Carcinoma in the Era of Immunotherapy

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Abstract

Introduction

Recent advances in our understanding of tumour immunology has led to new treatment options for patients with advanced Merkel cell carcinoma, a rare malignant skin cancer with a poor prognosis.

Cases

Case 1 – a 77-year-old man with pancreatic metastases from a Merkel cell carcinoma primary achieved a complete response with second line avelumab maintained for at least 36 months.
Case 2 – a 58-year-old man with metastatic Merkel cell carcinoma involving liver achieved a complete response with second line pembrolizumab sustained for at least 48 months.
Case 3 – a 57-year-old woman with extensive nodal metastases from a Merkel cell carcinoma primary did not respond to second line pembrolizumab and died.

Outcome

Three patients under our care with advanced Merkel cell carcinoma were treated with immunotherapy following traditional chemotherapy. Two patients with distant metastases to the pancreas and liver respectively achieved a sustained complete response of at least 36 months. One patient did not respond and died.

Conclusion

The treatment paradigm for advanced Merkel cell carcinoma has shifted dramatically with the advent of immunotherapy, the new standard of care in metastatic disease. These cases illustrate the dramatic responses that are possible but also underline the need for further research.

Introduction

Merkel-cell carcinoma (MCC) is a rare cutaneous malignancy arising from epidermal mechanoreceptors with an incidence of approximately 1 in 100,000, rising exponentially with age.[1] The majority of lesions arise on the head, neck or upper limb and may be misdiagnosed as a sebaceous cyst or lipoma. Rapidly growing, red-blue, fleshy lesions on sun-exposed skin (Figure 1), particularly in the elderly and/or immunosuppressed, should raise suspicion for MCC.[1] Whilst most cases are localized at diagnosis (65%), a minority present with distant disease (8%), conferring a poor prognosis with a 5-year overall survival of just 14%.[2]

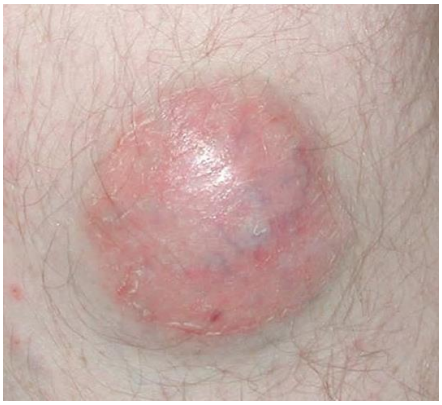

Figure 1. Merkel cell carcinoma (reproduced with permission from merkelcell.org)

The pathogenesis of MCC is associated with a double-stranded DNA polyoma virus (MCPyV) which can be isolated in about 80% of cases.[3] Although a constituent of the human skin microbiome, MCPyV can be incorporated into the tumour genome leading to the expression of several oncoproteins.[4,5] Elevated antibody titres to these oncoproteins may correlate with risk of recurrence and influence the intensity of surveillance.[6] In Ireland, testing for polyoma virus and antibodies is not routine. In viralnegative disease, ultraviolet radiation plays a prominent role in carcinogenesis leading to a high mutational burden. This is supported by several observations including the propensity of MCC to occur on sun exposed skin[1] and the correlation between regional incidence rates and UV solar index, with Australia possessing the highest rates worldwide.[7] Patients who are immunosuppressed due to B cell malignancies, organ transplantation or HIV infection are much more likely to be diagnosed with MCC.[8,9] Immunosuppression may facilitate greater replication of the polyoma virus and increase the likelihood of incorporation into the genome.

MCC is an aggressive cutaneous neuroendocrine tumour on the same histological spectrum as small cell lung cancer or high-grade neuroendocrine carcinomas and up until recently the preferred initial treatment option was chemotherapy with a combination of carboplatin and etoposide. Despite this approach outcomes in advanced disease are poor with a median progression-free survival of just 3 months and overall survival between 6-10 months.[10] However, the treatment paradigm has shifted radically in recent years with the emergence of immune checkpoint inhibitors, which have already proven effective in metastatic melanoma and cutaneous squamous cell carcinoma.[11,12]

The immune checkpoint refers to the receptor-ligand interaction between T lymphocytes and host cells that prevents autoimmunity. One such interaction involves the Programmed Death (PD) receptor on T cells and associated ligand (PDL1) expressed on host cells. Tumour cells can upregulate expression of PDL1 thereby suppressing immune-mediated destruction, but this camouflage can be lifted by inhibitors such as pembrolizumab, avelumab, and nivolumab. Herein we report our early experience in the treatment of advanced MCC with immunotherapy.

Case 1

A 77-year-old man presented with a painless lesion on his left upper lip. His past medical history included hypertension and smoking. There was no history of immunosuppression or autoimmunity, but he had significant sun-exposure having spent several months each year living in Spain. Excision biopsy was performed confirming a Stage I MCC (less than 2cm in maximum diameter). This was followed by adjuvant radiotherapy and workup did not reveal any evidence of local or distant metastases. Eight months later he represented with left sided cervical lymphadenopathy and a neck dissection was undertaken revealing a single 2.8cm deposit of MCC. Adjuvant radiotherapy was delivered. A year later surveillance imaging demonstrated a 5cm x 10cm mass in the pancreatic neck (Figure 2) with endoscopic ultrasound fine needle aspirate confirming a metastatic MCC deposit. There was associated retroperitoneal lymphadenopathy and low volume lung metastases. He underwent chemotherapy and although he could only complete two cycles of carboplatinetoposide due to Grade 4 fatigue, he achieved an excellent partial response. Based on a compassionate access programme, an anti-PDL1 antibody, avelumab (Bavencio^{TM}), was commenced for metastatic MCC. Of note the MCPyV status was not known. Within 3 months there was a complete radiological response (Figure 3) which has been maintained for at least 36 months with minimal adverse effects.

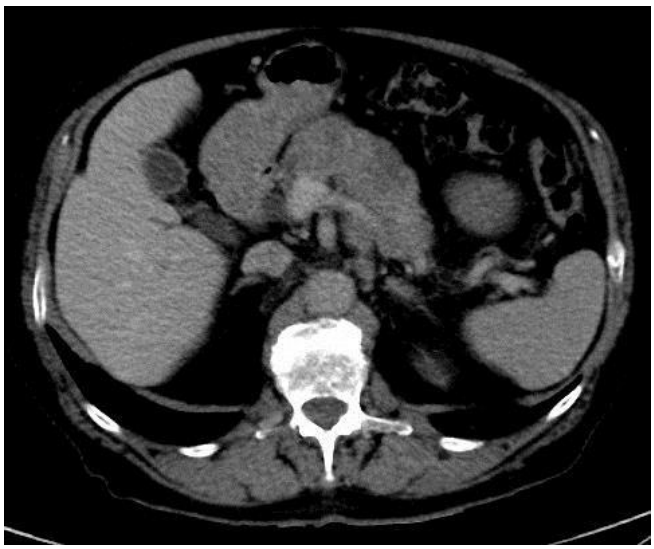

Figure 2. Pre-treatment axial CT-abdomen demonstrating the pancreatic mass.

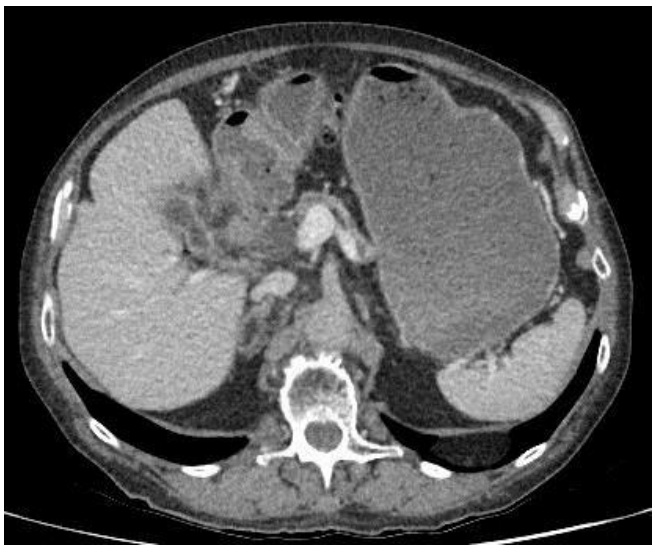

Figure 3. Complete response after 3 months of avelumab.

Case 2

A 58-year-old man with a background of psoriasis managed with an immunosuppressant biological agent, adalimumab, presented to his General Practitioner with a painless swelling on the dorsum of his left hand, growing over the preceding 3 months. The lesion was clinically diagnosed as a sebaceous cyst, but subsequent excision was difficult and therefore the patient was referred to a plastic surgeon for full excision. Immunohistochemical staining for synaptophysin, chromogranin and CK20 was positive confirming MCC. Imaging revealed pathological left-sided axillary lymphadenopathy and multiple liver metastases, biopsy of the latter confirmed Stage IV disease. Initial systemic treatment consisted of four cycles of chemotherapy with carboplatin and etoposide which induced a partial response. Based on emerging data supporting the role of immunotherapy in the metastatic setting, funding from the hospital was approved for the anti-PD1 antibody pembrolizumab (Keytruda^{TM}). Remarkably, the patient achieved a complete clinical and radiological response and completed 2 years of immunotherapy with no Grade 3 or 4 adverse events. Currently the patient remains off treatment with no measurable disease representing overall survival of at least 48 months.

Case 3

A 57-year-old woman with hypertension and monoclonal gammopathy of uncertain significance presented with painless left-sided groin swelling which had developed over a few months. Core biopsy of an inguinal lymph node established the diagnosis of advanced MCC. Staging with PET-CT confirmed Stage III disease with no distant metastases. Initially she received two cycles of carboplatin-etoposide with a partial response but within 1 month the adenopathy rapidly progressed requiring salvage radiotherapy. Subsequently pembrolizumab was commenced via a compassionate access programme, but further adenopathy developed in the retroperitoneum and left axilla therefore it was discontinued after 7 cycles. She underwent experimental electrochemotherapy in combination with pembrolizumab but there was no significant benefit. The patient died from progressive disease 18 months after the original diagnosis.

Discussion

This report describes our early experience treating advanced MCC, the management of which has been revolutionised in the last decade by the emergence of immunotherapy. The rationale for targeting the immune system in MCC is based on observations regarding its immunogenicity, namely its association with immunosuppression, UV radiation leading to mutational burden and the MCPyV.[1,3,5] Recent evidence suggests that a third of cases demonstrate a high mutational burden, a genetic state characterised by greater expression of neoantigens, thus providing more signals for an immune response.[13] However, although tumour mutational burden (TMB) and MPcyV status as well as PD-L1 expression have been shown to be associated with increased response rates, these have not been validated as predictive biomarkers and therefore were not assessed in our patients.

Randomised controlled trials are difficult to undertake in this disease given its rarity, but emerging data, albeit phase I/II trials, has shown significant durable activity in metastatic disease.

Immunotherapy with checkpoint inhibitors has recently been recommended as the standard of care in the US in the first line setting for advanced disease.[14]

Part A of the JAVELIN Merkel 200 study investigated avelumab in patients with metastatic MCC previously treated with chemotherapy.[15] In an exploratory analysis after 3 years of follow up the objective response rate was 33%, the median duration of response was 40.5 months and the 3 year survival rate was 32%. This resulted in FDA approval, the first in this context. In Part B of this trial patients who were treatment naïve received avelumab and an interim analysis has demonstrated a higher response rate of 62% and a median PFS of 9.1 months.[16] Our patient treated with avelumab had a complete and sustained response, which is even more remarkable because pancreatic metastases from MCC are typically fatal within 3-9 months.[17]

In the KEYNOTE-017 study, pembrolizumab was shown to produce a 56% response rate in chemotherapy naive patients with Stage IV MCC, independent of tumour PDL1 expression and MCPyV status.[18] The same study demonstrated an overall survival at 3 years of 64%, almost three times better than historical data with chemotherapy. Of the two patients we treated with pembrolizumab, one had a complete response and remains alive with no identifiable disease, whilst another had progression of disease and died. Although this is a small cohort of patients these vastly different outcomes reflect our incomplete understanding of tumour immunology in this aggressive disease.

There are also data to support the use of nivolumab in metastatic MCC. In the Checkmate 358 phase I/II trial, reported in abstract form, the response rates in treatment naïve patient were up to 73%.[19]

Initially, all three cases were treated in a conventional manner involving platinum-based chemotherapy before immunotherapy was commenced. It is possible that the two patients who achieved a significant response to chemotherapy could have experienced a sustained disease-free survival without the need for additional immunotherapy. However, this was considered highly unlikely as historically the median duration of complete response is just 6 months in metastatic disease.[10] Although chemotherapy is associated with a high response rate it is typically short-lived with median progression free survival of just 3 months.[10] Therefore the rationale to increase the likelihood of a durable response with the sequential addition of immunotherapy was strong and highly successful in two of the three cases achieving an overall survival of over 3 years.

Immune related adverse events have been well documented with immune checkpoint inhibitors, in particular in patients with pre-existing autoimmune conditions. None of our patients experienced any grade 3 or 4 adverse events from immunotherapy. One patient with psoriasis did notice increased activity of disease but this was managed effectively with topical treatment.

The correlation between immune-related toxicity and efficacy in metastatic melanoma has been reported with combination therapy, but there is no data to support this in metastatic MCC.[20] In the JAVELIN Merkel 200 study and the largest expanded access program (EAP) series the most common treatment related adverse effects of avelumab were infusion reaction, fatigue and rash, the majority

of which were grade II or less. However, the main toxicity of immunotherapy may prove to be financial.

Funding for immunotherapy in rare diseases such as MCC historically depended on philanthropy and compassionate access programmes. However, in 2019, avelumab was approved for reimbursement by the National Centre for Pharmacoeconomics (NCPE) for use in metastatic MCC after prior chemotherapy. Meanwhile, the FDA has approved avelumab in all settings for the treatment of metastatic MCC. The American National Comprehensive Cancer Network (NCCN) has recommended avelumab, pembrolizumab and nivolumab for the treatment of metastatic MCC and discouraged the use of systemic chemotherapy, unless there is a contraindication to immunotherapy or progression of disease after previous treatment with immunotherapy.[14]

Similarly to malignant melanoma, the potential of immunotherapy in the neoadjuvant and adjuvant management of MCC is also an exciting prospect. Recently, a phase I/II study demonstrated that just two doses of neoadjuvant nivolumab produced a pathological complete response in almost 50% of patients with resectable stage II-IV, regardless of PDL1, TMB and MCPyV status.[22] Clinical trials are ongoing to further evaluate these strategies but in the meantime there is sufficient evidence to recommend immunotherapy as a first line treatment in metastatic disease, offering hope to patients with an otherwise poor prognosis.

Declaration of Conflicts of Interest:

The authors have no conflicts of interest to declare.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P281

Poem

COVID-19: Welcome to the Vaccine

After a long wait…
in trouble and strait…
after all the times…,
pressing and tight…,
and the long path… in
the big plight…,
comes as good news..
a vaccine on the way…, will
be soon in use…
Let joy be released.., and
blessings perfuse..
Remember our loved ones
Let their souls rest.. now..
in repose…
and all who are alive…
defend their health cause..
What a big relief..!
Forgive my disbelief..!
Be just and fair….. Administer
it to everyone… vulnerable and at
the risk..
Knock at every door….
Remember all the poor…. from
every tongue..

What could be done… in
years and years…,
now in twelve months..!
Now is the time to live … in
peace... with no fears.. Yet,
keep up to the task…

Do not throw the mask..!

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Irish Medical Journal
Established 1867
Issue: Ir Med J; Vol 114; No. 2; P282

Obstetrics and Gynaecology Core Rotation Induction: Student Experience

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An orientation, or induction, session is meant to facilitate a student's learning experience, understanding of the program, and maximize social integration with students and faculty. Effective induction sessions have been shown to boost confidence, reduce anxiety, and improve the overall clinical experience of first-year medical students[1]. These results extend past medical education, as effective inductions have demonstrated success in the fields of forensics, psychiatry, post-graduate training, and high school[2,3,4]. In the field of post-graduate training, medical school graduates demonstrated decreased anxiety after undertaking a proper orientation program prior to beginning surgical training[3]. Although the benefits of a thorough and effective orientation may seem obvious, published research studies addressing the true value of induction is limited.

A pilot induction program was undertaken with students of the Royal College of Surgeons in Ireland (RCSI) on an obstetrics and gynaecology (OB/GYN) core rotation at Our Lady of Lourdes Hospital (OLOL) in Drogheda, Ireland. Students were from culturally diverse backgrounds, including North America, Europe, and the Middle East. The objective of this study was to identify gaps in student understanding of the goals of their OB/GYN rotation, with the aim of incorporating policy changes where deemed necessary.

A survey of subjective student experience of the day one OB/GYN rotation induction was collected from September 2019 to March 2020. The survey provided qualitatively assessed the level of agreement to a certain statement regarding: the timing, location, teaching, rotation goals, schedule and overall confidence. Answer choices ranged from *strongly agree* to *strongly disagree*. Students were also asked to leave comments where prompted.

The survey response rate was 93% (51/55). The induction timing and location facilities were deemed favourable by the majority of students surveyed (76-98%). Importantly, the teaching and content clarity was evaluated. Specifics about the rotation goals, daily schedule, and assessment schedule were less well received, with more students expressing a lack of understanding.

Although 75% (38/51) agreed or strongly agreed that goals and objectives were outlined in the session clearly, 69% (35/51) felt confident that they understood the goals of the rotation. The overall goal of the induction was to improve the confidence in students' ability to succeed in the rotation, of which over 76% (38/51) of students either agreed or strongly agreed.

On review of comments provided, some students reported that because they did not participate on the orientation day activities, they felt underprepared. The lack of ability to participate stemmed from a conflicting event scheduled. To avoid this outcome, necessary arrangements should be made to ensure that all students are able to attend the initial orientation before starting specific postings.

Student understanding of their education program is facilitated by an effective orientation[1,3]. Limited research regarding the true effectiveness and value of an induction day prompted this study to evaluate student self-confidence in their understanding of the rotation. Student feedback may be used to re-evaluate the structure of the program to facilitate quality improvement. Future studies should focus on the development and understanding of online learning methods.

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Irish Medical Journal
Established 1867
Issue: Ir Med J; Vol 114; No. 2; P283

Variant of Guillain-Barré Syndrome

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Dear Editor,

A 13-year-old previously healthy boy experienced an upper respiratory tract infection one week prior to his presentation, returning from a school trip to Paris.

On admission, neuro-ophthalmological examination revealed symmetrically mydriatic pupils, unresponsive to light and near stimuli. Accommodation was impaired. Ocular movements of both eyes were limited in all directions. Funduscopic examination revealed normal findings. Systemic neurological examination showed that the strength of the facial muscles as well as the upper and the lower limbs muscles was normal. Ataxic gait was present. Deep tendon reflexes were absent with bilateral flexor plantar responses. There was no evidence on history or examination of involvement of sensory, respiratory, and autonomic systems of sphincter functions. Nasal dysarthria was noted on examination.

Motor and sensory nerve conduction studies were within normal limits. The blink response testing was normal and suggested intact bilateral afferent trigeminal nerve and efferent facial nerve. The results of routine blood chemistry tests, anti-HSV, as well as a panel of serology tests of autoimmune disorders were unremarkable. PCR screen of peripheral blood for Meningococcal DNA was negative. The cerebrospinal fluid (CSF) analysis revealed clear CSF, normal pressure, and no blood cells, normal glucose and protein levels. CSF culture and PCR for possible organisms, such as bacteria, mycobacterium tuberculosis, herpes viruses, yielded negative results. Electrocardiogram and chest Xray were normal. CT brain and MRI brain and spine were normal. Stool analysis for *Campylobacter jejuni* was negative. CSF testing for anti-GQ1b and GM1 antibodies was negative.

Based on the clinical presentation Miller Fisher variant of Guillain-Barré Syndrome was the final diagnosis and intravenous immunoglobulin therapy was immediately initiated. The patient was treated with 0.4 g/kg/day IVIG over 5 days. The neurological symptoms dramatically resolved four days after the treatment. The patient was followed up in our outpatient clinic and one month after his hospitalisation he became symptom-free. During six months of observation no relapses were observed.

Miller Fisher syndrome is a rare, acquired nerve disease that is considered to be a variant of GuillainBarré syndrome. It is characterized by abnormal muscle coordination, paralysis of the eye muscles, and absence of the tendon reflexes. Symptoms may be preceded by a viral illness.

A distinctive feature of our patient was the absence of anti-GQ1b antibody. Up to 95% of the patients have anti-GQ1b antibodies during the acute phase of MFS, owing to the high specificity and sensitivity, these antibodies are useful to confirm the diagnosis; however, a negative result does not exclude the diagnosis.
Because of no difference in the treatment response between the patients with anti-GQ1b antibody positive and negative, IVIG was initiated immediately with a favourable outcome. We believe that very immediate initiation of IVIG, when only mild immunological injury to the axon occurs, can yield a favourable outcome.

In conclusion, in the case of acute bilateral mydriasis, associated with ophthalmoplegia, diplopia, areflexia and ataxia, which poses a diagnostic challenge to the clinician, the diagnosis of Miller Fisher syndrome should be considered even in the absence of CSF/serum anti-GQ1b antibody.

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Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P284

Trends in Antimicrobial Resistance in Children Admitted with *Escherichia coli* Urinary Tract Infections

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Urinary tract infections (UTI) are common in children, with *Escherichia coli* (*E.coli*) being the most common uropathogen. Current national guidelines recommend the empiric use of co-amoxiclav and gentamicin for hospitalised children over two months of age while urine culture and sensitivity is awaited[1]. Previous studies have demonstrated significant global variation in resistance rates though the overall prevalence of resistance is increasing[2]. As a broad-spectrum antibiotic, co-amoxiclav has become widely used both in hospitals and primary care settings to treat various infections including respiratory tract infections and UTIs. Up to 80% of antibiotics used in Europe are prescribed at primary care level[3] and co-amoxiclav is the most frequently prescribed antibiotic despite not being recommended as first line treatment for many community acquired infections[4]. The aim of this study was to identify the prevalence of antibiotic resistance in children admitted with UTI caused by *E.coli* and to assess the change in this prevalence over the past four years.

A retrospective chart review was conducted of all children admitted with UTI in 2015 and 2019. A UTI was defined as the presence of typical symptoms in a child with a pure growth of an organism with $>10^5$ colony forming units per milliliter on urine culture. Following 24-hour culture on chromogenic agar, organisms were identified in the laboratory using MALDITOF mass spectrometry. Automated susceptibility testing was performed using Vitek 2 (Biomerieux) and reported in line with European Committee Antimicrobial Susceptibility Testing guidelines.

The prevalence of resistance to commonly prescribed antibiotics increased over the four year study period in patients with UTI caused by *E.coli*. In 2015, *E.coli* was resistant to co-amoxiclav in 143/583 (24.5%) of samples. However, in 2019, the resistance rate had doubled, with resistance detected in 308 of 608 urinary isolates (50.1%).
Compared to 2015, in 2019 modest increases in resistance rates were seen in many other antibiotics including trimethoprim which increased from 164/593 (27.7%) to 172/607 (28.3%), ceftazidime increased from 15/594 (2.5%) to 33/608 (5.4%), ceftriaxone increased from 12/588 (2%) to 38/607 (6.3%), cefuroxime increased from 43/594 (7.2%) to 48/609 (7.9%), gentamicin increased from 19/594 (3.2%) to 28/609 (4.6%) and ciprofloxacin increased from 32/594 (5.4%) to 48/609 (7.9%).

E.coli causing UTI remains mostly susceptible to nitrofurantoin with resistance seen in just 3/594 (0.5%) and 2/607 (0.2%) of E. coli cultured from urinary tract specimens in 2015 and 2019 respectively. All isolates of *E.coli* causing UTI were found to be sensitive to meropenem in both 2015 and 2019.

This study highlights the importance of knowing local susceptibility data when prescribing antibiotics for children with UTI. Increasing prevalence of antibiotic resistance is common worldwide and Ireland is no exception. The doubling of resistance rates to co-amoxiclav is an area of particular concern as this is a component of current empiric antibiotic prescribing guidelines. Antimicrobial stewardship and appropriate prescribing of antibiotics remains vital in slowing the development of antimicrobial resistance. Local surveillance systems should be in place with regular review of data and guidelines by antimicrobial stewardship teams.

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Issue: Ir Med J; Vol 114; No. Irish Medical Journal Established 1867 *2; P285*

Improving Venous Thromboembolism (VTE) Prophylaxis in Tallaght Orthopaedics

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Dear Editor

A heightened risk of Venous Thromboembolism has long been associated with orthopaedic surgery. This holds true in both the trauma[1] and elective setting[2] and is due to a number of factors including immobilization with resultant stasis and the physiological insult of surgery with local tissue damage.[1]

A key focus of best practice guidelines is the prevention of venous thromboembolism. There is a gap between guideline recommendations and clinical practice and internationally adherence to these guidelines though improving, still leaves room for improvement.[3]

In Tallaght University Hospital we carried out a closed loop audit of venous thromboembolism prophylaxis within the Orthopaedic Department, to evaluate the department's performance on VTE prophylaxis and implement strategies and improve on the overall performance. The Tallaght Adult Medicines Guide VTE guidelines were used as our audit standard. These are derived from the 2018 NICE Guideline 89, the ACCP endorsed Padua Score and the National Medication Safety Improvement Programme's Preventing Clots in Hospitals Toolkit.

Cycle 1 consisted of a 2 day audit of orthopaedic inpatients in TUH on 2 separate timepoints in November and December 2019 consisting of 74 inpatients. Each patient's medical and nursing charts were examined to identify each patients reason for admission, VTE risk factors and contraindications to VTE prophylaxis. The patients Medication Kardex was then checked to see whether appropriate chemical and mechanical prophylaxis was prescribed. Finally each patient was examined to assess whether mechanical VTE prophylaxis was physically worn at that time.

Results of cycle 1 were then presented and discussed at a weekly orthopaedic education meeting. From this meeting a number of simple recommendations were made, including a re-emphasis on VTE prophylaxis, a focus on prescribing mechanical prophylaxis for those patients with contraindications to anticoagulation such as Spinal surgery patients. A Comprehensive flow sheet was also produced in collaboration with the consultants, and displayed prominently within the TUH Orthopaedic wards and offices, to act both as a guide and reminder.

Audit cycle was repeated in January 2020, 34 patients were included and results compared. In terms of appropriate chemical prophylaxis an improvement from 92% (68/74 incl 7/72 C/I) to 100% (34/34 incl 4/34 C/I) was observed. For mechanical prophylaxis, albeit from a lower base, appropriate prescribing improved 69%

(51/72 incl 3/72 C/I) to 78% (27/34 incl 4/34 C/I). Levels of application improved from 53% (38/71) to 70% (21/30).

Improvement in all areas of VTE prophylaxis between audit cycles was observed, with the excellent rate of appropriate chemical VTE prophylaxis. This study is relevant to other departments as it highlights the benefits of regular VTE prophylaxis re-education within hospitals.

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Issue: Ir Med J; Vol 114; No. 2; Irish Medical Journal Established 1867 *P286*

COVID-19: The Longest Ventilated Patient

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Dear Editor,

The case below is interesting in that it highlights the tiered escalation of treatment of a SARS-CoV 2 patient in the first wave of the pandemic in Ireland. Hopefully, through retrospective analysis of this case, some readers may learn valuable clinical insights, as at the time of writing we sit on the eve of an unprecedented surge in hospital cases.

A 76-year-old female presented with acute coronary syndrome. She became febrile 36 hours post admission but was otherwise asymptomatic. A SARS-CoV-2 swab was sent 2 days post presentation which returned positive. It was subsequently identified that she was a close contact of a COVID-19 community cluster and had been incubating the disease at presentation. Primary PCI was carried out 5 days after initial presentation. This was complicated by acute limb ischaemia, requiring left leg embolectomy and endarterectomy.

On day 9, the patient started to develop respiratory failure with increasing oxygen requirements and new ground glass opacities on chest imaging. Following further clinical deterioration, the patient met criteria for intubation and ventilation.

On day 18 with a significant rise in ferritin, the diagnosis of SARS-CoV-2 related secondary hemophagocytic lymphohistiocytosis (sHLH) was made. Tinzaparin, tocilizumab and steroids were commenced as per national recommendations. With persistent hypoxia the patient was began a proned ventilation regimen for 12hrs per day.

After 37 days on mechanical ventilation, percutaneous tracheostomy formation was carried out in the ICU setting. 79 days post intubation the patient was weaned off mechanical ventilation.

This case is interesting in terms of highlighting the multiple issues involved in caring for patients with SARS-CoV-2. It is understood that this patient may be the longest SARS-CoV-2 patient in Ireland successfully weaned from a ventilator.

VTE thromboprophylaxis in the SARS-CoV-2 patient, has received increasing attention of late, with evidence suggesting an underlying systemic endotheliitis driving the constellation of symptoms associated with SARS-CoV-2. It is speculated that SARS-CoV-2 infection was a precipitant of the initial coronary occlusion which caused the patient to present due to endothelial inflammation resulting in destabilisation of a pre-existing coronary plaque.

This patient developed a secondary hemophagocytic lymphohistiocytosis (sHLC). There are many recent studies examining the hyperinflammatory pathways associated with SARS-Cov-2 infection, including the RECOVERY trial.[1] This suggested patient who received dexamethasone 6mg once daily for up to 10 days had a reduced 28-day mortality if they required ventilation or oxygen therapy. (1) In the ventilated patient, ARDs becomes a hallmark of SARS-CoV-2 infection and proning has become the emerging trend.[2]

Interleukin-6 seems to play an important role in the SARS-CoV-2 inflammatory response. This is where treatment with tocilizumab comes into play. The inhibition of the IL-6 inflammatory pathway may continue to be of major significance with recent studies showing promising reductions in in-patient mortality for those treated with sarilumab vs. standard care.

In conclusion, this case demonstrates the multisystemic endothelial inflammatory response elicited by severe SARS-CoV-2 infection and the constellation of symptoms and complications that my present. Active surveillance and early recognition of these complications followed by early implementation of appropriate therapies aided the above patient to recover quite remarkably.

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Issue: Ir Med J; Vol 114; No. 2; P287

Irish Medical Journal
Established 1867

Letter in Response to Article "COVID-19: The First 100 Days in the South of Ireland"

Published in Issue: Ir Med J; Vol 113; No. 9; P185

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Dear Sir,

We are writing in response to the recent article "COVID-19: The First 100 Days in the South of Ireland" by Ní Bhuacalla, C et al.[1] This paper offers important insights into the initial COVID-19 experience in the South of Ireland and adds to our collective knowledge as a nation battling our biggest pandemic for 100 years. We wish to continue the discussion about the future potential challenges faced by the health service as we have found that the road to recovery for some healthcare workers (HCW) postacute COVID-19 infection can be long and arduous, irrespective of the initial severity of their acute COVID-19 infection.

It is widely reported that HCW have a higher overall incidence of COVID-19 infection[2] and are more vulnerable to contracting the virus than the general population given the nature of their work[3]. In our institution, it is apparent that the impact of the virus is unpredictable and can lead to significant functional limitations and restrictions to workload capacity. During the first wave, between March 13th and May 31st, 2020, 32% (1075) of staff were tested due to symptoms of COVID-19 and 35% (375) tested positive. The most common symptoms reported included fatigue, headache, cough, temperature and myalgia.

Some employers may have welcomed the updated return to work guidelines that stipulate a person may return to work after 10 days of isolation[4]. However, we would suggest that for a significant proportion of employees this may not be physically possible. We surveyed those who contracted Covid-19 illness during the first wave to review their progress. One hundred and seventy-three employees (46%) responded and 115 (67%) of those respondents experienced post-Covid symptoms beyond their 14-day isolation period, most commonly fatigue, cough and shortness of breath which resulted in reduced functional capacity upon returning to work. Thirty-eight (22%) continued to experience symptoms > 8 weeks after contracting COVID-19.

In total, 128 (62%) were unable to return to work following the 14-day isolation period and the average time to return to work post positive test was actually 30 days. At the time of writing, a number of staff members remain unable to return to their previous full clinical commitments or are simply unable to

return to work at all. The implications of these results are vast in terms of work force planning and the management of patient services in our increasingly strained health service.

Working in healthcare is challenging due to its many physical, mental and emotional demands. Transitioning back to this environment following illness is often optimally managed with the guidance and support of an occupational health and wellbeing department (OHWD). Their guidance can facilitate a graded return to work where appropriate, provide links to both physical and psychological support where needed and offer reassurance that employees are not alone in experiencing prolonged symptoms post infection.

Overall, we urge caution when returning employees to work post COVID-19 illness and to seek advice if unsure. It is imperative that strong support services are established to care for employees to enable them to care for their patients and one such support is the OHWD.

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