

Maternal sepsis: a 5-year single center review

C.A. McCormick¹, R. Gryson¹, S. Al Tikriti¹, M. Eogan¹, R.J. Drew².

1. Department of Obstetrics and Gynecology, Rotunda Hospital, Parnell Square E., Rotunda, Dublin 1, Ireland.
2. Clinical Innovation Unit, Rotunda Hospital, Rotunda Hospital, Parnell Square E., Rotunda, Dublin 1, Ireland.
3. Irish Meningitis and Sepsis Reference Laboratory, Children's Health Ireland (CHI) at Temple Street, Dublin 1, Ireland.
4. Department of Microbiology, Royal College of Surgeons in Ireland (RCSI), St. Stephen's Green, Dublin 2, Ireland.

Abstract

Aim

The aim of this study was to review cases and causes of maternal sepsis in a single tertiary unit over a five-year period (2018-2022).

Methods

Maternal sepsis cases were prospectively identified by the local surveillance. Data pertaining to each case was collected in an excel database accessed and analysed by the research team.

Results

41,887 women delivered babies weighing >500g during the study period. 82 women were recorded as having sepsis (0.2% or 1.96 per 1000 women). Of these, 32 cases (39%) occurred in the antenatal period, 19 (23%) were intrapartum and 31 (38%) occurred in the postnatal period. 11 (34%) of the antenatal cases had a diagnosis of pyelonephritis, with E.coli being the most frequently isolated organism (7). The majority (95, 18%) of intrapartum sepsis cases had chorioamnionitis. Postnatally the most common diagnosis was endometritis 14 (45%) followed by pyelonephritis 4 (13%). E.coli was isolated in 34 (41%) of sepsis cases overall.

Discussion

It is imperative that maternity services continue to focus on identification of cases, conditions and trends in order that appropriate staff and patient education and interventions can be encouraged and sustained to mitigate risk.

Introduction

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection¹. Between 2019 and 2021 sepsis was the fourth leading cause of direct maternal death in the UK and Ireland (excluding cases of COVID-19 infection). The mortality rate of sepsis secondary to pregnancy related infection has increased from 0.40 per 100,000 in 1985-87 to 0.73 per 100,000 maternities 2019-21.2

Locally the rate of clinically significant bacteraemia has been previously reported as 2.24 per 1000 live births (>500g)³. A second Dublin study from two other tertiary maternity hospitals reported a sepsis rate of 1.81 per 1000 pregnant women⁴. In these units maternal infection was most common in the postnatal period (47%), followed by intrapartum (36%) and less (17%) cases occurring in the antenatally. Both these studies only included women with positive microbiological cultures so likely underestimated the incidence of sepsis as it is now defined⁵. Interestingly the sepsis rate in our unit almost 100 years ago was not dissimilar to these rates at 2.8 per 1000 (but with a significantly higher mortality rate of 1.1 per 1000)⁶.

The aim of this study was to review cases of maternal sepsis over a five-year period (2018-2022), identify trends in aetiology/microbiology and consider potential areas to improve care and mitigate risk.

Methods

This was a retrospective review of sepsis cases in an urban stand-alone tertiary maternity center over a five year period between January 2018 and December 2022 inclusive. Maternal sepsis cases were identified by the local Sepsis Committee surveillance. Cases were identified by the Consultant Microbiologists, Infection Prevention and Control midwives or by the antibiotic pharmacists contemporaneously as part of their clinical service. The aim of this surveillance was to monitor sepsis rates and identify any significant trends. Data pertaining to each case was collected in a password protected excel database which was accessed only by this research team. Charts were reviewed to confirm classification of sepsis etiologies and ensure all gynecology cases were excluded from this particular analysis and the database was anonymized. Cases were defined as intrapartum if associated with symptoms of labor e.g. contractions or cervical change. Triggers for sepsis recognition were defined as per the Irish Sepsis Management Clinical Guideline 2021⁷. Data analysis was performed using chi square statistics on Microsoft excel 16.66.1. A p-value of <0.05 was considered statistically significant. Ethical approval was obtained from the hospital ethics committee (RAG-2002-030). Individual consent was not required as this was a retrospective non-interventional audit of existing data for quality improvement of patient care.

Results

There were 50,347 pregnancy episodes and 41,887 babies born weighing over 500g in our unit over the five year period. Eighty-two women were recorded as having sepsis (0.20% or 1.96/1000). The sepsis rate was 0.11% in 2018 and 0.27% in 2022.

Of these, 32 cases (39%) occurred in the antenatal period, 19 (23%) were intrapartum and 31 (38%) occurred in the postnatal period. There were no maternal deaths from sepsis during the study period.

The median age of women diagnosed in the antenatal period was 31 years (range 18-42). Their mean gestation was 26 weeks. Of the 32 women in the antenatal group 26 had live births. 15 women had an interval between sepsis and delivery, the mean interval was 13 weeks.

	Antenatal	Intrapartum	Postnatal	Total
Sepsis cases	32	19	31	82
Median age (years)	31	31	32	32
Age range	18-42	21-40	18-41	18-42
Mean gestation	26 (SD=7)	37 (SD=6)	N/A	N/A

Table 1: Demographics of sepsis cases

Of antenatal cases, 34% (n=11) had a diagnosis of pyelonephritis, with E. coli isolated in seven out of 11 cases. The second most common etiology of antenatal sepsis was respiratory viral infections (influenza/COVID-19) with 28% (n=9) of antenatal women with sepsis affected. The peak of viral infections in this study was in 2021.

Chorioamnionitis was diagnosed in 22% (n=7) of women with antenatal sepsis. All had preterm prelabour rupture of membranes (PPROM). Two had group B Streptococcus (GBS) isolated and five had E. coli positive cultures. In this subgroup there were two live births, three terminations of pregnancy in the interest of maternal health and two fetal demises (both mid trimester).

Overall, in the antenatal group 11 of 32 (34%) required inotropic support and were classified as having septic shock. Of those with PPRM who developed chorioamnionitis the rate of septic shock was higher (57%) than in the overall group.

Nineteen women had a diagnosis of intrapartum sepsis. The median age was 31 years (range 21-40). The etiology in the majority of these patients was chorioamnionitis (95%). There were three fetal losses (two pre-viability, one at term). Four women had a diagnosis of septic shock and required inotropes (21%).

The median age of women in the postnatal group was 32 years (range 18-41). The most common diagnosis was endometritis (45%) followed by pyelonephritis (13%) and viral infection (COVID-19/ influenza A or B) (13%). *E. coli* was isolated in 42% of all cases of postnatal sepsis. Only two women in this group (6%) required inotropic support and were diagnosed as having septic shock.

In total, over the five-year period studied 17 women required inotropic support (21%). A statistically significant ($p=0.024$) greater proportion of women had septic shock in the antenatal sepsis cohort (11/32) compared with the intrapartum (4/19) or postpartum group (2/31). Four pregnancies were delivered prior to viability or following intrauterine demise (two at 17 weeks, one at 19 weeks and one at 21 weeks gestation).

Sepsis screening tools such as the Modified Early Warning Score (MEWS) and systemic inflammatory response syndrome (SIRS) criteria, as outlined in the Maternity Sepsis Form HSE 20207, are widely used in healthcare settings to identify patients with sepsis 1. These scores identify triggers to promote a clinical response. The most common trigger for sepsis in this study was blood pressure (83% of cases triggered). The second most common trigger was respiratory (respiratory rate or oxygen saturations) (12%). No patient triggered based on liver function. Platelets, delirium, lactate and renal were less common triggers (10%, 6%, 2%, 1% respectively). 10 cases triggered on more than one criteria.

A significantly higher proportion of women in the intrapartum sepsis cohort met criteria for two sepsis triggers ($n=5$) compared with antenatal ($n=1$) or postpartum ($n=3$) cohorts ($p=0.036$).

Organism	Total	Antenatal			Intrapartum			Postnatal		
		Urinary tract	Genital tract	Other	Urinary tract	Genital tract	Other	Urinary tract	Genital tract	Other
<i>E. coli</i>	34	7	5			9		4	8	1
<i>COVID-19</i>	14			11			1			2
<i>GBS</i>	8		1			4			1	2
<i>Enterococcus</i>	4	1	1			1			1	
<i>Influenza</i>	3			1						2
<i>Streptococcus anginosus</i>	2		1						1	
<i>Morganella sp.</i>	2									2
Group A <i>streptococcus</i>	2								1	1
Group G <i>streptococcus</i>	1								1	
<i>Herpes simplex virus</i>	1			1						
<i>Enterobacter</i>	1									
<i>Klebsiella</i>	1	1							1	
Total	73	9	8	13	0	14	1	4	14	10

Table 2: Sepsis cases with confirmed organism isolated.

There were a total of 73 organisms identified in the 82 sepsis cases reviewed. Cases are listed by presumed source of infection and causative organism by trimester. Where two organisms were isolated, a case is listed twice. In 17 cases there were no significant organisms isolated.

Discussion

The rate of sepsis in this study, at 0.2% or 1.96/1000 women is similar to that previously reported (1.8 per 1000 pregnant women) in two other Dublin maternity hospitals⁴. There was a higher proportion of antenatal cases in our study compared with that previous study (39% vs 17% $p < 0.05$).

Additionally, bacteremia has previously been reported from another local tertiary center⁸. In this study over a four-year period 54 cases of bacteremia were reported giving a rate of 0.2%. Two women received a diagnosis of septic shock requiring admission to the Intensive

Care Unit. *E. coli* was the most common organism. Women who had sepsis antenatally most commonly had a urinary source whereas intrapartum and postnatal cases primarily had a genital source. These findings are similar to those of our study and a previously study in our unit which reported a clinically significant bacteremia rate of 2.24 per 1000 women between 2001 and 20143.

Of the 15 cases of pyelonephritis in our study population 11 had cultures positive for *E. Coli* (73%). A recent systematic review reported a 51% positive *E.coli* culture rate in maternal pyelonephritis cases⁹. The higher proportion of *E.coli* infection in our study population is interesting and deserving of further analysis.

E.coli was the most commonly isolated pathogen- 47% of culture positive cases. A previous study from our unit reported a lower rate of *E.coli* (37%) but higher Group B *Streptococcus* (GBS) (25% vs 11%) rate in blood culture positive patient samples³. This trend is concerning due to the potential for antimicrobial resistance. GBS is universally penicillin susceptible. However *E.coli* can develop antimicrobial resistance, potentially to multiple drugs¹⁰. This is most notably through the production of extended- spectrum beta lactamases (ESBL) enzymes leading to antimicrobial resistance. The incidence of these pathogens is increasing with 11.6% of invasive *E.coli* infections caused by ESBL producers in the Irish Health Protection and Surveillance Centre's 2018 annual report¹⁰.

Overall, the rate of sepsis appears to have increased over the study period, although similar to the most recent MBRACE metrics, this may be influenced by the fact that the study period was inclusive of the years of the COVID pandemic. In 2021 a significant proportion of women with sepsis tested positive for COVID-19 infection. It is notable that although the rate of respiratory viral infections decreased from 2021 to 2022, the rate of sepsis overall was higher in 2022 than any previous year. These trends should be considered in the wider context given the relatively small numbers in the setting of a standalone maternity hospital without an intensive care unit.

The National Sepsis Report 2020¹¹ demonstrates the stark difference between maternal sepsis and sepsis in the general medical and surgical populations. There were no maternal deaths from sepsis in pregnancy in 2019. In contrast in medical patients the rate was 19.1% and in surgical patients 24.5%. Baseline characteristics of these patients are different to maternity patients (age mid 70s and average of two comorbidities). The mortality rates in the group with septic shock was 37%. As already noted, there were no maternal deaths from sepsis in our unit during the study period, nevertheless the proportion of women with septic shock, particularly in the antenatal PPRM cohort, cannot be ignored. From the perspectives of both

maternal and fetal health it is vital to continue to develop, implement and evaluate clinical and laboratory strategies to identify the deteriorating patient to prompt responsive intervention in a timely fashion.

Increasingly the long-term adverse health outcomes following sepsis are being explored in the general adult population¹². While it is widely acknowledged that obstetric related sepsis carries acute risks for morbidity and mortality in both mother and baby, there is minimal literature on long term outcomes following maternal sepsis. Rates of severe maternal morbidity in Ireland have been stable at approximately 6 per 1000 since 2015¹³. Sepsis contributes to this morbidity and rates of ICU admission due to sepsis are monitored through the National Perinatal Epidemiology Centers Annual Report¹³. In 2022 3% of maternal ICU admissions were due to septic shock.

The difference between general hospital patients and maternity patients should also be considered in relation to physiological responses to sepsis. There are well described cardiovascular system alterations during pregnancy (increase in blood flow, blood volume, stroke volume, heart rate, decrease in systemic vascular resistance, oncotic pressure and blood pressure¹⁴). An awareness of these changes and a high clinical suspicion for sepsis are key to recognizing the deteriorating antenatal patient. In our study a higher proportion of women in the antenatal sepsis group required vasoactive supports (34% of antenatal cases vs 12% of intrapartum and postnatal groups combined). This may reflect the nature of their underlying sepsis pathology or could be a reflection of physiological changes of pregnancy, but it is an important trend to watch and also to include in sepsis education.

In conclusion approximately one in 511 women attending our unit had a prospectively recorded diagnosis of sepsis over this five-year study period, a period during which the rate of maternal sepsis increased, as did awareness of sepsis within maternity services and a time period during which the COVID-19 pandemic came and went. In contrast to previous studies from the same unit which identified the most common pathogens as *E. coli* and Group B *Streptococcus* we found *E. coli* and COVID-19 to be the leading causes of infection³. This variation highlights the importance of ongoing timely surveillance and responses, as well as the impact of pathogens and conditions which are not specifically caused by or related to pregnancy.

Declarations of Conflicts of Interest:

None declared.

Corresponding author:

C.A. McCormick,
Department of Obstetrics and Gynecology,
Rotunda Hospital,
Parnell Square E.,
Rotunda,
Dublin 1,
Ireland.

E-Mail: ciara1mcc1@gmail.com

References:

1. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Crit Care Med.* 11 01 2021;49(11):e1063-e1143. doi:10.1097/CCM.0000000000005337
2. Knight M, Bunch K, Felker A, Patel R, Kotnis R, Kenyon S, Kurinczuk JJ (Eds.) on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care Core Report - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2019-21. Oxford: National Perinatal Epidemiology Unit, University of Oxford 2023.
3. Drew RJ, Fonseca-Kelly Z, Eogan M. A Retrospective Audit of Clinically Significant Maternal Bacteraemia in a Specialist Maternity Hospital from 2001 to 2014. *Infect Dis Obstet Gynecol.* 2015;2015:518562. doi:10.1155/2015/518562
4. Knowles SJ, O'Sullivan NP, Meenan AM, Hanniffy R, Robson M. Maternal sepsis incidence, aetiology and outcome for mother and fetus: a prospective study. *BJOG.* Apr 2015;122(5):663-71. doi:10.1111/1471-0528.12892
5. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* Feb 23 2016;315(8):801-10. doi:10.1001/jama.2016.0287
6. Fitzgibbon G, Bigger JW. A CLINICAL AND BACTERIOLOGICAL INVESTIGATION OF PUERPERAL FEVER: IN THE ROTUNDA HOSPITAL, DUBLIN. *Br Med J.* Apr 25 1925;1(3356):773-4. doi:10.1136/bmj.1.3356.773
Health Do. Sepsis Management for Adults (including maternity)
National Clinical Guideline No. 26. 2021.
7. O'Higgins AC, Egan AF, Murphy OC, Fitzpatrick C, Sheehan SR, Turner MJ. A clinical review of maternal bacteremia. *Int J Gynaecol Obstet.* Mar 2014;124(3):226-9.

- doi:10.1016/j.ijgo.2013.08.023
8. Grette K, Cassity S, Holliday N, Rimawi BH. Acute pyelonephritis during pregnancy: a systematic review of the aetiology, timing, and reported adverse perinatal risks during pregnancy. *J Obstet Gynaecol.* Aug 2020;40(6):739-748.
doi:10.1080/01443615.2019.1647524
 9. Centre HHPs. Antimicrobial Resistance in Ireland 2018. In: HPSC DH, editor. 2019.
 10. Executive HS. National Sepsis Report 2020. 2020.
 11. Mostel Z, Perl A, Marck M, et al. Post-sepsis syndrome - an evolving entity that afflicts survivors of sepsis. *Mol Med.* 12 31 2019;26(1):6. doi:10.1186/s10020-019-0132-z 12.
 12. Nanda S, Nelson-Piercy C, Mackillop L. Cardiac disease in pregnancy. *Clin Med (Lond).* Dec 2012;12(6):553-60. doi:10.7861/clinmedicine.12-6-553.
 13. Leitao S, Manning E, Corcoran P, Keane J, McKernan J, Greene RA, on behalf of the Severe Maternal Morbidity Group. Severe Maternal Morbidity in Ireland Annual Report 2022. Cork: National Perinatal Epidemiology Centre, 2024
 14. Thompson MG, Kwong JC, Regan AK, et al. Influenza Vaccine Effectiveness in Preventing Influenza-associated Hospitalizations During Pregnancy: A Multi-country Retrospective Test Negative Design Study, 2010-2016. *Clin Infect Dis.* Apr 24 2019;68(9):1444-1453. doi:10.1093/cid/ciy73