

Prenatally Diagnosed Fetal Aneuploidy: Natural History and Subsequent Management

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Abstract

Aims

Our aim was to determine the number of cases of aneuploidy which were prenatally diagnosed in our tertiary referral unit from 2005-2015 and to analyse the subsequent outcomes of Trisomies 13, 18 and 21 (T13, T18 and T21).

Methods

This was a retrospective observational study. We firstly determined the total number of prenatally diagnosed aneuploidies. We then analysed their subsequent outcomes including average gestation at miscarriage or IUD, mode of delivery and neonatal outcome.

Results

402 cases of T13, T18 or T21 were identified of which 40% opted for expectant management. T18 was the most likely diagnosis to result in miscarriage, IUD or intrapartum death. The highest caesarean delivery rate was in T21.

Conclusion

With regards to T13 and T18, live birth rates show that some parents may achieve the goal of spending time with their baby in the immediate postpartum period. This information will act as a valuable resource in our counselling.

Introduction

The purpose of this study was to study the natural history and subsequent management of antenatally diagnosed aneuploidy in an Irish setting. We also wished to determine our own numbers of diagnoses and compile a resource to enable us to fully counsel our patients.

Prior to January 2018, expectant management was the only management course open to couples who did not desire, or were not in a position to travel abroad to the United Kingdom or elsewhere for termination of pregnancy for aneuploidy. Research from the United States of America would suggest that termination of pregnancy in the setting of aneuploidy can be as high as 81%¹. This study by Shaffer et al indicated that the type and severity of aneuploidy can be a contributory factor as to the likelihood of a woman opting for termination of pregnancy.

The Fetal Assessment Unit in the Rotunda hospital acts as a tertiary referral centre and the hospital cares for nearly ten thousand pregnant women per annum². Given the difficulties in accessing termination of pregnancy which Irish women have previously experienced and our busy fetal medicine service, we felt that we were in a unique position to examine both the natural history and subsequent management of prenatally diagnosed fetal aneuploidy.

Our objective was to examine the natural history of antenatally diagnosed aneuploidies and to specifically examine the outcomes of expectantly managed women with a diagnosis of Trisomy 13, Trisomy 18 and Trisomy 21.

Our aim was firstly to determine the number of diagnoses from our unit over a ten year period and secondly to create a resource to enable both our unit and units internationally to counsel couples as to potential outcomes should they wish to continue with a pregnancy following such a diagnosis.

Counselling after a prenatal diagnosis of aneuploidy is important to enable couples to make the correct decision for them and for their families^{3,4}.

In 2018, the Irish electorate voted to remove the eighth amendment from the constitution. Up to this point, termination of pregnancy was not legal in this jurisdiction, with the exception of intervention permitted in limited circumstances to save the life of the pregnant woman⁵.

The legislation and clinical pathways which have legalised termination of pregnancy in a broader range of circumstances have been written and the act was signed into law on 20th December 2018⁶.

Ireland is therefore in a unique position in an international context to examine the natural history and subsequent management of prenatally diagnosed aneuploidy when compared with jurisdictions where termination of pregnancy has heretofore been legalized.

Methods

This was a retrospective observational study. The Rotunda Hospital Fetal Assessment Unit has compiled a database of confirmed diagnoses of aneuploidies since 2005. We analysed this database from 2005-2015. As regards patient and public involvement, we did not specifically seek consent from the women involved in this review, however all cases were coded and anonymized. The database was anonymized, encrypted and stored in accordance with data protection law.

Firstly, we determined the number of the cases of confirmed aneuploidy. This comprised of women who had originally booked their pregnancies through our unit and women who had initially booked in a peripheral unit and were referred to our tertiary centre.

Secondly, we analysed their outcomes and categorised them into those who had opted for expectant management or those who had terminated their pregnancies

Finally, we analysed the outcomes specifically of those who had chosen expectant management after a diagnosis of Trisomy 13, Trisomy 18 or Trisomy 21. This clarified their mode of delivery if relevant or the timing of their miscarriage or intra-uterine fetal demise.

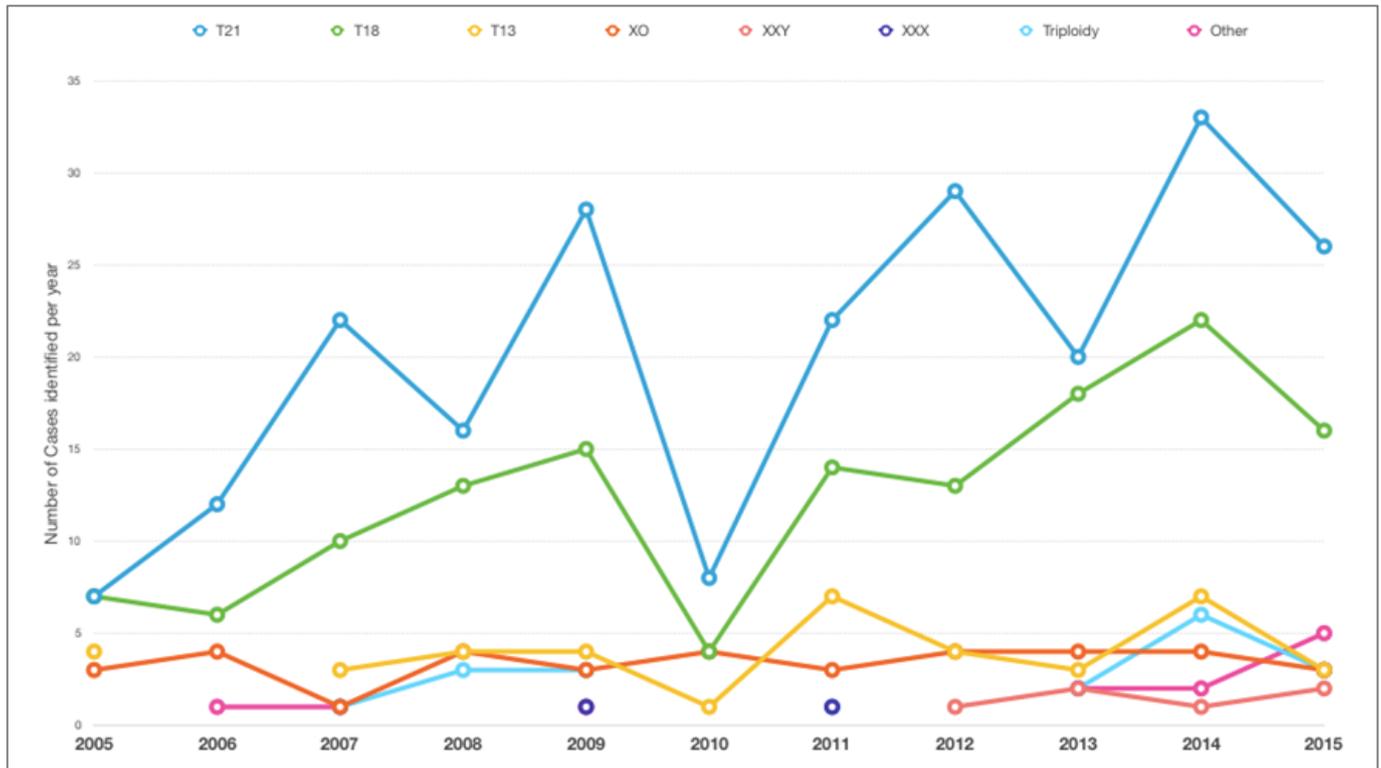
Patients were identified through the Fetal Assessment Unit database. Following same, their medical records were reviewed in order to clarify their outcomes.

All records were kept on site in the Rotunda hospital in compliance with GDPR and data was analysed using Microsoft Excel 2016. Approval was granted by the Rotunda Hospital Clinical Audit Committee.

Results

A total of 482 cases of fetal aneuploidy were diagnosed prenatally between 2005 and 2015 inclusively. This incorporated cases of Trisomy 21 (45.4%), Trisomy 18 (27.6%), Trisomy 13 (8%), Monosomy X (7.4%), Triploidy (3.8%) and others such as translocations (7.8%). The annual number of cases of each is depicted in Graph 1.

Graph 1. The number of cases of each chromosomal abnormality diagnosed from 2005-2015



402 cases were identified as Trisomy 21, Trisomy 18 or Trisomy 13. In total, 161 of 402 cases (40%) of these continued their pregnancies and were expectantly managed.

Trisomy 13

With respect to Trisomy 13, the rate of expectant management was 40% (n=16). As detailed in table 1, the incidence of miscarriage or intra-uterine death was 43.75% with average gestation of 25+3 wks at time of diagnosis of fetal loss. The live birth rate was 56.25% (n=9) (graph 2) with all reported cases ending in neonatal death (NND), ranging from 29 minutes to 12 days postpartum. The average gestation at delivery resulting in live birth was 35+4 weeks (248.6 days).

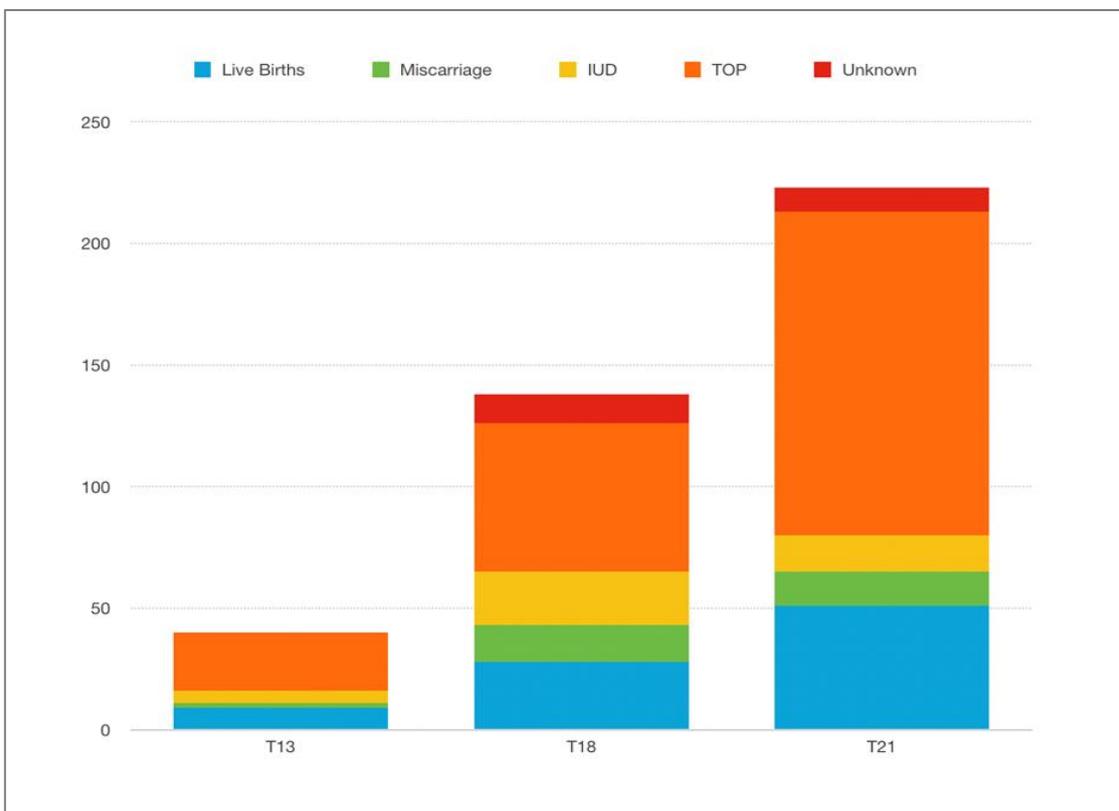
Table 1: Mode of delivery for patients who opted for expectant management and average gestation for miscarriage or intrauterine death (IUD)

Anomaly	Mode of Delivery	Average gestation for miscarriage (<24/40)	Average gestation for Intra-uterine Death (>24/40)
Trisomy 13 (n=16)	<u>Caesarean Section</u> 18.75% (n=3)	n=2 17 weeks 1 day	n=5 30 weeks 3 days
	<u>Live birth after vaginal delivery</u> 37.5% (n=6)		
	<u>Intrauterine Death/Miscarriage</u> 43.75% (n=7)		
Trisomy 18 (n=65)	<u>Caesarean Section</u> (n=9) 13.8%	n=15 15 weeks 1 day	n=22 33 weeks 4 days
	<u>Live birth after vaginal delivery</u> 29.2% (n=19)		
	<u>Intrauterine Death/Miscarriage</u> (n=37) 57%		
Trisomy 21 (n=80)	<u>Caesarean Section</u> 33.75% (n=27)	n=14 15 weeks 1 day	n=15 30 weeks 6 days
	<u>Live birth after vaginal delivery</u> 30% (n=24)		
	<u>Intrauterine Death/Miscarriage</u> 36.25% (n=29)		

Trisomy 18

50.8% (n=65) of Trisomy 18 cases diagnosed were expectantly managed. The incidence of miscarriage or IUD was 57% (n=37) (Table 1), while the rate of live birth was 43% (n=28) as depicted in Graph 2.

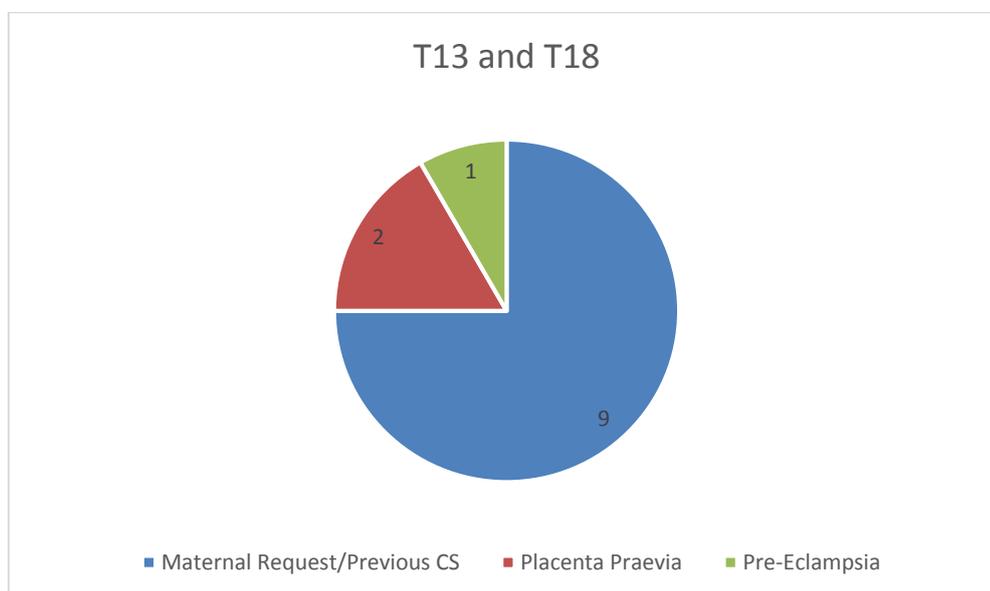
Graph 2: Documented outcomes in cases of T13, T18 and T21



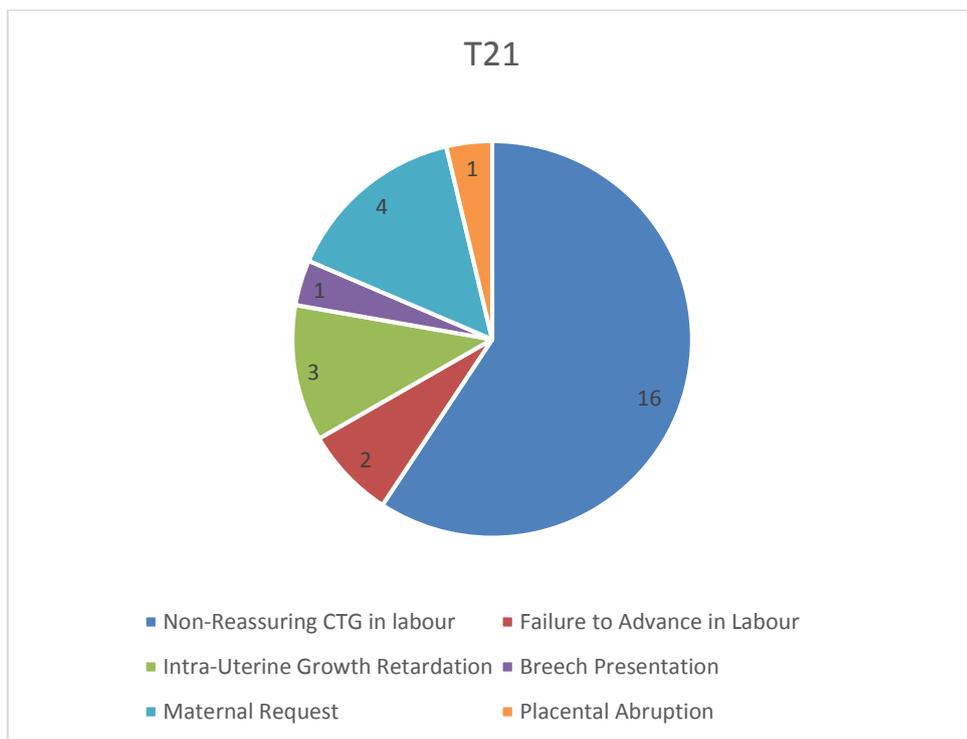
Trisomy 21

Finally, 35.9% (n=80) of Trisomy 21 cases were expectantly managed. The incidence of miscarriage or intra-uterine death (IUD) was 36.25% (n=29) as seen in Table 1. The live birth rate was 63.7% (n=51), which included 27 Caesarean sections. There were 5 documented cases of NND. Indications for Caesarean delivery are depicted in Graph 3(a) and 3(b).

Graph 3(a) Indication for Caesarean delivery in T13 and T18



Graph 3(b) Indication for Caesarean delivery in T21



Discussion

A review of this nature had not been done to date in our unit. We felt it was valuable to determine our numbers of antenatal diagnoses in order to better assist with resource planning and internal staff management. We have also determined the numbers of the patients who opted for expectant management or for termination of pregnancy. We are cognisant that these numbers may change in the future with the new legislation permitting termination of pregnancy in the case of fatal fetal anomaly. We have calculated the average age of fetal demise in the case of miscarriage or intrauterine fetal demise and this is a common query from our patients, which we are now better placed to address. This will enable our counselling after a diagnosis to be more succinct and accurate for our patients.

Furthermore, we have been able to quantify those who have had a live birth following a diagnosis of Trisomy 13, Trisomy 18 or Trisomy 21, and also their modes of delivery. Data collected regarding mode of delivery also holds significance as it can both help to inform patients of possible outcomes and reveals insight into documented existing co-morbidities in our patient cohort. For example, the main indications for Caesarean section in cases of Trisomy 13 or Trisomy 18 included antepartum haemorrhage, preterm prelabour rupture of membranes and pre-eclampsia, i.e. delivery for maternal indications. However in cases of Trisomy 21, indications such as breech presentation, unstable lie, absent end diastolic flow, gestational diabetes and maternal request were more commonly seen given the fact that Trisomy 21 is not a fatal anomaly.

We have confidence in the accuracy of our data presented given the fact that we have a large database compiled by the fetal assessment unit staff over a period of 10 years. We are also a large tertiary referral centre and as such, it is reasonable to assume that the findings for those who opt for expectant management may be reflected elsewhere and can act as a resource for clinicians and patients in peripheral units or international centres.

This review is limited to the patients of the Rotunda hospital only. Several patients included in this audit chose to continue their antenatal care in another tertiary centre and hence their outcomes are documented as unknown, significantly impeding data collection. A review of a nationally collated database would give a more reflective picture of management choices and outcomes, rather than being limited to the patients of one unit.

Our review has enabled us to collate a useful resource for women faced with a diagnosis of aneuploidy. In particular, it will be helpful in the decision making process for those considering expectant management as it may guide them as to the likelihood of experiencing a live birth or when a potential fetal demise may occur. Parents opting for

expectant management may do so in the hope of spending some time with their baby after delivery and this study has enabled us to counsel them more appropriately.

We think that a national database would be a useful addition and would encourage all units to prospectively gather their data in order that such a database can be collated.

In an international setting, clinicians may find this review of particular assistance. Due to the fact that termination of pregnancy has only recently been legalized, Ireland is in a unique position to compile a resource of this nature. Clinicians operating in countries where termination of pregnancy is a more routine decision following a diagnosis of aneuploidy may now be better equipped to fully counsel women who are considering expectant management as to their potential outcomes.

We aim to conduct a follow in study in one year's time to determine if there is any change in the management pathway that our patients choose in the event of a diagnosis of this nature.

Declaration of Conflicts of Interest:

The authors have no conflicts of interest to declare.

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