

Maternal and Fetal Outcomes of Triplet Gestation in a Tertiary Hospital in Oman

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نتائج الحمل ثلاثي التوائم في الأمهات والأجنة في مستشفى رعاية ثلاثي في سلطنة عمان

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ABSTRACT: Objectives: The aim of this study was to describe the fetal and maternal outcomes of triplet gestation and to report on the maternal characteristics of those pregnancies in a tertiary care centre in Oman. **Methods:** A retrospective study was undertaken of all triplet pregnancies delivered at Sultan Qaboos University Hospital, Muscat, Oman, between January 2009 and December 2011. **Results:** Over the three-year study period, there were 9,140 deliveries. Of these, there were 18 triplet pregnancies, giving a frequency of 0.2%. The mean gestational age at delivery was 31.0 ± 3.0 weeks, and the mean birth weight was $1,594 \pm 460$ g. The most common maternal complications were preterm labour in 13 pregnancies (72.2%), gestational diabetes in 7 (39%) and gestational hypertension in 5 (28%). Of the total deliveries, there were 54 neonates. Neonatal complications among these included hyaline membrane disease in 25 neonates (46%), hyperbilirubinaemia in 24 (43%), sepsis in 18 (33%) and anaemia in 8 (15%). The perinatal mortality rate was 55 per 1,000 births. **Conclusion:** The maternal and neonatal outcomes of triplet pregnancies were similar to those reported in other studies.

Keywords: Triplet Pregnancies; Morbidity; Perinatal Mortality; Fetus, complications; Preterm Births; Fertility; Oman.

الملخص: الهدف: هدفت هذه الدراسة إلى وصف نتائج الأمهات والأجنة للحمل ثلاثي التوائم وبيان الخصائص السريرية للأمهات في هذا النوع من الحمل في مستشفى رعاية ثلاثي في سلطنة عمان. **الطريقة:** هذه الدراسة الاستيعادية ضمت جميع حالات الحمل ثلاثية التوائم التي تمت ولادتها في مستشفى جامعة السلطان قابوس، مسقط، سلطنة عمان في الفترة ما بين يناير 2009 وديسمبر 2011. **النتائج:** خلال فترة الدراسة كان هناك 9,140 حالة ولادة. من تلك الحالات كانت هناك 18 ولادة ثلاثية التوائم بنسبة 0.2%. متوسط عمر الحمل عند الولادة كان 31.0 ± 3.0 اسبوع ومتوسط وزن الاطفال عند الولادة $1,594 \pm 460$ غ. أكثر المضاعفات شيوعا بين الامهات كانت الولادة المبكرة في 13 حمل (72.2%). سكري الحمل في 7 حالات (39%) وارتفاع ضغط الدم الحولي في 5 حالات (28%). شملت الدراسة 54 مولوداً. تضمنت المضاعفات عند هؤلاء المواليد مرض الغشاء الزجاجي في (46%) 25، اليرقان في (43%) 24، إنتان الدم في (33%) 18 وفقر الدم في (15%) 8 مواليد. بلغ معدل الوفاة في الفترة المحيطة بالولادة 55 لكل 1,000 ولادة. الخلاصة: نتائج دراستنا الخاصة بالأمهات والمواليد للحمل ثلاثي التوائم تماثل النتائج المنشورة في دراسات أخرى.

مفتاح الكلمات: الحمل ثلاثي التوائم؛ مرضية؛ معدل الوفاة في الفترة المحيطة بالولادة؛ جنين؛ مضاعفات؛ ولادة مبكرة؛ خصوبة؛ سلطنة عمان.

ADVANCES IN KNOWLEDGE

- This is one of the first studies in Oman on the prevalence of triplet pregnancies.
- This study also provides information on iatrogenic triplet pregnancies due to the use of fertility medications.

APPLICATION TO PATIENT CARE

- The results of this study will help in counselling couples on the neonatal outcomes of triplet pregnancies in Oman.

THE INCIDENCE OF TRIPLET AND HIGHER order multi-fetal gestation has risen several hundred percent since 1980, primarily due to the increasingly widespread availability of fertility therapies.¹ The natural incidence of spontaneous triplet pregnancy is approximately 1 in 6,000 to 8,000 births.² By comparison, triplet births accounted for

153.5 per 100,000 live births in 2009 in the USA, which is approximately 1 in 651 live births;¹ fewer than 20% of these were naturally conceived. In 2008, 15.5 per 1,000 women giving birth in England and Wales had multiple births compared with 9.8 per 1,000 in 1980. Up to 24% of successful *in vitro* fertilisation (IVF) procedures result in multiple pregnancies and

currently account for 3% of live births.³

Triplet pregnancies are associated with significantly increased risks of maternal and neonatal morbidity. These pregnancies have a significantly higher incidence and risk of diabetes, anaemia, amniotic fluid abnormalities, pregnancy-associated hypertension, eclampsia, incompetent cervix, antepartum haemorrhaging, the use of tocolytic drugs, Caesarean deliveries, placental abruption and placenta praevia. Overall maternal mortality associated with multiple births is 2.5 times the rate for single births.³ About 75–100% of triplets are born prematurely with an average gestational duration of 32 weeks.³ The overall stillbirth rate is 27.9 per 1,000 triplet births compared with 4.8 per 1,000 single births.³ Additional risks to the babies include intrauterine growth restriction with major congenital abnormalities; this is more common in multiple pregnancies (4.9%) than in singleton pregnancies.³

The present retrospective descriptive study was conducted to describe the fetal and maternal outcomes of triplet gestation and to report on the maternal characteristics of these pregnancies in a tertiary care centre in Muscat, Oman. It is hoped that the results of this study will assist in the future counselling of expectant couples regarding the outcomes of triplet pregnancies in this setting.

Methods

Sultan Qaboos University Hospital (SQUH) is one of three centres in Oman that provides tertiary maternity and neonatal care. Data were collected on all triplet pregnancies managed at SQUH from January 2009 to December 2011; they were gathered from the hospital information system, the labour ward registry and the Neonatal Unit records. All patients with triplet pregnancies who were followed-up antenatally and delivered in SQUH were included. Unless indications called for admittance, all patients were followed-up on an outpatient basis until almost their third trimester.

In women with regular periods, gestational age was calculated from the date of their last menstrual period if they were certain of this date. In cases of ovulation induction, the age was calculated by the known treatment dates and in patients who had undergone IVF by the date of embryo transfer. All of these calculations were complemented by early ultrasound dating in the first trimester.⁴ First trimester scans were performed to determine chorionicity and second trimester scans were used to identify anomalies. Serial growth scans and cervical length assessments by transvaginal ultrasounds were also

performed. Cervical cerclage was performed where indicated in patients with a short cervix (<2.5 cm) or a history suggestive of cervical incompetence. In some patients, a prophylactic cerclage was performed in the centres where they had received assisted reproductive technology (ART). Prophylactic steroid administration at 24–28 gestational weeks and admission for bed rest in the third trimester was offered to all patients, with an elective Caesarean section at 36–37 gestational weeks. In cases where there was a clinical indication of a fetal or maternal condition, an early delivery was planned. The total hospital stay was calculated from the date of admission to the date of discharge, including any antenatal and postnatal inpatient stays. The number of days spent immediately following the birth of a neonate was determined to be the neonatal hospital stay.⁴

In order to identify clinically relevant maternal and neonatal complications of triplet gestation, the following definitions were utilised.⁴ Preterm labour was defined as progressive cervical dilatation combined with uterine contractions at <37 weeks' gestation.⁴ Pre-eclampsia was defined according to National Institute for Health and Clinical Excellence (NICE) guidelines.^{5,6} The cut-off value to label a patient as anaemic was a haemoglobin level of less than 10.5 g/dL. Women were diagnosed with gestational diabetes mellitus (GDM) by glucose tolerance testing according to the Royal College of Obstetricians & Gynaecologists and NICE guidelines.³ A maternal temperature of 38 °C or more, persisting for more than 24 hours post-partum and requiring investigation and/or treatment was considered as febrile morbidity.⁴ Blood loss of more than 500 mL during vaginal delivery and more than 1,000 mL during Caesarean section was defined as post-partum haemorrhage.⁴

All neonates born were initially assessed by neonatologists; the ones requiring care were admitted to the Neonatal Intensive Care Unit (NICU) for further appropriate evaluation and management. Chest radiography was the investigation of choice by the neonatologists in the diagnoses of hyaline membrane disease and chronic lung disease. Transient tachypnoea of the newborn was defined as respiratory distress lasting <24 hours, after hyaline membrane disease had been ruled out by chest X-ray.⁴ The assessment and grading of intraventricular haemorrhage was done by a cranial ultrasound examination of the neonate. Sepsis was suspected on the basis of a clinical deterioration combined with either a raised C-reactive protein or an abnormal immature white cell count.⁴ Subsequently, sepsis was confirmed on the basis of the above investigations as well as positive cultures from wound swabs/fluids from otherwise sterile sites.⁴

Table 1: Frequency of triplet pregnancies by year

Year	Total deliveries	Triplets n (%)
2009	2,414	3 (0.12)
2010	3,396	7 (0.21)
2011	3,330	8 (0.24)

Necrotising enterocolitis (NEC) was diagnosed based on a clinical diagnosis by a neonatologist. If phototherapy was required, the neonate was labelled as having jaundice (hyperbilirubinaemia).⁴ If *patent ductus arteriosus* (PDA) was clinically significant and required either medical or surgical therapy, it was also added to the data.⁴ Retinopathy of prematurity was diagnosed and graded according to the standard international classifications^{7,8} by a paediatric ophthalmologist.⁴ A blood glucose level of less than 4 mmol/L requiring dextrose therapy was defined as hypoglycaemia and a body temperature of <36 °C was defined as hypothermia.

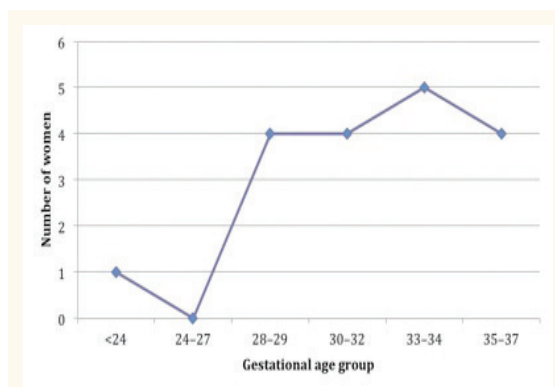
Descriptive statistics were undertaken using the Statistical Package for the Social Sciences (SPSS) Version 16.0 (IBM, Corp., Chicago, Illinois, USA). This study was approved by the College of Medicine Research & Ethics committees of Sultan Qaboos University, 4th November 2012 (ERC#625).

Results

From January 2009 to December 2011, 18 sets of triplets over 20 weeks' gestation were delivered at SQUH. The frequency of triplet pregnancy was 0.2% (18 triplets out of 9,140 total deliveries) [Table 1]. The gestational age at delivery varied from <24 weeks to 37 weeks [Figure 1]. There was a significant association between triplet pregnancy and infertility and the increased use of ART and ovulation induction. Of the 18 sets of triplets, 33% (6/18) were conceived via IVE, 28% (5/18) were conceived using gonadotropin stimulation, follicle-stimulating hormone (FSH) and intrauterine insemination (IUI), 28% (5/18) with clomiphene and IUI and 11% (2/18) were the result of spontaneous conception.

The maternal characteristics of the subjects are shown in Table 2. The mean maternal age was 29 ± 6 years. Mean gravidity was 2 ± 1 and parity was 1 ± 1. The mean gestational age at delivery was 31.0 ± 3.0 weeks and the mean antenatal hospital stay was 27 ± 20 days.

The most common maternal prenatal complications were preterm labor (72.2%), GDM (39%) and gestational hypertension (28%) [Figure 2].

**Figure 1:** Gestational age group of the neonates at delivery.

Out of the 18 pregnancies, 16 mothers had at least one antenatal complication. Fourteen had emergency Caesarean deliveries due to preterm labour occurring much earlier than their previously planned elective Caesarean sections. Only three patients (16.6%) had elective Caesarean deliveries and one (5.5%) had a vaginal delivery because she presented with preterm labour at <23 weeks' gestation. All 18 mothers received antenatal steroids at a mean gestational age of 26 ± 2 weeks [Table 2].

Regarding postnatal maternal complications, five women (27%) required blood transfusions; two (11%) were due to post-partum haemorrhaging with blood losses in excess of 1,000 mL. Three of the five women had pre-existing antenatal anaemia which was aggravated by the blood loss during their Caesarean delivery. Post-partum febrile morbidity occurred in one woman (5.5%) which required an extended hospital stay and resulted in endometritis and wound infection. The mean postnatal hospital stay was 6 ± 3 days.

The neonatal outcomes of the triplet pregnancies are shown in Table 3. Among the 54 neonates, the mean birth weight was 1,594 ± 460 g and the mean weight at the time of discharge from the NICU was 1,715 ± 415 g. Fifty (90%) neonates were admitted to the NICU and 34 (63%) required surfactants. The mean neonatal hospital stay was 24 ± 10 days [Table 3]. There were 3 (5%) neonatal deaths and the perinatal mortality rate was 55 per 1,000. The neonates who had early neonatal death were delivered at <23 weeks' gestation. Antenatal counselling was given to the parents regarding the poor prognosis of survival at this gestational age.

Among the 54 neonates, neonatal complications included hyaline membrane disease in 25 babies (46%), hyperbilirubinaemia in 23 (43%), sepsis in 18 (33%), anaemia in 8 (15%), PDA/atrial septal defect in 5 [9%] and NEC in 2 (4%) [Figure 3].

Table 2: Maternal characteristics of the triplet pregnancies (N = 18)

Characteristic	Mean ± SD	n (%)
Age in years	29 ± 6	-
Gravidity	2 ± 1	-
Parity	1 ± 1	-
History of infertility	-	16 (88)
Duration of infertility in years	6 ± 4	-
Gestational age at first visit in years	18 ± 9	-
Cervical length at first visit in mm	34 ± 9	-
Cervical cerclage	-	11 (61)
Gestational age at cerclage in weeks	16 ± 3	-
Cervical length at cerclage in mm	23 ± 7	-
Gestational age at steroid administration in weeks	26 ± 2	-
Gestational age at admission in weeks	28 ± 4	-
Gestational age at delivery in weeks	31 ± 3	-
Mode of delivery		
Emergency Caesarean	-	14 (78)
Elective Caesarean	-	3 (16.6)
Vaginal delivery	-	1 (5.5)
Postoperative complications		
Post-partum haemorrhage	-	2 (11)
Fever	-	1 (5.5)
Total hospital stay in days	27 ± 20	-
Postoperative stay in days	6 ± 3	-

SD = standard deviation.

Discussion

The majority of the triplet pregnancies in this study were conceived as a result of ART. Preterm labour of <34 gestational weeks (13/18) was the most common antenatal complication (72.2%) noted in this study. The mean antenatal hospital stay was 27 ± 20 days, which is very similar to other reports where the average antenatal stay was approximately 11–42 days.^{9,10} In

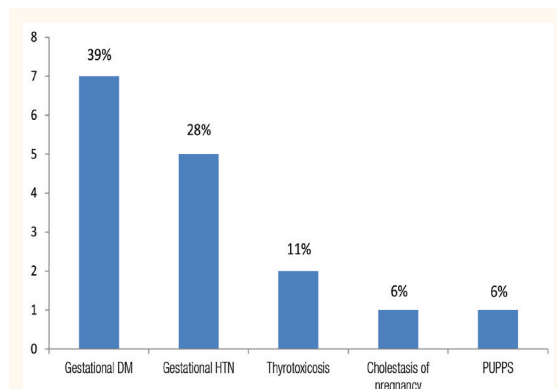


Figure 2: Maternal complications of the triplet pregnancies.

DM = diabetes mellitus; HTN = hypertension; PUPPS = pruritic urticarial papules and plaques of pregnancy.

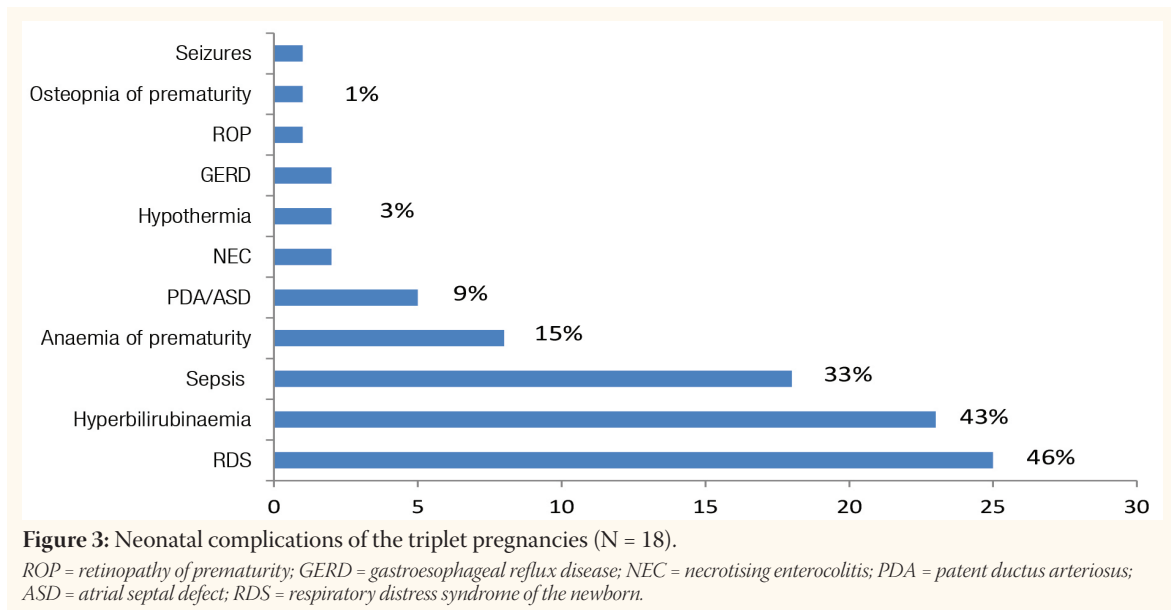
Table 3: Neonatal outcomes of the triplet pregnancies (N = 18)

Neonatal outcome	Mean ± SD	n (%)
Birth weight in g	1,594 ± 460	-
Gestational age in weeks	31 ± 3	-
Apgar score		
1 min	7 ± 2	-
5 mins	9 ± 1	-
Neonatal death	-	3 (5)
Intubation	-	40 (74)
Surfactant	-	34 (63)
NICU admission	-	50 (90)
Total NICU admission	24 ± 10	-
Weight at discharge in g	1,715 ± 415	-

SD = standard deviation; NICU = Neonatal Intensive Care Unit.

SQUH, routine antenatal admission for bed rest in the third trimester is offered despite the fact that retrospective analyses have not clearly demonstrated the benefit of bed rest for the prevention of preterm delivery. However, in a study of 20 triplet pregnancies, women with restricted activity delivered at a later mean gestational age than women with unrestricted activity (34.3 and 31.3 weeks, respectively).¹¹ Furthermore, a randomised prospective study of 19 triplet gestations compared inpatient bed rest after 24 gestational weeks with outpatient management. Bed rest was associated with an additional week's pregnancy duration, reduced frequency of pre-eclampsia (9% versus 31%) and a lower rate of neonatal intraventricular haemorrhage (1% versus 10%).¹² Similar findings were noted in non-randomised studies.¹³

The mean cervical length of women with triplet pregnancies is reported to be less than that of women with singleton pregnancies.¹⁴ In one study, women with triplet pregnancies delivering prior to 33 gestational weeks had shorter cervixes at 28, 30 and 32 weeks than those delivering after 33 weeks.¹⁴ The policy at SQUH during the present study was to monitor cervical length by ultrasound; when cervical length was found to be less than 25 mm (11/18), cervical cerclage was performed to reduce the risk of pregnancy loss and preterm labour. The mean gestational age for the cervical cerclage procedure was 16 weeks. In this study, five emergency cervical cerclages were performed. Six women had had prophylactic cerclage performed by the centres where they had received ART. The effectiveness of prophylactic cerclage is unproven, despite at least one small series suggesting efficacy.¹³ The largest study addressing this issue used a national database to compare the outcome of triplet pregnancies with cerclage (n = 248) to those without cerclage (n = 3,030).¹⁵ Both groups had similar rates of



preterm birth at <28 and <32 weeks, respectively.

Available evidence suggests that the effects of glucocorticoids on respiratory distress syndrome are influenced by plurality, with increasing plurality associated with a decreasing effect of the steroids. In a study of 906 triplet infants, 2,460 twin infants and 4,754 singletons, the odds ratios for respiratory distress syndrome among infants who received a complete course of antenatal steroids compared with singletons were 1.4 and 1.8 for twins and triplets, respectively.¹⁶ While these findings suggest that the appropriate dose of steroids might be higher in triplets than singletons, there are no data evaluating the efficacy of higher doses in multi-fetal gestations. Furthermore, in another study, plurality did not appear to influence the effect of glucocorticoids on the risk of intraventricular haemorrhage.¹⁷

It has been observed that the administration of one course of glucocorticoids is most helpful for fetuses who are delivering in the 28–32 gestational week window.^{4,16,17} In the current study, the mean gestational age for prophylactic steroid administration was 26 ± 2 weeks, although there were three sets of triplets who received steroids at less than 26 gestational weeks as they were preterm.

The most common maternal complications were GDM (39%) and gestational hypertension (28%). The results of the current study show that the prevalence of GDM appears to be increased in triplet compared to singleton pregnancies, although this has not been a consistent finding in all studies.^{18,19} In the current study, seven women developed GDM; five were managed using diet control and exercise and two required insulin for glycaemic control. The prevalence of pregnancy-associated hypertension is significantly

increased in triplets compared to singletons (adjusted odds ratio of 2.8).¹⁹ Five women in the current study developed gestational hypertension.

Pre-eclampsia complicates 20–46% of triplet pregnancies compared to 5% of singleton pregnancies.^{13,20–22} Pre-eclampsia occurs earlier and is more severe in multi-fetal gestations and the HELLP syndrome (haemolysis, elevated liver enzymes and low platelet count) is also more likely. Fortunately, no patients in the current study developed pre-eclampsia.

In the current study, 17 sets of triplets (94.6%) were delivered by lower segment Caesarean section; of these, 14 (78%) were by emergency lower segment Caesarean section and 3 (16%) were by elective Caesarean section. One woman (5.4%) spontaneously delivered vaginally because she presented in preterm labour at >23 weeks' gestation. This shows that the Caesarean section was the recommended mode of delivery in this tertiary centre for triplets.⁴ Lipitz *et al.* reported increased perinatal morbidity—in particular low Apgar scores—as well as asphyxia and respiratory complications among vaginally-delivered triplets;²³ however, such complications were rarely observed in studies where Caesarean sections were the chosen mode of delivery.⁸ A study from the Netherlands suggested that the safety of vaginal delivery is similar to that of Caesarean delivery.²⁴ However, there are no randomised controlled studies comparing the safety of Caesarean and vaginal deliveries. At present, there is no concrete evidence to justify changes in the existing practices regarding the mode of delivery for triplet pregnancies.

Post-partum haemorrhage was the most common complication in addition to post-partum pyrexia most probably due to endometritis in 5% of the women in

the current study, which was similar to reports from other studies.^{25,26}

The perinatal mortality rate in the current study was similar to that in the existing literature,²⁷ at 55 per 1,000 live births. The major reason for the high perinatal mortality rate was linked to the low birth weight and very low birth weight of the infants. The mean birth weight was $1,594 \pm 460$ g and the mean weight at discharge from the NICU was $1,715 \pm 415$ g.

The prevalence of chronic lung disease and retinopathy of prematurity for babies born at 28 gestational weeks or more were consistent with earlier reports.⁴ Although there are no reported rates of sepsis in the existing literature of triplet births, sepsis was the third major cause of neonatal morbidity in the current study, affecting 18 neonates (33%). It is a relevant and important finding, as sepsis is a known cause of death in very preterm infants. The outcomes for triplets born after 28 gestational weeks in SQUH were favourable.

It is hoped that these data will be useful for the counselling of couples planning to use ART and also in the management of women with triplet pregnancies. Additionally, this study highlights the maternal and fetal outcomes of this high-risk type of pregnancy under the current levels of obstetric and neonatal care. It will give some information to help care providers counsel patients based on their local data. However, this study is limited by its retrospective nature. The patients in the study were referred at different gestational ages from different centres. This means that they had received variable care before the referral, which makes it difficult to correlate the maternal and neonatal outcome with the care provided. Furthermore, the small sample size of the study and the fact that it is a single-centre experience makes it difficult to generalise the study outcomes to all triplets pregnancies in Oman.

Further research in the area of multi-fetal gestations and their outcomes is strongly recommended to improve the understanding of the outcomes of these pregnancies and standardise early obstetric care. This research should ideally take the form of a prospective study with a larger sample size.

Conclusion

The maternal and neonatal outcomes of triplet pregnancies in SQUH are similar to those reported in other studies. It is hoped that these results will reassure healthcare providers that their outcomes are in line with other international centres. It should also help to provide local information about maternal and neonatal outcomes of higher order births to those practitioners counselling couples planning assisted

reproduction and those counselling women with triplet pregnancies.

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