

Maternal and Early Perinatal Outcomes of Triplet Pregnancy: Study of 82 Triplets from a Single Perinatal Centre in South India

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Abstract

Objectives To study the recent trends in maternal and perinatal outcomes of triplet pregnancy from a perinatal centre in South India.

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Methods All triplet pregnancies booked at Fernandez hospital, Hyderabad (a tertiary care perinatal centre in South India), or those referred between 2000 and 2014 were included in the study. The maternal, fetal and neonatal outcome and any interventions like cerclage, steroid administration were studied.

Results There were 82 triplet deliveries over the study period of 15 years (82 per 69,584 live births). Most of them (78%) conceived with assistance and 83% of the triplets were trichorionic triamniotic. Anaemia and pregnancy induced hypertension were the commonest medical disorders (40.2 and 22%, respectively). Mean gestational age at delivery was 32 ± 2.8 weeks and 91% were delivered by caesarean section. Preterm labour and preterm pre-labour rupture of membranes were present in 29 and 15%, respectively. Antenatal steroids were administered in 87.8 and 53.7% had a cerclage. There were 20.7% growth restricted fetuses and 5.6% still births among the triplets. The mean birthweight among the live born neonates was 1.5 kg, and birthweight discordancy of >25% was seen in 14%. Among the live born neonates, 80% required admission to the neonatal intensive care unit, 11% had culture

positive sepsis, 3% had bronchopulmonary dysplasia, and 4% died during the hospital stay. None of them had periventricular leukomalacia or retinopathy requiring LASER. Mothers in the spontaneous conception group were younger and had more monozygotic triamniotic pregnancies than in the assisted conception groups (11.8 vs. 2.9%, $p = 0.001$). The incidence of PPROM was significantly more in the spontaneous conception group than in the ovulation induction, intrauterine insemination groups (29.4 vs. 2.9%, $p = 0.03$), we do not have an explanation for this. There was no difference in the other maternal, fetal or neonatal parameters based on the mode of conception.

Conclusion Though triplet pregnancies are encountered infrequently, obstetricians should be familiar with their management. Appropriate antenatal, perinatal care with neonatal support can result in optimal outcome.

Keywords Triplets · Maternal outcome · Fetal and neonatal outcome · Gestational age · Birthweight

Introduction

Multiple gestation has been increasing mainly due to increasing child bearing age and infertility treatment, though the rate has slowed down since 2005. Triplets in the USA peaked to 193.5 per 100,000 births in 1998 followed by a decrease to 153.4 per 100,000 by 2009 [1]. This slowdown is attributed to advances in infertility treatment. Regulations in embryo transfer and option of fetal reduction have resulted in less incidence of higher order multiples.

Triplet pregnancy is associated with increasing maternal and perinatal morbidity and mortality. Triplets when compared to twins have more of diabetes, anaemia, amniotic fluid abnormalities, hypertension, eclampsia, antepartum haemorrhage, preterm pre-labour rupture of membranes and caesarean delivery. There are perinatal complications like still birth, intrauterine growth restriction, twin to twin transfusion syndrome (TTTS), pre-maturity and its consequences like sepsis and long-term outcomes like cerebral palsy. Apart from this, the parents also face social, financial and psychological problems.

There are a number of studies on the outcome of twins but very few on the outcome of triplets. As we come across more number of triplets than other higher order multiples, more studies are needed here. The protocols and practices in surveillance and management of triplets have changed over the years. Available studies are not recent and have small numbers. An analysis on the outcomes in triplet pregnancies is useful to plan and to review the current practices in the management of triplet pregnancies. It is also essential to counsel the couples with triplet pregnancies.

Materials and Methods

In this retrospective observational study, all triplet pregnancies booked at and referred to Fernandez hospital between January 2000 and December 2014 were included.

The data were collected from the hospital database. All pregnant women diagnosed to have triplet pregnancy attended the multiple pregnancy clinic. Maternal monitoring included blood pressure, screening for gestational diabetes, haemoglobin every trimester. Fetal monitoring was done with serial ultrasound—early pregnancy scan between 8–10 weeks, 11–13⁺⁶ weeks scan, anomaly scan, growth scan 2–3 weekly from 26 weeks. Chorionicity was determined between 10 and 14 weeks. All the mothers were administered iron and calcium tablets from 16 weeks.

Pre-eclampsia or gestational hypertension was diagnosed according to Working Group on the National High Blood Pressure Education Program criteria. Gestational diabetes was diagnosed as per IADPSG criteria. Anaemia was diagnosed if the haemoglobin level was less than 11 g/dl. Anaemia was classified based on the ICMR criteria.

Cervical length screening was done at 16 and 20 weeks, if the cervix was ≤ 25 mm, the couple was counselled about cerclage/progesterone support. Progesterone was administered for those not opting for cerclage. Prophylactic steroids were administered at 26–30 weeks and in the earlier years were administered to all mothers with triplet pregnancy.

The mothers were delivered by caesarean section between 32 and 34 weeks. Earlier, we used to wait till term for vaginal delivery. In situations like fetal growth restriction and with preterm pre-labour rupture of membranes, timing of delivery was decided after discussing with the couple.

The criteria for neonatal intensive care unit (NICU) admission included birthweight less than 1800 g and gestation < 35 weeks or any symptomatic infant. All the neonates were managed as per the existing clinical protocols. The definitions of neonatal morbidities are uniform for the study infants.

Statistical analysis was done using SPSS 15. Frequencies and percentages and mean with standard deviation were used for various variables. Group comparisons were done between the various modes of conception. Categorical values were compared using Chi-square test and continuous variables with 't' test or Mann–Whitney test.

Maternal parameters like age, mode of conception, parity, cerclage, progesterone, complications such as anaemia, hypertensive disorders, gestational diabetes, antepartum haemorrhage, and post-partum haemorrhage and prevalence of medical disorders were noted. Preterm labour, preterm pre-labour rupture of membranes and mode of delivery were noted. Fetal parameters included chorionicity, fetal

reduction, miscarriage, anomalies, growth restriction and intrauterine fetal demise. Gestational age at delivery, 1' and 5' APGAR scores, birthweight, discordance, need for NICU admission, bronchopulmonary dysplasia, sepsis, periventricular leukomalacia and retinopathy of pre-maturity were the neonatal parameters. The study was approved by the institute review board of Fernandez Hospital.

Results

During the study period, a total of 69, 181 mothers delivered at our hospital. The incidence of triplet delivery was 82 per 69,584 live births (117 per 100,000 live births). Of the mothers who had triplet pregnancies, the mean maternal age was 27.3 ± 4.8 years. Mean maternal BMI was 25.73 ± 4.2 . Sixty-three (77%) pregnancies were booked at our hospital, and mean gestational age at booking was 17 ± 8.7 weeks. Fifty-nine (72%) were nulliparous. Seventeen had spontaneous conception, 35 ovulation induction or intrauterine insemination and 26 in vitro fertilisation (IVF). Majority (63) were trichorionic triamniotic (83%), 10 (13%) dichorionic triamniotic and 3 (4%) monochorionic triamniotic. Twelve percent ($n = 10$) of the women had pre-existing hypothyroidism, 12% had other medical disorders like asthma, epilepsy, thrombocytopenia, hypertension and supraventricular tachycardia. Two women had conceived with pre-existing diabetes mellitus (Table 1).

The most common complications were anaemia ($n = 34$, 40.2%, 1 severe degree), pregnancy induced hypertension ($n = 18$, 21.9%), gestational diabetes ($n = 13$, 15.8%), oligohydramnios ($n = 5$, 6.1%), polyhydramnios ($n = 5$, 6.1%) and antepartum haemorrhage ($n = 2$, 2.5%) (Table 2).

The foeto-maternal interventions included fetal reduction in 2, cerclage in 44, progesterone in 21 and antenatal steroids in 72 (Table 2).

The fetal complications included fetal anomalies in 4 (5%), miscarriages in 3, (4%), any fetal death in 11 (13%), growth restriction of any one fetus in 19 (23%) and foeto-fetal transfusion in 1. The anomalies included complex congenital heart disease, meningomyelocele, hydronephrosis, unilateral renal agenesis in one fetus each (Table 3).

Obstetric Outcome

Mean gestational age at delivery was 32 ± 2.8 weeks, 13 (16%) mothers delivered before 30 weeks, 31 (38%) delivered before 32 weeks and 51 (63%) delivered before 34 weeks. The mode of delivery was caesarean section in 75 (91%), and 46 (56.1%) had an emergency caesarean section. Five mothers had vaginal delivery (IUID of all 3 fetuses, gestational age <27 weeks ($n = 2$) and advanced

Table 1 Baseline characteristics

Variable	Percentage	
Maternal age	27.3 ± 4.8 years	
Mode of conception ($n = 78$)		
IVF	26	33.3
Ovulation induction + IUI	26 + 9 = 35	44.8
Spontaneous	17	21.7
Booked pregnancy	63	77.7
Gestational age at booking (mean + SD weeks)	17.0 ± 8.73	
Maternal BMI at booking	25.73 ± 4.2	
Nulliparous	59	71.9
Chorionicity ($n = 76$)		
TCTA	63	83
DCTA	10	13
MCTA	3	4
Pre-existing hypothyroidism	10	12
Pre-existing DM	2	2.4
Other pre-existing medical disorder	10	12

Table 2 Complications and interventions during pregnancy

Variable	Percentage	
Anaemia (Hb < 11 g/dl)	33	40.2
Severe anaemia (<7 g/dl)	1	1.2
Hypertensive disorder of pregnancy	18	22
Gestational hypertension	9	11
Pre-eclampsia	9	11
Eclampsia	1	1.2
HELLP	2	2.4
GDM on diet	9	11
GDM on insulin	4	4.9
Ante-partum haemorrhage	2	2.4
Fetal reduction	2	2.4
Cerclage	44	53.7
Progesterone	21	25.6
Oligohydramnios (SVP < 2 cm)	5	6
Polyhydramnios (SVP > 8 cm)	5	6
Antenatal steroids (complete)	72	87.8

labour at admission). Pregnancy was complicated by preterm pre-labour rupture of membranes in 12 (15%) and by preterm labour in 24 (29.2%) (Table 4). The incidence of post-partum haemorrhage was 8 (10%), wound infection 3 (4%) and 4 mothers required ICU stay (5%) for eclampsia, rectus sheath haematoma, tracheo-bronchitis and uterine artery rupture with massive haemoperitoneum (Table 4).

Table 3 Fetal complications of pregnancy

Variable		Percentage
Anomalies (any fetus)	4	4.8
Miscarriage	3	3.6
One fetal death	7	8.5
More than one fetal death	4	4.9
IUGR of any one fetus	19	23
IUGR of more than one fetus	10	12
Feto-fetal transfusion	1	1.2

Table 4 Perinatal complications

Variable		Percentage
Gestational age at delivery (weeks)	32 ± 2.8	
Pre-labour rupture of membranes	12	14.6
Chorioamnionitis	0	0
Preterm labour	24	29.2
Elective C-section	29	35.4
Emergency C-section	46	56.1
Vaginal delivery	5	6.1
Asphyxia of any one fetus (5 min Apgar <3)	1	1.2
Asphyxia of more than one fetus (5 min Apgar <3)	0	0
Post-partum haemorrhage	8	9.8
Wound infection	3	3.7
Maternal ICU admission	4	4.8
IUFD of any fetus	11	13
Miscarriage of any fetus	3	3.6

Neonatal Outcomes

Of the 82 pregnancies, 225 newborns were born alive, there were 5 miscarriages and 16 intrauterine fetal deaths. Discordancy in birthweight of 20% was seen in 18 and 25% discordancy in 14%. Among the live borns ($n = 225$), mean gestation and mean birthweight were 32.3 ± 2.6 weeks and 1.51 ± 0.42 kg. Fourteen (6.2%), 15 (6.6%) and 64 (28%) newborns had a birthweight <750, 751–999 and <1500 g, respectively. Median APGAR score was 7 (7–8) and 8 (7–8) at 1 and 5 min, respectively. The proportion of newborns requiring NICU admission was 80% ($n=180$) of the 225 live births. Among the newborns admitted to the NICU, 25 newborns (11%) had culture positive sepsis, 6 (3%) had bronchopulmonary dysplasia, and nine (4%) died during the hospital stay. None of the study infants had periventricular leukomalacia or retinopathy (Table 5).

On comparing the maternal, fetal and neonatal outcomes across the 3 groups based on mode of conception, women who conceived spontaneously were younger compared to

Table 5 Overall neonatal outcomes ($n = 225$ live births)

Variable		Percentage
Gestational age (weeks)	32.32 ± 2.6	
Mean birthweight (kg)	1.51 ± 0.42	
<0.750	14	6.2
0.750–0.999	15	6.6
<1.5	64	28
Median 1 min Apgar (range)	7 (7–8)	
Median 5 min Apgar (range)	8 (7–8)	
Discordancy 20–25%	08	14% (>25% disc)
25–30%	06	
>30%	26	
NICU admission	180	80
Culture positive sepsis	25	11
Bronco pulmonary dysplasia	6	3
Neonatal mortality	09	4

those conceived by IVF probably because older women more readily resorted to IVF. Monochorionic triamniotic triplets were more after spontaneous conception than any artificial reproductive technique (11.8 vs. 2.9%, $p = 0.001$) as given in Table 6. The incidence of PPRM was significantly more in the spontaneous conception group. There was no significant difference between three groups in parity, chorionicity, booking status, medical co-morbidities, antenatal complications, interventions, gestational age at delivery, mode of delivery, fetal, neonatal outcomes like birthweight, NICU admission, sepsis and other neonatal complications, neonatal deaths or maternal post-natal complications.

Discussion

There are a few studies describing triplet pregnancies, but most of them are before the year 2000. Recently, there has been improvement in maternal and neonatal care especially in developing countries. Ours is a large single-centre study with recent data showing the outcome of triplet pregnancies in the current scenario.

The incidence of triplet deliveries was 117 per 100,000 live births. The incidence of triplets in the USA in 2009 was 153 per 100,000 births [1]. The lower incidence of triplets in our study may be due to controlled ovarian stimulation, regulations on the number of embryos transferred and availability of option of fetal reduction.

In our study, 78% of the triplet pregnancies were secondary to infertility treatment, which is comparable to other studies (55–94%) [2]. In 83% of the triplets, the chorionicity was TCTA and this is similar to other reports. The increased prevalence of conception after ovulation

Table 6 Maternal, fetal and neonatal parameters—comparison between spont and IVF conception

Variable	Spontaneous (n = 17)	IVF (n = 26)	p value
Primigravida	7 (41.2)	17 (65.4)	0.11
MCTA	2 (11.8)	0	
TCTA	10 (58.8)	22 (84.6)	0.08
DCTA	3 (17.6)	3 (11.5)	
Booked	12 (70.6)	21 (80.8)	0.47
Hypothyroid	1 (5.9)	5 (19.2)	0.51
Gestational hypertension	3 (17.6)	3 (11.5)	0.73
Pre-eclampsia	1 (5.9)	0	
Severe PE	0	2 (7.7)	0.18
GDMD	1 (5.8)	4 (15.4)	0.87
GDMI	0	1 (3.8)	0.87
Anaemia (mild)	0	6 (23.1)	0.21
Anaemia (moderate)	6 (35.3)	5 (19.2)	0.21
Anaemia (severe)	1 (5.9)	0	0.21
Anomalies	1 (5.9)	1 (3.8)	0.96
Cerclage	8 (47.1)	16 (61.5)	0.46
Progesterone	3 (17.6)	7 (26.9)	0.63
PPROM	5 (29.4)	6 (23.1)	0.66
Fetal reduction	0	0	
Any fetal death	4 (23.5)	1 (3.8)	0.17
Fetal growth restriction	10 (58.8)	8 (30.8)	0.105
Preterm labour	6 (35.3)	7 (26.9)	0.56
Steroids	15 (88.2)	23 (88.5)	1.00
Discordancy	8 (47.1)	15 (57.7)	0.58
Antepartum haemorrhage	1 (5.9)	0	
LSCS	16 (94.1)	23 (88.5)	0.75
Mean age	25.8 ± 3.16	31 ± 5.4	0.001
POG at booking	19.2 ± 10.5	17.5 ± 7.98	0.54
Gestation at delivery	32.17 ± 2.07	31.46 ± 3.43	0.45
PPH	2 (11.8)	3 (11.5)	0.91
Birthweight kg	1.48 ± 0.402	1.42 ± 0.44	0.49
Gestational age at delivery weeks	32.3 ± 2	31.8 ± 3	0.31
NND	2 (4.5)	4 (5.5)	0.9
Sepsis	4 (9.1)	13 (17.8)	0.9
BPD	0	5 (6.8)	0.28
NICU admission	39 (89)	58 (80)	0.25

induction or intrauterine insemination (45%) may explain the high incidence of TCTA (83%). In contrast, Mazhar et al. [3] reported 61% prevalence of dichorionic placenta. The mean maternal age of 27.3 ± 4.8 years is similar to Mazhar et al. [3], but other studies [3, 4] reported age 30 years or above. Younger women seeking assisted conception may explain this.

Anaemia and hypertension were the commonest maternal complications in most of the studies, though the

incidence of anaemia was higher in our study (40.2%) in comparison with the other studies (18–24%). This may be because most of these studies considered haemoglobin less than 10 g/dl as anaemia, whereas 11 g/dl was taken as cut-off in our study (WHO) and by Mazhar et al. [3]. The incidence of pre-eclampsia varied from 4 to 26% in various studies [2], and it was 11% in our study. Gestational diabetes incidence was 5–14% in other studies, and it was 16% in our study. Antepartum haemorrhage was only 2.4% in our study.

In 27 mothers (32%), antenatal corticosteroids were administered anticipating preterm delivery while in the remaining 45 mothers, steroids were administered prophylactically. In most of the other studies, prophylactic steroids or cerclage was not routine but in our set-up, since most of the patients stayed far from the hospital, steroids were administered prophylactically between 28 and 31 weeks. In our study, 7 mothers had cerclage for short cervix or funnelling and 37 had prophylactic cerclage (most of them had undergone cerclage before being referred to us). Among the rescue cerclage group, 5 delivered after 34 weeks, 2 mothers delivered before 28 weeks.

The incidence of preterm labour was 29.2%; it was 50–78% in various other studies [2, 3]. This difference may be due to the widespread use of progesterone in recent times. Although delivery was planned at 34 weeks, more than 60% delivered before 34 weeks and by caesarean section (for reasons like preterm labour, Doppler compromise, abruption and severe pre-eclampsia). Mean gestational age at delivery was 33 weeks in studies by Mahzar et al. [3] and 31 weeks in study by Al Sunaidi et al. [2], and in our study it was 32 weeks.

The occurrence of post-partum haemorrhage was 9.8% similar to the other studies (3–9%) [2]. In our study, 51 out of the 246 fetuses (20.7%) were growth restricted similar to others. There were 16 still births in our study (6.5%) which is comparable to the other studies (3–7%) [2, 3]. One mother had stillbirth of all 3 fetuses secondary to antepartum uterine artery rupture. The incidence of congenital anomalies was 4.8% like in other studies (2–8%) [2, 3].

The mean birthweight of the neonates was 1.51 kg in our study, 1.4 kg in the study by Al Sunaidi et al. [2] and 1.6 kg in the other studies [3, 5]. Among the live born babies in our study, 80% required NICU admission and 83% newborns required NICU admissions as reported by Al Sunaidi et al. [2], respectively, but it was only 57% in the study by Mazhar et al. [3]. Culture positive sepsis was present in 10.7% of the live born neonates which is similar to most studies [2, 3]. Eighteen percent of the neonates showed birthweight discordance >20%, 14% above 25%. In the study by Mazhar et al. [3], 27.8% showed >25% discordancy. In twin pregnancies, discordance >20%

ranges from 14 to 40% (16%) [6]. There is a disparity among various studies in describing the degree of discordance, some consider 20% as significant, whereas the recent recommendations consider 25%. There were no cases of severe intraventricular haemorrhage in our study as in other studies. There were no cases of retinopathy requiring LASER in our study. The incidence of bronchopulmonary dysplasia (3%) was comparable to other studies. The neonatal mortality in our study was 3.8%, and it was 11, 16.6% in the studies by Al Sunaidi et al. [2], Mazhar et al. [3], respectively.

When comparing the maternal and neonatal outcome among triplets conceived spontaneously, ovulation induction and IVF, monochorionic triamniotic pregnancies (MCTA) triplets were seen significantly more in the spontaneous conception group. The incidence of PPROM was significantly more in the spontaneous conception group; we do not have an explanation for this. Other maternal and neonatal parameters were similar irrespective of the mode of conception which is similar to the other studies [5–7].

Merits and Demerits

This is one of the large series from a developing country, and it reflects possible outcomes to help in decision-making as well as counselling of couples. It also reflects on how appropriate specialised obstetric and neonatal care can maximise maternal and perinatal outcomes. It can be said with reasonable certainty that assisted reproductive techniques do not increase most of the possible complications.

The limitation of this study was that it was a retrospective analysis and in about 5% of women, the mode of

conception could not be ascertained. To have an observational study of this magnitude prospectively, it will take several years, but it will be worthwhile.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interests.

Ethical Approval This is an analysis of records over 15 years, approved by the institute research board and ethical committee.

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