CAHIERS MAGELLANES-NS
Volume 06 Issue 1
2024

ISSN:1624-1940
DOI 10.6084/m9.figshare.26207009
http://magellanes.com/

MATERNAL AND NEONATAL OUTCOMES IN TRIPLET GESTATIONS IN TERTIARY CENTER, SAUDI ARABIA

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Abstract:
Background: There are many studies that showed that multiple pregnancy is associated with increased risk for both mother and neonate, however, little is known about the situation in Saudi Arabia. Main objectives: Assessment of the maternal risk factors of triplet pregnancy, assessment of maternal outcomes and assessment of fatal and neonatal outcomes. Secondary Objectives: 1-Dose ceserian section reduce fetal/neonatal morbidity and mortality. 2-Any difference in outcome of triplete of ART or spontenious pregnancy
Methodology: This is retrospective cohort study that was conducted at NGHA, KAMC Riyadh covering triplet pregnancy who received antenatal care in the period between 2016-2021. The data sheet included bibliographic data in form of age, body mass index. Another section is about general obstetric information, regarding gravidity, parity, number of abortions, family history of twins, ART, mode of delivery and gestational age at delivery. All data was stored at the principal investigator office and access of the data was limited to the member of the research; data analysis was done by using SPSS software version 26.
Results: In this study, we retrospectively collected data from 42 women with triplet pregnancies. The mean age of the women was 30.57 years old (SD=5.18). Preterm birth was the most common complication of multiple gestation with all 42 triplet pregnancies (100%) terminating in PTB. Considering fetal outcomes, miscarriage was found to occur in two cases (4.8 %) and fetal restriction was reported in three mothers (7.1 %). Moreover, the neonatal respiratory distress (RDS) was reported in 78.6 % of pregnancies occurred in 33 pregnancies and 73 infants (Prevalence was 57.9 % of total births). Furthermore, early neonatal death (ENND) was reported in infants of 23.8 % of pregnancies occurred in 15 infants (11.9 %).
Conclusion: Triplet pregnancies are associated with higher risk of maternal, neonatal and infant morbidities and mortality. More interest should be performed for pregnant women with triplet pregnancies.

Keywords: Triplet pregnancies, Pregnant women, Neonatal, Maternal.

Introduction:

During the last two decades, there has been a 400 % increase in the rate of higher-order multiple births [1]. Multiple gestation in women refers to their pregnancy in which mother carries two or more than

ISSN:1624-1940
DOI 10.6084/m9.figshare.26207009
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two fetuses in her womb [2]. Two important factors are found to be associated with this huge increase including increased maternal age at pregnancy which may be associated with increased rates of spontaneous multiple births as well as increasing widespread availability of medical assistance for conception including ovulation induction and assisted reproductive technologies (ART), and in vitro fertilization (IVF) [3-6].

There are many studies that showed that multiple pregnancy is associated with increased risk for both mother and neonate [7-10]. Pregnant women with multiple pregnancies are at higher risk of miscarriage, anemia, hemorrhage, postpartum illness, hypertensive disorders and need for operative deliveries [2]. Moreover, neonatal complications include bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), retinopathy prematurity (ROP), respiratory distress syndrome (RDS), chronic lung disease, pneumothorax, intraventricular hemorrhage, hydrocephalous, patent ductus arteriosus (PDA), and perinatal mortality. Preterm delivery with low birth weight are the most common complications associated with triplet pregnancy, with about 75 % to 100 % of the triplets being born prematurely [11]. Neonatal complications are mainly associated with prematurity and intrauterine growth restrictions where the higher preterm delivery rates in multiple pregnancies imply the increased need for specialist neonatal resources because women with multiple pregnancies require more care as well as additional calories and proteins, and increased ANC visits at hospitals during pregnancy because of the increased complications rate [12].

The combination of the increasing number of triplet pregnancies and the possibility of complications facilitated the requirements and relevance of the present study. In this study, we aimed to assess maternal, fetal and neonatal outcomes of triplet pregnancy in feto-maternal department at NGH as tertiary center and compare it to international data.

Methodology:

This is retrospective cohort study that was conducted at NGHA, KAMC Riyadh covering triplet pregnancy who received antenatal care in the period between 2016-2021. Inclusion criteria included any triple pregnancy diagnosed by ultrasound done in fetomaternal medicine department at NGH, between 11-13 w, all fetuses still viable beyond 24 w, managed and delivered at NGH. Between 2016-2021. Exclusion criteria included triplet pregnancy with miscarriage before 24w.

Data collection sheet was written to extract all related information of the study population covering all aspects. The data sheet included bibliographic data in form of age, body mass index. Another section is about general obstetric information, regarding gravidity, parity, number of abortions, family history of twins, ART, mode of delivery and gestational age at delivery. Another section includes pregnancy complication, covering Fectoreduction, Gestational hypertension, Preeclampsia, Gestational Diabetes, Placenta Previa, Induction of labor, Post-Partum Hemorrhage, HDU admission, cesarean hysterectomy. In addition to fetal complication covering Preterm delivery, Small for Gestational Age, AFI abnormalities, IUFD of co-twin, fetal anemia, IUT and Fetal Malformation. The last section covers general information regarding the neonate, which contains RDS, LBW, NICU admission, jaundice, hypoglycemia, ENND, and neurological development at 3 and 6 months of life.

All data was stored at the principal investigator office and access of the data was limited to the member of the research; data analysis was done by using SPSS software version 26. Categorical data were presented as frequencies and percentages while numerical data was presented as mean and standard

ISSN:1624-1940
DOI 10.6084/m9.figshare.26207009
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deviation. Chi square test was used to assess the association between age group and categorical outcome variables such as PTL. Logistic regression wase used to adjust the comparison between the selected group with other characteristics. A test was considered significant if p-value.

Results:

In this study, we retrospectively collected data from 42 women with triplet pregnancies. The mean age of the women was 30.57 years old (SD=5.18) ranged between 22- 44 years old where 83.3 % of the women were younger than 35 years old. Moreover, the mean BMI of the sample was 32.9 Kg/M2 where only 11.9 % of the women had normal weight while 61.9 % were obese and 26.2 % were overweighted. The mean gravity among the participants was 3.47 while 9 participants reported no parity (21.4 %) and the mean parity among those with parity was 2.18. Moreover, 20 women had a previous abortion (47.6 %) with mean rate of abortion among the women of 1.65 times (Table 1).

Table 1: Maternal baseline characteristics (N=42).

		Count	Column N %
Age	< 35	35	83.3%
	35 or older	7	16.7%
	Mean (SD)	30.57 (5.18)	
BMI	Normal	5	11.9%
	Overweight	11	26.2%
	Obese	26	61.9%
	Mean (SD)	32.9 (6.95)	
Gravity	Mean (SD)	3.47 (2.02)	
Parity (N=33)	Mean (SD)	2.18 (1.54)	
Abortion (N=20)	Mean (SD)	1.65 (1.01)	

Moreover, among the women included in this study, none of them had diabetes mellitus while 7.1 % of them had hypertension and 21.4 % had hypothyroid. Furthermore, 40.5 % of the women had previous CS while 14.3 % had previous PTL and 28.6 % were on medications. Moreover, none of the participants had family history of twins and 26.2 % of them had US at 11-13 weeks of pregnancy. In vitro fertilization (IVF) was the main cause of pregnancy in 85.7 % of the women whole spontaneous pregnancy was reported in 14.3 % of the cases. Among the participants, 90.5 % of them delivered their baby through lower segment cesarian section (LSCS) while vaginal delivery was reported in one case (Table 2).

Table 2: The medical and family history of the participants as well as cause of pregnancy and mode of the delivery

		Count	Column N %
DM	No	42	100.0%
	Yes	0	0.0%
HTN	No	39	92.9%
	Yes	3	7.1%
Hypothyroid	No	33	78.6%

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Volume 06 Issue 1
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ISSN:1624-1940
DOI 10.6084/m9.figshare.26207009
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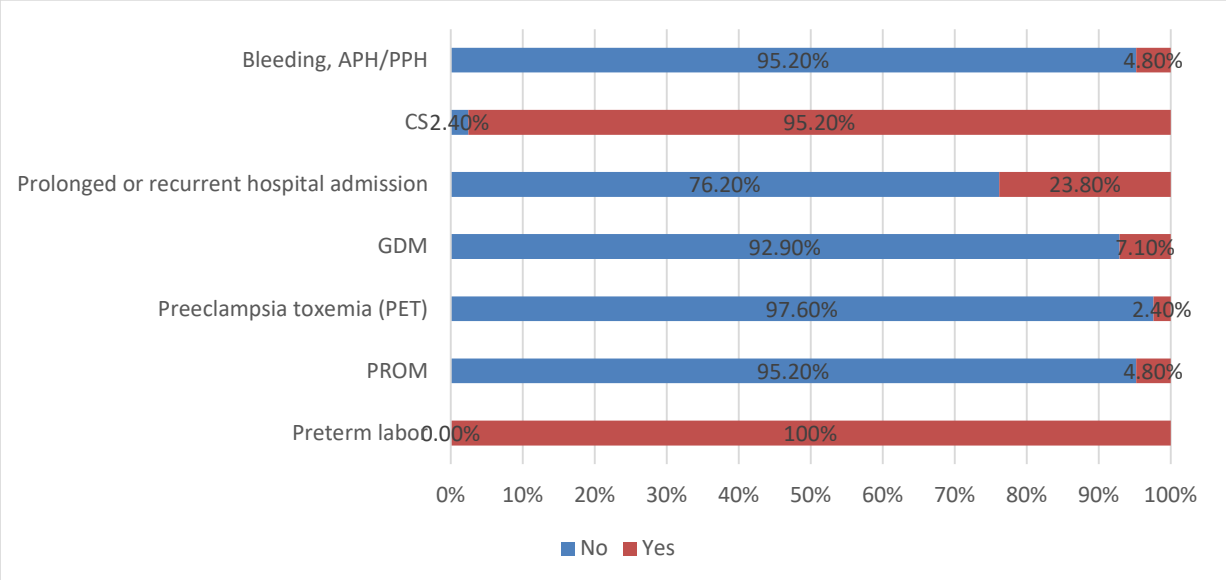
	Yes	9	21.4%
Previous CS	No	25	59.5%
	Yes	17	40.5%
Previous PTL	No	36	85.7%
	Yes	6	14.3%
Drug	No	30	71.4%
	Yes	12	28.6%
FHX of twins	No	42	100.0%
	Yes	0	0.0%
US at 11-13w	No	31	73.8%
	Yes	11	26.2%
IVF or spontaneous	Spontaneously	6	14.3%
	In vitro fertilization (IVF)	36	85.7%
mode of delivery	Classical CS	1	2.4%
	Lower segment Cesarian section (LSCS)	38	90.5%
	Spontaneous vaginal delivery (SVD)	1	2.4%
	LSCS+SVD	2	4.8%

Preterm birth was the most common complication of multiple gestation with all 42 triplet pregnancies (100%) terminating in PTB. Apart from PTB, combined for both types of multiple gestations, the most common obstetric complication was GDM in three pregnancies (7.1%) followed by premature rupture of membranes (PROM) in 2 pregnancies (4.8%). Moreover, 28.8 % of the women had prolonged or recurrent hospital admission and 95.2 % of women gave birth by CS (Figure 1).

Figure 1: Most common complication of multiple gestation (Maternal outcomes):



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ISSN:1624-1940
DOI 10.6084/m9.figshare.26207009
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Table 3: Fetal outcomes of women with triplet pregnancy

		Count	Column N %
Miscarriage	No	40	95.2%
	Yes	2	4.8%
Fetal growth restriction (FGR)	No	39	92.9%
	Yes	3	7.1%
Fetal anomaly	No fetal anomaly	36	85.7%
	Fetal anomaly in one infant	4	9.5%
	Fetal anomaly in two infants (Conjoint)	1	2.4%
	Fetal anomaly in three infants	1	2.4%
Fetal anemia	No	39	92.9%
	Yes	3	7.1%
IUF	No	41	97.6%
	Yes	1	2.4%
IUT	No	42	100.0%
	Yes	0	0.0%

Considering fetal outcomes, miscarriage was found to occur in two cases (4.8 %) and fetal restriction was reported in three mothers (7.1 %). Moreover, fetal anomaly was found in six cases (14.3 % of cases, 9 infants) where four cases were reported in one infant of the pregnancy, while one case was reported in two infants (conjoint) and one cases was reported in the three infants. Moreover, the prevalence of fetal anemia and IUF were 7.1 %, and 2.4 % respectively while no case was reported to have IUT (Table 3).

Moreover, the neonatal respiratory distress (RDS) was reported in 78.6 % of pregnancies occurred in 33 pregnancies and 73 infants (Prevalence was 57.9 % of total births) where 40.5 % of RDS occurred among the three infants while 23.8 % was found in one infant and 14.3 % was found in two infants. Moreover, 16.7 % of pregnancies results in low-birth-weight infants (17 infants, with prevalence of 13.4 %). NICU admission was reported in infants of 61.9 % of pregnancies with 60 infants (47.6 %) where the three infants of 33.3 % pregnancies needed NICU admission. Moreover, jaundice was reported in 83.3 % of the pregnancies with total 52 infants (41.2 %) while no case was reported to have hypoglycemia. Furthermore, early neonatal death (ENND) was reported in infants of 23.8 % of pregnancies occurred in 15 infants (11.9 %) (Table 4).

Table 4: Neonatal outcomes

	Pregnancies		Infants	
	Count	Column N %	Count	Column N %

ISSN:1624-1940
DOI 10.6084/m9.figshare.26207009
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RDS	No RDS	9	21.4%	53	42.1 %
	RDS in one infant	10	23.8%	10	7.9 %
	RDS in Two infants	6	14.3%	12	9.5 %
	RDS in three infants	17	40.5%	51	40.5 %
LBW	No LBW	35	83.3%	111	88.1 %
	LBW in one infant	2	4.8%	2	1.58 %
	LBW in Two infants	0	0.0%	0	0.0 %
	LBW in three infants	5	11.9%	15	10.32 %
NICU admission	No NICU admission	16	38.1%	66	52.4 %
	NICU admission in one infant	6	14.3%	6	4.76 %
	NICU admission in Two infant	6	14.3%	12	9.52 %
	NICU admission in three infants	14	33.3%	42	33.32 %
Jaundice	No Jaundice	7	16.7%	74	58.7 %
	Jaundice in one infant	23	54.8%	23	18.3 %
	Jaundice in Two infants	7	16.7%	14	11.1 %
	Jaundice in three infants	5	11.9%	15	11.9 %
Hypoglycemia	No Hypoglycemia	42	100.0%	126	100 %
	LBW in one infant	0	0.0%	0	0.0%
	LBW in Two infants	0	0.0%	0	0.0%
	LBW in three infants	0	0.0%	0	0.0%
ENND	No ENND	32	76.2%	111	88.1 %
	ENND in one infant	6	14.3%	6	4.8 %
	ENND in Two infants	3	7.1%	6	4.8 %
	ENND in three infants	1	2.4%	3	2.3 %

In table 5, we showed the relation between incidence of CS and infant and neonatal mortality. The results showed that there is a significant relation between CS and mortality where miscarriage was found in 100 % of cases with normal delivery while the infant mortality rate among mothers with CS was 2.4 % (P=0.000). Moreover, the neonatal mortality rate was 22 % of pregnancies (10.4 % of infants) in women who underwent CS compared with 100 % of those did not undergo CS. Moreover, we did not find any significant difference in infant or neonatal mortality according to the cause of pregnancy however, the infant mortality rate was 0.0 % in those with spontaneous pregnancy and 5.6 % in those with IVF (P=0.554) (Table 5).

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ISSN:1624-1940
DOI 10.6084/m9.figshare.26207009
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Table 5: The relation between incidence of CS, IVF and infant and neonatal mortality

		CS					IVF or spontaneous				
		No		Yes		P-value	Spontaneous		In vitro fertilization (IVF)		P-value
Miscarriage	No	0	0.0%	40	97.6 %	0.000 *	6	100.0 %	34	94.4 %	0.554
	Yes	1	100.0 %	1	2.4%		0	0.0%	2	5.6%	
ENND	No ENND	0	0.0%	32	78.0 %	0.004 *	4	66.7%	28	77.8 %	0.761
	In one infant	0	0.0%	6	14.6 %		1	16.7%	5	13.9 %	
	In two infants	1	100.0 %	2	4.9%		1	16.7%	2	5.6%	
	In three infants	0	0.0%	1	2.4%		0	0.0%	1	2.8%	

Discussion:

The introduction and development of the assisted reproductive technologies has had an important impact on the increased incidence of multiple births within Saudi Arabia [13] as well as Kuwait [14] and United States [15]. The main cause being that since the early 1995s, with the indiscriminate use of ovulation inducing medications by general practitioners without regulatory bodies that defines the number of embryos which can be reposited per IVF cycle where in most cases, at least 3 or more embryos were reposited per IVF cycle [16]. In our study, IVF was applied in 85.7 % of the cases and spontaneous pregnancy was the responsible for six cases (out of 42) with prevalence of 14.3 %. This is different from the results of previous studies which showed that spontaneous prevalence of triplets is one in 10,000 pregnancies [17]. Globally, 45 % of pregnancies resulting through IVF are multiple gestations [18].

Multiple gestation is associated with increased risk for maternal and neonatal complications including GDM, pregnancy induced hypertension, intrauterine growth restriction, preeclampsia, anemia, postpartum hemorrhage, low birth weight, preterm birth, and neonatal morbidity and mortality [19,20]. Preterm labor was the main maternal complications occurred in all pregnancies with triplets (N=42, 100 %). This is in agreement with many previous study which showed the incidence of preterm birth among triplets differs from 64 % to

ISSN:1624-1940
DOI 10.6084/m9.figshare.26207009
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almost 100 % [16, 21-25]. Two Saudi studies had reported a preterm labor incidence of 69-80 % as the most common complication in higher order gestation [13,26]. Other studies that were conducted in the Middle East reported similar results including two studies conducted in Kuwait [14,16], and one study in Egypt [27]. However, the prevalence of preterm labor was significantly higher than found among single pregnancies as reported in many previous studies including study of Abdelhady S et al who reported a prevalence of preterm labor in 7.01 % of single pregnancies [27], study of Gurung A et al of 9.3 % [28], study of Wagura et al of 18.3 % [29], and according to World Health Organization (WHO), the rate of preterm birth ranges between 5- and 18 % among 184 countries [30]. Moreover, in our study, mean gestational age at birth of 30.6 (3.9) weeks which is lower than reported in some previous studies among triplets as study of Chibber R et al who reported mean gestational age at delivery of 33.2 weeks [16], study of Mansouri H et al who reported a gestational age at delivery of 33.9 (SD=4.1) weeks [13], and study of Abu Heija et al, who reported a mean gestational age at delivery of 31.7 (SD=4.2) weeks [31].

Other maternal complications that were reported among mothers in this study included prolonged or recurrent hospital admission and development of gestational diabetic mellitus in 7.4 % of the mothers. Different studies conducted in Arab countries had reported that prevalence of GDM among women with multiple pregnancies was ranged between 3.8-12 % [13,14,21,31].

Among infants, the crude perinatal mortality rate (defined as the sum of the number of perinatal deaths (stillbirths and early neonatal deaths) divided by the number of pregnancies of seven or more months' duration) in this study was 166.7 per 1,000. This is an improvement over earlier studies which reported a mortality rate of 312 per 1,000 from the studies conducted in western countries [15,32,33]. However, this is higher than reported by some other studies including study conducted in USA with mortality of 103 per 1,000 births [24], as well as two studies conducted in Saudi Arabia which showed mortality rate of 67.7 per 1,000 and 159 per 1,000 births [13,31]. Moreover, neonatal respiratory distress (RDS) was the main complications reported among 57.9 % of the newborns. Similarly, pre-maturity and respiratory distress syndrome are the most common causes of morbidity in most studies [34,35].

Similar to results obtained in this study, pre-maturity and respiratory distress syndrome are the most common causes of morbidity in most studies [11,12].

In our study, pregnancy outcome did not differ with mode of conception which is also reported in a previous study [26]. Mode of conception was not associated with infant or neonatal mortality. This is similar to the results of Molines L et al who showed that there was no significant association between assisted conception and neonatal morbidity and mortality (aOR 0.67, 95% CI [0.25, 1.77], P = 0.422) [36]. However, in another study conducted by Luke B et al, the authors showed that IVF was associated with increased risk for neonatal morbidity as preterm labor and prematurity as well as infant mortality [37] and this was also reported in another study [38]. On the other hand, cesarean section triplets have lower perinatal mortality rates compared with vaginally delivered triplets [39,40]. For this reason, our obstetricians' consensus is to do cesarean section for triplets and higher-order pregnancies and that probably is the reason for higher cesarean section deliveries for triplets in the present study.

Conclusion:

In conclusion, triplet pregnancies are associated with higher risk of maternal, neonatal and infant morbidities and mortality. Preterm labor, recurrent hospital admission were the main maternal complications while fetal anomaly and RDS were the main infant and neonatal complications. The

ISSN:1624-1940
DOI 10.6084/m9.figshare.26207009
http://magellanes.com/

mortality rate of infant during pregnancy and among newborns was 166.7 per 1,000. Moreover, improvement of IVF techniques that allow for more control on the number of ovaries is important and would increase the safety of pregnancy. More interest should be performed for pregnant women with triplet pregnancies.

Acknowledgement:

We thank the participants who all contributed samples to the study.

Ethical approval

Ethical approval was obtained from the research ethics committee of King Abdullah International Medical Research Center with Application number: [NRC21R/477/10]. An informed consent was obtained from each participant after explaining the study in full and clarifying that participation is voluntary. Data collected were securely saved and used for research purposes only.

Funding

The study did not receive any external funding.

Conflict of interests

The authors declare that there are no conflicts of interest.

Informed consent:

Written informed consent was obtained from all individual participants included in the study.

Data and materials availability

All data associated with this study are present in the paper.

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