Original Article

Maternal Risk Factors and Perinatal Outcome of Fetal Growth Restriction

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ABSTRACT

Background: Worldwide, Fetal growth restriction is a leading cause of stillbirth, neonatal mortality, and morbidity. Several maternal factors influence fetal growth and increases the risk of fetal growth restriction. Our study aimed to determine the risk factors and perinatal outcome of fetal growth restriction at Tribhuvan University teaching hospital, Maharajgunj, Kathmandu.

Methods: A prospective study was conducted in the department of Obstetrics and Gynecology at Tribhuvan University teaching hospital. A total of 140 Pregnant women at > 28 weeks period of gestation clinically diagnosed as FGR and fulfilling the inclusion criteria were enrolled in this study. The data was analyzed using SPSS 23. The association between various risk factors and FGR was studied using the binary logistic regression.

Results: Among the 140 FGR fetuses, 27.9 % (39) belonged to the <10th percentile (Mild Fetal growth restriction) and 72.1%(101) belonged to<5th percentile (Severe Fetal growth restriction). Maternal age more than 35 years was found to be statistically significant as a risk factor in the severe Fetal growth restriction group. Among the maternal co-morbidities, hypertensive disorder of pregnancy was found to be the most common co-morbidity followed by heart disease and thyroid disorders. The Fetal growth restriction neonates requiring neonatal intensive care unit (NICU) stay was 42 (30%) and the median neonatal intensive care unit stay was 4 days. The fetal morbidities associated with fetal growth restriction were prematurity,respiratory distress syndrome(RDS), sepsis, meconium aspiration syndrome(MAS) and neonatal jaundice (NNJ). Among the 140 FGR babies, 138 were live born and there were 2 neonatal deaths (NND).

Conclusions: In our study ,advanced maternal age is found to be a significant risk factor for Fetal growth restriction and gestational hypertension is the most common comorbidity associated with Fetal growth restriction. Therefore, identification of such women, their regular antenatal checkups, fetal surveillance and timely intervention are crucial for better perinatal outcome.

Keywords: Fetal growth restriction, fetal outcome, risk factors.

INTRODUCTION

Fetal growth restriction (FGR) is defined as the failure of the fetus to meet its growth potential due to a pathological factor, most commonly placental dysfunction.[1]The definition of FGR should be based on a combination of measures of fetal size percentile and Doppler abnormalities. But in low-resource settings, FGR may be defined in the same way as small for gestational age(SGA).[2] Worldwide, FGR is a leading cause of stillbirth, neonatal mortality, and short- and long-term morbidity. In the Asian continent, it accounts for approximately 75% of all affected infants.[3]The prevalence of SGA births across the 12 hospitals observed in Nepal was 11.9%.[4]Our study aimed to determine the risk factors and perinatal outcome of FGR at Tribhuvan University teaching hospital (TUTH), Maharajgunj, Kathmandu.

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METHODS

A prospective observational study was conducted in the Department of Obstetrics and Gynecology, TUTH after taking ethical approval from Institutional review Committee (reference no: 133 (6-11)2078-2079). The duration of study was conducted over a period of one year (October 2021- September 2022). The study population comprised pregnant women >28 weeks POG diagnosed as FGR during the antenatal visit and those fulfilling the inclusion criteria (singleton, live, cephalic, confirmed gestational age, symphysial fundal height (SFH) lagging the gestational age by 4cm) were enrolled in the study.

The exclusion criteria included pregnancies less than 28 weeks period of gestation, twin pregnancies, congenital anomalies, intrauterine fetal demise (IUFD) and newborns with birth weight more than 10th percentile for gestational age.

A non -probability purposive sampling method was used. A sample size of 140 participants was calculated, using Cochran's formula where prevalence of FGR was 10%, taking margin error as 5%, considering 95%Confidence interval and 80% power.[5]

The patients were admitted from OPD and labour room of department of obstetrics and gynecology, TUTH. A detailed history was taken regarding the maternal age, parity, period of gestation, BMI, antenatal visits, prior history of FGR, uterine malformation and maternal morbidities like chronic hypertension, gestational hypertension, overt diabetes mellitus, gestational diabetes mellitus (GDM), anemia, heart disease, thyroid disorders and systemic lupus erythromatosis (SLE). General and obstetric examination was done. All baseline investigations and ultrasound for fetal biometry, estimated fetal weight (EFW), amniotic fluid index (AFI), and doppler findings were performed.

After delivery, the new-borns were classified as < 10th percentile FGR (Mild FGR) and < 5th percentile FGR (Severe FGR) using WHO birth chart.Perinatal outcomes were assessed in terms of birth weight, apgar score, mode of delivery, delivery outcome (live/stillbirth/ NND), NICU admission, need for resuscitation, neonatal sepsis, prematurity, respiratory distress syndrome and hyperbilirubinemia.

Mothers and newborns were followed till discharge from hospital.

All the data was entered in a structured proforma and analyzed using SPSS 23 Inc., Chicago, USA. Categorical variables were described using frequency with percentage and continuous data were described using mean and median. The association between various risk factors and FGR was studied using the binary logistic regression.

RESULTS

Among the140 pregnant women,127 (90.7%) were in the 20-34 years age group and 13 (9.3%) were >35 years age group. Among the 140 FGR fetuses, 27.9 % (39) belonged to the <10th percentile (Mild FGR) and 72.1% (101) belonged to<5th percentile (Severe FGR).

On analyzing the risk factors of fetal growth restriction, maternal age was found to be statistically significant in (Severe FGR) <5th percentile FGR. It was found that mothers aged more than 35 years of age were 3.4 times more likely to deliver FGR babies, as compared to mothers of 20-34 years age in the <5th percentile FGR.

Table 1. Baseline Maternal characteristics.

Variables	Category	Number (n=140) Percent (%)
Age	20-34	127 90.7
	>35	13 9.3
Parity	Nulliparous	83 59.3
	Multiparous	57 40.7
BMI	Underweight	7 5
	Normal	113 80.7
	Overweight	15 10.7
	Obese	5 3.6
Maternal Comorbidity	Present	56 40
	Absent	84 60
Uterine anomaly	Yes	6 4.3
	No	134 95.7
Birth spacing	<3 years	15 10.7
	>3 years	37 26.4
	None	88 62.9
Previous IUGR	Yes	5 3.6
	No	135 96.4
ANC visit type	Booked	122 87.1
	Un-booked	18 12.9

Table 2.Risk Factors associated with FGR. (<5th percentile)			
Variables	5th percentile Small forgestational age N=101	Odds Ratio (95% Confidence Interval)	p-value
Age			
20-34 years	95 (94.1%)	Reference	Reference
>35 years	6 (5.9%)	3.464 (1.084 - 11.067)	0.036*
Parity			
Nulliparous	60 (59.4%)	0.982 (0.463 - 2.083)	0.963
Multiparous	41 (40.6%)	Reference	Reference
Period of gestation			
28-37 weeks	48 (47.5%)	1.049 (0.501 - 2.197)	0.899
>37 weeks	53 (52.5%)	Reference	Reference
BMI			
Underweight	6 (5.9%)	0.461 (0.053 - 3.990)	0.482
Normal	83 (82.2%)	Reference	Reference
Overweight	9 (8.9%)	1.844 (0.605 - 5.620)	0.282
Obese	3 (3%)	1.844 (0.294 - 11.582)	0.514
Maternal Comorbidity			
Present	41 (40.6%)	0.915 (0.429 - 1.951)	0.817
Absent	60 (59.4%)	Reference	Reference
Uterine anomaly			
Yes	5 (5%)	0.505 (0.057 - 4.468)	0.539
No	96 (95%)	Reference	Reference
Previous IUGR			
Yes	4 (4%)	0.638 (0.069-5.894)	0.692
No	97 (96%)	Reference	Reference
ANC visit type			
Booked	87 (86.1%)	Reference	Reference
Un-booked	14 (13.9%)	0.710 (0.219 - 2.308)	0.569
*indicates statistically significant. p<0.05 were considered statistically significant.			

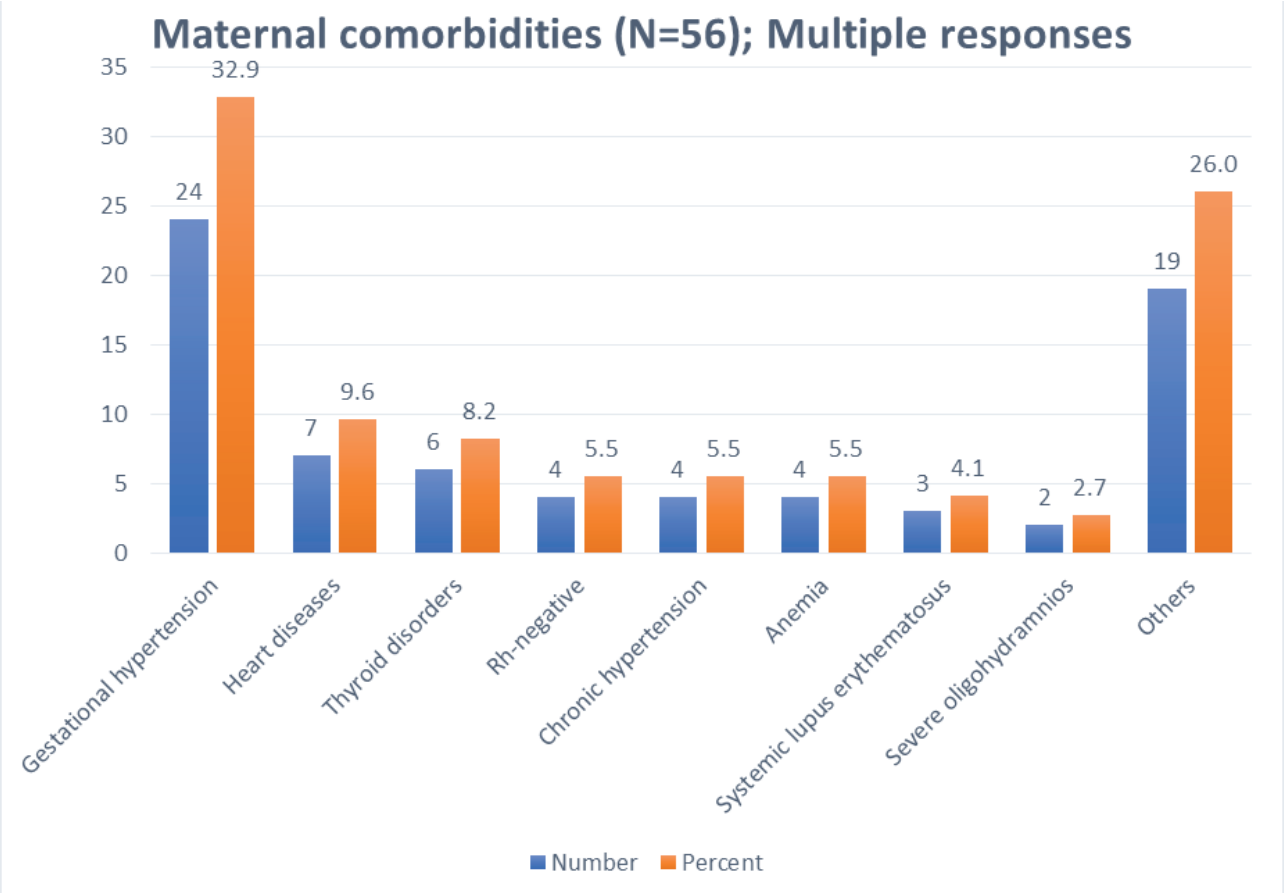

Figure 1.Distribution of maternal comorbidities in the pregnant women.

Of the total mothers who delivered FGR babies, 40% (56 of them) had any forms of maternal comorbidities. Gestational hypertension was the most common comorbid condition present in 32.9% of the mothers with any form of comorbidity which was followed by heart diseases (9.6%), thyroid disorders (8.2%), Rh-negative (5.5%), chronic hypertension (5.5%), anemia (5.5%), systemic lupus erythematosus (4.1%) and severe oligohydramnios (2.7%).

Table 3. Fetal Outcome in patients with fetal growth restriction.

Variable	Category	Number (n=140) Percentage (%)
Birth weight (kg)	Range (0.93-2.6) Mean 2.1 SD= 0.401	
< 10th percentile FGR (Mild FGR)	Yes	39 27.9
< 5th percentile FGR(Severe FGR)	Yes	101 72.1
Period of gestation (POG)	28-37 weeks > 37 weeks	67 47.9 73. 52.1
Mode of Delivery	Vaginal Caesarean section	53 37.9 87 62
Delivery outcome	Live Still birth NND	138 98.6 0 0 2 1.4
Apgar score at 5 minutes	> 7 < 7	123 87.9 17 12.1
Resuscitation	Yes	32 22.9
Fetal morbidity	Yes	42 30

The mean birth weight of newborns was 2.1 kg with SD of 0.40. The lowest birth weight of newborn was 900gms and highest weight was 2.6 kg. Out of the total 140 newborns delivered, 72.1% (101) belonged to the <5th percentile (Severe FGR) and 27.9% (39) belonged to the < 10th percentile (Mild FGR). Regarding delivery, 52.1 % of women delivered at >37 weeks POG and 62.1% were delivered by caesarean section.

Out of 140 neonates delivered, 138 (98.6%) were alive, there were 2 (1.4%) NND and no still births.One hundred and twentythree (87.9%) newborns had good 5minute Apgar score (>7) at time of birth. Only 32 (22.9) % newborns required any form of resuscitation and 42 (30 %) newborns required NICU stay. Median NICU stay = 4 days (Inter-quartile range = 4 days)

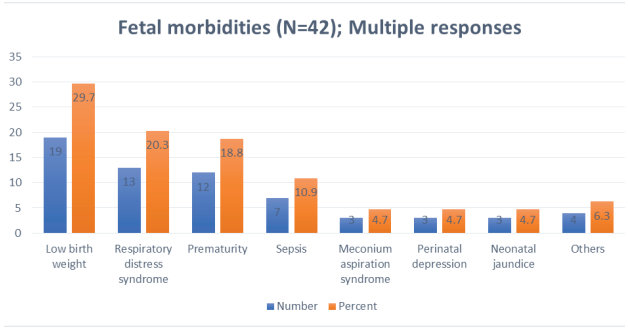

Figure 2. Fetal morbidities in FGR babies.

Of the total FGR babies delivered, 42 of them (30%) had any forms of fetal morbidities. Low birth weight requiring NNU/NICU admission was seen in 29.7% of the babies followed by respiratory distress syndrome (20.3%), prematurity (18.8%), sepsis (10.9%), MAS (4.7%), perinatal depression (4.7%) and NNJ (4.7%). Other morbid conditions found were transient tachypnea, congenital pneumonia, grossly distended urinary bladder and thrombocytopenia.

DISCUSSION

Worldwide, FGR is a leading cause of stillbirth, neonatal mortality, and short- and long-term morbidity. In a prospective study by Shrestha et al, most of the pregnant women with SGA fetuses were 20-34 years age group and most were nulliparous, which is comparable to that in our study.In our study, maternal age was found to be statistically significant risk factor in 5th percentile (Severe FGR).Mothers aged more than 35 years of age were 3.4 times more likely to deliver FGR babies as compared to mothers of 20-34 years age.The presence of co-morbid conditions like chronic hypertension and diabetes associated with advanced maternal age could be potential co-founders for this condition. Similarly in a case control study by Odibo et al, advanced maternal age was found to be an independent risk factor for FGR suggesting that screening for FGR is indicated in women of 35 years or older.[6,7]

In our study, 52.1 % of women delivered at >37 weeks POG. In a retrospectivestudy by Trudell AS, the cumulative risks of stillbirth rose from 28/10,000 SGA at 37 weeks to 77/10,000 at 39 weeks.This could be because the risk of MAS in this population increased significantly after 40 weeks. Similarly, in a retrospective cohort study by Pillodi RA, the risk of stillbirth increased with gestational age with the risk of stillbirth at each week of gestation inversely proportional to growth percentile.[8,9]

Most women in our study 113 (80.7%) were found to have normal Body mass index(BMI). Whereas, in a systematic review and meta-analysis by Liu L et al of over 1.6 million Chinese mothers examined the quantitative effect of maternal BMI on adverse neonatal outcomes.Maternal overweight or obesity was associated with macrosomia, large for gestational age(LGA), Preterm birth (PTB) and neonatal asphyxia, while maternal underweight was associated with LBW and SGA.[10]

In our study, hypertensive disorders of pregnancy was found to be the most common comorbid condition present in 42.9% of women. Fetal growth restriction results from inadequate placentation associated with early onset pre-eclampsia. Similarly, a Dutch population-based prospective cohort study showed that compared to women with no hypertension in pregnancy, women with preeclampsia had increased risk of SGA infants.[11]

In our study, 62.1% of women delivered by caesarean section which is comparable to study by Shrestha A et al where 82.2% of women with IUGR were delivered by LSCS.

The high rate of caesarean section could be attributed to the abnormal doppler findings on ultrasound, failed inductions and associated maternal co-morbidities like severe preeclampsia requiring early obstetric intervention.[12]

In our study, <5th percentile FGR (Severe FGR) comprised 71.4% newborns whereas <10th percentile FGR (Mild FGR) comprised 28.6% newborns. In a study by Zhang-Rutledge K, < 5th percentile FGR were likely to have worse antepartum and neonatal outcomes than those with an estimated fetal weight in the 5th to 10th percentiles. In a retrospective cohort study by Pilliod RA, maximum risk of intrauterine fetal death (IUFD) among postterm

pregnancies was 43.9 IUFDS per10,000 at risk fetuses at 5thpercentile and 26.3 for 10th percentile FGR.[9,13]

The Apgar score at 5 minutes was >7 in 87.9% newborns which is comparable to study by Hasmasanu et al. The good apgar score in most new borns could be attributed to early intervention by caesarean section as well as the availability of pediatrician for neonatal resuscitation. [14]

Prematurity was found in 48.7% of newborns with FGR. RDS was seen in 68.4% of preterm babies.Similarly in a systematic review of studies of FGR diagnosed before 32 weeks of gestation,the most common neonatal morbidities were RDS (34 %), retinopathy of prematurity (13 %), and sepsis (30 %).Chronic hypoxia adversely affects the structural development of airways and pulmonary vasculature in immature lungs. Furthermore, intrauterine hypoxia and acidosis may interfere with surfactant synthesis.Therefore, the possible increased risk for RDS may be caused by reduced or impaired release of surfactant or a diminished response to endogenous and exogenous corticosteroids.[15]

Among the 140 FGR babies, 138 were live born and there were 2NND. Out of 2 NND, one had RDS of prematurity and other had MAS.The good perinatal outcome in our study could be attributed to early diagnosis, vigorous monitoring and timely intervention.

Mention the limitations of this study: The limitation of our study was single centre study with small sample size. Also, our study didn't study early versus late FGR for which we can recommend further study with large sample size.

Recommendation: As our study identified, advanced maternal age as a significant risk factor for fetal growth restriction, women who belong to this group should be adviced regular antenatal visits and fetal surveillance for good perinatal outcome.

CONCLUSIONS

Our study identified advanced maternal age as a significant risk factor for FGR and gestational hypertension as the most common maternal comorbidity associated to FGR. Hence identification of such cases, their regular antenatal checkups, fetal surveillance and timely intervention are crucial for better perinatal outcome as seen in our study.

CONFLICT OF INTEREST

None.

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