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ORIGINAL ARTICLE

Maternal Predictors of Intrauterine Growth Retardation

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ABSTRACT

Objective: To identify maternal factors associated with intrauterine growth restriction (IUGR).

Study Design: A case-control study.

Place and Duration of Study: Neonatal Unit of The Aga Khan Hospital for Women (AKHW), Karimabad, from January 2014 to December 2015.

Methodology: Cases were IUGR live born babies (n=90), while control were appropriate-for-gestational age (AGA) babies (n=180). Information recorded in pre-designed proforma included gestational age and birth weight of baby, demographics of mothers, pregnancy related medical and obstetric complications. Data were analysed through SPSS-19. Multivariable logistic regression was used to determine the maternal factors associated with the intrauterine growth restriction.

Results: Maternal factors associated with IUGR after adjusting for confounders in the multivariable model included younger age (OR=0.9, CI=0.8-0.9), poor gestational weight gain (OR=3.0, CI=1.6-6.1) and history of previous abortion (OR=3.06, CI=1.1-8.0). Significant interaction was found between pregnancy-induced hypertension (PIH) and parity of mother, primary-para mother with PIH having an increased risk for IUGR babies (OR=10.1, CI=1.0-23.2).

Conclusion: Young age, primigravida status, low gestational weight gain, previous history of abortion, PIH and GDM have strong association with IUGR; hence, special consideration is essential to overcome these issues in order to improve maternal and neonatal health.

Key Words: *Intrauterine growth retardation. Gestational diabetes. Low gestational weight gain.*

INTRODUCTION

Intrauterine growth retardation (IUGR) represents the second leading cause of perinatal morbidity and mortality in non-anomalous fetuses, after prematurity.[1,2] IUGR refers to the fetus whose birth weight less than 10th centile for gestational age and displays signs of chronic hypoxia or malnutrition.[3]

IUGR is observed in 23.8% of newborns around the world; and significant global burden approximate 75% of IUGR neonates are contributed by the Asian continent.[4] In Pakistan, the incidence of IUGR is around 25%,[5] more than the WHO criteria for triggering a public health action. It is mainly due to a pathologic slow-down in the fetal growth pace, resulting in a fetus that is unable to reach its growth potential.

There are multiple factors associated with high incidence of IUGR and there is a strong positive correlation exists between fetal, placental and maternal factors, but maternal factors *per se* significant cause of IUGR.[4] Poor maternal nutrition, poor maternal weight gain, maternal anemia, inadequate prenatal care, short interpregnancy interval, pregnancy-induced hypertension (PIH), gestational diabetes (GDM), maternal infection, and maternal chronic illness are major maternal risk factors.[6] Healthy dietary habit, avoidance of unhealthy lifestyles, receiving proper prenatal care, and close antenatal surveillance of high risk pregnancy may help in declining the risk for IUGR.

The objective of this study was to identify maternal factors associated with IUGR. A comprehensive understanding of these factors will help in providing early interventions to improve the perinatal outcome due to IUGR.

METHODOLOGY

This study was carried as a case-control study in the Neonatal Unit of The Aga Khan Hospital for Women (AKHW), Karimabad, Karachi, from January 2014 to December 2015. Babies born after 32 weeks gestation, without lethal congenital anomalies were included. Cases were IUGR neonates (defined as babies with abnormal Doppler ultrasound and weight less than 10 percentile for gestational age); and controls were appropriate for gestational age (AGA) neonates with normal Doppler ultrasound as per American College of Obstetricians and Gynecologists (ACOG) definition. The case-control ratio was kept at 1:2. Cases and controls were selected retrospectively from hospital records during the study period. Data was retrieved using ICD discharge codes, and medical records were reviewed in detail.

A pre-designed proforma was filled by reviewing the clinical notes which entailed information about basic

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demographic information like, gestational age, birth weight, gender, mode of delivery, Apgar score, maternal age, maternal weight, maternal illness during pregnancy, antenatal care (ANC) visit, inter-pregnancy interval, previous IUGR births, amniotic fluid index, and umbilical artery blood flow. The study was carried out after obtaining approval from the Institutional Ethical Review Committee.

Gestational age (recorded as completed weeks) was calculated from maternal last menstrual period (LMP) and was categorised as preterm less than 37 weeks and term as 37 weeks or above.

As per routine practice, birth anthropometries were measured by staff nurse in labour room or operation theatre by using standardised equipment. Weight was measured without clothes using standard weighing balance in kilogram (kg) and length by a non-stretchable measuring tape in centimeter (cm). The calibration of the weighing scale was checked regularly before each measurement in order to avoid error. All measurements were recorded in a structured proforma during file review and plotted on specific WHO growth charts (Fenton growth chart), and percentiles was noted. Maternal age at the time of delivery was recorded. Maternal weight and height at the time of initial visit was used to calculate body mass index (BMI) for mother. Gestational weight gain was calculated by difference in the maternal weight at the time of 1st visit during 1st trimester and at the time of delivery and categorised into poor weight gain <10 kg and good weight gain >10 kg.

Pregnancy-induced medical disorders and obstetrical complications like placenta previa, abruptio placentae, anemia, PIH; and GDM was also obtained. Inter-pregnancy interval was estimated by the number of months between the conception of current pregnancy and the previous delivery, abortion or stillbirth.

The statistical analysis was computed by using the SPSS version 19. Mean ±SD was calculated for continuous variables; while for qualitative variables frequencies and percentages were analysed. Cross-tabulation was done to see the independent variables across the categories of outcome (IUGR and AGA). Chi-square test was applied for categorical variables and independent sample t-test was applied for measureable variables, and p <0.05 considered as significant. Multivariable logistic regression was performed to analyse the association between maternal factors and intrauterine growth restriction. Multivariable analysis was calculated for the variables found to be stastically significant or with p-value ≤0.20 in univariate analysis.

RESULTS

In this study, 90 cases and 180 controls were recruited for analysis. Table I shows the distribution of various characteristics between cases and controls. Mothers of cases were younger 26.7 ±4.4 years compared to mothers of controls 28.0 ±4.4 years (p=0.025). There was low weight gain during pregnancy among cases as 80% (n=72) had poor weight gain compared to 60% (n=108) among controls. Among cases, 58% (n=52) were primi compared to 66% (n=119) among controls; and this was not found to be significantly different. Significantly, higher proportion of cases had history of previous abortion 21% (n=19) compared to controls 8% (n=15). A higher proportion of cases had history of GDM 16.7% (n=15) compared to about 4% (n=7) in controls. Similarly, history of PIH was positive more in cases 13.3% (n=12) than controls 4% (n=7).

Logistic regression analysis showed that increasing age of mother was protective against IUGR adjusted OR 0.93 (95% CI: 0.88-0.99, p= 0.006). On the other hand, women who had poor weight gain during pregnancy

Table I: Comparison of characteristics of cases and controls.

Variable	Case 90	Control 180	p-value
Gender			
Male	49 (54.4)	93 (51.7)	
Female	41 (45.6)	87 (48.3)	0.667
Age of mother[a]	26.7 (±4.4)	28.0 (±4.4)	0.025
BMI of mother			
Normal	43 (47.8)	82 (45.6)	0.926
Underweight	12 (13.3)	23 (12.8)	
Overweight	22 (24.4)	51 (28.3)	
Obese	13 (14.4)	24 (13.3)	
Weight gain during pregnancy			
Poor	72 (80)	108 (60)	
Good	18 (20)	72 (40)	0.001
Parity			
Primi	52 (57.8)	119 (66.1)	
Multi	38 (42.2)	61 (33.9)	0.180
Previous abortion			
Yes	19 (21.1)	15 (8.3)	
No	71 (78.9)	165 (91.7)	0.003
Anemia during pregnancy			
Yes	25 (27.8)	48 (26.7)	
No	65 (72.2)	132 (73.3)	0.846
Variable	Case	Control	p-value
GDM			
Yes	15 (16.7)	7 (3.9)	
No	75 (83.3)	173 (96.1)	<0.001
PIH			
Yes	12 (13.3)	7 (3.9)	
No	78 (86.7)	173 (96.1)	0.004
Multiple gestation			
Yes	4 (4.4)	17 (9.4)	
No	86 (95.6)	163 (90.6)	0.0148
Antenatal visit			
<2	2 (2.2)	4 (2.2)	
2-4	16 (17.8)	19 (10.6)	
>4	72 (80)	157 (87.2)	0.249
Weight of mother[a]	57.9 (±12.4)	57.8 (±12.5)	0.923
Height of mother[a]	155 (±5.3)	154.3 (±5.6)	0.811
Interpregnancy interval[a]	0.95 (±1.86)	0.59 (±1.12)	0.099

[a] Continuous variable: Means and standard deviations are reported
BMI = Body Mass Index; GDM: Gestational Diabetes Mellitus;
PIH = Pregnancy Induced Hypertension.

Table II: Regression analysis of factors associated with intrauterine growth retardation.

Variables	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Gender				
Male	1	0.667	--	
Female	0.89 (0.58-1.49)	0.026	0.93 (0.85-0.97)	0.006
Age[a]	0.93 (0.88-0.99)			
Weight[a]	1.0 (0.98-1.02)	0.922	--	
Height[a]	1.03 (0.98-1.08)	0.259	--	
BMI				
Normal	1			
Under	1.0 (0.45-2.19)	0.990	--	
Over	0.82 (0.44-1.53)	0.538		
Obese	1.03 (0.48-2.23)	0.934		
Weight gain				
Good	1		1	
Poor	2.67 (1.47-4.84)	0.001	3.09 (1.65-6.15)	0.001
Parity				
Primary`	1		1	
Multi	1.43 (0.85-2.40)	0.181	1.33 (0.66-2.72)	0.427
Previous abortion				
No	1		1	
Yes	2.94 (1.41-6.12)	0.004	3.06 (1.17-8.0)	0.023
Variables	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Anemia				
No	1			
Yes	1.06 (0.60-1.87)	0.846	--	
GDM				
No	1		1	
Yes	4.94 (1.93-12.62)	0.001	3.34 (1.22-9.17)	0.019
PIH				
No	1		1	0.036
Yes	3.80 (1.448-10.02)	0.007	3.10 (1.08-8.94)	
Multiple gestation				
No	1		1	
Yes	0.45 (0.14-1.37)	0.158	0.44 (0.13-1.49)	0.188
Antenatal visits				
>4	1			
2-4	1.84 (0.89-3.78)	0.099		
1	1.09 (0.20-6.09)	0.922	--	
Pregnancy interval (years)				
2 or more	1			
Less than 2	0.82 (0.43-1.60)	0.56	--	

[a] Continuous variable; BMI = Body Mass Index; GDM = Gestational Diabetes Mellitus; PIH = Pregnancy Induced Hypertension.

were at almost three times higher risk of IUGR adjusted OR 3.09 (95% CI: 1.65-6.15, p=0.001). History of previous abortion was associated with three times higher risk of IUGR compared to those without history of previous abortion adjusted OR 3.06 (95% CI: 1.17-8.0, p=0.023). There was more than three times higher risk adjusted OR 3.34 (95% CI: 1.22-9.17, p=0.019) of IUGR among women with history of GDM. History of PIH was also found to be associated with significant risk of IUGR adjusted OR 3.1 (95% CI: 1.08-8.94, p=0.036). Multiple regression analysis is shown in Table II.

DISCUSSION

Obstetric and maternal risk factors for IUGR are well described in many studies. We found significant differences for maternal predictors as age, parity, weight gain, previous history of abortion, GDM and PIH between the IUGR and AGA after adjusting for probable confounding.

Maternal age is one of the important risk factors associated with birth weight of the neonate. The relationship between maternal age and IUGR was found significant when compared between cases and control. Maternal age less than 27 years was one of the predictors in this study, similar findings were observed in studies conducted by Jamal *et al*. and Taj,[7,8] while in comparison with Odibo *et al*. study, who observed a strong association between increasing maternal age and risk of IUGR.[9]

Primigravida mothers are at risk to deliver IUGR babies. It has been evident that the birth weight increases with

parity (up to 4-5 births) but declines afterward.[10] Proportion of primigravida was high in this study; similar findings were also reported by different studies from Pakistan and India.[8,11,12]

Inadequate nutrition is not uncommon factor of impaired fetal growth. Here, maternal weight and height on first visit was used to calculate BMI. Studies from neighbouring countries have shown that BMI, pre-pregnancy body weight, and weight gain during pregnancy had significant effect on birth weight.[13,14] There was no significant association between maternal nutritional status (BMI) and the IUGR births, in contrast with results observed in study by Taj *et al*. and Acharya.[8,12]

Weight gain during pregnancy has strong, positive impact on fetal growth suggesting that energy balance is an important determinant of birth outcomes.[15] Low weight gain reflects deficiency of calorie and micro-nutrients, which are essential for fetal growth.[16] In this study, poor gestational weight gain was also a significant factor of IUGR, mothers with poor weight gain during pregnancy had three times risk of delivering babies with IUGR as compared to mothers with good gestational weight gain. These findings were consistent with different Indian studies which showed poor gestational weight gain, for even short-term, places the fetus at risk for IUGR.[17-20] Improving maternal weight prior to conception and pregnancy weight gain are possible strategies to improve birth weight.

Anemia is a common problem in pregnant women in developing countries. In this study, anemia in pregnancy Hb <10 gm%) was not significantly associated with IUGR. It was found 27.8% of mothers with anemia (p=0.8). This is in contrast with studies at Goa and Karnataka, which have shown 49% (p<0.001) and 76% (p=0.01) of mothers had anemia, respectively.[11,12]

Maternal diabetes causes long term changes in placenta and may cause fetal growth restriction[16], GDM is found in 10% of women with IUGR.[21] This study has shown strong association between IUGR and GDM, there was more than three times higher risk of IUGR among mothers with GDM; this finding is not consistent with study by Taj.[8]

Hypertensive conditions are responsible for one-third of all fetal growth retardation.[22] PIH is a frequent cause of placental insufficiency. In this study, PIH was associated with higher risk of IUGR with adjusted odds ratio 3.1 (p=0.036). This is consistent with study by Taj, Thompson *et al*. and Burke.[8,23,24] Burke reported pre-eclampsia with a combined odds ratio of 5.4 (p<0.001),[24] while the incidence of IUGR among preeclamptic women was 22.2%, found in study by Viller.[25]

The present results also suggest negative effect of previous history of abortion on fetal growth. Similar finding was observed in study by Motghare. However, no such relation was seen in study by Aghamolaei *et al*.[26]

Although sample size calculation was not done prior to the study; however, post-hoc power calculations showed that the sample had enough power for observed ORs.

CONCLUSION

Several maternal risk factors of IUGR were identified. Awareness of these predictors, not only helps in proper preventive care but also helps in prompt diagnosis of IUGR. Nutritional intervention could help increase maternal weight during pregnancy. Screening and proper management of GDM and PIH would help in reduction of incidence of IUGR in the community which would eventually help in succeeding the goal of reduced neonatal mortality and morbidity.

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