



ASSESSMENT OF MATERNAL RISK FACTORS FOR INTRAUTERINE GROWTH RETARDATION (IUGR) AMONG NEWBORNS IN A TERTIARY CARE HOSPITAL IN EASTERN INDIA: A CASE CONTROL STUDY.

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ABSTRACT

Introduction: Intrauterine growth retardation (IUGR) ranks as the second leading cause of perinatal illness and death. Several studies have identified multiple risk factors linked to IUGR. The present study aims to explore the maternal factors contributing to IUGR among term newborns in eastern India.

Methodology: A case-control study was conducted in a medical college in Kolkata with 64 subjects in each group. Data collected using a semi-structured questionnaire and maternal clinical records. Data analyzed using STATA MP/16 by appropriate statistical tests.

Results: Mothers of cases were older (27.9 ± 5.58 years) compared to mothers of controls (26.4 ± 5.19 years). There was significantly lesser weight gain during pregnancy among cases (7.01 ± 2.13 Kg.) compared to (10.4 ± 2.5 Kg) among controls ($p < 0.05$). The mean maternal height of cases was also significantly lower than the controls. A significantly higher proportion of cases ($p < 0.05$) had history of diabetes mellitus (15.6%), hypothyroidism (37.5%) and liquor abnormalities (22%) compared to controls (4.7%, 12.5% and 4.7% respectively). Univariate logistic regression analysis showed height of mother (OR: 0.86), weight gain during pregnancy (OR: 0.48), bad obstetrics history (OR: 6.2), hypothyroidism (OR: 4.2) and liquor abnormalities (OR: 5.6) were significantly associated with IUGR. In multivariable logistic regression factors like height of mother (AOR: 0.82), weight gain during pregnancy (AOR: 0.48) and liquor abnormalities (AOR: 29.5) retained their significance ($p < 0.05$).

Conclusion: Screening of identified risk factors like maternal weight gain, hypothyroidism, liquor abnormalities, etc. and effective management of diabetes mellitus and pregnancy-induced hypertension (PIH) can contribute to decreasing the occurrence of IUGR in the population.

Keywords: intrauterine growth restriction, risk factor, hypertension, diabetes mellitus

INTRODUCTION:

IUGR (intrauterine growth retardation) or FGR (fetal growth restriction) by a strict clinical definition refers to a situation where the fetus has failed to achieve its normal biologic/genetic growth potential due to a pathologic cause.^{1,2,3} Worldwide the incidence of IUGR is 23.8 % of all newborn births and out of which about 75 % of this burden is contributed by the Asian countries.⁴

IUGR is the second most common cause of neonatal deaths and the most common cause of intra uterine fetal deaths.⁵ IUGR can significantly increase the risk of adverse events in antenatal (chronic fetal distress, fetal death), intranatal (meconium aspiration, birth asphyxia, respiratory distress syndrome, hypoglycaemia, hypothermia, bronchopulmonary dysplasia), and post-natal periods. IUGR increases the risk for neurodevelopmental impairment in children.⁶ The IUGR infant is known to be at a higher risk to develop long term problems like short stature, cognitive delay, poor academic performance, epilepsy, cerebral palsy, behaviour and intellectual disorders, learning disabilities and various psychiatric conditions in later life.^{7,8} IUGR is also related to development of adverse cardiological remodelling which leads to hypertension and various other cardiological diseases in adult life.⁹ It can lead to late adverse outcomes like the metabolic syndrome in adult life with diabetes, obesity, hypertension and chronic heart diseases.¹⁰ These long term morbidities leads to increased health costs to the society by way of increased health care and special education needs.¹¹

IUGR is loosely used interchangeably with the term SGA (small for gestational age) which by definition is a fetus who has a birth weight for gestational age below the 10th centile based on a gender specific reference population.¹² It is based on the cross sectional evaluation (prenatal or postnatal). SGA includes 2 groups of fetuses namely constitutionally normal small babies who are normally small for their gestational age due to certain inherent factors like maternal height, parity, ethnicity, etc. and these babies do not have any risk of increased perinatal morbidity or mortality. The second group of SGA babies are the babies with true pathological growth restriction (FGR or IUGR) which resulted in the weight to fall below the 10th centile for the age and sex, and who have a greatly increased risk of developing various complications during the perinatal and postnatal period which lead to significant increase in perinatal mortality and morbidity. Hence some babies with SGA may not have IUGR and conversely some babies with IUGR may be above the 10th centile for age and sex and hence may not meet the criteria of SGA. To accurately differentiate between normal SGA and true IUGR/FGR we need fetal growth curves which have been customised and tailor made to the local population under study¹³, as well as analysis of fetal growth trajectories.¹⁴

Since IUGR is considered to be the most common cause of SGA babies and vast majority of studies done on IUGR in India as well as abroad choose to ignore the subtle differences between SGA and FGR SGA(IUGR) babies, we also in this study have not attempted to make any distinction between the two and have used the terms IUGR and SGA interchangeably.^{15,16} The fetal growth is a very strong predictor of the final outcome of the pregnancy and is a result of various physiological and pathological factors which act to influence the fetal growth.¹⁷⁻¹⁹

The causes of IUGR are multifactorial (maternal, fetal, placental, environmental and genetic) with many factors sometimes playing simultaneous roles in its occurrence.^{15,20} In our study we aim to analyse mainly the maternal risk factors and their association with IUGR. In a recent meta-analysis¹⁵ which was conducted after a systematic review of various studies on risk factors of IUGR in South Asian population in the last decade, some common maternal risk factors associated with IUGR identified were rural area, low-socioeconomic status, non-registered, lesser antenatal visits, grand multiparity, history of IUGR in previous pregnancy, bad obstetric history, anemia, TORCH infections;¹⁶ hilly area, younger age. heavy manual work HDP (hypertensive disorders of

pregnancy)²¹; Primigravida, poor gestational weight gain, history of abortion;²² low socioeconomic status and malnutrition;^{23,24} Low maternal educational status, maternal age, number of ANC visits, maternal height, primiparity, anemia;²⁵ Low maternal BMI, Hypothyroidism, Smoking, GDM (Gestational diabetes mellitus);²⁶ Younger maternal age, multiparity, preeclampsia, chronic hypertension, primigravida, low blood sugar levels.²⁷⁻²⁹

As it can be understood that each geographical region in South Asia reported its own set of unique maternal risk factors which were most significant in their own context with respect to development of IUGR. There is a scarcity of similar data from Eastern India and particularly from West Bengal which prompted us to conduct this study to identify the most important maternal risk factors in this part of our country so that local measures could be best tailored to combat the problems most prevalent in our context. The socioeconomic dynamics of the population in this part of the country has changed significantly post the covid pandemic with many people having lost jobs, etc. which may have adversely impacted the physical, mental and emotional health of the mothers. An increase in the incidence of IUGR has also been noted in the post covid era in these parts of the country as observed by the rising trend of IUGR deliveries in our hospital which is a tertiary level hospital catering to a huge population of over 10 million people covering an area over 10,000 square kms. The risk factors are very dynamic and keep changing with time and, also from population to population and therefore there is a very pressing need to identify the present-day risk factors (particularly, in the post pandemic context) which are most significant in the population of this part of our country so that preventive steps are directed most specifically to these problems effectively to reduce the burden of IUGR. Many of these risk factors are modifiable and early identification can prevent occurrence of IUGR. We wish to do this study with regards to the population around this part of West Bengal (South 24 Parganas) as because no studies have been done in this semi urban region and finding this data will help us to significantly lower the incidence of IUGR by identifying the modifiable maternal risk factors with the most strength of associations.

OBJECTIVES:

1. To determine the maternal risk factors associated with IUGR in term neonates.
2. To find out the association of IUGR with maternal risk factors.

METHODOLOGY:

A case-control study was conducted in a medical college in Kolkata. Cases were consenting singleton mothers with known duration of amenorrhea delivering term babies with birth weight less than 2.5 kg.; and controls were consenting mothers delivering term babies having birth weight of 2.5 – 4 kg. The case-control ratio was 1:1. Cases and controls were selected from hospital records during the study period.

The Exclusion criteria:

- Multiple pregnancies
- Mothers with babies born with congenital anomalies and dysmorphism

The sample size was calculated using the formula:

$$n = \frac{r+1}{r} \frac{(p^*)(1-p^*)(Z_{1-\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

- r = ratio of case and controls, 1 for equal number of cases and controls
- P* = Average proportion exposed = (proportion of exposed cases + proportion of exposed controls)/2
- Z_{1-β} = Standard normal variate for power = 0.84 for 80% power
- Z_{α/2} = Standard normal variate for level of significance = 1.96 for 5% α

- $p_1 - p_2$ = Effect size or Difference in proportion expected based on previous studies. p_1 is proportion in cases and p_2 is proportion in controls
 - Considering proportion of controls and cases with exposure as 84% and 62% respectively from the study done by Dr. Rahul Surve & Dr Abhay Jain.
 - Sample size cases: 64
 - Sample size controls: 64
 - Total sample size: 128
- Sampling method: Convenience sampling

The study was carried out after obtaining approval from the Institutional Ethical Review Committee. Data collected using a pre-designed schedule was filled by reviewing the clinical notes which entailed information about basic demographic information like, gestational age, birth weight, gender, mode of delivery, maternal age, maternal weight, maternal illness during pregnancy, antenatal care (ANC) visit, inter-pregnancy interval, previous IUGR births, placental & amniotic fluid abnormalities, etc. 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 schedule 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.

Data collected were compiled in Microsoft Excel and analyzed using STATA-MP16 software. Mean $\pm$ 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 statistically significant or with p -value <0.20 in univariate analysis.

RESULTS:

In this case control study, an equal number of cases and controls (64 in each group) were studied. Cases were mothers of term IUGR babies (weighing < 2.5 Kg.), while controls included mothers of term babies having birth weight $\geq$ 2.5 Kg. Table-1 depicts the socio-demographic profile of cases and controls. As per Modified BG Prasad classification for socioeconomic class, IUGR babies were more prevalent among the mothers belonging to middle class(48.5%) and lower middle class (32.8%), compared to control group where more number of babies (51.6%) were born to mothers belonging to upper middle class, and this difference was found to be statistically significant ($p < 0.05$). No significant difference was found between the case and control group in other socio-demographic characteristics like family size, mother's occupation, type of house, religion, educational status, etc.

Table-1	Demographic profile of the cases and controls
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Characteristics		Case	Control	Chi square test
Number of family members	<5 members	43	33	$\chi^2=3.2$
	≥ 5 members	21	31	$p=0.07$
House type	Pucca	55(86%)	50(78%)	$\chi^2=1.32$
	Semipucca	4 (6.2%)	14 (22%)	$p=0.25$
	Kuccha	5(7.8%)	0	
Occupation of mother	Homemaker	57(89%)	58(90.6%)	$\chi^2=0.085$
	Working	7(11%)	6 (9.4%)	$p= 0.77$
Religion	Hindu	50 (78%)	44 (68.7%)	$\chi^2=1.44$
	Muslim	14 (22%)	20(31.3%)	$p=0.23$
Education	Primary (class VIII)	20(31.3%)	14(21.9%)	$\chi^2=5.97$
	Secondary (class X)	30(46.8%)	26(40.6%)	$p=0.201$
	Higher secondary	5(7.8%)	13(20.3%)	
	Graduate	5(7.8%)	8(12.5%)	
	Post graduate	4(6.3%)	3(4.7%)	
Socioeconomic class	Upper	0 (0%)	5 (7.8%)	$\chi^2= 31.07$
	Upper middle	9(14%)	33(51.6%)	$p<0.0001$
	Middle	31(48.5%)	10(15.6%)	
	Lower middle	21(32.8%)	14(21.9%)	
	lower	3(4.7%)	2(3.1%)	

Table-2 Maternal Information			
Characteristics	Case (Mean $\pm$ SD)	Control (Mean $\pm$ SD)	p-value
Maternal age	27.9 $\pm$ 5.58	26.4 $\pm$ 5.19	0.138
Maternal weight (kg) at 1 st visit	54.47 $\pm$ 8.2	56.9 $\pm$ 10.9	<0.001
Maternal height (cm)	152.8 $\pm$ 2.9	154.8 $\pm$ 4.5	0.003
No. of ANC visits	9.14 $\pm$ 3.3	6.79 $\pm$ 2.4	<0.001
Weight gain in pregnancy (kg)	7.01 $\pm$ 2.13	10.4 $\pm$ 2.5	<0.001
Mean family income	11898 $\pm$ 4226.8	21875 $\pm$ 10648	<0.001
Gap between pregnancy	3.88 $\pm$ 2.70	4.45 $\pm$ 2.85	0.423
Resting hours	7.9 $\pm$ 1.6	8.7 $\pm$ 2.6	0.037
Intake of Iron tab	198 $\pm$ 48.5	195 $\pm$ 45.3	0.748
Intake of FA tab	210 $\pm$ 69	194 $\pm$ 61.8	0.171

Table-2 shows the distribution of various maternal characteristics between cases and controls. Mothers of cases were older (27.9 $\pm$ 5.58 years) compared to mothers of controls (26.4 $\pm$ 5.19 years). There was significantly lesser weight gain during pregnancy among cases (7.01 $\pm$ 2.13 Kg.) compared to (10.4 $\pm$ 2.5 Kg) among controls ($p<0.05$). The mean maternal height and weight at first visit of cases (152.8 cm and 54.4 kg.) was also significantly lower than those of the controls (154.8 cm and 56.9 kg.) and it was statistically significant ($p<0.05$). The average monthly family income of the controls was almost twice that of the cases (INR 21875 vs INR 11898).

Table-3 Maternal risk factors associated with IUGR (N=128)			
Risk factors	Cases (n=64) n (%)	Control (n=64) n (%)	p-value
Multiparity	25 (39.1)	23 (36)	0.71
BOH (prematurity, abortion)	27 (42.1)	7 (10.9)	<0.001
Preeclampsia	3(4.7)	2(3.1)	0.64
Eclampsia	3(4.7)	0	0.08
Multiple pregnancies	2(3.1)	0	0.154
PROM*	5(14.1)	1(1.6)	0.09

Anemia in mother	11(17.2)	9 (14.1)	0.626
Thalassemia in mother	2(3.1)	0	0.154
Diabetes	10(15.6)	3(4.7)	0.04
Hypothyroidism	24(37.5)	8 (12.5)	0.001
Hypertension	7 (10.9)	5 (7.8)	0.54
Tobacco intake in mother	1(1.6)	1(1.6)	1
UTI* in mother	5 (14.1)	1 (1.6)	0.094
Placental abnormality	2 (3.1)	0	0.154
Liquor abnormalities	14 (21.9)	3 (4.7)	0.004
* UTI-Urinary tract infection; PROM-Premature rupture of membranes			

Table-3 shows the association of various maternal risk factors with cases and controls. Among the cases 39% were multipara compared to 36% among controls, but the difference was not statistically significant. A higher proportion of mothers (42%) had bad obstetric history (abortion/IUD/prematurity) compared to controls (11%) and the difference was statistically significant ($p < 0.001$). A significantly higher proportion of cases ($p < 0.05$) had history of diabetes mellitus (15.6%), hypothyroidism (37.5%) and liquor abnormalities (22%) like oligohydromnios, polyhydromnios & meconium stained liquor compared to controls (4.7%, 12.5% and 4.7% respectively). Although other maternal obstetrics/medical conditions like pre-eclampsia, eclampsia, multiple pregnancies, PROM, anaemia (hemoglobin < 10 gm%), thalassemia, hyperthyroidism and hypertension were found to be more prevalent among the cases, their associations with IUGR were not statistically significant.

Univariate logistic regression analysis showed that socio-economic status below middle class (OR: 8.9, CI: 3.7, 21.1), height of mother (OR: 0.86, CI: 0.78, 0.95), weight gain during pregnancy (OR: 0.48, CI: 0.36, 0.62), heavy physical work (OR: 0.3, CI: 0.1, 0.98), bad obstetrics history (OR: 6.2, CI: 2.5, 15), hypothyroidism (OR: 4.2, CI: 1.7, 10.3) and liquor abnormalities (OR: 5.6, CI: 1.5, 20.9) were significantly associated with IUGR. In multivariable logistic regression, socio-economic status below middle class (AOR: 4.7, CI: 1, 20), height of mother (AOR: 0.82, CI: 0.69, 0.99), weight gain during pregnancy (AOR: 0.48, CI: 0.3, 0.7), heavy physical work (AOR: 0.13, CI: 0.1, 0.7) and liquor abnormalities (AOR: 29.5, CI: 2.8, 312) retained their significance ($p < 0.05$) [Table-4]. McFadden's Pseudo- R^2 for the model was 0.55.

Table-4 Univariate and multivariable logistic regression showing factors associated with IUGR				
Variables	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age	1.05 (.98 – 1.12)	0.139		
SE class <middle class	8.9 (3.7 – 21.1)	0.000	4.7 (1 – 20)	0.000
Education <VIII	1.62 (.73 – 3.6)	0.232		
Height	0.86 (0.78 – 0.95)	0.005	0.82 (0.69 – 0.99)	0.04
Weight gain	0.48 (0.36 – 0.62)	0.000	0.48 (0.3 – 0.7)	0.000
Heavy Physical Work	0.3 (0.1 – 0.98)	0.03	0.13 (0.01 – 0.7)	0.02
Multipara	1.3 (0.64 – 2.5)	0.48		
H/O Previous abortion	1.25 (0.75 - 2)	0.38		
Bad obstetric history	6.2 (2.5 – 15)	0.000	3.6 (0.98 – 13.5)	0.052
Pre-eclampsia	1.5 (0.25 – 9.4)	0.65		
Hypothyroidism	4.2 (1.7 – 10.3)	0.002	2.9 (0.7 – 11.9)	0.13
Liquor abnormality	5.6 (1.5 – 20.9)	0.009	29.5 (2.8 – 312)	0.005
PROM	5.3 (0.6 - 47)	0.13		

DISCUSSION:

Various studies have extensively documented obstetric and maternal risk factors associated with Intrauterine Growth Restriction (IUGR). Maternal age has been reported as a factor influencing

neonatal birth weight, with a significant association between lower maternal age and IUGR observed in studies by Jamal et al. and Taj.^{30,31} However our study did not find such relationship, whereas Odibo et al. noted a strong correlation between increasing maternal age and IUGR risk.¹⁷

First-time mothers (primigravida) are at higher risk of delivering IUGR babies.³³ There were more number of primigravida mothers in our study, a trend consistent with findings from studies in Pakistan and India.^{30–32} Inadequate nutrition, notably poor gestational weight gain, is implicated in impaired fetal growth,³³ with our study showing poor weight gain during pregnancy as a significant risk factor for IUGR. This aligns with prior research from India indicating that insufficient gestational weight gain elevates the risk of IUGR.^{34–36} Addressing maternal weight pre-conception and during pregnancy represents a potential avenue for improving birth outcomes.

Although anemia is prevalent among pregnant women in developing nations, our study did not find a significant association between anemia and IUGR. This differs from studies by Surve et al., Motghare et al. and Acharya et al., who reported higher rates of anemia (84.6%, 49% & 76% respectively) among pregnant women with IUGR.^{16,25,37} Maternal diabetes is known to impact placental function and fetal growth; our findings demonstrate a strong association between DM and IUGR, with 15.6% mothers having IUGR had DM ($p=0.04\%$), which differs with study by Taj et al.³² Hypertensive conditions, including Pregnancy-Induced Hypertension (PIH), contribute substantially to fetal growth restriction³⁸ and our study shows higher proportion of cases with hypertension but it was not statistically significant ($p>0.05$). This differs with previous research by Taj et al., Thompson, and Burke,^{32,39,40} who reported significant association between PIH and IUGR. Additionally, our study suggests a significant negative influence of previous abortion history on fetal growth, consistent with findings by Motghare.²⁵ However, this relationship was not observed in a study by Aghamolaei et al.⁴¹

CONCLUSION:

Several maternal risks factors for intrauterine growth restriction (IUGR) like weight gain during pregnancy, maternal height, diabetes mellitus, hypothyroidism, liquor abnormalities, etc. were recognized. Recognizing these indicators will not only aid in appropriate preventive measures but also facilitate timely detection of IUGR. Implementing nutritional interventions may support maternal weight gain during pregnancy. Screening and effective management of gestational diabetes mellitus (GDM), hypothyroidism and hypertension (PIH) can contribute to decreasing the occurrence of IUGR in the population, ultimately meeting the objective of reducing neonatal mortality and morbidity.

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