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Original Research Article.

Frequency, Risk Factors and Outcome of Clinical Management of Intrauterine Growth Restricted Infants in a Tertiary Care Hospital in Bangladesh

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ABSTRACT

Background: Fetal growth is a complex process which depends on nutrient and oxygen availability and transport from the mother to the fetus across the placenta. This involves hormones and growth factors as well as maternal and fetal genes. The failure of the fetus to reach his or her full potential for growth is called intrauterine growth restriction (IUGR) and implies risk for adverse short- and long-term outcomes.

Objective: To study the frequency, risk factors and outcome of the clinical management of IUGR infants in the NICU of a tertiary care hospital.

Methods: This case control study was conducted from August 2015 to July 2016 in the department of Neonatology, Bangabandhu Sheikh Mujib Medical University (BSMMU). Prior approval from Institutional Review Board (IRB) for this research work was taken.

After taking consent from parents/Guardians, particulars of the neonates, antenatal, natal and postnatal history were recorded in a data collection form. All Newborn in the NICU during study period were the study population. Newborn who meet the inclusion criteria were divided into two groups as case group (IUGR babies) and control group (AGA babies). The risk factors were identified by taking face to face interview of mother regarding prenatal period whereas the outcome of clinical management was observed by the caution and careful NICU follow up of the baby. Data were analyzed by statistical package for social sciences (SPSS) version 20. At first frequency of IUGR was found among all admitted newborn. Risk factors were analyzed to calculate the odds ratio. Then risk factors were analyzed with chi square test to find out significant risk factors. P values less than 0.05 (95% CI) were considered statistically significant.

Results: The frequency of IUGR babies in this one year study was found 11.86%. Congenital malformation (p=0.02) was found as significant fetal risk factor. Congenital CMV infection was found in 16.3 % case of IUGR babies. Maternal weight (p=<0.001), height (p=<0.001), socioeconomic status of mother (p=0.001), Inter pregnancy Interval (p=0.04), placental insufficiency (p=0.001), Pregnancy Induced hypertension (p=0.001) are significant maternal risk factor. Hypoglycemia (p=0.007) and hyperbilirubinemia (p=<0.001) were found significant co-morbidities. Length of hospital stay was significantly higher among IUGR babies (p= 0.001) that proclaim the outcome of clinical management. In case group 16.3% and in control 8.2% babies expired even after providing all available standard clinical management. Most of the patients died due to sepsis in both the groups. But the mortality showed no significant differences as outcome of clinical management.

Conclusion: IUGR babies in BSMMU was 11.86%. Maternal weight, height, inter pregnancy interval, socioeconomic status, Pregnancy induced hypertension, placental insufficiency, less ANC visits were maternal risk factors for IUGR babies.

Key words: Frequency, Risk Factors, IUGR Infants.

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INTRODUCTION

Intrauterine growth restriction (IUGR) is one of the major public health issues in developing countries like Bangladesh. It may be defined as the rate of fetal growth that is subnormal form the perspective of the growth potential of a specific infant according to race and gender.[1] Some authors defined it as the weight of the fetus below the 10th percentile of appropriate gestational time and gender.[2] IUGR has got significant importance due to its approach towards post neonatal, infant and childhood mortality and morbidity.[3]

IUGR incidence is singleton pregnancies is 3-7%.[4] Among them IUGR infants are frequently observed in Asian continent accounting for approximately 75% of all affected infants.[1] Bangladesh claimed the highest rank in the statistics of IUGR babies in Asian continent.[5]

IUGR may be caused by maternal, placental or fetal factors individually or altogether. Nearly one third of this problem may be due to genetic causes and rest two-third are due to fetal environment.[6] Among them elderly age of mother, inter-pregnancy interval, mothers health status, behavioural status and maternal infection are significant maternal risk factors.[7] Besides, the imbalance between supply of nutrient by the placenta and the demand of fetus is a significant fetal risk factor. Besides, congenital malformation, inborn error of metabolism and chromosomal mismatched conditions are also vital risk factors for IUGR.[7] Recently, it was claimed that maternal, fetal and placental genes polymorphisms are also accounted as risk factors for IUGR with the radical advancement of molecular biology and genetics.[8]

The aim of this study is to identify the frequency, risk factors and to observe the outcome of clinical management of IUGR infants.

METHODS

This case control study was conducted from August 2015 to July 2016 in the department of Neonatology, Bangabandhu Sheikh Mujib Medical University (BSMMU).

All Newborn in the NICU during study period were the study population. All the IUGR babies were labeled as case (Group- A) and the babies of the same gestational age were labeled as control (Group-B). After taking consent from the parents/guardians, particulars of the neonates, antenatal, natal and postnatal history were recorded in a data collection form. The risk factors were identified by taking face to face interview of mother regarding prenatal period whereas the outcome of clinical management was observed by careful NICU follow up of the baby. Maternal weight was taken by digital weight machine [SALTER], height was measured by stediometer and BMI was calculated by weight in kg divided by height in square meter. The infant's medical records were reviewed to identify antenatal, natal and postnatal risk factors and were recorded in a data collection form.

Here the mothers who's antenatal records properly maintained were included in the study; otherwise the case/control was excluded for lacking appropriate data. Information from ultrasonography report during pregnancy were collected. Placental insufficiency was confirmed by Doppler ultrasonography.

Clinical examination was done to search for any congenital anomalies, neurologic and metabolic abnormalities. The newborn infants were weighed without clothing soon after birth on an electronic scale (infant-type) with a precision of 10 g [Model 914, SALTER].

The OFC of the infant was taken by measuring tape & length was taken by infantometer, expressed as centimeter. Gestational age was calculated on the basis of ultrasonography findings and New Ballard scoring. Newborns were classified as large for gestational age, appropriate for gestational age, and IUGR when their birth weight was respectively above the 90th percentile, between the 90th and 10th percentiles, and less than the 10th percentile of the weight for gestational age from the Lubchenco chart for the determination of body proportionate. For detection of congenital CMV infection IgM & IgG for CMV was sent. When Anti CMV Ig G was found more than fourfold then urine for CMV DNA was done by PCR method. When CMV DNA was detected in urine it was labeled as congenital CMV infection. The infant of both group were under follow up to find out co-morbidities and outcome during hospital stay.

After collection, data were entered into a personal computer and were edited, analyzed, plotted in graphs and tables. Data were analyzed by chi square test, Mann Whitney U tests, using the statistical package for social sciences (SPSS) version 20.

Frequency of IUGR were calculated by percentage of total admitted newborn. Risk factors were analyzed to calculate the odds ratio. Then risk factors were analyzed with chi square test to find out significant risk factors. P values less than 0.05 (95% CI) were considered statistically significant.

RESULTS

The frequency of IUGR infants in BSMMU was 11.86% (73 in 615 admitted Newborn).

The frequency of LSCS is more in both case and control group. But the magnitude is more in IUGR group.

Majorities of deliveries in both groups took place in BSMMU, Thirty six (73.5%) and forty one (83.7%) were in case and control group respectively. Whereas 13(26.5%) and 8(16.3%) of case and control were delivered at other hospitals respectively.

Male and female sex were equal in both group 29 (59%) and 20(41%) respectively. There was statistically significant difference regarding maternal weight and total ANC visits of mothers between both groups (Table-1).

Table 1: Comparison of baseline characteristics of the study groups (n=98; 49 in each group)

Characteristic	Case (IUGR) (n=49)	Control (AGA) (n=49)	P-value
Maternal age (year)	24.09±5.1	23.33±5.03	0.25^{NS}
Maternal weight (kg)	47.05±9.19	52.15±8.59	**$<0.001^{S}$**
Total ANC visits (No.)	2.31±1.45	4.45±1.45	**$<0.001^{S}$**
BMI (kg/m^2)	23.33±1.93	24.54±2.1	0.078^{NS}

S: significant; NS: not significant; Statistics were calculated by Mann-Whitney U test; P-value is significant <0.05

Table 2: Fetal risk factor in both groups (n=98; 49 in each group)

Variables	Cases (IUGR) (n=49)	Control (AGA) (n=49)	OR (95% CI)	P-value
Intrauterine infection (Cytomegalovirus)				
Yes	8 (16.3%)	----	-----	**------**
No	41 (83.7%)	----	-----	
Congenital malformation				
Yes	9 (18.4%)	1 (2.1%)	10.8	**0.02S**
No	40 (81.6%)	48(97.9%)	(1.3-88.92)	
Multiple gestation				
Yes	4 (8.2%)	1 (2.1%)	4.27	0.2 NS
No	45 (91.8%)	48 (97.9%)	(0.459-39.545)	

Table 3: Maternal Risk factors associated with IUGR babies (n=98; 49 in each group)

Characteristics	Case (IUGR) (n=49)	Control (AGA) (n=49)	OR (95% CI)	P-value
Maternal age (years)				
<20 years	4 (8.2%)	2 (4.1%)	2.09 (0.364-11.94)	0.4**NS**
20-34 years	38 (77.5%)	44 (89.8%)	1	
≥35 years	7(14.3%)	3 (6.1%)	2.56 (0.62-10.49)	
Maternal weight				
≤45 kg	25 (51%)	12 (24.5%)	4.94 (2.65-9.21)	**<0.001S**
45-55 kg	16 (32.7%)	20 (40.8%)	2.07 (1.12-3.82)	
≥55 kg	8 (16.3%)	17 (34.7%)	1	
Maternal height				
≤1.45 meters	26(53.1%)	5(10.2%)	11.09 (5.23-23.56)	<0.001S
1.46-1.55 meters	15(30.6%)	31(63.3%)	1.05 (0.56-1.86)	
>1.55 meters	8(16.3%)	13(26.5%)	1	
BMI (kg/m2)				
<18.5	8(16.3%)	7 (14.3%)	0.92 (0.52-1.66)	0.14 **NS**
18.5-24.99	32(65.3%)	35 (71.4%)	1.95 (0.86-4.42)	
≥25	9(18.4%)	7 (14.3%)	1	
Parity				
1	29 (59.2%)	32 (65.3%)	0.97 (0.61-1.62)	0.43 **NS**
2	15 (30.6%)	14 (28.6%)	1	
≥3	5 (10.2%)	3 (6.1%)	1.81 (0.68-4.61)	
Inter pregnancy interval				
<24 months	14 (28.6%)	9 (18.4%)	2.69 (1.17-6.13)	**0.04S**
24-48 months	18 (36.7%)	27 (55.1%)	1	
>48 months	17 (34.7%)	13 (26.5%)	2.14 (1.02-4.56)	
Socioeconomic status of mothers				
Lower	40 (81.6%)	30 (61.2%)	2.6 (1.5-3.9)	**0.001S**
Middle	8 (16.3%)	17 (34.7%)	1	
Upper	1 (2.1%)	2 (4.1%)	1	
Placental Insufficiency				
Yes	26 (53.1%)	3(6.1%)	16.99	**<0.001S**
No	23 (46.9%)	46 (93.9%)	(4.67-61.87)	
Previous IUGR				
Yes	5 (10.2%)	1 (2.1%)	5.47	**0.09NS**
No	44 (89.8%)	48 (97.9%)	(0.61-48.51)	
Pregnancy Induced HTN				
Yes	24 (49%)	8 (16.3%)	4.85 (1.89-12.38)	**0.001S**
No	25(51%)	41 (83.7%)		
Chronic medical illness				
Yes	14 (28.6%)	7 (14.3%)	7.8 (1.725-13.27)	0.53 **NS**
No	35 (71.4%)	42 (85.7%)		

OR: Odds ratio; P-value was calculated by chi-square test; S: significant; NS: Not significant

Table 4: Distribution of Co-morbidities of neonates in both groups (n=98; 49 in each group)

Co-morbidities	Case (IUGR) (n=49)	Control (AGA) (n=49)	P-value
Hypothermia			
Present	4 (8.2%)	2 (4.1%)	0.39^{NS}
Absent	45 (91.8%)	47 (95.9%)	
Hypoglycemia			
Present	10 (20.4%)	1 (2.1%)	**0.007^{S}**
Absent	39 (79.6%)	48 (97.9%)	
Perinatal Asphyxia			
Present	10 (20.4%)	8 (16.3%)	0.79^{NS}
Absent	39 (79.6%)	41 (83.7%)	
Sepsis			
Present	32 (65.3%)	22 (44.9%)	0.07^{NS}
Absent	17 (34.7%)	27 (55.1%)	
Polycythemia			
Present	3(6.1%)	1(2.1%)	0.31^{NS}
Absent	46(93.9%)	48(97.9%)	
Hyperbilirubinemia			
Present	43 (87.6%)	27 (55.1%)	
Absent	6 (12.4%)	22 (44.9%)	**<0.001^{S}**
Respiratory distress			
Present	24 (49%)	18 (36.7%)	
Absent	25 (51%)	31 (63.3%)	0.23^{NS}

Table 5: Distribution of clinical management outcome (n=98, 49 in each group)

Variables	Case (IUGR) (n=49)	Control (AGA) (n=49)	p value
Length of hospital stay			
24 - <72 hour	1 (2.1%)	6 (12.2%)	**0.001^{S}**
3 - <7 days	10 (20.4%)	17 (34.7%)	
7 - <14 days	9 (18.3%)	15 (30.6%)	
≥14 days	29 (59.2%)	11 (22.5%)	
Death			
Yes	8 (16.3%)	4 (8.2%)	0.23^{NS}
No	41(83.7%)	45(91.8%)	

P value was calculated by chi square test; S: significant; NS: not significant; P-value <0.05 significant

Congenital malformation (P=0.02) has the significant contribution for IUGR. (Table-2)

Maternal weight (P=<0.001), height (P=<0.001), inter pregnancy interval (P=0.04), socioeconomic status (P=0.001), placental insufficiency (P=<0.001), pregnancy induced HTN (P=0.001) are significant contributing factors. (Table-3)

The co-morbidities of neonates where hypoglycemia (p= 0.007) and hyperbilirubinemia (p = < 0.001) showed the significant difference (Table-4). Among the outcome of clinical management of IUGR babies length of hospital stay (p= 0.001) showed significant differences between the groups. (Table-5)

DISCUSSION

The frequency of IUGR babies was found in BSMMU 11.86% which is much lower than another previous Bangladeshi study where it was reported as 39.4%.[9]

National Neonatal Perinatal Database of India reported the incidence of IUGR to be 9.65% among hospital born live birth infants.[10] Previous study showed an association with female sex which has been reported as a significant risk factor in study from Africa.[11] But in this study it was found that neonates' sex distribution is almost equal in both groups. According to the study of Singh et al.[12] LBW was significantly associated with total number of ANC visits. Current study also showed that less ANC visit was significantly associated with higher incidence of IUGR. In this study previous history of growth restriction was not significantly related with IUGR. But it was found significant by Thompson et al.[13] and Sharon and Gilberto.[14] IUGR babies were more frequently observed among the poor socioeconomic background. Several studies also revealed similar result.[15-17]

H. S. Joshi et al.[18] studied on 256 mothers and their newborn babies and concluded that placental insufficiency was one of the prime maternal risk factors that supported our study. Similar picture was drawn by Visser et al.[19] In this study, IUGR babies developed sepsis (65.3%), hypothermia (8.2%), hypoglycemia (20.4%), perinatal asphyxia (20.4%), polycythemia (6.1%), hyperbilirubinemia (87.6%), respiratory distress (49%). Nelson KB et al.[20] found hypoglycemia and hyperbilirubinemia as statistically significant complications. Placental insufficiency was recognized as a risk factor (p=0.001) in this study, as it was also mentioned

by Krishna Usha et al.[21] Pregnancy induced hypertension was found as risk factor (p=0.001) for IUGR which was also found significant by Victoria M Allen et al.[22]Inter pregnancy interval showed significance (P=0.04) in contributing as a risk factor for developing intrauterine growth restriction which was similar with Yadav et al.[23] and in contrast with Roy et al.[24] The overall outcome of clinical management revealed that in IUGR group 8(16.3%) babies died and 41(83.7%) were survived. Among them 6 babies died due to sepsis & congenital heart disease. Rest 2 babies were died due to perinatal asphyxia. Length of hospital stay (p=0.001) were significantly more in IUGR group.

CONCLUSION

Frequency of IUGR babies in BSMMU was 11.86%. Maternal weight, height, inter pregnancy interval, socioeconomic status, Pregnancy induced hypertension, placental insufficiency, less ANC visits were maternal risk factors for IUGR babies. Congenital malformation was found as fetal risk factor. Congenital CMV infection was found in 16.3 % of IUGR babies. Hypoglycemia and hyperbilirubinemia were significant co-morbidities of IUGR babies. IUGR babies had longer hospital stay than AGA babies. Deaths were more in IUGR babies but was not statistically significant.

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