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Original Article

A Study to Evaluate the Clinical Profiles of Asymmetric and Mixed Types of Intrauterine Growth Retardation

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Abstract

Introduction: The prevalence of intrauterine growth restriction (IUGR) is about 28% in the general population. IUGR poses increased risk of fetal mortality and morbidity and also contributes to developmental origin of health and disease. Of the three types of IUGR, Type III is more common in developing countries. This study evaluates the clinical profiles of Type II and Type III IUGR and also to evaluate any differences between the two types.

Materials and Methods: This cross-sectional, observational, and analytical study was conducted on 86 pregnant women with gestational age of more than 24 weeks, clinically diagnosed as IUGR and confirmed by ultrasound. They were followed up till discharge in the postnatal period. Any significant antenatal, intranatal, or postnatal events were recorded.

Results: There were increased incidences of oligohydramnios, preterm birth, and requirement of cesarean section which are increased in the cases of IUGR, more in Type II than in Type III IUGR. Furthermore, there were significant differences in maternal Vitamin D levels between the low and normal birth weight groups in Type II IUGR.

Conclusion: IUGR is associated with increased risk of preterm birth and operative delivery. Deficient maternal serum Vitamin D levels are a risk factor for low birth weight in asymmetric IUGR only, though further studies need to be conducted in this regard.

Key words: Asymmetric intrauterine growth restriction, Cesarean section, Mixed intrauterine growth restriction, Oligohydramnios, Preterm birth, Type II intrauterine growth restriction, Type III intrauterine growth restriction, Vitamin D

INTRODUCTION

Intrauterine growth restriction (IUGR) is defined as a velocity of fetal growth less than the normal fetus growth potential for a specific neonate as per the race and gender. Any fetus with sonographic estimated weight below the 10th percentile for gestational age (GA) is considered to have IUGR.[1]

The prevalence of IUGR is about 28% in the general population. The prevalence of IUGR is higher in Asia than elsewhere. It has been shown that 52% of stillbirths are associated with IUGR and 10% of perinatal mortality is a consequence of IUGR.[1] Apart from the increased risk of mortality, IUGR neonates also face many short-term and long-term complications, including fetal origin of adult disease, which has been recently replaced with "developmental origin of health and disease."[2]

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Clinically, three categories of IUGR can be identified depending on the time of onset and the pathological process:[1]

1. Type I or symmetrical or intrinsic IUGR – this occurs as a result of growth inhibition early pregnancy. It accounts for 2030% of growth retardation. This type of IUGR leads to reduced number of cells in fetus and overall decreased growth potential caused by intrauterine infection, chromosomal disorders, and congenital malformation. All parameters, i.e. head and abdominal circumference, length, and weight are below 10th percentile for gestation age; hence, these infants have a normal ponderal index

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2. Type II or asymmetrical or extrinsic IUGR – this occurs as a result of restriction of nutrient supply *in utero*, i.e. uteroplacental insufficiency. It accounts 7080% of growth restriction. The onset occurs usually after 28 weeks of gestation. This type of IUGR has near-normal total number of cells, but the cell size is reduced. There is brain-sparing effect so that the head growth remains normal but abdominal growth slows down. The ponderal index is low with low birth weight (LBW) and abdominal circumference and fetal length leads to decrease amniotic fluid and chronic hypoxia and may result in fetal length
3. Type III or intermediate IUGR or mixed IUGR – it is a combination of Type I and Type II resulting in decreased number as well as decreased cell size accounts for 510% of all growth retarded.

Type I IUGR is due to early insult in multiplication of cells during fetal growth which is intrinsic pathological process genetically determined independent of any micronutrient deficiency while Type II and Type III IUGR are caused by extrinsic factors such as most of micronutrient deficiency result due to uteroplacental insufficiency results in poor differentiation of cells during fetal growth. Of the micronutrients, Vitamin D has been hypothesized as a cause for fetal growth restriction. The link between maternal Vitamin D status and fetal growth, as measured most frequently by infant birth weight and birth length, has been explored by a number of investigators with mixed result.[3] Thus, clearly, Type II and Type III IUGR may be preventable, to some extent, by addressing the modifiable factors.

Although there have been some comparative studies between symmetric (Type I) and asymmetric (Type II) IUGR, no studies were found involving mixed (Type III) IUGR. As Type III IUGR is usually seen in the developing countries[1] and also as Type II and Type III IUGR may be associated with preventable risk factors, therefore, this study was undertaken to understand the clinical profiles of Type II and Type III IUGR and also to evaluate any differences between the two types.

MATERIALS AND METHODS

This cross-sectional, observational, and analytical study was undertaken after approval of the Institutional Ethics Committee.

A total of 86 pregnant women attending antenatal clinic with gestation age more than 24 weeks and clinically diagnosed as IUGR were included in the study, after confirmation by the sonographic parameters. Pregnant women having any major comorbidities such as diabetes, parathyroid or bone disease, and anemia or any major high-risk condition associated with the current pregnancy such as antepartum hemorrhage, placenta previa, and pre-eclampsia were excluded from the study.

A written informed consent was obtained from each participant. Demographic details and routine obstetric history were recorded. Physical and obstetric examination was done. Routine investigations were carried out. Apart from that, the serum Vitamin D3 levels, serum calcium levels, and serum alkaline phosphatase levels were also recorded.

All the patients were followed up till discharge in the postnatal period. Any significant antenatal, intranatal, or postnatal events were recorded.

Statistical Analysis

The data were analyzed using SPSS. Qualitative data were analyzed using Chi-square test (Fisher's exact test when any cell value was <5) and quantitative data were analyzed by unpaired *t*-test. $P < 0.05$ was considered to be statistically significant.

RESULTS

Of the total 86 cases, the incidence of Type II IUGR was 84% (72 cases) and of Type III IUGR was 16% (14 cases). The overall prevalence of oligohydramnios, operative delivery by lower segment cesarean section (LSCS), and LBW is as per Table 1.

The prevalence of oligohydramnios was more in Type III IUGR group and the difference was statistically significant [Table 2].

No statistically significant differences were found in either the incidence of preterm deliveries ($P = 0.24$) or the birth weight ($P = 0.25$) in the two groups [Table 3].

The requirement of operative delivery (LSCS) was also significantly more in Type III IUGR group [Table 4].

On comparing the maternal serum levels of Vitamin D3, it was found that there was on overall deficiency [Table 5].

Table 1: Distribution of the characteristics in the study group

Parameter	Number of cases	Percentage
Oligohydramnios	39	45
Operative delivery (LSCS)	42	49
LBW (<2.5 kg)	55	64
Deficiency of Vitamin D3 (<50 nmol/L)	83	97
Deficiency of calcium (<8 mg/dL)	18	21
Neonatal death	1	1.2

LSCS: Lower segment cesarean section, LBW: Low birth weight

However, when grouped as per the type of IUGR, there was no statistically significant difference. However, when grouped as per the birth weight of the neonate, the group with LBW had a much lower maternal serum Vitamin D3 and that was statistically significant.

Table 2: Prevalence of oligohydramnios in Type II and Type III IUGR

Parameter	Type II IUGR (%)	Type III IUGR (%)	*P* value	Statistical significance
Oligohydramnios				
Present	25 (35)	14 (100)	<0.0001	Significant
Absent	47 (65)	0		

IUGR: Intrauterine growth restriction

Table 3: Comparison of incidence of preterm deliveries as per the type of IUGR

Parameter	Type II IUGR (%)	Type III IUGR (%)	*P* value	Statistical significance
Preterm delivery	20 (28)	3 (21)	0.24	Not significant
Term delivery	52 (72)	11 (79)		

IUGR: Intrauterine growth restriction

Table 4: Mode of delivery in Type II and Type III IUGR

Parameter	Type II IUGR (%)	Type III IUGR (%)	*P* value	Statistical significance
Delivery by LSCS	31 (43)	11 (79)	0.015	Significant
Normal/assisted	41 (57)	3 (21)		

IUGR: Intrauterine growth restriction, LSCS: Lower segment cesarean section

Maternal serum calcium levels were normal [Table 5] and no significant differences were found in terms of the type of IUGR or birth weight.

When maternal serum Vitamin D3 levels were compared in terms of birth weight in the Type II and Type III IUGR groups, no significant intergroup differences were found ($P > 0.05$). The only significant difference was found in the intragroup comparison in the Type II IUGR group [Table 6].

DISCUSSION

Fetal or IUGR is associated with perinatal mortality and morbidity. A satisfactory definition of IUGR has been suggested by the American College of Obstetricians and Gynecologists as describing "a fetus that fails to reach his potential growth."[2]

The recognition of IUGR begins with an accurate GA. Many studies have been conducted regarding the risk factors of IUGR. There have been some studies comparing the symmetric (Type I) and asymmetric (Type II) IUGR. However, no study was found regarding the studies profile of mixed IUGR. Therefore, this study was undertaken to compare the risk factors of asymmetric and mixed IUGR.

Oligohydramnios

The overall incidence of oligohydramnios is 15%.[4] However, in the study by Lin *et al.*,[5] the incidence of oligohydramnios was found to be significantly higher

Table 5: Intergroup comparisons of maternal serum levels of Vitamin D3 and calcium as per the type of IUGR and birth weight of the neonate

Parameter	Serum Vitamin D3 (in nmol/L)			Serum calcium (in mg/dL)		
	Mean±SD	*P* value	Significance	Mean±SD	*P* value	Significance
Type of IUGR						
Type II	27.52±10.23	0.189	Not significant	8.54±1.03	0.149	Not significant
Type III	24.96±9.57			8.82±0.88		
Birth weight						
Low	25.51±9.95	0.026	Significant	8.58±1.00	0.494	Not significant
Normal	29.92±9.96			8.59±1.03		

IUGR: Intrauterine growth restriction, SD: Standard deviation

Table 6: Intragroup comparison of maternal serum Vitamin D3 levels (in nmol/L) according to birth weight of the baby in the Type II and Type III IUGR groups

Type II IUGR				Type III IUGR			
LBW	Normal birth weight	*P* value	Statistical significance	LBW	Normal birth weight	*P* value	Statistical significance
Mean±SD	Mean±SD			Mean±SD	Mean±SD		
25.94±9.94	30.13±10.37	0.046	Significant	23.57±9.75	28.45±7.58	0.205	Not significant

LBW: Low birth weight, IUGR: Intrauterine growth restriction, SD: Standard deviation in the IUGR group (29%) compared to non-IUGR group. Accordingly, in the present study, the incidence of oligohydramnios in IUGR was 45%.

All the cases of mixed IUGR were associated with oligohydramnios, in contrast to only 35% association in case of asymmetric IUGR.

Preterm Birth (Before 37 Weeks)

The overall preterm birth rate is 57% of the live births.[6] In the present study, the overall incidence was much higher (36.5%). Although IUGR has been hypothesized as a risk factor for preterm labor, the mechanisms of the relationship remain unknown. It has been hypothesized that IUGR increases susceptibility to preterm labor due to the changing balance of synthetic and metabolizing enzymes and hence increasing the availability of prostaglandins (key stimulants of labor).[7]

As per the study by Lin *et al*.,[8] the incidence of preterm labor was less in the cases of asymmetric IUGR as compared to symmetric IUGR.

In the present study, the incidence of preterm labor was slightly more with asymmetric IUGR than mixed IUGR. However, the difference was not statistically significant.

Cesarean Section

The overall cesarean section rate in India is 17.2%.[9] However, in the study by Boers *et al*.,[10] the cesarean section rate in the cases of IUGR was 44%. Accordingly, in the present study, the cesarean section rate was 49%.

In the study by Connor *et al*.,[11] the cesarean section rate was found to be significantly higher in the symmetric IUGR group (12%) than in the asymmetric IUGR group (5%).

In the present study, the rate was more in the case of mixed IUGR (79%) than in the case of asymmetric IUGR (43%).

Birth Weight

The incidence of LBW in India varies between 25% and 30% and of which 60% and 65% are due to IUGR.[12] In accordance, the incidence of LBW in the present study was found to be 64%.

As per the studies by Lin *et al*.[8] and Connor *et al*.,[11] it was concluded that the birth weight was more in cases of asymmetric IUGR than in symmetric IUGR.

In the present study, no statistically significant difference was found in the incidence of LBW between the asymmetric and mixed IUGR groups.

Vitamin D3

In the present study, the prevalence of deficiency of Vitamin D3 in IUGR cases was 97%. This is in accordance to the high prevalence of Vitamin D deficiency in cases of IUGR in the studies by Nageshu *et al*. (68%),[13] Aly *et al*. (66%),[14] Hollis *et al*. (84%),[15] and in the systematic review by Aghajafari *et al*.[16]

It was also found in this study that the birth weight of the neonate was associated with maternal serum Vitamin D3 levels. The mean maternal serum Vitamin D3 level was significantly lower in the group with LBW babies than with normal birth weight babies. This was in accordance with the study by Nageshu *et al*.[13] and with the systematic review by Aghajafari *et al*.[16] However, these were in contrast to the study by Gale *et al*.[17]

When analyzed according to the type of IUGR, statistically significant difference was found between maternal serum Vitamin D3 levels in low and normal birth weight groups in the asymmetric IUGR group. However, this difference was not significant in the mixed IUGR Group. Thus, maternal serum Vitamin D3 levels have a significant impact on the birth weight of the neonate in the case of asymmetric IUGR.

Limitations

The study was limited by the outpatient department attendance of the pregnant women with IUGR. Therefore, the results may not be generalized.

CONCLUSION

It can be effectively concluded from the study that the incidences of oligohydramnios, preterm birth, and requirement of cesarean section are increased in the cases of IUGR. Furthermore, these incidences are significantly different in the asymmetric (Type II) and mixed (Type III) IUGR cases. Low levels of maternal serum Vitamin D3 lead to LBW, particularly in cases of asymmetric IUGR. Thus, the deficiency of maternal serum Vitamin D3 as a risk factor for LBW in IUGR is supported only in case of asymmetric IUGR but not in mixed IUGR, though further studies need to be conducted in this regard.

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