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Risk Factors Associated with Intrauterine Growth Restriction: A Case-Control Study

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ABSTRACT

Intrauterine growth restriction (IUGR) is a significant contributor to perinatal morbidity and mortality in low- and middle-income countries. **Objectives:** To determine maternal and clinical risk factors for IUGR among pregnant women at a tertiary care hospital in Karachi. **Methods:** This case-control study was conducted in the Department of Obstetrics and Gynecology, Kharadar General Hospital, from November 2023 to April 2024. A total of 188 women were enrolled, including 94 cases (women with IUGR) and 94 controls (women without IUGR). Data on sociodemographic characteristics, anemia, pregnancy-induced hypertension (PIH), thyroid dysfunction, and nutritional status were collected using predefined operational definitions. Logistic regression determined the independent risk factors. **Results:** The mean maternal age was 30.3 ± 4.2 years among cases and 29.3 ± 4.5 years among controls. Anemia and hypothyroidism were significantly associated with IUGR in multivariate analysis (aOR=4.23; 95% CI: 1.60–11.19; p=0.004 and aOR=6.04; 95% CI: 1.61–22.68; p=0.008, respectively). PIH showed significance in univariate analysis but lost significance after adjustment. Maternal underweight and hyperthyroidism were not independently associated with IUGR. **Conclusions:** Maternal anemia and hypothyroidism emerged as independent risk factors for IUGR, highlighting the need for routine screening and early interventions during pregnancy to improve neonatal outcomes.

INTRODUCTION

Increased perinatal morbidity and mortality are associated with intrauterine growth restriction (IUGR), which restricts the fetal growth potential. It is characterized by a birth weight below the 10th percentile for gestational age, affecting approximately 30 million infants worldwide each year, particularly in low- and middle-income countries [1, 2]. In Pakistan, IUGR contributes to an estimated 20–24% of live births, representing a significant cause of neonatal complications and mortality [3]. The etiology of IUGR differs between developed and developing regions. In high-income countries, placental insufficiency is a primary factor, whereas in resource-limited settings, maternal anemia, malnutrition, infections, and inadequate antenatal care are more prominent [4, 5]. Previous studies have also highlighted pregnancy-induced hypertension and thyroid dysfunction as major maternal contributors [6, 7]. These risk factors not only increase the likelihood of intrauterine growth restriction but also predispose affected infants to lifelong health consequences such as impaired neurodevelopment and metabolic disorders [8, 9]. As different studies highlighted the pool of risk factors, some factors like illiteracy, maternal mid-upper arm circumference <23, body mass index, altitude, small placental size, and small for gestational age are also known predictors of IUGR [10, 11].

Despite its importance, research on IUGR in Pakistan has largely focused on prevalence rather than determinants. Comprehensive data on maternal and clinical factors linked

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to intrauterine growth restriction (IUGR) in local populations are currently limited. Identifying such risk factors is essential for guiding obstetricians toward early diagnosis, preventive measures, and timely interventions. This study aims to assess maternal risk factors associated with IUGR and provide baseline data that may support national strategies to reduce perinatal morbidity and mortality.

METHODS

This case-control study was conducted in the Department of Obstetrics and Gynecology, Kharadar General Hospital, from November 2023 to April 2024, after obtaining ethical approval from the Hospital Ethical Review Committee (Ref. No. CPSP/REU/OBG-2022-207-11626). Written informed consent was taken from all participants. Pregnant women aged 18–45 years with more than 20 weeks of gestation attending the antenatal clinic were included, while those with multiple pregnancies, a history of renal failure or chronic liver disease, or unbooked status were excluded. The sample size was calculated using the WHO sample size calculator, based on the reported frequency of anemia among cases and controls (29.6% and 12.9%, respectively), with 80% power and a 95% confidence level, yielding a total of 188 participants (94 in each group). Non-probability consecutive sampling was applied to recruit both cases and controls. Participants were categorized into two groups: cases (women with intrauterine growth restriction, IUGR) and controls (women without IUGR). Baseline demographic and clinical data, including age, residence, family income, height, weight, BMI, parity, gravida, and number of children, were recorded on a predesigned proforma, and all patients were managed as per hospital protocols. Anemia, PIH, thyroid disorders, and maternal underweight were defined using standard clinical criteria. Data analysis in SPSS version 26 included descriptive statistics and binary logistic regression to identify IUGR-related factors. Variables with p <0.25 from univariate analysis were included in the model, showing no multicollinearity. Adjusted odds ratios with 95% confidence intervals were reported, considering confounders such as age, residence, income, parity, gravidity, and number of children, with significance set at p ≤0.050.

RESULTS

A total of 188 women participated in the study, consisting of 94 cases with Intrauterine Growth Restriction (IUGR) and 94 controls without IUGR. Both groups predominantly included women aged ≤30 years (53.2% in cases, 64.9% in controls), with no significant age difference (p=0.225). Income levels were similar, with 44.7% in both groups earning between 30,000 to 50,000 PKR (p=0.205). Urban residency was higher among both groups (62.8% cases, 69.1% controls), showing no significant difference (p=0.356). Notably, significant differences were observed in parity and gravidity: controls had a higher percentage of primigravida (46.8% vs. 27.7% in cases, p=0.007) and nulliparity (51.1% vs. 33% in cases, p=0.003) (Table 1).

Table 1: Baseline Characteristics of Patients According to Groups (N=188)

Variables	Groups	Case (with IUGR) N=94	Control (without IUGR) N=94	p-Value
Age Groups (Years)	≤ 30	50 (53.2%)	61 (64.9%)	0.225
	31–35	32 (34.0%)	22 (23.4%)	
	> 35	12 (12.8%)	11 (11.7%)	
Family Monthly Income (Rs)	< 30,000	27 (28.7%)	18 (19.1%)	0.205
	30,000–50,000	42 (44.7%)	42 (44.7%)	
	> 50,000	25 (26.6%)	34 (36.2%)	
Residence	Urban	59 (62.8%)	65 (69.1%)	0.356
	Rural	35 (37.2%)	29 (30.9%)	
Gravida	Primigravida	26 (27.7%)	44 (46.8%)	0.007
	Multigravida	68 (72.3%)	50 (53.2%)	
Parity	Nulliparous	31 (33.0%)	48 (51.1%)	0.003
	Primiparous	36 (38.3%)	36 (38.3%)	
	Multiparous	27 (28.7%)	10 (10.6%)	

Participants in both groups were similar in age, with no significant difference observed. However, controls had notably higher BMI and hemoglobin levels than cases, and both differences were statistically significant (p < 0.001) (Table 2).

Table 2: Descriptive Statistics of Study Patients According to Groups (N=188)

Variables	Cases (with IUGR)	Controls (without IUGR)	p-Value
Age (Years)	30.36 (±4.2)	29.31 (±4.53)	0.100
BMI (kg/m^2)	23.39 (±4.39)	28.66 (±5.57)	<0.001
Hemoglobin (g/dl)	10.37 (±1.89)	11.58 (±1.26)	<0.001
Family Income (Rs)	41,000 (±12,000)	46,000 (±12,700)	0.023

Anemia, underweight status, PIH, and thyroid dysfunction showed significant associations with intrauterine growth restriction (IUGR). Anemia was five times more common in IUGR cases than controls [OR=5.08; 95% CI: 2.71–10.41; p=0.005]. Underweight women had a threefold higher risk of IUGR [OR=3.24; 95% CI: 1.22–8.63; p=0.014]. PIH was also about three times more frequent among cases [OR=3.09; 95% CI: 1.29–7.39; p=0.009]. Thyroid dysfunction was significantly more prevalent in IUGR cases [OR=4.12; 95% CI: 2.19–7.76; p=0.005], with hypothyroidism showing a strong association [OR=13.97; 95% CI: 4.72–41.31; p=0.005], while hyperthyroidism showed no link (p=0.519) (Table 3).

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Table 3: Risk Factors Associated with Intrauterine Growth Restriction(N=188)

Variables	Category	Case (IUGR) (N=94)	Control (No IUGR) (N=94)	Total	p-Value	OR [95% CI]
Anemia	Yes	49 (52.1%)	16 (17.0%)	65	0.005	5.08 [2.71 – 10.41]
	No	45 (47.9%)	78 (83.0%)	123		
Underweight	Yes	17 (18.1%)	6 (6.4%)	23	0.014	3.24 [1.22 – 8.63]
	No	77 (81.9%)	88 (93.6%)	165		
Pregnancy-Induced Hypertension (PIH)	Yes	21 (22.3%)	8 (8.5%)	29	0.009	3.09 [1.29 – 7.39]
	No	73 (77.7%)	86 (91.5%)	159		
Thyroid Dysfunction	Yes	51 (54.3%)	21 (22.3%)	72	0.005	4.12 [2.19 – 7.76]
	No	43 (45.7%)	73 (77.7%)	116		
Hypo-thyroidism	Yes	36 (38.3%)	4 (4.3%)	40	0.005	13.97 [4.72 – 41.31]
	No	58 (61.7%)	90 (95.7%)	148		
Hyper-thyroidism	Yes	11 (11.7%)	14 (14.9%)	25	0.519	0.75 [0.33 – 1.77]
	No	83 (88.3%)	80 (85.1%)	163		

OR = Odds ratio, CI=Confidence Interval

Multivariate analysis identified anemia and hypothyroidism as significant predictors of IUGR after controlling for confounders, with adjusted odds ratios of 4.23 and 6.04, respectively. Thyroid dysfunction showed a marginal association, while factors such as underweight status, pregnancy-induced hypertension, age, gravida, and parity were not significantly linked to IUGR. The model achieved a 74.5% classification accuracy, correctly identifying IUGR status in most participants (Table 4).

Table 4: Multivariate Analysis Showing the Factors Associated with IUGR(N=188)

Variables	p-Values	Adjusted OR	95% CI for OR	
			Lower	Upper
Age Groups				
≤30	0.430	1.61	0.49	5.28
31–35	0.420	1.65	0.486	5.57
>35	–	Ref	–	–
Gravida				
Primigravida	0.890	0.89	0.159	5.02
Multigravida	–	Ref	–	–
Parity				
Nulliparous	0.070	0.18	0.027	1.18
Primiparous	0.130	0.45	0.162	1.26
Multiparous	–	Ref	–	–
Anemia				
Yes	0.004	4.23	1.60	11.19
No	–	Ref	–	–
Pregnancy-Induced Hypertension				
Yes	0.620	1.315	0.446	3.87
No	–	Ref	–	–
Thyroid Dysfunction				
Yes	0.068	2.24	0.942	5.32
No	–	Ref	–	–
Hypothyroidism				
Yes	0.008	6.04	1.61	22.68
No	–	Ref	–	–
Underweight				
Yes	0.990	0.992	0.261	3.77
No	–	Ref	–	–

Model Accuracy = 74.5% Ref= References, CI=Confidence Interval

DISCUSSION

Hypoxia, impaired neurodevelopment, and metabolic disorders later in life are among the negative neonatal outcomes that IUGR causes globally [12, 13]. The burden is particularly high in low- and middle-income countries, including Pakistan, where limited antenatal screening and nutritional deficiencies are common [14]. According to Sinha et al., the incidence of IUGR was 2.13%, with the majority of cases (48%) occurring in women aged 21–25 years. A separate case-control study reported that 51.9% of IUGR cases fell within the 21–25 age group, followed by 37.0% in the 26–30 age group, and 11.1% in women over 30 [15]. In the control group, the distribution was 40.7% (21–25 years), 48.2% (26–30 years), and 11.1% (>30 years). Several other studies have also identified younger maternal age as a significant risk factor for IUGR. In our study, anemia was found to be a strong independent risk factor for IUGR, with a fivefold higher likelihood among cases. These findings are consistent with previous reports highlighting anemia and antepartum hemorrhage as major contributing factors [16-19]. Hemoglobin deficiency reduces oxygen-carrying capacity, leading to chronic fetal hypoxia and growth restriction. We categorized thyroid dysfunction according to standard pregnancy-specific criteria. The significant association between hypothyroidism and IUGR in our study aligns with prior evidence that maternal thyroid insufficiency impairs placental and fetal development [20, 21]. The distinction between subclinical and overt hypothyroidism is important, as both conditions may increase the risk of adverse pregnancy outcomes, though overt hypothyroidism has a stronger effect on fetal growth restriction. Hypothyroidism remained significant in multivariate analysis, supporting prior evidence that maternal thyroid dysfunction interferes with placental and fetal metabolism, thereby increasing the risk of IUGR. However, some studies reported no association, possibly due to geographical variation [22]. Maternal underweight and hyperthyroidism were not associated with IUGR in multivariate analysis, although underweight status has been identified as a significant risk factor in other studies [17, 23]. Current findings suggest that nutritional and metabolic disturbances may exert their effects indirectly through anemia rather than BMI alone. In our study, the mean BMI was significantly higher among controls compared to cases, suggesting that maternal obesity may

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play a protective role against IUGR. Several studies have reported similar findings, indicating that higher maternal BMI is often associated with increased nutrient availability and placental growth, which may reduce the likelihood of restricted intrauterine growth [24, 25].

However, this does not imply that obesity is beneficial, as excessive maternal weight is independently linked to gestational diabetes, preeclampsia, and cesarean delivery. This study has certain limitations. First, as a single-center case-control study, the findings may not be generalizable to all populations. Second, definitions of IUGR vary across the literature, with some studies using <2 kg birth weight and others using <10th percentile for gestational age, which may introduce comparability bias. Third, only maternal clinical and biochemical factors were considered; fetal and placental parameters such as Doppler indices and congenital anomalies were not assessed. Fourth, the cross-sectional nature of measurements limited the ability to establish temporality between risk factors and IUGR. Lastly, although regression analysis was performed, residual confounding from unmeasured variables such as dietary intake, micronutrient supplementation, and socioeconomic influences cannot be fully excluded.

CONCLUSIONS

Intrauterine growth restriction remains a significant public health concern, particularly in low- and middle-income countries. This study identified maternal anemia and hypothyroidism as independent risk factors, underscoring the importance of routine screening and timely management during pregnancy. Early detection and treatment of these modifiable conditions, coupled with improved antenatal care and nutritional support, may reduce the burden of IUGR and improve neonatal outcomes. Future multicenter prospective studies incorporating both maternal and fetal factors are recommended to strengthen the evidence base and guide preventive strategies at the population level.

Authors' Contribution

Conceptualization: MA
Methodology: MM, MA
Formal analysis: SI
Writing and Drafting: SI
Review and Editing: SI, MM, MA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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