Research Article

Risk Factors of Intrauterine Growth Restriction: A Case-Control Study

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Abstract

Objective: To investigate the association between maternal age, parity, and hypertension and the risk of intrauterine growth restriction (IUGR) among women delivering at Bethesda Hospital, Yogyakarta.

Methods: A case–control study was conducted using medical record data of patients who delivered at Bethesda Hospital, Yogyakarta, between January 2015 and December 2021. A total of 62 subjects were included, comprising 31 cases with IUGR and 31 controls without IUGR.

Results: Bivariate analysis using the Chi-square test demonstrated that maternal hypertension was a significant risk factor for IUGR ($p = 0.032$; OR = 3.906), indicating that mothers with hypertension were nearly four times more likely to have pregnancies complicated by IUGR. In contrast, maternal age ($p = 0.115$) and parity ($p = 0.446$; OR = 1.681) were not statistically significant risk factors for IUGR.

Conclusion: Maternal hypertension was identified as a significant risk factor for IUGR among pregnant women delivering at Bethesda Hospital, Yogyakarta. Conversely, maternal age and parity were not significantly associated with IUGR in this study. The lack of association may be partly attributable to the relatively small sample size and limited statistical power to detect weaker associations.

Keywords: age, hypertension, IUGR, parity.

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INTRODUCTION

Intrauterine growth restriction (IUGR) is defined as a condition in which a fetus fails to reach its genetically determined growth potential. This condition is primarily caused by placental insufficiency and several other contributing factors and is characterized by impaired oxygen and nutrient supply to the fetus.[1] IUGR and Small for Gestational Age (SGA) are distinct but related conditions. SGA refers to a fetus with a birth weight below the 10th percentile for gestational age in a reference population who may otherwise be healthy. In contrast, IUGR describes an SGA fetus with clinical evidence of growth restriction and signs of intrauterine malnutrition.[1]

The highest incidence of IUGR has been reported in South Asia, with prevalence rates of 39% in Bangladesh, 21% in India, and 18% in Pakistan. Other Asian countries, including Sri Lanka, Cambodia, and Vietnam, have reported IUGR incidences of 13%, 12%, and 11%, respectively.[2] In Indonesia, the overall incidence of IUGR has been reported to be 4.4%, with the highest prevalence observed in Papua (27%), followed by East Nusa Tenggara (20.3%) and South Sumatra (19.5%).[3-5] In Yogyakarta City, the incidence of low birth weight (LBW) in 2019 was recorded at 6.08%.[6]

The high incidence of IUGR is a major public health concern due to its significant impact on fetal and neonatal morbidity and mortality. IUGR is associated with various adverse perinatal outcomes, including prematurity, cerebral palsy,

and intrauterine fetal death. Furthermore, it is linked to long-term health consequences that extend into adulthood, such as metabolic syndrome, obesity, hypertension, and chronic cardiovascular disease.[7,8]

METHODS

This study was a retrospective, non-experimental analytical study employing a case–control design. Secondary data were obtained from the medical records of mothers who delivered at Bethesda Hospital, Yogyakarta, between January 2015 and December 2021. The study population was selected using rigorous, predefined criteria to minimize selection bias. A total of 62 subjects were included, comprising 31 cases and 31 controls.

The case group consisted of mothers whose fetuses were diagnosed with Intrauterine Growth Restriction (IUGR). Antenatal diagnosis of IUGR was based on ultrasonographic findings, defined as an estimated Fetal Weight (EFW) or Abdominal Circumference (AC) below the 10th percentile for gestational age, accompanied by evidence of placental insufficiency, indicated by abnormal umbilical artery Doppler studies. The inclusion criteria for the case group were: antenatal diagnosis of IUGR as defined above; availability of data on maternal age, parity, and maternal blood pressure during pregnancy; and term delivery (gestational age ≥ 37 weeks). The exclusion criteria for the case group included stillbirths, preterm births (< 37 weeks of gestation) without documented evidence of IUGR, and pregnancies with documented congenital anomalies.

The control group consisted of mothers who were not diagnosed with IUGR (EFW ≥ 10th percentile for gestational age) and who delivered neonates with birth weights Appropriate for Gestational Age (AGA). Controls were selected using a frequency-matching approach to ensure comparability with the case group in terms of hospital setting and delivery period. Inclusion criteria for the control group were: term delivery (≥ 37 weeks of gestation); delivery of AGA neonates; absence of antenatal or postnatal diagnoses of IUGR or small for gestational age (SGA); and availability of data on maternal age, parity, and maternal blood pressure during pregnancy. Exclusion criteria included stillbirths, preterm births, documented congenital anomalies, and any maternal or fetal conditions other than IUGR that could severely affect fetal growth.

To ensure the reliability and validity of the secondary data, a standardized data extraction form was developed and piloted on five non-study medical records prior to the main data collection. Data extraction was performed primarily by the first author. Data accuracy was further ensured through quality control procedures, whereby the second author independently cross-checked a random sample of 10% of the extracted data against the original medical records. Any discrepancies were reviewed and resolved by consensus with the third author, an obstetrics and gynecology physician, to maintain data integrity before final analysis.

Data analysis consisted of univariate and bivariate analyses. Univariate analysis was presented in tabular form to describe the study variables. Bivariate analysis was conducted to assess associations between exposure variables and IUGR using the Chi-square test. When the assumptions of the Chi-square test were violated (i.e., expected cell counts < 5 in more than 20% of cells), Fisher's exact test was applied. Cramer's V was used to assess the strength of association for categorical variables in contingency tables larger than 2 × 2. This study adhered to ethical principles in medical research, with strict measures taken to ensure the confidentiality and anonymity of all study participants.

RESULTS

The characteristics of the 62 study participants (31 cases and 31 controls) are summarized in Table 1. Analysis of categorical characteristics, including occupation, education level, and residence, showed no statistically significant differences between the IUGR and non-IUGR groups, with p-values ranging from 0.063 to 0.800. The most common occupation among mothers in the IUGR group was private-sector employment (35.5%). High school education was the most prevalent educational level in the IUGR group (45.2%). Most mothers in both groups resided in Yogyakarta (38.7% in the IUGR group and 45.2% in the non-IUGR group), followed by Sleman.

The associations between the hypothesized risk factors maternal age, parity, and hypertension and the incidence of IUGR were examined using the Chi-square test, with the results presented in Table 2. Bivariate analysis revealed that hypertension was the only variable significantly associated with the incidence of

IUGR at Bethesda Hospital, Yogyakarta (p = 0.032). Mothers diagnosed with hypertension had a significantly higher likelihood of having pregnancies complicated by IUGR compared with non-hypertensive mothers. Specifically, 71.4% of mothers in the IUGR group had hypertension, whereas the majority of mothers in the control group were non-hypertensive (61%). The calculated odds ratio (OR) was 3.906, indicating that mothers with hypertension were nearly four times more likely to experience IUGR than mothers without hypertension.

Maternal age was not significantly associated with the occurrence of IUGR (p = 0.115). Most mothers in both the case and control groups were within the age range of 20–35 years. Parity was also not identified as a statistically significant risk factor for IUGR (p = 0.446). Although the proportion of primiparous mothers was slightly higher in the IUGR group (56.7%) than in the control group, this difference was not statistically significant (OR = 1.681).

Table 1. Sample Characteristics

Characteristic	IUGR				*P-value*
	Yes		No		
	n	%	n	%	
Occupation					
Housewife	9	29.0	11	35.5	
Private Sector Employment	11	35.5	9	29.0	0.800
Entrepreneur	4	12.9	6	19.4	
Others	7	22.6	5	16.1	
Education					
Junior High School	3	9.7	4	12.9	
High School	14	45.2	12	38.7	
Diploma	4	12.9	3	9.7	0.425
Bachelor	10	32.3	12	38.7	
Residence					
Yogyakarta	12	38.7	14	45.2	
Sleman	4	12.9	5	16.1	
Bantul	3	9.7	4	12.9	
Kulon Progo	2	6.5	3	9.7	0.063
Gunung Kidul	2	6.5	2	6.5	
Others	8	25.8	3	9.7	

Table 2. Chi-Square Test Results

Characteristic	IUGR				% Total	*P-value*	OR
	Yes		No				
	n	%	n	%			
Age**							
< 20	4	100	0	0	100		
20-35	22	45.8	26	54.2	100	0.115**	-
>35	5	50	5	50	100		
Parity							
Primipara	17	56.7	13	43.3	100	0.446	1.681
Multipara	14	43.8	18	56.2	100		
Hypertension							
Hypertension	15	71.4	6	28.6	100	0.032*	3.906
Non-Hypertension	16	39	25	61	100		

NOTE (*): There is a relationship between the independent variable and the dependent variable (p<0.05);
Cramer's V test is used for variables with more than two columns.

DISCUSSION

Maternal hypertension was found to be significantly associated with the incidence of IUGR (p = 0.032), with an odds ratio (OR) of 3.906, indicating that hypertensive mothers are nearly four times more likely to experience IUGR than non-hypertensive mothers. This finding is consistent with previous studies that have consistently identified maternal hypertension as a significant risk factor for IUGR (p = 0.004; OR = 2.48).[9] Hypertension during pregnancy increases resistance in the fetoplacental blood vessels, leading to reduced placental perfusion and, consequently, impaired fetal development and lower birth weight. Furthermore, a hypoxic placenta may release antiangiogenic factors into the maternal circulation, triggering inflammatory responses, endothelial dysfunction, and elevated maternal blood pressure. This pathological process increases fetoplacental vascular resistance, thereby reducing oxygen and nutrient transfer from mother to fetus and ultimately resulting in intrauterine growth restriction.[10–12] The magnitude of the association observed in this study (OR = 3.906) highlights the critical importance of strict blood pressure monitoring and management during pregnancy.

The bivariate analysis showed no significant association between maternal age and the incidence of IUGR (p = 0.115). Although existing literature suggests that pregnancies in mothers younger than 20 years or older than 35 years carry a higher risk of IUGR due to incomplete placental development in younger mothers and reduced placental blood flow in older mothers the low number of subjects in these extreme age groups in the present study may have contributed to the lack of statistical significance.[13,14] This finding contradicts several previous studies that reported a significant association between maternal age and IUGR.

Similarly, parity was not significantly associated with IUGR in this study (p = 0.446). This result contrasts with earlier research that demonstrated a significant relationship between parity and IUGR.[15] Previous studies have suggested that primiparous women may have a higher risk up to 4.66 times greater due to ongoing vascular adaptation in the uterine environment, making them more sensitive to pregnancy-related physiological changes. In contrast, multiparous women generally have a more mature reproductive system that supports improved placental development.[16] The absence of a statistically significant association in the present study (OR = 1.681) may be explained by the limited sample size, which reduced the statistical power to detect meaningful differences.

The study also found that high school education was the most prevalent educational level among mothers with IUGR. This finding differs from some previous studies that reported higher IUGR risk among mothers with lower or no formal education. Higher maternal education is generally associated with improved health literacy, better access to health information, and greater awareness of pregnancy-related complications.[17] Additionally, maternal occupation has been identified as a factor related to IUGR incidence, as pregnant women engaged in moderate to high levels of physical activity at work may be at increased risk due to inadequate rest and suboptimal nutritional intake.[2,16]

Several limitations of this study should be acknowledged. First, the retrospective case-control design based on secondary medical record data carries inherent risks of information bias due to missing or incomplete records, as well as selection bias, since the study population was derived from a single healthcare institution, potentially limiting the generalizability of the findings. Second, the relatively small sample size (n = 62) may have limited the statistical power of the bivariate analyses, possibly contributing to the non-significant findings for known risk factors such as maternal age and parity (p > 0.05). Future studies are therefore recommended to employ prospective cohort designs or multi-center approaches with larger sample sizes to improve statistical power and external validity. Further research should also explore additional confounding variables and intermediate biological mechanisms, such as detailed maternal nutritional status and specific subtypes of hypertensive disorders during pregnancy.

CONCLUSION

This study concludes that maternal hypertension is a significant risk factor for IUGR, with hypertensive mothers being nearly four times more likely to experience this condition than non-hypertensive mothers. In contrast, maternal age and parity were not significantly associated with the incidence of IUGR. Clinically, these findings underscore the importance of heightened surveillance in pregnant women with hypertension. Enhanced

monitoring, including regular ultrasonography and Doppler assessments, should be prioritized to enable early detection and timely management of IUGR, thereby reducing neonatal morbidity and mortality. Future research should involve larger, multi-center prospective studies to improve statistical power and external validity. Such studies should also address the limitations of retrospective data by incorporating standardized, real-time measurements of potential confounding factors and further investigating the pathophysiological mechanisms of IUGR across diverse clinical settings.

ETHICAL CLEARANCE

This research followed a protocol approved by Health Research Ethic Committee of the Bethesda Hospital Yogyakarta, with reference protocol number: No.14/KEPK-RSB/1/22. The study design follows all ethical principles to protect participants' rights, ensure confidentiality, and minimize risks, aligns with national and international human research procedures.

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