Diyala Journal of Medicine

ORIGINAL RESEARCH
Published: 25 June 2024
Doi: 10.26505/DJM.26028540505

Serum Ferritin Level as a Predictor for Intra Uterine Growth Restriction

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Abstract

Background: Maternal serum ferritin is being explored as a potential predictor for Intrauterine Growth Restriction (IUGR). Early detection of IUGR is crucial for improving perinatal outcomes and reducing associated mortality and morbidity.

Objective: To evaluate the role of elevated maternal serum ferritin in predicting the risk of developing IUGR.

Patients and Methods: A prospective case-control study was conducted at Al-Batool Teaching Hospital, Diyala, involving 51 pregnant women divided into two groups based on pregnancy status. Demographic data, obstetric history, and risk factors for IUGR were collected through a questionnaire, and blood samples were taken to measure hemoglobin and serum ferritin levels.

Results: The study found that the mean serum ferritin level was significantly higher in the patient group (209.89±50.95 ng/ml) compared to the control group (66.91±37.49 ng/ml), with a p-value of <0.001. The mean birth weight was significantly lower in the patient group (1873.81±425.62 g) compared to the control group (3078.67±415.56 g), also with a p-value of <0.001. There were no significant differences in age and hemoglobin levels between the two groups.

Conclusion: Elevated maternal serum ferritin levels may suggest an increased risk of IUGR, emphasizing the need for further research to validate its role as a predictive marker.

Keywords: Intrauterine Growth Restriction (IUGR), Serum Ferritin, Pregnancy, Predictive Marker, Perinatal Outcomes.

OPEN ACCESS

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Received: 5 May 2024
Accepted: 5 June 2024
Published: 25 June 2024

Introduction

Intrauterine growth restriction (IUGR) is a significant cause of prenatal morbidity and mortality [1,2,3]. As there is no definitive treatment, predicting IUGR is a key priority in prenatal healthcare [1,2,3]. Serum ferritin, an iron storage protein, has emerged as a crucial biomarker in this context [4], [5]. Ferritin levels are regulated by cellular iron status, with higher intracellular iron concentrations resulting in increased ferritin expression [4]. However, ferritin is also an acute-phase protein, and its serum concentrations can be influenced by inflammation and other factors [4]. Recent

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studies have examined the potential of maternal serum ferritin levels during pregnancy, particularly in the 30–32-week gestational period, to predict the development of IUGR [1]-[3]. The objective of this review is to synthesize the current evidence on the significance of serum ferritin as an indicator of IUGR risk. Iron is known to be an important micronutrient for proper cellular function in all organ systems including the brain as it is needed for neural &glial energy metabolism, neurotransmitter synthesis and myelination [6,7]. Iron deficiency is the most common cause of anemia in pregnancy and , according to World Health Organization (WHO), is defined as the hemoglobin concentration of less than 11 g/dL while low ferritin is defined as serum ferritin (SF) level of less than 10µg/L. Pregnant ladies are grouped into three predelivery concentrations and two SF levels according to WHO grouping: non anemic when Hb≥ 11g/dL, mild to moderate anemic Hb ≥ 7-10.9g/dL and severely anemic (Hb<7 g/dL; and into normal (SF ≥10µg/L and low(SF<10µg/L [8,9]. Many studies revealed that maternal iron deprivation with subsequent low iron stores and iron deficiency anemia in infants may affect cognitive, emotional, motor and neurophysiological development in these infants [10,11]. Pregnant woman requires more iron to meet the expansion in maternal blood volume and fetal red cell mass. Although maternal iron absorption is increased during pregnancy, but still about 50% of pregnant ladies have anemia, mostly iron deficiency anemia with subsequent effect on iron transfer to the fetus [12,13]. Physiological anemia of pregnancy (which is due to maternal blood volume expansion) can be differentiated from iron deficiency anemia in that physiological anemia of pregnancy is normochromic normocytic [14]. Serum ferritin concentration reflects body iron stores and correlates with bone marrow iron, although elevated serum ferritin level is considered as an acute phase reactant that increases in many inflammatory conditions [15,16]. Fetal growth restriction (FGR) affects about 10% of infants with increased perinatal mortality and morbidity [17,18]. Worldwide, a major cause of FGR is maternal malnutrition. Prenatal identification of FGR is crucial as early detection and management is associated with better outcomes and decreasing perinatal mortality and morbidity [19,20].

Patients and Methods

Study design

A prospective case-control study was done in Al-Batool Teaching Hospital, Diyala, during the period from July 2017 –February 2018. Fifty-one pregnant women were included in our study and after taking informed consent from all participants, they were divided into two groups. Group A (30 ladies with normal pregnancy) and Group B (21 pregnant ladies with clinical and ultrasonic features of IUGR). Both groups filled in a questionnaire that included demographic data of the patients, past obstetric history, any risk factors of IUGR (as previous IUGR, hypertension, poverty, maternal malnutrition, cyanotic heart disease etc.). Blood was drawn from antecubital fossa and complete blood count & serum ferritin level was measured.

Statistical Analysis

This is a prospective study, demographic data were presented mean ± SD, comparison

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between two groups were done by using unpaired t-test.

Results

In our study, the two groups of mothers were comparable in terms of age, birth weight, hemoglobin and serum ferritin levels Table (1). Regarding the age and hemoglobin level, there were no significant differences between the two groups. The mean age of the first group (control) was 29.73 ± 7.18 and the second group (patient) was 30.52 ± 6.85. While the mean hemoglobin level in the control was11.31 ± 0.93 and the patient was 11.5 ± 0.88. Whereas birth weight values differed among the two groups (p0.001), the mean birth weight in the control group was 3078.67 ± 415.56 and in the patient, group was 1873.81 ± 425.62. Serum ferritin values differed significantly among the two groups (p0.001), it was within the normal range in the first group (control) with the mean of 66.91 ± 37.49 whereas maternal serum ferritin was higher in the second group (patient) with the mean of 209.89 ± 50.95.

Table (1): Comparison of numeric data between control and patient groups by unpaired t- test.

Parameters	Control N=30 Mean±SD	Patients N=21 Mean±SD	P-Value
Age(yr)	29.73±7.18	30.52±6.85	0.693*
Bodyweight(g)	3078.67±415.56	1873.81±425.62	<0.001*
Hemoglobin (g/dl)	11.31±0.93	11.5±0.88	0.452*
S. Ferritin (ng/ml)	66.91±37.49	209.89±50.95	<0.001*

The Table (1) shows a comparison of numeric data between the control group (N=30) and the patient group (N=21). The parameters evaluated include age, body weight, hemoglobin, and serum ferritin levels. The mean age was similar between the control group (29.73±7.18 years) and the patient group (30.52±6.85 years), with a non-significant p-value of 0.693, indicating no statistically significant difference in age between the two groups. However, the mean body weight was significantly lower in the patient group (1873.81±425.62 g) compared to the control group (3078.67±415.56 g), with a p-value of <0.001, suggesting that the patient group had a significantly lower body weight. The mean hemoglobin levels were not significantly different between the control group (11.31±0.93 g/dl and the patient group (11.5±0.88 g/dl), with a p-value of 0.452, indicating no statistically significant difference in hemoglobin levels. Importantly, the mean serum ferritin level was significantly higher in the patient group (209.89±50.95 ng/ml) compared to the control group (66.91±37.49 ng/ml), with a p-value of <0.001. This suggests that higher serum ferritin levels are associated with the patient group, which may be a predictor for intrauterine growth restriction, the key findings from this table are the significantly lower body weight and significantly higher serum ferritin levels in the patient group compared to the control group, while age and hemoglobin levels were not significantly different between the two groups.

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Table (2): Comparison of categorical data between control and patient groups by unpaired t-test.

Parameters		Control N=30 No. (%)	Patients N=21 No. (%)	P-value
Gestational age	Term	29 (96.7)	0 (0)	<0.001*
	Preterm	1 (3.3)	21 (100)	
Gravida	1	3 (10.0)	1 (4.8)	0.958**
	2-4	18 (60.0)	12 (57.1)	
	≥5	9 (30.0)	8 (38.1)	
Parity	0-1	6 (20.0)	7 (33.3)	0.693**
	2-4	19 (63.3)	10 (47.6)	
	≥5	5 (16.7)	4 (19.0)	
Abortion	0	15 (50.0)	8 (38.1)	0.725**
	1	12 (40.0)	12 (57.1)	
	≥2	3 (10.0)	1 (4.8)	
Risk factors	Negative	22 (73.3)	2 (9.5)	<0.001**
	DM	6 (20.0)	1 (4.8)	
	HT	2 (6.7)	6 (28.6)	
	IUGR	0 (0)	7 (33.3)	
	Miscellaneous	0 (0)	7 (33.3)	

The Table (2) presents a comparison of categorical data between the control group (N=30) and the patient group (N=21) for various parameters, including gestational age, gravida, parity, abortion, and risk factors. For gestational age, 96.7% of the control group had term pregnancies, while 100% of the patient group had preterm pregnancies, with a highly significant p-value of <0.001.

This indicates that the patient group had a significantly higher rate of preterm births compared to the control group. The distribution of gravida (number of pregnancies) and parity (number of births) was similar between the control and patient groups, with no statistically significant differences (p-values of 0.958 and 0.693, respectively). The number of abortions was also comparable between the two groups, with no significant differences (p-value of 0.725).

Regarding risk factors, the majority (73.3%) of the control group had no identified risk factors, while in the patient group, a significant proportion had various risk factors, including hypertension (28.6%), intrauterine growth restriction (IUGR) (33.3%), and miscellaneous conditions (33.3%). The difference in the distribution of risk factors between the groups was statistically significant (p-value <0.001), the key findings from this table are the significantly higher rate of preterm births and the presence of various risk factors, such as hypertension and IUGR, in the patient group compared to the control group, while the distribution of gravida, parity, and abortions was similar between the two groups.

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Table (3): Correlation between numeric parameters within the control group.

		Age	B. W	Hb	Serum ferritin
Age	R	1.000	-0.099	0.016	-0.174
	P		0.602	0.932	0.359
B. W	R		1.000	0.249	0.374
	P			0.185	0.042
Hb	R	R		1.000	0.542
	P	P			0.002

This Table (3) presents the correlation analysis between various numeric parameters within a group of patients. The study appears to be investigating the relationship between serum ferritin levels and intra-uterine growth restriction (IUGR). The Table (3) shows the correlation coefficient (r) and the corresponding p-value (p) for each pair of variables, which include age, birth weight (B.W.), hemoglobin (Hb), and serum ferritin. The results indicate that there is a moderate positive correlation between age and birth weight (r = 0.350), but this correlation is not statistically significant (p = 0.120). Similarly, there is a weak negative correlation between age and hemoglobin levels (r = -0.137), but this correlation is also not statistically significant (p = 0.555). The correlation between age and serum ferritin levels is very weak and positive (r = 0.034), and it is not statistically significant (p = 0.885).

When examining the relationship between birth weight and other variables, the table shows a moderate negative correlation between birth weight and hemoglobin levels (r = -0.357), but this correlation is not statistically significant (p = 0.112). The correlation between birth weight and serum ferritin levels is weak and negative (r = -0.132), and it is not statistically significant (p = 0.569), the table indicates a moderate positive correlation between hemoglobin and serum ferritin levels (r = 0.400), and this correlation is approaching statistical significance (p = 0.073).

Overall, the results presented in this table do not show a statistically significant correlation between serum ferritin levels and intra-uterine growth restriction. The study may need to investigate other factors or expand the sample size to better understand the potential relationship between these variables.

Table (4): Correlation between numeric parameters within patients' group.

		Age	B. W	Hb	Serum ferritin
Age	R	1.000	0.350	-0.137	0.034
	P		0.120	0.555	0.885
B.W	R		1.000	-0.357	-0.132
	P			0.112	0.569
Hb	R			1.000	0.400
	P				0.073

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This Table (4) presents the correlation analysis between various numeric parameters within a group of patients. The study appears to be investigating the relationship between serum ferritin levels and intra-uterine growth restriction (IUGR). The first row of the table shows the correlation coefficients (r) and p-values (p) for the relationships between age and the other variables. There is a moderate positive correlation between age and birth weight (r = 0.350), but this correlation is not statistically significant (p = 0.120). The correlation between age and hemoglobin levels is weak and negative (r = -0.137), and it is also not statistically significant (p = 0.555). Finally, the correlation between age and serum ferritin levels is very weak and positive (r = 0.034), and it is not statistically significant (p = 0.885).

Moving to the second row, the table shows the correlations involving birth weight. There is a moderate negative correlation between birth weight and hemoglobin levels (r = -0.357), but this correlation is not statistically significant (p = 0.112). The correlation between birth weight and serum ferritin levels is weak and negative (r = -0.132), and it is also not statistically significant (p = 0.569). The third row of the table presents the correlation involving hemoglobin. There is a moderate positive correlation between hemoglobin and serum ferritin levels (r = 0.400), and this correlation is approaching statistical significance (p = 0.073), the results presented in this table do not show a statistically significant correlation between serum ferritin levels and intra-uterine growth restriction. The study may need to investigate other factors or expand the sample size to better understand the potential relationship between these variables.

Discussion

The study aimed to evaluate the potential of serum ferritin levels as a predictor for intrauterine growth restriction (IUGR). The findings revealed significant differences between the control and patient groups in terms of serum ferritin levels, birth weight, and the presence of risk factors.

The patient group exhibited significantly higher serum ferritin levels (209.89 ± 50.95 ng/ml) compared to the control group (66.91 ± 37.49 ng/ml), with a p-value of <0.001 [3]. This suggests that elevated serum ferritin levels could be associated with IUGR, making it a potential biomarker for early detection. The higher serum ferritin levels in the patient group could be indicative of an inflammatory response or oxidative stress, which are known to contribute to adverse pregnancy outcomes [2]. Additionally, the mean birth weight was significantly lower in the patient group (1873.81 ± 425.62 g) compared to the control group (3078.67 ± 415.56 g), with a p-value of <0.001 [3]. This aligns with previous studies that have shown a correlation between high serum ferritin levels and low birth weight, further supporting the hypothesis that serum ferritin could be a useful predictor for IUGR.

The study also found that the patient group had a significantly higher rate of preterm births (100%) compared to the control group (3.3%), with a p-value of <0.001 [4]. This is consistent with the literature indicating that preterm birth is a common complication in pregnancies affected by IUGR [1].

Interestingly, there were no significant differences in age and hemoglobin levels

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Published: 25 June 2024
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between the two groups, suggesting that these factors do not play a significant role in the development of IUGR in this study population [3]. This highlights the importance of focusing on serum ferritin levels and other potential biomarkers for early detection and management of IUGR, the study provides compelling evidence that elevated serum ferritin levels are significantly associated with IUGR. These findings could pave the way for further research to validate serum ferritin as a reliable biomarker for early detection of IUGR, potentially improving maternal and fetal outcomes.

The morbidity associated with FGR may not affect the antenatal period only but may extend to childhood and even adulthood periods and thus early detection and management is important [21,22]. In this study we found that serum ferritin is higher in patient with IUGR compared to normal pregnancy, this agrees with Neeta Bindal [22], NemanjaVisnjevas [23] and Vsoubasi [24] who found that serum ferritin is higher in a group of patient who develop IUGR this can be explained by the fact that fetal growth is regulated by the balance between fetal nutrient demand and maternal placenta nutrient supply. Iron deficiency has its known effect in pregnancy as it increases fetal corticotropins and fetal cortisol causing inhibition of fetal growth [36].

Various studies showed that lower level of trans ferritin receptor expression in placenta is associated with preeclampsia and IUGR. This leads to decrease extraction of iron by placenta from maternal serum leading to increase maternal serum ferritin. In addition, placental iso ferritin levels also decrease in IUGR [24]. Our study showed that IUGR occurs in approximately 33.3% of the patients with a previous history of IUGR, which agrees with the study of V Soubasi [24].

Conclusions

The study found that elevated maternal serum ferritin levels may be associated with an increased risk of Intrauterine Growth Restriction (IUGR). However, there was no statistically significant correlation between serum ferritin levels and IUGR, indicating the need for further validation before it can be used as a standalone predictive marker.

Recommendations

Conduct further longitudinal studies to better understand the relationship between serum ferritin levels and the development of Intrauterine Growth Restriction (IUGR).

Explore a multifactorial approach when studying the potential link between elevated serum ferritin and IUGR to account for various influencing factors.

Validate the role of elevated maternal serum ferritin as a predictive marker for IUGR through additional research.

Consider monitoring maternal serum ferritin levels during pregnancy, particularly in the 30-32-week gestational period, to potentially predict the risk of IUGR development. Emphasize the importance of early detection of IUGR through the evaluation of maternal serum ferritin levels to improve perinatal outcomes and reduce associated mortality and morbidity.

Acknowledgement:

The study was conducted at Al-Batool Teaching Hospital, Diyala, from July 2017 to February 2018, involving 51 pregnant women who provided informed consent. The

ORIGINAL RESEARCH
Published: 25 June 2024
Doi: 10.26505/DJM.26028540505

authors acknowledge the participants for their involvement in the research.

Source of funding: Patients with IUGR had significantly higher serum ferritin levels compared to those with normal pregnancies, suggesting a potential link between elevated serum ferritin and IUGR. The study also highlighted the importance of considering a multifactorial approach and conducting longitudinal studies to better understand the relationship between serum ferritin levels and IUGR development.

Ethical clearance: This study was conducted according to the approval of College of Medicine/ University of Diyala and in accordance with the ethical guidelines of the Declaration of ethical committee of the College (Document no. 2024IFM854).

Conflict of interest: Nil

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Diyala Journal of Medicine

ORIGINAL RESEARCH
Published: 25 June 2024
Doi: 10.26505/DJM.26028540505

مستوى الفيريتين في الدم كمؤشر لتقييد النمو داخل الرحم

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الملخص

خلفية الدراسة: يتم استكشاف فيريتين مصل الأم كمؤشر محتمل لتقييد النمو داخل الرحم (IUGR). يعد الكشف المبكر عن IUGR أمرا بالغ الأهمية لتحسين نتائج الفترة المحيطة بالولادة والحد من الوفيات والمراضة المرتبطة بها.

اهداف الدراسة: لتقييم دور ارتفاع فيريتين مصل الأم في التنبؤ بخطر الإصابة ب IUGR.

المرضى والطرائق: أجريت دراسة مستقبلية للحالات والشواهد في مستشفى البتول التعليمي في ديالى، شملت ٥١ امرأة حامل مقسمة إلى مجموعتين بناء على حالة الحمل. تم جمع البيانات الديموغرافية وتاريخ التوليد وعوامل الخطر ل IUGR من خلال استبيان ، وتم أخذ عينات الدم لقياس مستويات الهيموجلوبين والفيريتين في الدم.

النتائج: وجدت الدراسة أن متوسط مستوى الفيريتين في الدم كان أعلى بكثير في مجموعة المرضى (٢٠٩,٨٩±٥٠,٩٥ نانوغرام / مل) مقارنة بالمجموعة الضابطة (٦٦,٩١±٣٧,٤٩ نانوغرام / مل) ، مع قيمة p تبلغ <٠,٠٠١. كان متوسط الوزن عند الولادة أقل بكثير في مجموعة المرضى (١٨٧٣,٨١±٤٢٥,٦٢ جم) مقارنة بالمجموعة الضابطة (٣٠٧٨,٦٧±٤١٥,٥٦ جم)، أيضا بقيمة p تبلغ <٠,٠٠١. لم تكن هناك فروق ذات دلالة إحصائية في العمر ومستويات الهيموغلوبين بين المجموعتين.

الاستنتاجات: قد يشير ارتفاع مستويات الفيريتين في مصل الأم إلى زيادة خطر الإصابة ب IUGR ، مما يؤكد الحاجة إلى مزيد من البحث للتحقق من دوره كعلامة تنبؤية.

الكلمات المفتاحية: تقييد النمو داخل الرحم (IUGR) ، مصل الفيريتين ، الحمل ، العلامة التنبؤية ، نتائج الفترة المحيطة بالولادة.

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تاريخ استلام البحث: ٥ آيار ٢٠٢٤

تاريخ قبول البحث: ٥ حزيران ٢٠٢٤

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