e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(3); 256-261

Original Research Article

Prospective Cross-Sectional Study to Evaluate the Validity of Serum Ferritin Level as a Marker of Preterm Labor

Rashmi Singh[1], Amrita Rai[2], N. K. Bariar[3]

[1]Assistant Professor, Department of Pathology, Patna Medical College & Hospital, Patna, Bihar, India.
[2]Assistant Professor, Department of Obstetrics & Gynecology, Patna Medical College & Hospital, Patna, Bihar, India.
[3]Professor and HOD, Department of Pathology, PMCH, Patna, Bihar, India

Received: 03-01-2022 / Revised: 10-02-2022 / Accepted: 18-03-2022
Corresponding author: Dr. Amrita Rai
Conflict of interest: Nil

Abstract

Aim: To evaluate the value of serum ferritin level as predictor in preterm labor.

Method: The Department of Obstetrics and Gynecology, Patna Medical College & Hospital, Patna, Bihar, India, conducted this cross-sectional study on 200 pregnant women with labour pain. They were divided into two groups i.e. group I (preterm N=100) and group II (term N=100).

Results: The rate of nulli parity was substantially greater in the preterm delivery group than in the term delivery (P 0.001). With a sensitivity, specificity, and diagnostic accuracy of 75.2 percent, 65.3 percent, and 75.0 percent, respectively, a ferritin level of 36.4 ng/mL was determined as the optimum cut-off for preterm delivery when compared to term delivery.

Conclusion: Considering the results of other studies, it can be stated that ferritin level can be used to detect patients at risk for preterm delivery.

Keywords: Serum ferritin, preterm labor, PROM

Introduction

Preterm labor complicates 8 to 10 percent of all pregnancies and is the leading cause of perinatal morbidity and mortality. [1] In 65 percent cases of preterm birth, there is always a predisposing cause, however, in 35 percent cases of preterm birth, there is no obvious etiology. [2] Although the pathophysiology of preterm labor remains incompletely defined, a growing body of evidence is emerging that links occult upper genital tract infection with subsequent spontaneous preterm labor. [3] Recently, in asymptomatic women, several serum (G CSF and ferritin) and cervicovaginal (fetal fibronectin, interleukin 6 and lactoferrin) inflammatory markers have been shown to be potent predictors of spontaneous preterm delivery in otherwise asymptomatic women. [4]

The causes of preterm labor (PTL) include multiple pregnancies, infections, and chronic conditions such as diabetes and high blood pressure. The reports also suggest that PTL may be due to one or more of the pathophysiologic processes such as amnio-chorionicdecidual or

systemic inflammation, activation of the maternal or fetal hypothalamic-pituitary-adrenal axis, decidual hemorrhage, or pathologic distension of the uterus. But a clear understanding of the molecular mechanism has not developed yet. [5] Many maternal and biochemical data as well as other demographic and behavioral factors have been used and tried for the prediction of PTD but none of them have succeeded.[6]

Ferritin is also a primary intracellular storage protein that holds iron in an insoluble and non-toxic state, while it has been reported to increase in a number of acute-phase reactions such as inflammation. [7] Maternal subclinical infection may increase ferritin level as an acute phase reactant and cause spontaneous rupture of the membranes. [8] Some studies have reported that ferritin level could be used as a predictor of preterm delivery [9-11]; however, the results of studies in this area are controversial. Hence, this study aims to evaluate the value of serum ferritin level as predictors in preterm labor.

Material & Methods:

The Department of Obstetrics and Gynecology, Patna Medical College & Hospital, Patna, Bihar, India, conducted this cross-sectional study on 200 pregnant women with labour pain. Ethical permission was obtained from the institutional ethical committee.They were divided into two groups

Group 1: 100 pregnant women who had preterm deliveries

Group 2: 100 pregnant women who had term deliveries

Inclusion criteria

Single pregnancy and gestational age of above 24 weeks.

Exclusion criteria

Anemia (hemoglobin level of less than 9.7 g/dL in the second trimester and less than 9.5 g/dL in the third trimester), elevated serum iron levels (above 178 μg/dL in the second trimester, and above 193 μg/dL in the third trimester), chronic infectious diseases, multiple pregnancies, fetal anomalies, fetal intrauterine death, severe polyhydramnios, diabetes mellitus, alcohol consumption, smoking and drug abuse, ferritin level enhancers including rheumatoid arthritis, hemochromatosis, hyperthyroidism, adult-onset Still's disease, leukemia, Hodgkin's lymphoma, and multiple blood transfusions.

Methodology

After the participants gave their written agreement detailed medical and clinical history was recorded. In addition, the research team noted maternal risk factors such as PROM, early pregnancy vaginal bleeding, overweight and obesity, insufficient maternal weight gain during pregnancy, age less than 18 or over 40 years, foetus congenital abnormalities, a time interval of less than 18 months between pregnancies, history of preterm delivery, anaemia (haemoglobin less than 10 g/dL), history of preterm delivery in first-degree relatives, and intrauterine growth (longer than 12 hours).

Thereafter, blood samples were taken from the subjects under sterile conditions and stored at room temperature in iron-free tubes. Within two hours, the samples' serums were separated and refrigerated at minus 20°C. With a completely automatic analyzer, the level of serum ferritin was determined using a particle enhanced immunoturbidimetric technique. A completely automatic spectrophotometer was also used to measure haemoglobin levels.

Statistical Analysis

SPSS 25 software was used for data entry and analysis and $P < 0.05$ was set as the level of significance. Chi-square and independent sample t test were utilized. The cut-off points for ferritin level for preterm delivery were also determined and

its efficiency (sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy) calculated using the receiver operating characteristics curve (ROC curve) and area under the curve (AUC).

Results:

Table 1 compares the study groups' pregnancy state and risk variables for premature delivery. The rate of nulliparity was substantially greater in the preterm delivery group than in the term delivery (P 0.001). Furthermore, preterm deliveries had significantly higher rates of PROM, vaginal bleeding in early pregnancy, overweight and obesity, history of preterm delivery in the patient and her first-degree relatives, and extended leakage than term (P 0.05).

Table 2shows Furthermore, ferritin levels were substantially higher (P 0.05) in preterm deliveries in patients with PROM or a prolonged leakage; however, there was no significant difference in ferritin levels between patients with PROM or a prolonged leakage in term deliveries.

Table 3 illustrate the ferritin cut-offs for premature delivery. With a sensitivity, specificity, and diagnostic accuracy of 75.2 percent, 65.3 percent, and 75.0 percent, respectively, a ferritin level of 36.4 ng/mL was determined as the optimum cut-off for preterm delivery when compared to term delivery.

Table 1: Comparison of pregnancy status and risk factors of preterm delivery between study groups

	Preterm (n=100)	Term labour (n=100)	***P* value***
Pregnancy status			**<0.001**
Nulliparous	49	42	
Primiparous	38	40	
Multiparous	13	18	
PROM	61	45	**<0.001**
Early pregnancy vaginal bleeding	16	8	**0.045**
Overweight and obesity	41	51	**<0.001**
Inadequate weight gain during pregnancy	3	0	0.072
Age <18 years or >40 years	5	3	0.291
Congenital fetal malformations	2	1	0.109
Less than 18 months between pregnancies	5	6	**0.020**
History of preterm labor	10	2	**<0.001**
Anemia (Hb<10 g/dL)	2	2	0.242
History of preterm labor in first-degree relatives	5	2	**0.005**
IUGR	6	3	**0.031**
Polyhydramnios	3	2	0.271
Uterine malformations	4	0	**0.010**
Prolonged leakage (longer than 12 hours)	11	4	**<0.001**

Table 2: Comparison of ferritin level in preterm and term deliveries

			Ferritin level (ng/mL)	*P* value*
Preterm labor (n =100)	**PROM**	No	**51.3 ± 22.5**	**0.003**
		Yes	**72.4 ± 38.2**	
	Prolonged leakage (longer than 12 hours)	No	**53.5 ± 23.5**	**<0.001**
		Yes	**111.3 ± 53.4**	
Term labor (n =100)	**PROM**	No	**32.4 ± 21.5**	0.592
		Yes	**34.3 ± 21.7**	
	Prolonged leakage (longer than 12 hours)	No	**37.3 ± 22.6**	**0.383**
		Yes	**48.4 ± 11.7**	

Table 3. Diagnostic efficacy of ferritin cut-off levels for preterm delivery

Comparison groups	Ferritin cut-off level(ng/mL)	Sensitivity	Specificity	PPV	NPV	Accuracy
Preterm vs. term deliveries	36.4	75.2%	65.3%	70.3 %	75.3 %	75 %

Discussion:

Preterm labor is the single most important complication of pregnancy in the absence of congenital abnormality, as it is recognized as a worldwide problem responsible for more than 80% of neonatal deaths and more than 50% of long term morbidity in the surviving infants. [12] Pregnancy tends to predispose to vaginocervical infection due to altered vaginal ph. The choriondecidual interface is infiltrated by macrophages following bacterial colonization and ferritin is produced as an acute phase reactants. [13]

Nandiniet al. [14] did a study on 100 pregnant women and divided into two groups, group 1(preterm delivery, case group) and group 2 (term delivery, control group). Findings of their study showed serum ferritin levels were significantly higher in preterm labor and its values ranged from 4.4 μg/dl to 841.2 μg/dl and 9.8 μg/dl to 67 μg/dl in preterm and control patients respectively.

The normal vaginal bacterial population assists in inhibiting the growth of pathologic vaginal organisms. If the normal vaginal ecosystem is altered, there is a greater chance of proliferation of pathogenic organisms. [15] Serum ferritin initiates to decrease normally from the beginning of second trimester and its level in maternal serum at time of labor reach one third the value of infant cord sample. When there is physiologic stress in acute or chronic infection the level of ferritin can elevate markedly, also increase with tissue damage or if there is liver disease or cancer. Ferritin in these cases reflects a status of an acute phase reaction rather than being an indicator of nutritional status. [16]

Overall, consistent with previous studies, our study showed that serum ferritin level in preterm deliveries was higher than those in term delivery. Given that in our study, women in preterm and term groups had labor pain and the results showed higher

ferritin level in preterm delivery than in term delivery, we suggest that ferritin level measurement, even at the onset of delivery pain, could help to predict the risk for preterm delivery. [17] However, it is suggested to conduct further multicenter prospective studies to evaluate the predictive value of serum ferritin levels in different high-risk groups and compare it with other biochemical parameters of preterm delivery such as fetal fibronectin.

Conclusion:

Therefore, considering the results of other studies, it can be stated that ferritin level can be used to detect patients at risk for preterm delivery. A ferritin level of 36.4 ng/mL was determined as the optimum cut-off for preterm delivery when compared to term delivery and showed diagnostic accuracy of 75%.

References:

1. Dutta DC. 1998. Textbook of obstetrics. 6th ed. Calcutta: New Central Book Agency (P) Ltd., pp. 324-35.
2. Arias F, Tomich P. 1982. Etiology and outcome of low birth and preterm infants. ObstetGynaecol60:277.
3. Leonardo CHB, Cresfor SAA, James SA, Siegel E, Wilcon S. 1990. Work related physical excretion and risk of preterm low birth weight delivery. PediatrPerinatEpidemiol4: 161-74.
4. Pushpo D, Jagdish WMA. 1991. A study of serum ferritin level in preterm labor. J ObstetGynaecol India 41: 269-73.
5. Auray-Blais C, Raiche E, Gagnon R, Berthiaume M, Pasquier JC (2011): Metabolomics and preterm birth.Int J Mass Spectrom.,307:33-38.
6. Tsiartas P, Holst RM, Wennerholm UB, Hagberg H, Hougaard DM, Skogstrand K, et al (2012): Prediction of spontaneous preterm delivery in women with threatened preterm labour.BJOG.,119:866-873.
7. Chen X, Scholl TO, Stein TP. Association of elevated serum ferritin levels and the risk of gestational diabetes mellitus in pregnant women: The Camden study. Diabetes Care 2006;29:1077-82. doi: 10.2337/diacare.2951077.
8. Zhang Q, Ananth CV, Li Z, Smulian JC. Maternal anaemia and preterm birth: a prospective cohort study. Int J Epidemiol. 2009;38:1380-9. doi: 10.1093/ije/dyp243.
9. Abdel-Malek K, El-Halwagi MA, Hammad BE, Azmy O, Helal O, Eid M, et al. Role of maternal serum ferritin in prediction of preterm labor. J ObstetGynaecol. 2018;38:222-25.
10. El-Shahawy HF, Hendawy SF, Hassanin AS, El-Azeem MMA. Estimation of Serum Ferritin Level in Preterm Labour. Egypt J Hosp Med. 2017;68(3)
11. Weintraub AY, Sheiner E, Mazor M, Levy A, Tevet A, Paamoni O, et al. Maternal serum ferritin concentration in patients with preterm labor and intact membranes. J Matern Fetal Neonatal Med. 2005;18:163-6.
12. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. The lancet 2008;371(9606):75-84.
13. Xiao R, Sorensen TK, Frederick IO, El-Bastawissi A, King IB, Leisenring WM et al. Maternal second-trimester serum ferritin concentrations and References 35 subsequent risk of preterm delivery. Paediatric and perinatal epidemiology 2002;16(4):297-304.
14. Nandini M D, Shetty H V, Rupakala B V, Usha S M R, Priyadarshini K S, Manjula H S,VictoriaKsh (2015): serum ferritin levels in preterm labor. International Journal of Recent Trends in Science and Technology, 14(2): 477-480.
15. Singh B, Goswami B, Gupta N, Bajaj AD, Mallika V. Potential biochemical markers for preterm labor: a pilot study

in north India. Indian Journal of Clinical Biochemistry 2011;26(1):41-5.
16. Movahedi M, Saiedi M, Gharipour M, Aghadavoudi O. Diagnostic performance and discriminative value of the serum ferritin level for predicting preterm labor. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences 2012;17(2):164.
17. Mohammed, ebtehag mustafa. (2020). Explanatory Factor analysis to determining the risk factors of cardiovascular disease: A hospital-based case-control study. Journal of Medical Research and Health Sciences, 3(8).