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

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(4); 112-117

Original Research Article

Prospective Hospital Based Assessment of the Serum Ferritin Level as A Marker of Preterm Labor

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Received: 17-01-2022 / Revised: 15-02-2022 / Accepted: 21-03-2022
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Conflict of interest: Nil

Abstract

Aim of the study: To evaluate the value of serum ferritin level as predictors in preterm labor

Patients and Method: This is a prospective study, conducted at the Department of Obstetrics & Gynecology, Nalanda Medical College & Hospital, Patna, Bihar, India, over a period of 7 months. The sample collected from the pregnant ladies who visited the outpatient clinic.

Results: The mean level of iron in preterm was (72.0±24.9) and (70.5±27.4) for full-term women with no significant differences (P=0.5). S. ferritin were highly significant decrease in full term than that in preterm (P<0.001) the level of the serum ferritin declined with progression of the gestational age in preterm labor, and the mean gestational age at delivery time was below the 36 weeks.

Conclusion: The findings of the present study showed that serum ferritin level can be used to find patients at risk of preterm delivery.

Keywords: Serum ferritin, preterm labor, third trimester

Introduction

Preterm delivery is a delivery occurring prior to 37 weeks of gestation. Every year, about 15 million babies are born prematurely, more than one in 10 of all babies born around the world, and its complications are the leading cause of mortality of children less than 5 years, causing about one million deaths annually[1,2]. The pathophysiology of preterm delivery is not yet fully understood, however, it has several risk factors such as a history of preterm delivery, a history of abortion, vaginal bleeding, moderate to severe anemia at 12 weeks of gestation, inadequate weight gain during pregnancy, and uterine and cervical problems[3]. There is evidence indicating that prelabor rupture of membranes (PROM) is the most important cause of preterm delivery, which may be caused by subclinical infection and chronic inflammation of the uterus[3]. Under such conditions, microorganisms produce prostaglandins directly or through

phospholipase A2 production, resulting in uterine contraction and cervical relaxation[4].

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 [5]. One particularly interesting potential marker is ferritin. Ferritin is an iron storage protein synthesized by a variety of tissues primarily the liver, spleen, bone and placenta. It is also released by infiltrating leukocytes, in response to acute and chronic infection. Several previous investigations have indicated an association between elevated serum ferritin concentration and preterm delivery [6].

In response to the call for early detection of PTD, several diagnostic biomarkers are currently in development. According to the main role of inflammation on appearance and progression of preterm delivery, it is hypothesized that measuring serum ferritin level as a sensitive inflammatory marker can effectively predict this event in the high risk group. Some investigators have reported a relationship between elevated serum ferritin concentrations and preterm labor. [7]

Hence the aim of the present study was to evaluate the value of serum ferritin level as predictors in preterm labor.

Material & Methods:

This is a prospective cross-sectional study, conducted at the Department of Obstetrics & Gynecology, Nalanda Medical College & Hospital, Patna, Bihar, India, over a period of 7 months. The sample collected from the pregnant ladies who visited the outpatient clinic.

Methodology

A total of 180 pregnant ladies between the age 18-40 years, with gestational age between (30-34) weeks (based on the last menstrual period and early U/s scan). Full history was taken from the ladies, with general obstetrical, medical and surgical history, and full general physical and obstetrical examination was carried to all respondents. We sent the respondents for U/s to confirm the gestational age, Hb and PCV%, S. iron, S. ferritin, and other investigations according to the patient's condition. The pregnant ladies with no sign and symptoms of anemia and their Hb ≥11g/dl were included in the study. The samples were sent for S. iron, S. ferritin. All patients' data entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 23 used in this study. In all statistical analysis, level of significance (p value) set at ≤ 0.05 and the result presented as tables and/or graphs.

Results:

Table 1: Association between Hb and hematocrit with gestational age:

No statistical association were found between the studied groups regarding Hb level (P=0.2), while significant increase in hematocrit in full-term were found (P=0.001) (table 1)

Table 1: Association between Hb and hematocrit with gestational age

	Gestational age		P value
	Preterm	Full-term	
	Mean±SD	Mean±SD	
Hb (g/dl)	10.8±0.5	10.4±0.7	0.200
Hematocrit (%)	30.6±2.9	33.8±2.5	0.001

The mean level of iron in preterm was (72.0±24.9) and (70.5±27.4) for full-term women with no significant differences (P=0.5). S. ferritin were highly significant decrease in full term than that in preterm (P<0.001) (table 2)

Table 2: Association between S. Iron and S. ferritin with type of term

		Type of gestational age	
	Preterm Mean±SD	**Full-term Mean±SD**	**P value**
Iron level (Mg/dl)	72.0±24.9	70.5±27.4	**0.501**
S. Ferritin level (ng/ml)	71.5±14.8	20.7±12.9	<0.001

Table 3 show that the level of the serum ferritin declined with progression of the gestational age in preterm labor, and the mean gestational age at delivery time was below the 36 weeks.

Table 3: level of serum ferritin according to GA in preterm labor

GA at time of sample collection	No. of patients	No. of patients who delivered preterm	S. Ferritin level (Mean±SD)	Mean of GA at delivery (Mean±SD)
30 wks	30	20	100.2±20.4	28.9±1.3
31 wks	22	3	95.8±8.0	27.1±2.4
32 wks	43	16	90.7±18.7	30.4±0.9
33 wks	56	27	71.5±17.9	32.8±0.8
34 wks	29	14	60.5±9.6	36.3±0.6
Total	180	90	-	-

Table 4 show that Hb in preterm [in primigravida was (10.2±1.4) and decrease in multigravida (12.9±1.2) but with no significant association (p=0.5)]
For s. ferritin: in preterm [in primigravida the level was (20.3±10.4) and increase in multigravida (21.4±13.2) with no difference (P=0.5), and in full-term [hb was (21.4±6.9) and decrease to (19.8±15.3) with no significant differences were found (p=0.05).

Table 4: Relation between S. Hb and S. ferritin with gestational age

	Gestational age					
	Preterm Mean±SD		**P value**	**Full-term Mean±SD**		**P value**
	Primigravida	Multigravida		Primigravida	Multigravida	
	Mean±SD	Mean±SD		Mean±SD	Mean±SD	
Hb (g/dl)	10.2±1.4	12.9±1.2	0.5	9.3±0.5	12.8±0.8	0.5
S.Ferritin level (ng/ml)	20.3±10.4	21.4±13.2	0.5	21.4±6.9	19.8±15.3	0.05

Validity of the test to diagnose preterm was assessed by using cutoff value of S. ferritin at 30.3 ng/L and the AUC was (81%) show that sensitivity was (91.5%),

specificity (94.6%), NPV (95%), PPV (60.3%) and the accuracy of the test was (95.0%), all these were found in (table 5)

Table 5: Validity test of the S. Ferritin

Cutoff value of S. ferritin	Sensitivity	Specificity	NPV	PPV	Accuracy
30.3 (ng/L)	91.5%	94.6%	95%	60.3%	95.0%

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 [8].

Pregnancy tends to predispose to vaginocervical infection due to altered vaginal pH. The chorion-decidual interface is infiltrated by macrophages following bacterial colonization and ferritin is produced as an acute phase reactants [9].

The purpose of this analysis was to explore whether serum ferritin levels which may be raised in any infective process could be used as a marker of preterm labor. Preterm delivery is commonly associated with anaemia and poor maternal weight gain during pregnancy. It was found that the relationship between anaemia and preterm delivery was specific to iron deficiency anaemia and the risk was more than double [10]. Anaemia during the second trimester has also been shown to be positively associated with spontaneous preterm birth although anaemia later in pregnancy was negatively associated with preterm birth [11].

Nandini et al highlighted that the mean ferritin level in women with preterm and normal vaginal delivery was 81.296 ng/mL and 28.576 ng/mL, respectively, which was significantly higher in women with preterm delivery [12].

Another case control study was done by Movahedi et al. [13] on 222 singleton pregnancies, 69 (31.1%) had preterm delivery and 153 (68.9%) had term delivery.). Women who delivered before 37 weeks had a higher mean serum ferritin concentration than those who delivered after 37 weeks of gestation (26.7 ± 5.5 ng/ml vs. 19.8 ± 3.6 ng/ml, P <0.001). Receiver operator characteristic (ROC) curve was constructed to the serum ferritin values to determine the level that would predict preterm delivery with reasonable sensitivity and specificity. Serum ferritin level of 22.5 ng/ml yielded the best combination with sensitivity of 78.3%, specificity of 83.0%, positive predictive value of 67.5%, and negative predictive value of 89.4% for prediction of preterm delivery. [13]

Although treatment of lower genital tract infection (bacterial vaginosis) has been shown to reduce the occurrence of spontaneous preterm delivery in some high risk population, it is unclear whether such infections are causal or merely associated with a concurrent occult chronic upper genital tract infection. However, in two small, randomized trials, a prolonged course of metronidazole plus ampicillin resulted in a substantial delay in delivery, a reduction in the incidence of preterm delivery and lower neonatal morbidity, as compared with placebo [14]. In practice, pregnant women with asymptomatic upper genital tract infection are not routinely screened or treated. Thus, the high serum ferritin level in the study group is most likely a part of acute phase reaction to a subclinical infection. Its treatment could have a substantial effect on the incidence of preterm delivery of infants with low

birth weight. These findings are consistent with earlier studies. [14, 15]

Conclusion:

From the present study it may be concluded that serum ferritin level may be considered as an important parameter for detecting preterm labor. In the cases of high level of serum ferritin, treatment may be instituted to prevent preterm birth. The result of the study adds to the existing evidence that high serum ferritin level is a risk factor for preterm birth. So, timely detection and intervention could easily prevent high serum ferritin related adverse pregnancy outcome.

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