

The Association Between Maternal Serum Ferritin Level and Preterm Labor

Fayza Ahmed Andegani^{1*}, Safaa M Al-Hasani², Seham Yahia Kutbi¹, Doaa Ahmed¹, Reem Adnan³ and Khulud Yahya Khati¹

¹King Abdulaziz Hospital, Saudi Arabia

²Salam Medical Services, Saudi Arabia

³Ibn Sina National College for Medical Studies, Saudi Arabia

***Corresponding Author:** Fayza Ahmed Andegani, King Abdulaziz Hospital, Saudi Arabia.

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Abstract

Objective: To compare the serum ferritin levels in women with preterm labor (PTL) with those in normal gravid women.

Method: The present study includes total 100 participants that comprise 50 women presenting with preterm onset of labor followed by delivery and 50 women who delivered at term served as controls.

Results: Mean serum ferritin levels in patients with preterm labor were 20.18 ng/ml. The mean serum ferritin in control subjects was 163.87 ng/ml.

Conclusion: The findings of this study have shown that the assessment of concentrations of serum ferritin in preterm was within normal range therefore cannot be a reliable method of detection preterm labor meanwhile serum ferritin concentration found to be significantly high in term labor.

Keywords: Maternal Serum Ferritin Level; Preterm Labor

Introduction

Preterm labor was defined as regular uterine contractions in patients before 37 completed weeks of gestation with intact membranes with 4 cm or more of cervical dilatation observable during a 2 hours period [1].

Preterm delivery is one of the leading causes of perinatal morbidity and mortality. An estimated one million babies die annually from preterm birth complication. It accounts for nearly 70% of the neonatal deaths and 50% of the long term neurological sequelae [2].

Many of the surviving infants suffer serious morbidity such as respiratory distress syndrome, broncho pulmonary dysplasia, intraventricular haemorrhage, retrolental fibroplasia and developmental problems [3].

In 40% cases of preterm birth, there is no obvious etiology. Although the pathophysiology of preterm labour remains incompletely defined, a growing body of evidence is emerging that links occult upper genital tract infections with subsequent spontaneous preterm labour. Multiple gestations and history of a preterm delivery are the two most significant risk factors for preterm labour [4,5].

Currently the accepted markers of onset of preterm labor are assessment of fetal fibronectin in cervicovaginal secretions and cervical dilatation [2].

Ferritin which has a central role in iron homeostasis, it also released by infiltrating leukocytes, in response to acute and chronic infection. Several previous investigations have showed an association between elevated serum ferritin concentration and preterm delivery. The presence of increased levels of ferritin may reflect an acute phase reaction to subclinical genital tract infection or inflammation [6].

Aim of the Work

The aim of this study is to evaluate the relation between maternal serum Ferritin level and preterm labor to assess its value as a predictive test.

Methodology

Design of the study

- Case - control study.
- Sample size justification: The sample size was estimated to be 98 cases, so we approximately included 100 cases. It was calculated by two-sided binomial test with a confidence level of 99% (alpha-error, 0.01) and assumed a prevalence rate of PTL of 50% (case: control ratio, 1:1).
- This study will be carried out at King Abdulaziz hospital-Jeddah.

Patients subdivided into 2 groups:

- **Group A:** Study group (50 cases) patients presented with established preterm labor within 24 weeks to 36 weeks gestation.
- **Group B:** Control group (50 cases) patients with uncomplicated pregnancies who delivered at full-term.

Inclusion criteria:

- Singleton pregnancy.
- Gestational age between 24 - 36 weeks.
- Parity: primipara or multipara.
- Patients with hemoglobin concentration > 10 gm %.

Exclusion criteria:

- Anemia (hemoglobin \leq 10 gm/dl).
- Iron overload state.
- Congenital uterine abnormalities and incompetent cervix.
- Multiple pregnancy.

- Polyhydramnios.
- Preterm premature rupture of membrane.
- Diabetes mellitus.
- Pre-eclampsia and eclampsia.
- Liver disease.
- Renal disease and malignancy.
- Foetal congenital anomalies.

All patients enrolled in this study will be subjected for the following:

- Verbal consent: Will be obtained from the pregnant women who are included in the study.
- Complete history taking.
- General, abdominal and pelvic examination.
- Investigations in the form of:
 - Ultrasonography to ensure fetal life, gestational age and excludes congenital fetal malformation.
 - Blood samples were taken for measurement of
 - Complete blood picture.
 - Serum ferritin concentration.

Measurement of serum ferritin level

Blood sample was taken from all women at 24 - 40 weeks of gestation. Assay of Ferritin was performed using Enzyme-Linked Fluorescent Assay (ELFA) technique.

Three milliliters of venous blood sample were taken from all women at 28 - 36 weeks were drawn from the antecubital vein using a disposable plastic syringe and left to clot for 30 minutes. The sample was then centrifuged and serum was separated and kept at -20°C till assay time. Serum ferritin levels were measured by ELFA technique [7].

Data management and analysis

Data will be collected, revised, coded, tabulated and introduced to a PC using IBM® SPSS® Statistics version 23 (IBM® Corp., Armonk, NY, USA).

Outcome measures

- **Primary outcome measures:**
 - Relation between maternal serum ferritin level and preterm labour.
- **Secondary outcome measures:**
 - If serum ferritin can be used as a predictive method for preterm labour.
 - Neonatal outcome:
 - Admission to ICU.
 - Neonatal death.

Results

100 respondent’s women included in the study; where constitute from 2 different types of pregnant women who had have either pre-term birth or term birth. No differences in Mean age for both types with mean for almost 32 years old. Women with preterm cases have a greater number of pregnancies (mean = 4) than women with term cases (mean = 3). Both have same number of delivery, while number of abortions were higher in preterm cases than in term cases (means = 2 compare to 1).

Pregnancy type	Preterm		Term		P-value
	Mean	STD	Mean	STD	
Age	32.38	6	31.62	7	.553
Number of pregnancies	4	3	3	2	.016
Number of Delivery	3	2	3	2	.121
Number of Abortion	2	1	1	1	.138

Table 1: Sample demographic profile (n = 100).
STD: Standard Deviation.

Table 2 showed statistically significant differences between preterm cases and term cases in related to the age after last menstrual cycle, and age based on sonar (P-value less than 0.05). It showed that Term cases have higher age of pregnancy in both after last menstrual cycle, and age based on sonar.

		Preterm		Term		P-value
		Mean	Standard Deviation	Mean	Standard Deviation	
Age after last menstrual cycle	Week	33.14	3	38.88	1	.000
	Day	5	2	3	2	
Age based on sonar	Week	33.18	3	38.76	1	.000
	Day	5	1	4	2	

Table 2: Measures the relation between age of pregnancy and term and preterm labour.

Table 3 showed statistically significant differences between preterm cases and term cases in related to the Ferritin concentration (P-value less than 0.05). It showed that Term cases have higher concentration with mean = 163.87 compare to mean = 20.18 for preterm cases. As well as table shown the status of ferritin level either normal or not normal in both preterm and term cases; where Preterm cases had had higher normal level of ferritin (47%) compare to 17% in term cases.

Mean		Preterm		Term		P-value
		Standard Deviation	Mean	Standard Deviation	Mean	
Ferritin concentration		20.18	54.96	163.87	164.57	.000
Type of Ferritin level		Count	Table N %	Count	Table N %	.000
	Normal	47	47.0%	17	17.0%	
	Not Normal	3	3.0%	33	33.0%	

Table 3: Measures the relation between maternal serum ferritin level and term and preterm labour; And Measures if serum ferritin can be used as a predictive method for preterm labour.

In table 4 showed statistically not significant relationship between BMI index in both preterm and term cases (P-value = .766).

		Preterm		Term		P-value
		Count	Table N %	Count	Table N %	
BMI index	Healthy	11	11.0%	11	11.0%	.766
	Underweight	1	1.0%	0	0.0%	
	Overweight	11	11.0%	12	12.0%	
	Obesity I	14	14.0%	13	13.0%	
	Obesity II	11	11.0%	9	9.0%	
	Obesity III	2	2.0%	5	5.0%	

Table 4: Measures the relation between weight measures and term and preterm labour.

The relationship between maternal serum ferritin level and BMI shown on table 5 were the relationship was not statistically significant as P-value more than 0.05.

Correlations			
		Ferritin concentration	BMI
Ferritin concentration	Pearson Correlation	1	-.023-
	Sig. (2-tailed)		.818
	N	100	100
BMI	Pearson Correlation	-.023-	1
	Sig. (2-tailed)	.818	
	N	100	100

Table 5: The relation between maternal serum ferritin level and BMI.

Discussion

Most studies done in the past show that ferritin levels are higher in preterm labor than term, and therefore can be used as an indicator to predict preterm labor [8,9]. However, in our study we do not find the similar outcome. Scholl et. al discovered that pregnant women with iron deficiency anemia at about 17 weeks have a high risk of preterm delivery. Serum ferritin is sensitive to stored iron in the body, however they are increased in acute or chronic inflammation. Many studies have attributed increased ferritin concentrations with several pregnancy related complications. Normally, preterm labor is caused by infections which may be a reason of increased ferritin concentration, since it is an acute phase reactant. Similar to our study, one study was done among 150 pregnant women to evaluate the concentration of serum ferritin with respect to labor onset. Seventy percent of women had low ferritin due to iron deficiency anemia. Only 11% of the pregnant women with preterm labor had a higher than 20 ug/L [10]. A study done to assess the predictiveness of serum ferritin levels in spontaneous preterm delivery showed that ferritin levels may be increased, but that is more likely reflecting an acute phase reaction of the underlying infection causing the preterm delivery. Additionally, most of the genital tract infections that cause preterm delivery are clinically undetected. Raman., et al. noticed a significant increase in the ferritin levels in women with eclampsia or pregnancy induced hypertension. Therefor suggesting that ferritin concentrations are not reliable [11].

In this study, we evaluated serum ferritin levels between groups with term and preterm labors. Our study shows no association between increased ferritin levels and preterm labor. Rather, the study showed increased ferritin levels with term deliveries as compared to preterm labors (47% vs 17%). This shows that more studies must be done to assess whether ferritin is a good predictor or not.

Conclusion

The findings of this study have shown that the assessment of concentrations of serum ferritin in preterm was within normal range therefor cannot be a reliable method of detection preterm labor meanwhile serum ferritin concentration found to be significantly high in term labor.

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