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Serum Ferritin Levels with Some Hematological Parameters in Women with Preterm Labour or PPROM

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Abstract

Preterm labour is defined as the presence of uterine contractions of sufficient frequency and intensity to cause progressive effacement and dilation of the cervix prior to term gestation between (24- 37) weeks of gestation**.**Aim of current study aims at conducting and detecting the serum ferritin level could be use as predictor in women with preterm labour. So to decrease morbidity and mortality among the mother and her baby by predicting early labour .Patient and Method:The study was conducted at the Department of Obstetrics and Gynecology at Tikrit Teaching Hospital,included 100(study and control)laboring women attending to hospital, patients included in the study were subdivided into two groups:fifty of them were preterm labour cases(gestational age between 24-37) and 50 of them had intact membranes and the other 50 were with preterm premature rupture of membranes.the second group consist of 100 patients with gestational age more than 37 weeks.all patient were subjected to the Hematological investigations(HB%,PCV,and serum ferritin). Results:In this study the patients were of comparable age with a mean age of the preterm labour group of 23.45+4.18 ranging from16-35 years, so gestational age distribution of both group, the preterm group women had a mean gestational age (34 weeks) which is significantly lower than those of the term pregnant women (38 weeks).All groups were comparable in terms of hemoglobin and PCV level ($p>0.05$), while there was higher serum iron and higher serum ferritin level in the preterm group compared to the control group ($p<0.0001$).only serum ferritin was higher in those PPROM($P<0.0001$)while the other parameter were not significantly different in there level between the two groups.Preterm group **showed** significant higher of serum iron of preterm from control ($P<0.0001$)and preterm premature ruptured membranes PPROM from control ($P<0.0001$).The serum ferritin showed a significantly higher level in preterm labour from control ($P<0.0001$) and significantly higher level in preterm premature ruptured membranes PPROM than control group ($P<0.0001$).**Conclusion** Elevated serum ferritin level could be use as a predictor for prediction of spontaneous preterm delivery and PPROM at high risk of these complication, although it is worth mentioning that a larger study population .

Keywords: *Serum ferritin; hematological parameters; women with preterm labour;PPROM.*

Introduction

For reasons related to etiology, out come and recurrence risk, preterm labour should be divided into three gestational groups**:** mildly preterm at 32^{+0} to 36^{+6} weeks (incidence 5.5%), **moderately** preterm 28^{+0} to 32^{+6} weeks (incidence 0.7%) and **extremely** preterm birth at 24^{+0} to 27^{+6} weeks (incidence 0.4%) **[1,2,3].**

The incidence of preterm labour in developed world between 7 to 12%**[1].** There has been a small gradual rise in the incidence of preterm labour associated with assisted reproduction and an increased tendency to obstetric intervention. The rate of preterm labour prior to 32 weeks has remained relatively stable at 1-2%. About one quarter of preterm labour is elective deliveries, usually for pre-eclampsia, intrauterine growth restriction, or maternal disease. The remainder is due to preterm labour and delivery. The incidence is at

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its lowest in women in their 20s.The risk is increased in teenagers and in women in their 30s [1, 3].

There are relatively frequent causes of preterm labour approximately 5-10% of patients with preterm labour have infection outside the uterus; most common is urinary tract infection [4].Romero and Mazor has presented the evidence suggesting that extra uterine infection may cause preterm labour by mechanism involving productionof IL and TNF by maternal macrophage which in turn will trigger the production of PG by amnion [4].

Early differentiation between true & false labor is difficult before there is demonstrable cervical effacement & dilatation .Painful or painless uterine contractions, symptoms such as pelvic pressure, menstrual-like cramps, watery vaginal discharge & lower back pain have been empirically associated with impending PTL[5].

Women at high risk of preterm labour will initially be detected based on past obstetrical history[6]Ferritin is a large protein shell(Molecular weight 450,000) comprised of 24 subunits,covering an iron core containing up to 4000 atomsof iron [7] ferritin occurs in virtually all cell of body and also in tissue fluids,it mainly located in the spleen, liver, and bone marrow,it is also found in the mucosal cell of the small intestine, placenta,kidney,testes,skeletal muscles and circulating plasma[8,9]

Ferritin act as the soluble storage form of iron in tissue (hemosiderin is relatively insoluble).It may serve other functions as well although these are controversial. It is found in most cells of the body, especially macrophages, hepatocytes, erythrocytes. Synthesis occurs in the liver and the rate correlates directly with the cellular iron content. Control of ferritin synthesis occur post-transcriptionally (at the mRNA level).There are iron-and cytokine-responsiv elements in ferritin mRNA. Increased iron or cytokine (suchIL-1, IL-6) promotes ferritin translation resulting in increased iron storage. This is one of the causes of iron sequestration that occurs in animals with chronic or inflammatory disease and will reduce serum iron value. The function is not known,but the concentration correlate well with the amount of stored iron in normal(and most diseased) subjects. It has been proposed that extra cellular ferritin has an important role in host defense against bacteremia by stimulating oxidative metabolism[6,10], in women receiving routine prenatal care,low serum ferritin level is indicated of low iron store,but high serum, ferritin concentration appear to represent an acut-phase reaction and predict preterm delivery[11].In pregnancy, serum ferritin concentration is maximum at 12-16 weeks gestation, and then falls with advancing gestation to reach a nadir at the third trimester[6]

Because of previously reported very strong association between preterm birth and intrauterine infection, and because other inflammatory conditions have been associated with elevated ferritin level, it was hypothesized that sub clinical maternal infection was responsible for both elevated ferritin level and for the spontaneous preterm birth[12,13].Serum ferritin could be useful to identify preterm labour in pregnancy.to account for the association between elevated serum ferritin concentration and spontaneous preterm delivery we suggest that the production of ferritin or the release of ferritin from tissue may be of an acute phase reactant associated with an upper genital tract infection. Themechanism of such association may be secondary to the increased production of ferritin by macrophages that infiltrate in to the choriondecidual interface after bacterial colonization[12,14]

Aim of current study aims at conducting and detecting the serum ferritin level could be use as predictor in women with preterm labour. So to decrease morbidity and mortality among the mother and her baby by predicting early labour by The current study was done aiming to measure the serum ferritin level with some other hematological parameters in women with preterm labour or PPROM and compare them to that of control group composed of term pregnant women in order .

Patient and Method

The study was conducted at the Department of Obstetrics and Gynecology at Tikrit Teaching **Hospital,**included 100(study and control)laboring women attending to hospital and fulfilling the following criteria(Cervical dilatation >3cm; Fully effaced cervix; Uterin contraction 3/10m), While laboring women with the following criteria were excluded(Anemia (hemoglobin<10.5g/dl); diabetes mellitus; Pr e-eclampsia, eclampsia; Polyhydramnios; Iron overload stats;Liver disease; Renal disease;Chronic infectious diseases;Smoker;Fetal congenital anomalies; Blood transfusion; Drugs, iron, thyroid drug; Haematological disorder;Multiple pregnancy.

The patients included in the study were subdivided into two groups:

1. fifty of them were preterm labour cases(gestational age between 24-37) and 50 of them had intact membranes and the other 50 were with preterm premature rupture of membranes.Gestational age was calculated by combined information from last menstrual period and first trimester ultrasound.
2. The second group consist of 100 patients with gestational age more than 37 weeks.All patient were subjected to the following:
   a. Hematological investigations(HB%,PCV,and serum ferritin)

b. Abdominal ultrasound to check for gestational age,and also to exclude congenital anomalies.

c. Serum ferritin was assayed by UBI Mgiwelltm Ferritin quantitative test system.

Estimation of serum ferritin: The serum ferritin (SF)was assayed by UBI Magiwelltm Ferritin quantitative test system. This is a solid phase enzyme-linked immunosorbent assay (ELISA).Using the mean absorbance value for sample, determine the corresponding concentration of ferritin in ng/ml for the standard curve.

Expected value and sensitivity of ferritin for female 10-12ng/ml, Hb and packet cell volume were estimated by automated coulter.Serum iron was estimated by standard method recommended by the international committee for standardization Hematology. The concentration (X) of each reference was plotted against its absorbance(y) on a full logarithmic graph paper and a standard curve was drawn. Ferritin values of samples were obtained by reference to the standard curve following the obtaining of the **equation** between (x) and (y). Obtained from the standard curve. (Figure 1).

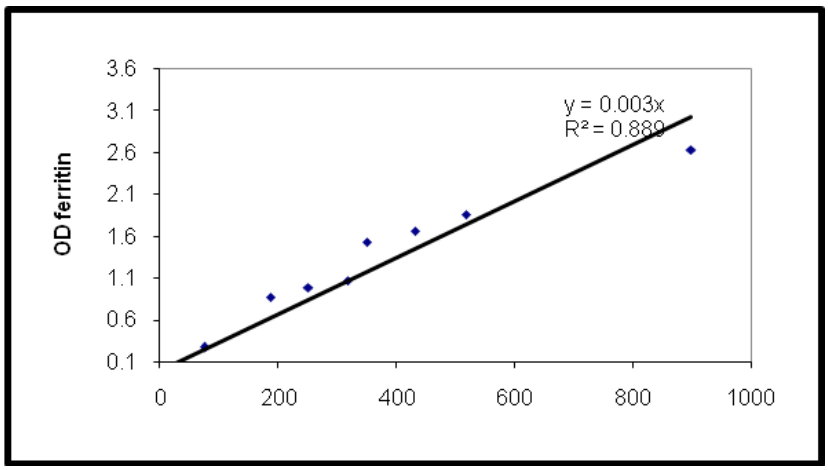

Figure 1: The standard curve for ferritin concentration.

Statistical Analysis: Statistical analysis was performed using (Statistical Packages for Social Sciences version 15) analysis software.

Finding: In this study the patients were of comparable age with a mean age of the preterm labour group of 23.45+4.18 ranging from 16-35 years, While the mean age of control group was 24.75+4.18 ranging from 15-35 years as show in Table 1.

Table 1:The Maternal Age (years) Distribution in the Studied Groups

Age (Years)	Preterm Labour No	Preterm Labour %	Control No	Control %
15-19	18	18.0	12	12.0
20-24	47	47.0	33	33.0
25-29	28	28.0	44	44.0
30-34	4	4.0	7	7.0
35	3	3.0	4	4.0
Mean+SD (min-max)	23.45±4.14 (16-35)		24.75±4.18 (15-35)	

P=0.086 (Not significant using Pearson chi-squared test at level of significance)

Table 2 showed the gestational age distribution of both group, the preterm group women had a mean gestational age (34 weeks) which is significantly lower than those of the term pregnant women (38 weeks).

Table 2: The Gestational Gge (weeks) Distribution in the Studied Groups.

Gestational age (weeks)	Preterm Labour No	Preterm Labour %	Control N0	Control %
24-29	9	9.0	-	-
30-31	6	6.0	-	-
32-33	4	4.0	-	-
34-35	64	64.0	-	-
37	17	17.0	34	34.0
38-39	-	-	42	42.0
40-42	-	-	24	24.0
Mean± SD	34.02±2.23 (28-36)	34.02±2.23 (28-36)	38.46±1.6 (37-42)	38.46±1.6 (37-42)

P=0.0001(Significant using Pearson chi-squared test at 0.05 level of significance)

All groups were comparable in terms of hemoglobin and PCV level (p>0.05) as it is shown in table 3, while there was higher serum iron and higher serum ferritin level in the preterm group compared to the control group (p<0.0001).

Table 3: The Hemoglobin, PCV, Serum Iron and Serum Ferritin Levels in the Studied Groups

	Pre-term labour men±SD	Control	Pvalue
Hb(g/dl)	11.80±0.76 (11.00-13.40)	11.88±0.74 (11.00-13.30)	0.445
PCV%	0.36±0.03 (0.30-0.40)	0.37±0.02 (0.33-0.40)	0.355
Iron(Mg/dl)	23.45±9.38 9.87-48.70	19.44±4.83 (12.40-30.20)	0.0001*
Ferritin(ng/ml)	25.81±7.69 (0.50-40.00)	9.24±5.50 (0-19.50)	0.0001*

Data were presented as Mean± SD(Range)

Regarding the comparison of the preterm labour with intact membrane groups with the (PPROM)group, as it is shown in table 4.only serum ferritin was higher in those PPROM(P<0.0001)while the other parameter were not significantly different in there level between the two groups.

Table 4:The hemoglobin, PCV, serum iron, and serum ferritin level in the studied groups.

	Preterm labour	Preterm PROM labour	P value
Hb(g/dl)	11.79±0.82 (11.0-13.40)	11.8±0.70 (11.0-13.00)	0.927
PCV%	0.36±0.03 (0.30-0.40)	0.36±0.02 (0.30-0.40)	-
Iron(Mg/dl)	21.79±5.75 (16.70-48.70)	25.12±11.80 (9.87-48.50)	0.076
Ferritin(ng/ml)	19.98±5.62 (0.5-26.00)	31.64±4.31 (25.50-40.00)	0.0001*

Data were presented as Mean± SD(Range), *highly Significant using t-test for two independent means at 0.05 level of significant.

Table (5): The hemoglobin, PCV, serum iron, and serum ferritin levels in the studied groups.

	Preterm Labour	PPROM	Control	P value for preterm x control	P value for PPROM xcontrol
Hb (gl/dl)	11.79±0.82	11.80±0.70	11.88±0.74	0.509	0.558
PCV%	0.36±0.03	0.36±0.02	0.37±0.02	0.449	0.424
Iron(mg/dl)	21.79±5.75	25.12±11.8	19.44±4.83	0.009*	0.0001*
Ferritin (ng/ml)	19.89±5.62	31.46±4.31	9.24±5.50	0.0001*	0.0001*

*highly significant using t-test for two independent means at 0.05 level of significance.

Table 5 showed the comparison between preterm labour and preterm premature rupture of membranes PPROM with that of control term pregnant women regarding different hematological parameters .Preterm group showed significant higher of serum iron of preterm from control (P<0.0001)and preterm premature ruptured membranes PPROM from control (P<0.0001). The serum ferritin showed a significantly higher level in preterm labour from control (P<0.0001) and significantly higher level in preterm premature ruptured membranes PPROM than control group (P<0.0001).These findings were demonstrated graphically for serum ironand serum ferritin levels.

Discussion

The prediction of which pregnancies will end in preterm birth is a reasonable goal for several reasons. First, predicting which women might have a preterm delivery may allow us to initiate appropriate risk – specific treatment. Second, it may help us to define a population of women who are at risk so that we can study a particular treatment. Finally, being able to predict which women will have a subsequent preterm birth may allow us to gain important insights into the mechanisms or pathways that ultimately lead to a preterm birth.[10,15]

Elevated serum ferritin level during the thired trimester are predictive of early spontaneous preterm delivery, possibly because these reflect an acute-phase reaction to sub clinical infection that are closely associated with premature delivery.[8]

Serum ferritin was 19.98±5.6290.50-26.00) and in PPROM group was 31.64±4.31(25.50-40.00), in the control group serum iron was19.44±4.83(12.40-30.20), and serum ferritin was 9.24±5.50(0-19.50). These finding are consistent with the study carried out by Saha *etal*., who found serum ferritin in the preterm labour group was (23.24±12.13), and in PPROM group was (29.44±28.41),compared to control group which was (8.69±3.7), and that carried out by Robert L who found high, but not low,plasma ferritin level, especially at 26 weeks, were strongly associated with subsequent preterm delivery.[1,15]

The possible explanation for higher serum ferritin level in patients with preterm labour and PPROM in this context could be iron overload or latent chorioamnionitis, and as iron overload has been excluded in the study by considering various hematological parameters, thus the high serum ferritin obtained in the preterm and PPROM is most likely a part of acute phase reaction to a sub clinical infection while Gopal *etal.,* reported a negative relation between serum ferritin level and preterm labour.[2,8]

In this study serum iron was significantly higher in control group 19.44±4.83 than in preterm labour 21.79±5.75 and PPROM25.12±11.80 while Kaneshige studied several hematological parameters during pregnancy he observed an increase in serum iron level in the first trimester as compared to that of non-pregnant women, then in third trimester giving a weak inverse correlation between serum iron and period of gestation.

Conclusion

Elevated serum ferritin level could be use as a predictor for prediction of spontaneous preterm delivery and PPROM at high risk of these complication, although it is worth mentioning that a larger study population such conclusion.

Conflict of Interest: Non

Source of Findings: Self findings.

Ethical Clearance: This research was carried out with the patient's verbal and hospital approval before the cases was taken.

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