

Original Article

The study of the relationship of serum ferritin and uterine contractions in pregnant women referred to medical centers of Isfahan

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Abstract

BACKGROUND: Prenatal care is performed in order to diagnose high risk cases. Researchers have shown the significant relationship between high serum ferritin levels and preterm delivery. Preterm labors are one of the major risk factors in prediction of preterm delivery. Hence we performed this study in order to determine the frequency distribution of serum ferritin level and the relationship between serum ferritin level and preterm labors too.

METHODS: A descriptive and analytic research was performed on 267 pregnant women who referred to health centers of Isfahan. Data was collected using a questionnaire with interview, results of serum ferritin levels and hospital documents. Data was analyzed with T-test and SPSS software.

RESULTS: Serum ferritin levels according to 10, 25, 50, 75 and 90 percentiles are categorized in series of 8.6, 12.7, 20, 30.3 and 42.5 ng/ml; so samples were divided into six groups. A significant relationship between serum ferritin levels (after 28-30 weeks of pregnancy) and preterm labors was found ($p = 0.029$).

CONCLUSION: Considering the significant relation between serum ferritin and uterine contractions that are not caused by other reasons like smoking, it can be used as an indicator to find women who may have early uterine contractions. Our findings suggest that further researches about ferritin and related factors and pregnancy outcome are needed.

KEY WORDS: Serum ferritin, uterine contractions, preterm labors.

IJNMR 2009; 14(4): 162-167

Hygiene and health of the child is in close contact with mother's hygiene and health and also her access to health services; as examples of these services we can mention prenatal care with the goal of diagnosing high risk pregnancies, predicting and preventing pregnancy complications as preterm delivery, which is one of the most controversial in midwifery medicine regarding 10% preterm deliveries.¹ A considerable number of researches are performed to recognize the high risk group of preterm deliveries. One of the most important researches done in this field is the study of Goldenberg et al which inspects the relationship between serum ferritin level in pregnant women and some pregnancy complications. This study shows a significant relation-

ship between high levels of serum ferritin in 26th week of pregnancy and preterm delivery and also low birth weight.²

In addition, some researchers suggest the relationship between serum ferritin level more than 30 $\mu\text{g}/\text{dl}$ in 26th week and 40 $\mu\text{g}/\text{dl}$ in the 34th week of pregnancy and preterm delivery.³ Serum ferritin is a high molecular weight glycoprotein which can be observed in the range of 20-120 ng/ml in healthy women in fertility ages and is the main protein for iron storage.⁴ In iron deficiency anemia and severe protein deficiencies, serum ferritin level will be decreased and we expect an increase in serum ferritin level during infection and inflammation.⁴

On the basis of latest national survey studies done by health research institute of Tehran

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Research Article of Isfahan University of Medical Sciences, No: 811140

University of Medical Sciences on women in fertility ages in urban and sub urban regions, 28.5% of women had a normal serum ferritin level in the range of 20-25ng/ml and 15.2% experienced positive iron equilibrium (balance) with 100-299 ng/ml ferritin level, and 6-10% showed extra iron on laboratory data. It means that, the last group had ferritin level above 200 ng/ml.⁵

Many researches are conducted to define the relation between high serum ferritin level and undesirable termination of pregnancy.

As ferritin is an acute phase protein, its high serum concentration is attributed to sub clinical infections² or hypovolemia⁶ and in some cases, mother's increased serum iron.⁷ On the other hand, preterm labors as a marker to define patients who experience a preterm delivery, are studied widely and many researchers' report an increased uterine contraction in woman who finally experience pain and preterm delivery.⁸

In this regard, a study performed in Isfahan which estimated the prevalence of about 20% for preterm labors. This study suggests, preventing early contractions is more beneficial than therapy and it is economically, culturally and socially more cost-effective.⁹ Regarding national researches and revealed data, we decided to assess the relationship between serum ferritin level and incidence of preterm labors in pregnant women who were referred to Isfahan Health Centers.

Our goal was to determine the frequency distribution of ferritin level in 28-30 weeks of pregnancy and also investigate the relationship between serum ferritin level and incidence of preterm labors. Regarding lack of data on this subject and really few researches done in this field, we think results of this study would be of great benefit to target population.

Methods

This survey is a descriptive analytical study designed in a two-phase prospective form, performed in 2002 in Isfahan Health Centers. Target populations were pregnant women with Hb level of 11 g/dl or above in routine laboratory

examinations at first trimester of pregnancy, who had daily use of one ferrous sulfate tablet from the 4th month of pregnancy. We enrolled participants who were under supervision of Health Centers, from 12th week of pregnancy.

We excluded cases with concurrent conditions that may cause increased serum ferritin level and preterm delivery as hemoglobinopathy, hyperthyroidism, acute myocardial infarction and hematologic malignancies.

Data were gathered through validated questionnaire based on available data in libraries and accessible articles.^{2,7,10}

The questionnaire was filled out through interview, data of prenatal care files, delivery documents and also serum ferritin examination results. To obtain better reliability, all participants were examined in the same laboratory and data was analyzed by a clinical-anatomical specialist via Eliza method. Exclusion and inclusion criteria were considered to enroll each case into the study. We used data from common prenatal laboratory examinations, health centers and doctor's offices. In cases with suspicion of hematologic disease, assurance was obtained by the view point of a specialist and tests which confirmed the absence of any hematologic disease.

Then sampling was done on pregnant women in 26-30th week of pregnancy who had the mentioned criteria. The sampling was done in mentioned weeks because in the third trimester of pregnancy the fetus's need for iron is optimum, so we have a physiological decrease in iron which may be proceeding decrease in mother's serum ferritin,¹¹ that can have effect on the results.

Many researches done, have studied ferritin in different weeks of pregnancy and measuring its relation with termination of pregnancy. They have found statistical meaningful relationship between high amount of ferritin and pregnancy complications in 28-30 weeks of pregnancy.^{2,7,12} Preterm labors in this research are those contractions which occur after 20th weeks of pregnancy in participants by the diagnosis of the gynecologist, which caused less than 3 cm dilation of

cervix, resulted in hospitalization and medication ($MgSO_4$ and other tocolytics, one or both of them with or without antibiotic).^{13,14}

After getting written consent, 4cc blood was taken from each participant then at the end of each day, samples were sent to the Jihad Daneshgahi Lab under special conditions and their ferritin was measured by one technician and one laboratory specialist by Eliza method.

In the second phase, each participant was followed to the end of delivery time and data related to occurrence and condition of preterm labors was confirmed after reports from the patients via studying hospital files and specialists' viewpoints.

Sample size was calculated by the followed formula:

$$n = \frac{Z^2 \left(1 - \frac{R}{2}\right) \delta^2}{d^2} = 267$$

$$\delta = 27.5, d = 3.3, z \left(1 - \frac{\alpha}{2}\right) = 1.96$$

where $\sigma = \frac{R}{4} = 24.5$ and R is the normal ferritin level range, regarding Radium co. kit (R = 110).

Researcher studied 322 cases, because of the condition of the study and probability of miss

ing data. Analyses was done using t-test and SPSS software version 10 and $p < 0.05$ was considered as statistical significance.

Results

Regarding the research results, ferritin level considering 10, 25, 50, 75 and 90 percentiles are classified in ordered series of 8.6, 12.5, 20, 30.3 and 42.5 ng/ml, so participants were divided into 6 groups (Table 1). The frequency distribution of pregnant mothers by ferritin percentiles and preterm labors is shown in table 1. The incidence of preterm labors was 3.6% in group with ferritin level lower than 8.6 ng/ml. In the second group (ferritin level of 8.6-12.5ng/ml) 10.7% of women experienced preterm labors. Finally, the incidence of preterm labors in other groups was 21.4%, 23.2%, 28.6% and 12.5%, respectively. Therefore with increasing ferritin levels, the incidence of preterm labors was increased.

Average and standard deviation for all participants are in the following order: 23.18 and 14.93 ng/ml; and minimum and maximum ferritin levels are 1.6 and 92 ng/ml consecutively.

Table 1. The frequency distribution of pregnant mothers by ferritin percentiles and preterm labors

Ferritin levels	Preterm labors		Without Preterm labors		Total	
	Percent	Number	Percent	Number	Percent	Number
8.6 <						
Percentile < 10	3.6	2	12.3	26	10.5	28
First group						
8.6-12.2						
(10-24) percentile	10.7	6	15.2	32	14.2	38
Second group						
12.3-20.2						
(25-49) percentile	21.4	12	25.6	54	24.7	66
Third group						
20.3-30.6						
(50-74) percentile	23.2	13	25.1	53	24.7	66
Fourth group						
30.7-42.4						
(75-89) percentile	28.6	16	11.8	25	15.4	41
Fifth group						
42.5 ≤						
Percentile ≥ 90	12.5	7	16	21	10.5	28
Sixth group						
Total	100	56	100	211	100	267

Table 2. Mean and standard deviation of serum ferritin levels by uterine contractions

Ferritin levels	serum ferritin levels Mean (SD)	Number	Percent
Preterm labors			
With	27.09 (14.53)	56	21
Without	22.16 (14.95)	211	79
Total	23.18 (14.93)	267	100

In addition to this, considering results from 267 cases, 56 cases (21%) got preterm labors and the average level of ferritin in this group (with preterm labors) was 27.09 (14.53) ng/ml and in the group without preterm labors, ferritin level was 22.16 (14.95) ng/ml, so with using T-test analysis, the average of ferritin level in the group with uterine contraction was significantly greater than the other group ($P = 0.029$) (Table 2).

Discussion

On the basis of our results, ferritin levels regarding 10, 25, 50, 75 and 90 percentiles are in order of 8.6, 12.5, 20, 30.3 and 42.5 ng/ml. According to Scholl's survey, ferritin levels of 28th week of pregnancy of the cases regarding 10, 25, 50, 75 and 90 percentiles were reported in order of 1.9, 7.2, 51.1, 25.8 and 41.5 ng/ml.¹²

In another research ferritin level of the optimum percentile was also 42 μ g/l and the relationship between pregnancy complications and ferritin level over or below mentioned levels were studied.¹⁵

Also results from this research suggest that the average of ferritin level in the group which got preterm labors was considerably more than the group that didn't get any preterm labors ($P = 0.029$). Anupam in a study like us showed that the serial serum ferritin levels in subjects in the term group showed a declining trend with advancing gestation as seen in normal pregnancy. However, in the preterm group, a rising trend was observed. Further, serum ferritin levels of higher than 30 micro g/dl at 26th week and higher than 40 micro g/dl at 34th week were found to have a reasonable sensitivity and specificity for predicting preterm delivery. Therefore a serum ferritin concentration of

higher than 40 micro g/dl and a rise in serum ferritin concentration with increasing gestation should alert the clinician regarding the possibility of preterm delivery.³ We did not find any other studies regarding ferritin relation with preterm labors as expressed in this article. However, as it was mentioned before Goldenberg et al reported a meaningful relationship between high plasma ferritin level (above 30 μ g/l) and preterm delivery especially in 26th week of pregnancy and they think that high ferritin level might be a sign of an acute phase reaction.² In their idea high level of ferritin and very preterm delivery might put forward a chorioamniotic infection. Yet more studies are essential to make serum ferritin tests more practical for screening. Tamura et al concluded that high viscosity of serum ferritin has a reverse correlation with gestational age at the time of birth. But other factors determining iron status and other acute phase reactants are not significantly related to gestational age at the time of birth so increased levels of serum ferritin in second trimester of pregnancy can predict a spontaneous preterm delivery in 32nd week or before. Perhaps this ferritin level can reflect an acute phase reaction with regards to subclinical infections which is significantly related to preterm delivery.¹⁵ Saha et al reported higher ferritin level in women with preterm delivery in comparison to control group; they also suggested ferritin to have a pivotal role in prediction of preterm delivery.¹⁶ Bacterial colonization of the choriodecidual interface induces production of cytokines, including tumor necrosis factor alpha, interleukin-1 alpha, interleukin-1 beta, interleukin-6, interleukin-8 and granulocyte colony-stimulating factor, leading to pros-

taglandin synthesis and release, neutrophil activation, and synthesis are release of metalloproteases. The prostaglandins stimulate preterm labors; the metalloproteases weaken the chorioamniotic membranes and remodel and soften cervical collagen.¹⁴

Iams et al, regarding preterm labors, thought that these activities in women with preterm deliveries, occur a few weeks before the time of birth and also there is significantly more contractions in twin pregnancies.¹⁷ Other researchers also pointed out hidden increase in preterm labors which appears 48-72 hours before preterm pains.^{8,13,18} Regarding mentioned studies and considering accompaniment of hidden and non-hidden infections of mother's urogenital system with preterm labors which can probably cause a preterm delivery, it is probable that increase in serum ferritin in these mothers is because of this kind of infections.

Still for better judgment, studies with bigger sample sizes which can define serum iron con-

dition and plasma volume of the pregnancy, is also essential.

Considering the importance of this subject, it is hopeful that the results of this research can be used for promoting further studies in the field of ferritin and its relationship with pregnancy complications and also other important factors relating ferritin such as nutrition, infections, economical and social situations. There is a hope to gain new methods for screening.

The Authors declare that have no conflict of interest in this study and ethical committee approved the study.

Acknowledgements

This article is the outcome of a research project, which is performed by the support of the vice chancellor for research of the Isfahan University of Medical Sciences. We thank the authorities of this chancellor and also we want to thank Dr. Baradaran, the head of Jahad Deneshgahi Laboratory for her kind support.

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