Section: Obstetrics & Gynecology

Original Research Article

STUDY OF SERUM FERRITIN LEVELS IN PRETERM LABOUR AND ITS PERINATAL OUTCOME IN TERTIARY CARE CENTRE

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Received *: 28/10/2023*
Received in revised form *: 04/12/2023*
Accepted *: 22/12/2023*

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DOI:10.5530/ijmedph.2023.4.29

Source of Support: Nil,
Conflict of Interest: Nonedeclared

Int J Med Pub Health
2023; 13 (4); 141-146

ABSTRACT

Background: Preterm labour is defined as regular uterine contractions leading to cervical changes before 37completed weeks of gestation and after period of viability. Preterm birth is responsible for 30-40% of neonatal mortality worldwide. Identifying pregnant women at risk of preterm delivery will enable them an easy access to tertiary care centres for further management. **Aim:** To evaluate serum ferritin levels in preterm labor and perinatal outcome in a tertiary care centre during 2years period from 2019-2022. **Objective:** To compare the serum ferritin levels in patients of preterm labor and low risk pregnant women with same gestational age.

Materials and Methods: A case control study was performed in the department of Obstetrics and Gynecology in Niloufer hospital, Osmania medical college, Hyderabad 2019-2022. Source of samples and data was take from the Department of Obstetrics & Gynecology, Niloufer hospital, Hyderabad and Department of Biochemistry, Osmania medical college/ Osmania General Hospital, Hyderabad. 100 subjects are taken as sample size after obtaining the consent in the study group & divided into 2 groups. Group 1 included women with spontaneous preterm labor and Group 2 included control group- women.

Results: Among 50 cases of pre term labour, majority 39 (78.0%) were belonging to pre term (32 to 36 weeks), followed by 18 (18.0%) were in very pre term (28 to 32 weeks). Among 50 cases included in the study, majority of the cases i.e., 31 (62.0%) was delivered by normal vaginal delivery and 19(38.0%) delivered by emergency LSCS.Among50cases, majority of the cases i.e., 49 (98.0%) of the pregnancies ended up with alive babies and 01 (2.0%) had still birth. CRP was positive in 02 (4.0%) cases and negative in 48 (96.0%) of cases. Vaginal swab was negative in all 50 (100%) cases. The mean WBC in cases was 12868.86 ± 3814.83 and in controls was 11057.80 ± 2301.67. Mean WBC levels were higher among cases than controls which is statistically significant in difference of WBC levels between cases and controls. The mean serum ferritin levels were 40.298 ± 19.64 in cases and 20.343 ± 6.82 in controls. The mean serum ferritin levels were significantly higher among cases than controls & in very pre term labour was 35.15 ± 13.87. The mean serum ferritin levels were highest in preterm category followed by very pre term. The mean WBC levels in very pre term labour was 13055.55 ± 2950.47. The mean WBC levels were highest in very preterm followed by preterm &found to be statistically insignificant.

Conclusion: Serum ferritin levels are elevated in preterm labor compared to low risk women of same gestational age. Elevated maternal serum ferritin levels in early pregnancy are associated with an increased risk of pre term labour. The usefulness of early pregnancy ferritin levels in identifying women at risk of pre term labour warrants further investigation.

Keywords: Serum ferritin, Preterm labor, Term labour, Pregnancy, Hb, CRP.

INTRODUCTION

Preterm labor is defined as the onset of labor before 37 completed weeks (259days of pregnancy) of gestation and after reaching the age of viability. The age viability depends on the definition adopted by the state which varies from 20 to 28 weeks.[1] Preterm labor and its complications of preterm delivery remain a major health problem. Incidence of preterm birth in developed countries is 10 to 12%. In india the preterm birth rate is 18% and it is one of the causes of neonatal mortality, in addition it contributes to significant morbidity like intra ventricular haemorrhage, transient tachyopnea of new born, neonatal jaundice, respiratory distress syndrome, necrotizing enterocolitis and sepsis & prolonged NICU stay.

It is estimated that 15 million preterm births occur each year with 1.1 million infants dying from preterm birth complications.[4] Prevention of preterm birth is the single most important challenge to modern obstetrics today, progress in this area has been hampered by lack of understanding of basic mechanism responsible for premature labor and delivery. Preterm labor is a pathological condition caused by multiple etiologies. Intra amnionic infection as a primary cause of preterm labor in pregnancies within tact membranes accounts for 25 to 40 percent of preterm births. The microbial invasion of the reproductive tract can lead to preterm birth.[6]Causes of preterm labor include infections such as bacterial

vaginosis, medical disorders like hypertension, preeclampsia, maternal diabetes, asthma, thyroid disease, heart disease.[8]It may be due to various pathophysiological process such as amnio-chorionic decidual or systemic inflammation, activation of maternal or fetal pituitary adrenal axis, multifetal pregnancy,[9]pregnancies conceived with assisted reproductive technology.[10]40%ofpretermbirthsare idiopathic,35% follow preterm prelabor rupture of membranes (PPROM) and 25% are iatrogenic because of obstetric and medical complications of pregnancy. PPROM and preterm labor are linked to pathological process such as inflammation and infection of membranes. There are many biomarkers to predict preterm labor, serum ferritin is one of the marker

Which increase in infection and inflammation. Ferritin is an intracellular iron storage protein which increases in inflammatory conditions along with other acute phase reactant.[7,8]

Aim

To evaluate serum ferritin levels in preterm labor and perinatal outcome in a tertiary care centre during 2-year period from 2019-2022.

Objectives

To study the role of serum ferritin as a marker of preterm labor.

To compare the serum ferritin levels in patients of preterm labor and low risk pregnant women with same gestational age.

MATERIAL AND METHODS

Setting: A case control study was performed in the department of Obstetric and Gynecology in Niloufer hospital, Osmania medical college, Hyderabad.

Type of study: case control study

Source of Samples and Data

1. Department of Obstetrics &Gynecology, Niloufer hospital, Hyderabad.
2. Department of Biochemistry,
3. Osmania medical college/Osmania General Hospital, Hyderabad.

100 subjects included in the study were divided into 2 groups.

Group 1 included women with spontaneous preterm labor and Group 2 included control group-womenwith same gestational age.

Table 1: Classification of study subjects

Group	Subject	Number
Group1	Women with pretermlabor(cases)	50
Group2	Normal pregnant Women With same gestational age (control)	50

Ethical clearance was obtained to conduct the study, from the institutional ethics committee of Osmania Medical College.

Informed consent was taken from all the individuals who took part in the study.

Inclusion Criteria

Group-1

1. Women who give informed written consent.
2. Women with spontaneous onset of labour with gestational age between 28 to 36 wks.
3. Hb>10 gm% iv) singleton live pregnancy

Group-2 Normal pregnant women with same gestational age.

Exclusion Criteria

1. Diabetes, hypertension and preeclampsia.
2. Thyroid disease and renal disease
3. Haemochromatosis, liver disease
4. Acute and chronic inflammatory disease
5. Multiple pregnancy
6. Polyhydramnios
7. Uterine anomalies
8. Cervical incompetence
9. Intrauterine fetal demise
10. Alcoholics and smokers

Methodology

After obtaining informed consent 50 pregnant women in

Preterm labor (cases) and 50 normal pregnant women (control) of after 28weeks of gestation and before37 completed weeks of gestation.

Group A: 50 gravid women in spontaneous preterm labor constituted the case study group.

Group B: 50 normal (uncomplicated) pregnant women with gestational age between 28 to 36 weeks registered in obstetric and gynecology outpatient department constituted the control group.

Detail obstetric, medical and menstrual and medical history taken.

Accurate gestational age was calculated from the last menstrual date and confirmed by early trimester ultrasound. Patient was clinically evaluated Relevant investigations sent. For both the groups under aseptic precautions veni puncture done and collected plain blood sample. And sent to laboratory for serum ferritin level estimation.

Criteria to document preterm labor

- 4 contractions in 20 minutes with progressivechange in the cervix.
- Cervical dilatation more than 1 cm
- Cervical effacement of ≥80%

Outcome of the labor was documented. Data obtained were statistically analysed and inferred accordingly.

Serumferritin Method

Two steriles and wich immunoassay using direct chemiluminometric Technology.

RESULTS

Among cases and control, majority of cases and controls were in the age group of 25 years or less 59 (59.0%) followed by 26 to 30 years 33 (33.0%) and least 8 (8.0%) were above the age of31years.There was almost equal representation of cases and controls across all age groups. The distribution of the cases and control subjects based on age is represented in. [Table 1]

Majority of cases and controls were 37 (37.0%) gravida 2 followed by Primi gravida - 35 (35.0%) and least were grand multies - 10 (10.0%). There was almost equal representation of various parity categories across cases and controls. The distribution of cases and controls based on parity is presented in table 2.

Among 50 cases of pre term labour, majority 39 (78.0%) were belonging to pre term (32 to36weeks), followed by18 (18.0%) were in very pre term (28to32weeks) and least 2 (4.0%) were in extreme pre term category. [Table 2]

Among 50 cases included in the study, majority of the casesi.e.,31 (62.0%)was delivered by normal vaginal delivery and 19 (38.0%) delivered by emergency LSCS. The distribution of cases based on mode of delivery is represented in. [Table 4]

Among 50 cases, majority of the casesi.e.,49 (98.0%) of the pregnancies ended up with alive babies and 01 (2.0%) had still birth. Table 5 and figure 5 represents the distribution of cases based on outcome of pregnancy.

Among 50 cases included in the study, CRP was positive in 02 (4.0%) cases and negative in 48 (96.0%) of cases. Vaginal swab was negative in all 50 (100%) cases. [Table 5]

The mean Hb in cases was 11.49 ± 1.03 and in control subjects was 11.59 ± 1.08 Mean Haemoglobin level among cases was slightly lower than that among controls. This difference was not found to be statistically significant.

[Table 6]

The mean WBC in cases was 12868.86 ± 3814.83 and in controls was 11057.80 ± 2301.67. Mean WBC levels were higher among cases than controls. This difference in WBC levels between cases and controls was found to be statistically significant. Table 8 and figure 8 represents the difference in WBC levels between cases and controls. [Table 7]

The means serum ferritin levels were 40.298 ± 19.64 in cases and 20.343 ± 6.82. The mean serum ferritin levels were significantly higher among cases than controls. The difference in ferritin levels between cases and controls is represented in table 9.

The serum ferritin levels in extreme pre term labour were 35.60 ± 6.50 and in very pre term labour was 35.15 ± 13.87. The mean serum ferritin levels were highest in pre term category followed by extreme pre term and least in very pre term. This difference was not found to be statistically significant. [Table 8]

The mean WBC levels in extreme pre term labour was 16500.00 ± 4666.90 and in very pre term labour was 13055.55 ± 2950.47. The mean WBC levels were highest in extreme pre term followed by very pre term and least in pre term category and found to be statistically insignificant. [Table 9]

The haemoglobin in extreme pre term labour was 11.55 ± 0.63 and in very pre term labour was 11.38 ±1.57.The mean Hb levels were highest in pre term followed by extreme pre term and least in very pre term category. This difference was not found to be statistically significant. [Table 10]

Table1: Age wise distribution of cases and controls

Age group	Group		Total
	Cases	Controls	
25 or less	30 (50.8)	29 (49.2)	59 (59.0)
26-30	15 (45.5)	18 (54.5)	33 (33.0)
31-35	5 (62.5)	3 (37.5)	8 (8.0)
Total	50	50	100

Table 2: Distribution of cases and controls based on parity

Parity	Group		Total
	Cases	Controls	
Primi	19 (54.3)	16 (45.7)	35 (35.0)
Gravida-2	18 (48.6)	19 (51.4)	37 (37.0)
Gravida-3	8 (44.4)	10 (55.6)	18 (18.0)

4and above	5 (50.0)	5 (50.0)	10 (10.0)
Total	50	50	100

Table 3: Distribution of cases based on category of preterm labour

Category of preterm	Frequency	Percent
Extreme preterm	2	4.0
Very pre term	9	18.0
Pre term	39	78.0
Total	50	100.0

Table 4:

Mode of delivery	Frequency	Percent
EmergencyLSCS	19	38.0
NVD	31	62.0
Total	50	100.0

Table 5: Distribution of cases based on outcome of pregnancy

Outcome	Frequency	Percent
Alive	49	98.0
Still birth	01	2.0
Total	100	100.0

Table 6: Distribution of cases based on CRP

CRP	Frequency	Percent
Negative	48	96.0
Positive	02	4.0
Total	100	100.0

Table 7: Difference in Haemoglobin levels between cases and controls

Hb%	Mean	SD	t	p
Cases	11.49	1.03	0.471	0.639
Controls	11.59	1.08		

Table 8: Difference in WBC levels between cases and controls

WBC	Mean	SD	t	p
Cases	12868.86	3814.83	2.874	0.005
Controls	11057.80	2301.67		

Table 9: Difference in Ferritin levels between cases and controls

Ferritin	Mean	SD	t	p
Cases	40.298	19.64	6.784	0.001
Controls	20.343	6.82		

Table 10: Comparison of serum ferritin levels across different categories of preterm labour

Category	Mean	SD	F	P
Extreme preterm	35.60	6.50	0.458	0.635
Verypreterm	35.15	13.87		
Preterm	41.72	21.13		

Table 11: Comparison of WBC levels across different categories of preterm labour

Category	Mean	SD	F	P
Extreme pre term	16500.00	4666.90	0.987	0.380
Very pre term	13055.55	2950.47		
Pre term	12639.56	3950.14		

Table 12: Comparison of Haemoglobin levels across different categories of pre term labour

Category	Mean	SD	F	P
Extremepreterm	11.55	0.63	0.204	0.816
Verypreterm	11.38	1.57		
Preterm	11.64	0.98		

DISCUSSION

Pre term birth is one of the leading causes of neonatal mortality in the absence of congenital anomalies in developing countries. Measure should be taken to identify, prevent preterm deliveries and treat this preterm neonate as early as possible. Hence present study was planned to assay the serum ferritin levels in preterm labour and its effect on perinatal outcome. The purpose of the analysis ofthis studywas to determine whether serum ferritin levels can be used as a marker for preterm labour.

Mean WBC levels were higher among cases than controls. This difference in WBC levels between cases and controls was found to be statistically significant. The haemoglobin in extreme pre term labour was 11.55 ± 0.63 and in very pre term labour was 11.38 ± 1.57.The mean Hb levels were highest in pre term followed by extreme pre term and least in very pre term category. This difference was not found to be statistically significant whereas the mean WBC levels were highest in extreme pre term followed by very pre term and least in preterm category and found to be statistically insignificant.

The relationship between maternal Fe status and the risk of preterm delivery is uncertain.[5] Both low and elevated maternal Fe levels have been associated with the risk of preterm birth.[6]While some randomised trials of Fe supplementation in pregnancy have reported a reduction in preterm births,[7] the most recent Cochrane,[3] and systematic reviews,[4] of intervention trials have found no significant effect of Fe supplementation in pregnancy on the risk of pre term birth. In contrast, there are several observational studies that have found an association between elevated serum ferritin (a biomarker of Fe stores) in the second trimester and an increased risk of sPTB.[1,5,7]Potential mechanisms resulting in elevated ferritin levels being linked to the risk of sPTB include the following: intra-uterine infection; failure of the maternal plasma volume to expand; infection and inflammation . Ferritin production is increased with infection and inflammation as part of the acute-phase response; therefore, interpretation of these studies is challenging. In the present study, the means serum ferritin levels were 40.298 ± 19.64 in cases and 20.343 ± 6.82. The mean serum ferritin levels were significantly higher among cases than controls. This is similar to the study of Khambalia et al, found increased odds of sPTB in association with elevated ferritin concentrations. Inconsistent findings across studies may be related to differences in study populations and the severity of sPTB, reduced numbers of women in certain categories of exposure and/or outcome, and the types of confounders included in adjusted analyses. Previous studies have mostly been cross-sectional and limited to serum ferritin measurements later in pregnancy or at the time of birth.[8,9]

In the present study, the mean serum ferritin levels were highest in pre term category followed by extreme pre term and least in very pre term. This difference was not found to be statistically significant. Khambalia et al found serum ferritin levels were associated with increased odds ofs PTB(<37weeks)and the sub category moderate- to-lates PTB(34–36 weeks). In the study by Saha et al, mean ferritin levels in control PPROM, Spontaneous pre term labour is8.69±3.7,29.4±28.4,23.24±12.13mg/ lrespectively. In that study there was a significant difference between control group and preterm labour group. However, in retrospective study by Gopal et al, there is no relation between serum ferritin levels and spontaneous labour. In the study by Valappil et al, which compared the ferritin levels of 50 patients with preterm premature rupture of membranes (PPROM), 50 with spontaneous preterm labour and 50 normal pregnant women with matching hemoglobin and gestational age reported that there was significant difference in mean ferritin values between control group and PPROM group. But there was no statistical difference in ferritin values between control group and spontaneous preterm labour indicated byapvalueof0.180.This lack of significant statistical difference may be due to Multifactorial cause of pre term labour.

CONCLUSION

This Study found significant difference in serum ferritin levels between spontaneous preterm labour and low risk pregnant women with same gestational age. Subclinical infections has significant role in preterm labour. Thus from the present study proved that the serum ferritin can be used as bio marker in predicting the pregnant women at risk for preterm delivery and thus helps obstetrician identify pregnant women at risk. This woman can receive early treatment and guidance regarding neonatal care. It can be taken as guide in small settings also.

Conflict of Interest: None
Funding Support: Nil.

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