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Original Research Article

Study of serum ferritin levels in preterm labour and its perinatal outcome in tertiary care centre

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ABSTRACT

Background: Pregnant women at risk of preterm birth may be easily identified and sent to tertiary care centres for further therapy. Numerous biomarkers are being investigated for their ability to predict preterm labour; serum ferritin is one of these indicators. It is an intracellular protein that has a role in iron storage and is also an acute phase reactant that is increased during acute and chronic infections.
Objective: To evaluate serum ferritin levels in preterm labour and perinatal outcome in a tertiary care centre during 2 years.
Materials and Methods: A case control study was conducted in collaboration with the Department of Obstetrics and Gynecology at Osmania Medical College, Hyderabad, from 2019 to 2022. After receiving permission, one hundred participants with an average age of 25 years who visit Niloufer hospital are included in the research and separated into case (Group 1) and control (Group 2) groups. Group 1 consists of women who had spontaneous preterm labour, whereas Group 2 consists of pregnant women of the same gestational age who are considered controls.
Results: Among 50 instances of preterm labour, 39 (78.0 percent) were classified as preterm (32 to 36 weeks), whereas 11 (22.0 percent) were classified as very preterm (28 to 32 weeks). The majority of the 50 patients included in the research, 31 (62.0 percent), were born by normal vaginal delivery, while 19 (38.0 percent) were delivered using emergency LSCS. CRP was positive in two patients (4.0 percent). The mean WBC levels in cases were much greater than those in controls, and the difference is statistically significant. Serum ferritin levels were 40.298 19.64 in cases and 20.343 6.82 in controls. Serum ferritin levels were substantially higher in cases than in controls on average. The mean WBC levels were greatest in extremely preterm infants, followed by preterm infants; however, this difference was determined to be statistically insignificant.
Conclusion: Ferritin levels are much higher in preterm labour patients than in low-risk women of the same gestational age. Serum ferritin levels may be utilised as a biomarker in high-risk premature labour.

1. Introduction

Preterm labour is defined as the commencement of labour before the 37th week (259th day of pregnancy) and after the viability phase has passed. The time of viability varies depending on the state's definition, which ranges from 20 to 28 weeks. Preterm labour and the difficulties that come with it are still a big health issue. Preterm birth occurs 10 to 12 percent of the time in industrialised nations. Preterm birth is one of the leading causes of neonatal death in India, contributing to significant morbidity such as intraventricular haemorrhage (IVH), transient tachypnea of

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the newborn (TTN), neonatal jaundice, respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), sepsis, and prolonged NICU stay.[1]

Each year, 15 million preterm births are predicted to occur, with 1.1 million newborns dying as a result of preterm birth complications. Preterm birth prevention is the single most critical problem facing modern obstetrics today, yet progress has been limited by a lack of knowledge of the core mechanisms that cause early labour and delivery.

Preterm labour is a medical disorder that may be caused by a variety of factors. Infections such as bacterial vaginosis, medical diseases such as hypertension, preeclampsia, maternal diabetes, asthma, thyroid disease, and heart disease are all causes of premature labour.[2]

Preterm birth may be caused by microbial invasion of the reproductive system. It might be caused by a variety of pathophysiological mechanisms, including amnio-chorionic decidual or systemic inflammation, multi-fetal pregnancy, or pregnancies created by assisted reproductive technologies. In pregnancies with intact membranes, intra-amniotic infection is the leading cause of premature labour, accounting for 25 to 40% of preterm deliveries. Preterm births are idiopathic in 40% of cases, followed by preterm prelabor rupture of membranes (PPROM) in 35% of cases, and iatrogenic in 25% of cases due to obstetric and medical difficulties during pregnancy.[3–6] Preterm labour and PPROM are connected to pathogenic processes such as membrane inflammation and infection. Serum ferritin is one of several indicators that may be used to predict premature labour. Ferritin is an internal iron storage protein that, like other acute phase reactants, rises in infection and inflammation.

2. Materials and Methods

A case control study was conducted in collaboration with the Department of Obstetrics and Gynecology at the Department of Biochemistry. The institutional ethics committee granted approval for the study's conduct. (IEC number- ECR/300/Inst/AP/2013/RR-19)All people who participated in the research provided informed consent. The study's 100 individuals were separated into two groups. Women experiencing spontaneous preterm labour were included in Group 1, whereas pregnant women with the same gestational age were included in Group 2.

2.1. Inclusion criteria

Group-1: women with spontaneous onset of labour with gestational age between 28 to 36wks, Hb>10 gm%, singleton live pregnancy

Group-2: normal pregnant women with same gestational age.

2.2. Exclusion criteria

Diabetes, hypertension, preeclampsia, thyroid disease, renal disease, haemochromatosis, liver disease, acute and chronic inflammatory disease, multiple pregnancy, polyhydramnios, uterine anomalies, cervical incompetence, intrauterine foetal death, and alcoholics and smokers were excluded from the study.

Complete obstetric, medical, menstrual, and medical histories are obtained. The gestational age was determined accurately using the last menstrual period and verified using early trimester ultrasonography. The patient was assessed clinically. Under aseptic conditions, blood samples were obtained from both groups and forwarded to a laboratory for serum ferritin level determination.

2.3. Criteria to document preterm labour

1. 4 contractions in 20 minutes with cervical changes that progressed.
2. Cervical dilatation more than one centimetre.
3. Cervical effacement of up to 80%.

The outcome of the labour was recorded, and the data collected were statistically analysed and inferred. Ferritin was quantified using a sandwich immunoassay based on direct chemiluminiscent technology on Advia Centaur.

3. Results

Table 1: Age and paritywise distribution of cases and controls

Age group	Cases N(%)	Controls N(%)	Total
25 or less	30(50.8)	29(49.2)	59(59)
26 -30	15(45.5)	18(54.5)	33(33)
31-35	5(62.5)	3(37.5)	8(8)
Total	50	50	100
Parity			
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)
4 and above	5 (50.0)	5 (50.0)	10 (10.0)

Majority of cases and controls were in the age group of 25 years or less (59%) followed by 26 to 30 years 33 (33.0%) and least 8 (8.0%) were above the age of 31 years. Distribution of cases and controls are almost equal all among age groups. Most of the subjects 370% are 2nd gravid, followed by Primi gravida 350% and least were grand multies10%. There was almost equalrepresentation of various parity categories across cases and controls.

Among 50 preterm labour cases 31(62.0%) were normal vaginal deliveries and 19 (38.0%) were emergency LSCS; 49 (98.0%) out of 50 cases delivered live babies and 01 (2.0%) had still birth.

Table 2: Mode of delivery and outcome in Grouup-1 (cases) N=50

Mode of delivery	Frequency	Percent
Emergency LSCS	19	38.0
NVD	31	62.0
Outcome		
Alive	49	98.0
Still birth	01	2.0

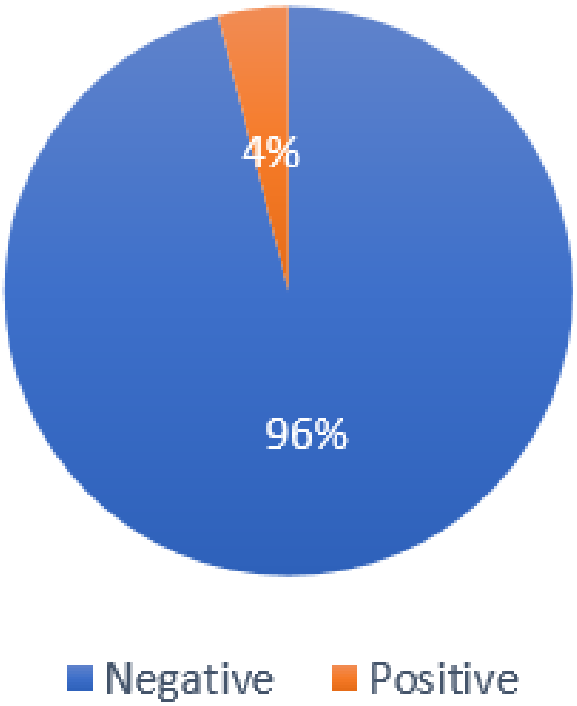

Figure 1: Distribution of cases based on CRP

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 culture was negative in all 50 (100%) cases.Figure 1

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. Figure 2

Table 3: Difference in Ferritin levels between cases and controls

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

P<0.01 *is considered significant*

The mean serum ferritin levels in patients were 40.298 ± 19.64 and in controls were 20.343 ± 6.82. Cases had considerably higher mean serum ferritin levels than controls.Figure 3

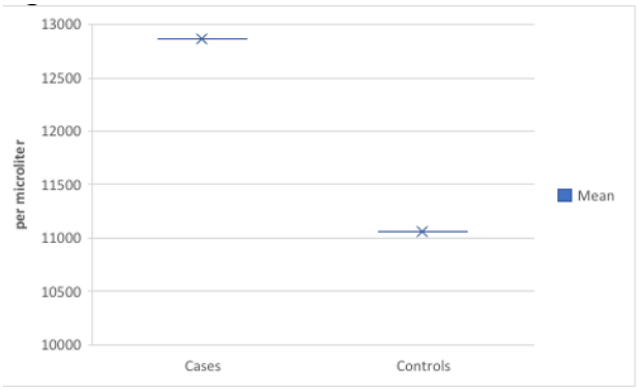

Figure 2: Difference in WBC levels between cases and controls

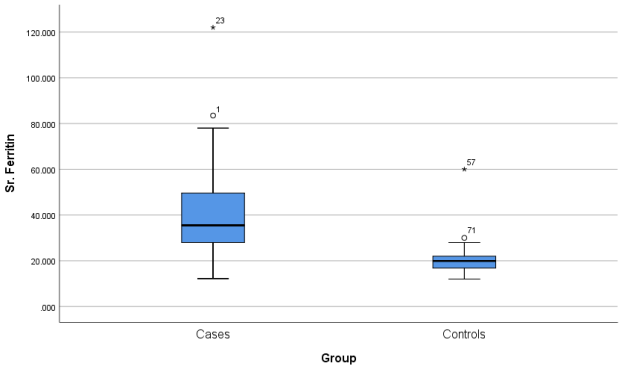

Figure 3: Difference in Ferritin levels between cases and controls

4. Discussion

In the absence of congenital abnormalities, preterm delivery is one of the top causes of infant death in underdeveloped nations. Preterm births should be identified, prevented, and this preterm neonate treated as soon as feasible.[7] As a result, the current research was designed to examine serum ferritin levels in preterm labour and their impact on perinatal outcomes. The goal of this study's research was to see whether serum ferritin levels might be utilised as a predictor of preterm labour. Serum ferritin levels begin to drop in the second trimester. At the time of birth, maternal serum ferritin levels may be 1/3rd of those seen in the newborn cord sample.[8] Ferritin levels have long been known to rise sharply in the presence of physiologic stress, such as acute or chronic infection, tissue injury, or liver illness or cancer. In many circumstances, ferritin represents the state of an acute phase response rather than being a nutritional indication.[9] The majority of cases and controls in this research were aged 25 years or younger (59.0 percent), followed by 26 to 30 years. Thirty-three percent (33%) and at least eight percent (8.0%) were above the age of

thirty-one. The majority of cases and controls were gravida 2 (37 percent), followed by Primi gravida (35 percent), and grand multies (ten percent) (10.0 percent). There was no difference in parity between preterm and term labour individuals in this research, regardless of age or parity. The majority of the patients in the research, 31 (62.0 percent), were born by normal vaginal birth, whereas 19 (38.0 percent) were delivered using emergency LSCS. The majority of the pregnancies, 49 (98.0 percent), resulted in live infants, while one (2.0 percent) resulted in a stillbirth. Infection and inflammation cause a rise in serum ferritin, which is an acute phase reactant. Preterm labour may be caused by a variety of factors, one of which being infection. Due to a change in vaginal pH, pregnancy puts you at risk for vagino-cervical infections. Bacterial colonisation also causes macrophages to penetrate the chorio decidual interface. High serum ferritin levels in pregnant women who seem to be in good health can aid the obstetrician in anticipating preterm birth and taking necessary treatment. CRP was positive in 02 (4.0 percent) of the 50 cases studied, while it was negative in 48 (96.0 percent) of the cases. All 50 instances (100%) had a negative vaginal swab. Khambalia et al. discovered that women who had a spontaneous preterm birth (sPTB) had substantially higher first-trimester CRP concentrations, but no link between sPTB and soluble transferrin receptor (sTfR) concentrations (a biomarker of Fe delivered to tissues). These findings imply that serum ferritin levels rise as part of the acute-phase response, and that the inflammatory process associated with sPTB may be seen as early as the first trimester. [Khambalia et al 2015].[10]

The absence of Hb data, which is regularly conducted throughout pregnancy but gathered by diverse health care providers and local labs, is a major restriction. Although there is some evidence of a U-shaped association between Hb concentrations in early pregnancy and the risk of preterm delivery, the function of maternal Hb in preterm birth is still unclear. The mean haemoglobin level among patients was somewhat lower than that of controls in this research. However, there was no statistically significant change. Hemoglobin has no effect on current delivery as term or preterm in this research. Cases had greater mean WBC levels than controls. It was discovered that the difference in WBC counts between patients and controls was statistically significant. In very preterm labour, the haemoglobin level was 11.55 ± 0.63, and in very preterm labour, it was 11.38 ± 1.57. Extreme preterm had the highest mean WBC counts, followed by extremely preterm, and then Preterm, which was statistically insignificant. This is in line with the findings of Mei Zhu et al, who discovered that preterm labour individuals had higher WBC levels than term labour subjects. [Mei Zhu et al 2020].[11]

There is no clear link between maternal Fe(iron) status and the risk of preterm birth. Fe levels in the mother, both low and high, have been linked to the risk of premature delivery.[12,13] While some randomised studies of Fe supplementation in pregnancy have demonstrated a decrease in preterm births, the most current Cochrane and systematic reviews of intervention trials have revealed that Fe supplementation in pregnancy had no meaningful impact on the risk of premature delivery. Several observational studies, on the other hand, have shown a link between greater blood ferritin (a biomarker of Fe storage) in the second trimester and a higher risk of sPTB.[9]

Intrauterine infection, inability of the maternal plasma volume to increase, infection, and inflammation are all possible factors that lead to high ferritin levels being associated to the risk of sPTB.[13] As part of the acute-phase response, ferritin synthesis rises in response to infection and inflammation, making interpretation of these findings difficult. The mean serum ferritin levels in the current research were 40.298 ± 19.64 in cases and 20.343 ± 6.82 in controls. Cases had considerably higher mean serum ferritin levels than controls. This is comparable to the findings of Khambalia et al, who discovered an increased risk of sPTB in those with high ferritin levels.[10]

Inconsistent results among studies might be due to variations in research populations and the severity of sPTB, as well as lower numbers of women in particular categories of exposure and/or outcome and the kinds of confounders included in adjusted analyses. Previous research has primarily been cross-sectional, with serum ferritin levels taken later in pregnancy or at the time of delivery. The mean serum ferritin levels in this research were greatest in the preterm group, followed by severe preterm (<28wks), and extremely preterm (28-32wks). This difference was determined to be non-significant statistically. Serum ferritin levels were linked to an elevated risk of sPTB (<37 weeks) and the subcategory moderate-to-late sPTB (34–36 weeks), according to Khambalia et al.[10]

Saha et al[14] found that mean ferritin levels in control, PPROM, and spontaneous preterm labour are 8.69±3.7, 29.4±28.4, and 23.24±12.13 mg/l, respectively, in their research. There was a significant difference between the control and preterm labour groups in that research. However, Gopal et al found no link between serum ferritin levels and spontaneous labour in a retrospective investigation.[15]

Valappil et al[3] found a significant difference in mean ferritin values between the control group and the PPROM group in a study that 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 haemoglobin and gestational age. However, a p value of 0.180 suggested that there was no significant difference in ferritin readings between the control group and spontaneous preterm labour. This lack of statistical significance might be attributed to the complex nature of premature labour.

5. Conclusion

The serum ferritin levels of spontaneous preterm labour and low-risk pregnant women of the same gestational age were observed to vary significantly in this study. Preterm labour is influenced by subclinical infections. Thus, the current research demonstrated that serum ferritin may be utilised as a biomarker to predict pregnant women at risk for preterm birth, assisting obstetricians in identifying these individuals. These mothers will be able to obtain early treatment and advice on neonatal care. It may also be used as a guide in small contexts.

6. Source of Funding

None.

7. Conflict of Interest

None.

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