International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Serum Ferritin Level as a Marker of Preterm Labor- A Prospective Observational Study

Dr. Priyanka H S[1], Dr. Shamili K[2], Dr. Varija T[3], Dr. Soujanya Hyati[4], Dr. Bhukke Bhavya[5]

[1]Postgraduate, Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari

[2]Assistant Professor, Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari

[3]Professor, Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari

[4]Postgraduate, Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari

[5]Postgraduate, Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari

Abstract: ***Introduction: Prematurity is a major healthcare problem throughout the globe. Preterm labor (PTL), defined as the labour starts between 28 weeks and before 36 weeks 6 days of gestation. The causes and mechanisms of PTL remain unknown which limit the prediction and prevention of PTL. Ferritin is also a primary intracellular storage protein that holds iron in an insoluble and nontoxic state, while it has been reported to increase in a number of acute - phase reactions such as inflammation. It has been hypothesized that subclinical maternal infection is responsible for increase in maternal serum ferritin levels and spontaneous preterm PROM. The study is planned with objective to study serum ferritin in preterm and term pregnancy. Materials & methods: A prospective Observational study conducted in Department of OBG, Vijayanagar Institute of Medical Sciences, Ballari over a period of 6 months consist of 70 subjects. All patients with diagnosis of preterm labor (>28 weeks and <36 weeks 6 days of gestation) and controls who ≥37 weeks of gestation. All pregnant women who fulfill the diagnostic criteria that is >28 weeks and <42 weeks of gestation above 18 years of age. Antenatal steroids will be administered to mother. Patient will be monitored both intrapartum and postpartum. Newborn is assessed by APGAR scores, any admission to NICU and followed till early neonatal period. Results: Majority of cases and controls were in the age group of 25 years or less (51.4%) followed by 26 to 30 years 29 (41.4%) and least 5 (7.1%) were above the age of 31 years. Distribution of cases and controls are almost equal all among age groups. Most of the subjects 38.5% are 2nd gravid, followed by Primi gravida 50.0% and least were grandmulties 11.4%. There was almost equal representation of various parity categories across cases and controls. Among 35 preterm labour cases 23 (65.7%) were normal vaginal deliveries and 12 (34.2%) were emergency LSCS; 34 (97.8%) out of 35 cases delivered live babies and 01 (2.2%) had still birth in cases. In Control 35 preterm labour cases 19 (54.2%) were normal vaginal deliveries and 11 (31.4%) were emergency LSCS; 34 (97.8%) out of 35 cases delivered live babies and 01 (2.2%) had still birth in cases. The mean serum ferritin levels in patients were 42.299 ± 21.68 and in controls were 22.350 ± 8.86. Cases had considerably higher mean serum ferritin levels than controls. Conclusion: High serum ferritin level is associated with premature delivery and serum ferritin level may consider as a marker for preterm labor. In cases with high serum ferritin, prophylactic treatment and early intervention may be considered to prevent preterm birth and to improve pregnancy outcome.***

Keywords: Preterm Labor, Serum Ferritin, APGAR scores

1. Introduction

Prematurity is a major healthcare problem throughout the globe. Preterm labor (PTL), defined as the labour starts between 28 weeks and before 36 weeks 6days of gestation. The causes and mechanisms of PTL remain unknown which limit the prediction and prevention of PTL. [1] It is a major cause of mortality of premature infants and can result in a series of long - term complications in survivors. [2] Complications of PTL are the main reasons which cause deaths of children under 5 years of age. [3] It has been postulated that infection is a major etiologic agent in the pathogenesis of preterm labor PTL and preterm premature rupture of membranes PROM. [4] Direct sampling of amniotic fluid in these situations has demonstrated the pathogenic microorganisms or markers of infection such as raised total leukocyte count TLC, cytokines, leukocyte esterase and low glucose level which indicate invasion by microorganisms. [5]

Ferritin is also a primary intracellular storage protein that holds iron in an insoluble and nontoxic state, while it has been reported to increase in a number of acute - phase reactions such as inflammation. [6] It has been hypothesized that subclinical maternal infection is responsible for increase in maternal serum ferritin levels and spontaneous preterm PROM. The study is planned with objective to study serum ferritin in preterm and term pregnancy. [7]

2. Materials & Methods

A prospective Observational study conducted in Department of OBG, Vijayanagar Institute of Medical Sciences, Ballari over a period of 6 months study period. Study will be conducted from 01st August 2023 to 31st January 2024.

All patients with diagnosis of preterm labor (>28 weeks and <36 weeks 6 days of gestation) and controls who ≥37 weeks of gestation.

Inclusion criteria

All pregnant women aged 18 years and above with >28 weeks and <42 weeks of gestation.

Exclusion criteria Maternal factors

- Anemia (hemoglobin <10.5g/dl)
- Iron overload states is excess iron in the body organs like liver, heart and endocrine for example hemochromatosis, thalassemia, blood transfusions.
- Chronic infective disease like HIV, Hepatitis B, SLE
- Any acute infections
- Multiple pregnancy
- Polyhydramnios/ Oligohydramnios
- Medical conditions like SLE, Rheumatoid arthritis
- Uterine anomalies
- Diabetes mellitus
- Pre - eclampsia - eclampsia
- Liver disease
- Renal disease
- Cardiac disease
- Malignancy
- Alcoholics or smokers

Fetal factors

- IUGR with doppler changes
- Fetal malformation
- Intrauterine fetal demise

Method of collection of data (Including sampling procedure, if any)

Data Collection

Pregnant women fulfilling the eligibility criteria will be considered after taking informed consent and demographic details, patients will be divided in two equal groups.

- In group A, preterm labor 28 weeks to <36 weeks 6 days of gestation (PTL) and
- In group B, control group who delivered at 37 or more weeks gestation.
- Both groups will be compared by sending serum ferritin levels by drawing 5ml of blood collected from large peripheral vein under aseptic condition in plain vial on admission after confirming that the patient is in labour.

Antenatal steroids will be administered to preterm mother. Patient will be monitored both intrapartum and postpartum. Newborn is assessed by APGAR scores, any admission to NICU and followed till early neonatal period.

Data Analysis

Database software SPSS 21.0 VERSION. Analysis will be carried out. Test of significance using Chi square test will be done and p value <0.05 will be considered significant.

3. Results

Table 1: Age wise distribution of cases and controls

Age group	Cases, N (%)	Controls, N (%)	Total
25 or less	19 (54.2)	17 (48.5)	**36 (51.4)**
26 - 30	14 (40.0)	15 (42.8)	**29 (41.4)**
31 - 35	2 (5.7)	3 (8.5)	**5 (7.1)**
Total	**35 (100)**	**35 (100)**	**70 (100)**

Majority of cases and controls were in the age group of 25 years or less (51.4%) followed by 26 to 30 years 29 (41.4%) and least 5 (7.1%) were above the age of 31 years. Distribution of cases and controls are almost equal all among age groups.

Table 2: Parity wise distribution of cases and controls

Parity	Cases, N (%)	Controls, N (%)	Total
Primi	18 (51.4)	17 (48.5)	**35 (50.0)**
Gravida - 2	14 (40.0)	13 (37.1)	**27 (38.5)**
Gravida - 3	3 (8.5)	5 (14.2)	**8 (11.4)**

Most of the subjects 38.5% are 2nd gravid, followed by Primi gravida 50.0% and least were grandmulties 11.4%. There was almost equal representation of various parity categories across cases and controls.

Table 3: Mode of delivery and outcome in cases and controls

Mode of delivery	Cases, N (%)	Controls, N (%)
Emergency LSCS	12 (34.2 %)	11 (31.4 %)
NVD	28 (80%)	19 (54.2%)
Outcome Alive	34 (97.8%)	34 (97.8%)
Still birth	01 (2.8%)	01 (2.8%)

Among 35 preterm labour cases 28 (80%) were normal vaginal deliveries and 12 (34.2%) were emergency LSCS; 34 (97.8%) out of 35 cases delivered live babies and 01 (2.2%) had still birth in cases. In Control 35 preterm labour cases 19 (54.2%) were normal vaginal deliveries and 11 (31.4%) were emergency LSCS; 34 (97.8%) out of 35 cases delivered live babies and 01 (2.2%) had still birth in cases.

Table 4: Difference in Ferritin levels between cases and controls

Ferritin	Mean units	SD	T	P
Cases	42.299	21.68	8.79	0.001
Controls	**22.35**	**8.86**		

The mean serum ferritin levels in patients were 42.299 ± 21.68 and in controls were 22.350 ± 8.86. Cases had considerably higher mean serum ferritin levels than controls.

Ferritin Normal range: Female: 11.1–264 ng/mL and Male: 17.9–464 ng/mL

4. Discussion

In the absence of congenital abnormalities, preterm work is the most significant consequence for pregnancy, increasing newborn morbidity and death. [8] Premature delivery represents 75 percent of perinatal mortality and responsible for 50% of long - term morbidity. Approximately 30%–35% of preterm birth are caused by medical indication, about 40–45% by spontaneous work, and about 25–30% by early membrane breakdown. [9]

Ferritin plays a key function in hosting protection against bacterial invasion by sequestering iron, which is a necessary ingredient for bacterial development. Placental iso ferritin, which is a placental ferritin type, was expressed as syncytiotrophoblast and deciduum macrophages. [10 - 14] This research was performed from May 2020 to February 2021 at Benha University Hospital. The population of the research included 90 pregnant women, split in two groups: the full - term population (n=64) and the preterm population (n=26). The findings indicated that serum ferritin levels were

substantially higher in the preterm group compared to the full - term group, because the p value was <0.0001.

Our research is in agreement with the study performed at the Obstetrics and Gynecology Department, Menoufia University Hospital between March 2017 and March 2019 by Ibrahim Saif Elnasr, per 100 pregnant women between 20 to 24 weeks of gestation, 85, of whom were born at full term (37: 39 weeks). [15] Of these, 15 were premature (33 - 36 weeks) and there were no significant differences in maternal age between term and premature group as the mean age for the term was 28.11, and 26.93 for the premature group was 0.35. In terms of the average gestational age at time of birth, there was a large statistically significant difference in terms of 38.8 and 35.2 P was <0.001 in a preterm group.

Naim A, conducted this research to evaluate the usefulness of cervical changes as a predictor of preterm labour for 154 women at the Maimonides Medical Center, 20 of whom experienced preterm labour at 13 percent.

Several studies have examined the relationship of serum ferritin with premature birth. In the research by Movahedi, 222 single - ton pregnancies were referred to in Isfahan as University Hospital clinics. In terms of serum ferritin concentration, preterm delivery group (n = 69) and delivery group (n = 153) were compared. The mean concentration of the women preterm delivered is greater than that of the preterm ferritin (26.7±5.5 ng/ml) vs (19.8±3.6 ng/ml) p - value < 0.001. The cutoff value for serum ferritin in this research was 22, 5 ng/mL, with 78, 3 percent sensitivity and 83 percent specificity. [17]

This is in line with research by Nandini M D. Group 1 (preterm delivery, case group) and group 2 of 100 pregnant women split into two groups (term delivery, control group). Study findings revealed substantially higher levels of serum ferritin in preterm labour, ranging from 4.4µg/dl to 841.2µg/dl and from 9.8µg/dl to 67µg/dl, respectively, in preterm and control individuals. The mean ferritin serum levels of 81, 29µg/dl were higher in the study group compared with 28, 57µg/dl in the control group and the P value was statistically significant (0.0062). [18]

Our trial coincides with Cetinkaya, where 91 pregnant women have risked premature work and 83 pregnant women have been diagnosed as a control group. They observed that serum ferritin concentrations in the study groups were substantially greater in comparison to the control group. [19]

Beta, conducted case - control research, comprising 30 spontaneous delivery cases before to 34 weeks and 90 matching tests after 37 weeks, which investigated the potential usefulness of blood ferritin levels in the first quarter of pregnancy for predicting spontaneous pre - term work. The research showed that serum ferritin was unlikely to be helpful in screening for spontaneous early preterm work at 11 to 13 weeks of gestation, because a comparison of two groups in respect of serum ferritin was not statistically different (p value = 0.725). [20]

Another case - control research was conducted to examine the link between serum ferritin and premature labour. Serum samples were collected at 24 weeks gestation, case definition was based on a spontaneous birth at 32 weeks or less (n=32) and spontaneous delivery at 37 weeks or longer (n=31). The serum ferritin levels were negatively related to gestational age (p - value =0.34), and the study found that higher serum ferritin levels are predictive of early spontaneous preterm delivery in the second trimester, possibly reflecting an acute phase reaction to subclinical infections that are closely linked to premature employment. [21]

El - Shahawy, also demonstrated that preterm ferritin levels at 30 - 34 weeks and ferritin levels over 55 ng/mL were substantially higher than uncomplicated pregnancy levels at the same gestation age with a sensitivity of 96.7 and a specificity of 96.7% were a predictor of early birth. [22]

This contradicts with the Adathila Sanoop A, research. [23] Their goals were to compare the levels of ferritin in 50 PPROM patients, 50 spontaneous preterm labour and 50 hemoglobin - associated pregnant women at the same gestational age. The mean ferritin levels between the control unit and the spontaneous preterm labour group were not statistically significantly affected by a p - value of 0.180.

5. Conclusion

High serum ferritin level is associated with premature delivery and serum ferritin level may consider as a marker for preterm labor. In cases with high serum ferritin, prophylactic treatment and early intervention may be considered to prevent preterm birth and to improve pregnancy outcome.

References

[1] Sameshima. Hiroshi. "Definition and Diagnosis of Preterm Labor. " Preterm Labor and Delivery Springer, Singapore. vol.5, pp.715, 2020.
[2] M. Movahedi, M. Saiedi, M. Gharipour, O. Aghadavoudi. Diagnostic performance and discriminative value of the serum ferritin level for predicting preterm labor. J Res Med Sci. vol.17, pp.164–6, 2012.
[3] E. Arpi, & F. Ferrari, Preterm birth and behavior problems in infants and preschoolage children: A review of the recent literature. Developmental Medicine & Child Neurology. vol.55 (9), pp788–796, 2013.
[4] Broumand & Farzaneh. "The diagnostic value of cervicovaginal and serum ferritin levels in midgestation time to predict spontaneous preterm delivery. " Nigerian medical journal: journal of the Nigeria Medical Association. vol.55.4, pp.321, 2014.
[5] Hazem FE–shahawy, sherifFHendawy, Alaa. SHassanin, AbdEl–Azeem, MMONA. Estimation of serum ferritin level in preterm labor. The Egyptian journal of Hospital medicine 68 (3), 1469 - 1474, 2017.
[6] C. P. Howston, M. V. Kinney, J. E. lawn, savethechildren, MarchofDimes, PMNCH and WHO, Born too soon; the Global Action, report on preterm birth, Geneva Switzerland 2012.3.

[7] Chiaravoltolini, Michela. Toricelli, Nalhalieconti, Francasalvellucei, Filebeez. Reproductive sciences 20 (11), 1274 - 1292, 2013.
[8] Ozlem Guzeloglu - Kayisli, Umit A Kayisli, Nihan Semerci, Murat Basar, Lynn FBuchwalder. Catalin S Buhimschi. Mechanisms of chorioamnitis - associated pre term birth: interleukin - 1 beta inhibits progesterone receptor expression in decidua cells. The journal of pathology 237 (4), 423 - 434, 2015.
[9] Lannon SMR, Vanderhoeven JP, Eschenbach DA, Gravett MG, Adams Waldorf KM. Synergy and interactions among biological pathways leading to pre term premature rupture of membranes. Reprod Sci., 2014; 21: 1215–27.
[10] Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. The Lancet 2012; 379 (9832): 2162 - 2172.
[11] Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH, et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bulletin of the World Health Organization 2010; 88 (1): 31 - 38.
[12] Kamali Fard M, Alizadeh R, Sehati Shafaei F, Gojazadeh M. The effect of lifestyle on the rate of preterm birth. Journal of Ardabil University of Medical Sciences 2010; 10 (1): 55 - 63.
[13] Goffinet F, Maillard F, Fulla Y, Cabrol D. Biochemical markers (without markers of infection) of the risk ofpre term delivery. Implications for clinical practice. EurJObstetGynecolReprodBiol 2001; 94: 59–68.
[14] Wwang, M A Knovich, lG Coffman, Frank M Torti, Suzy V Torti. Serum ferritin; past, present and future, Biochimicaet Biophysica Acta (BBA) - GeneralSubjects1800 (8), 760 - 769, 201059.
[15] Rundell K, Panchal B. Preterm Labor: Prevention and Management. American family physician 2017; 95 (6): 366 - 72
[16] Abdel - Malek K, El - Halwagi MA, Hammad BE, Azmy O, Helal O, Eid M et al. Role of maternal serum ferritin in prediction of preterm labour. Journal of Obstetrics and Gynaecology 2018; 38 (2): 222 - 5.
[17] Movahedi M, Saiedi M, Gharipour M, Aghadavoudi O. Diagnostic performance and discriminative value of the serum ferritin level for predicting preterm labor. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences 2012; 17 (2): 164.
[18] Singh B, Goswami B, Gupta N, Bajaj AD, Mallika V. Potential biochemical markers for preterm labor: a pilot study in north India. Indian Journal of Clinical Biochemistry 2011; 26 (1): 41 - 5.
[19] Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. The lancet 2008; 371 (9606): 75 - 84.
[20] Arosio P, Levi S. Cytosolic and mitochondrial ferritins in the regulation of cellular iron homeostasis and oxidative damage. Biochimica et Biophysica Acta (BBA) - General Subjects 2010; 1800 (8): 783 - 92.
[21] Maity B, Ueno T. Design of bioinorganic materials at the interface of coordination and biosupramolecular chemistry. The Chemical Record 2017; 17 (4): 383 - 98.
[22] Farag AH, Mohammed MM, Ellaithy MI, Salama HA. Blind vaginal fetal fibronectin swab for prediction of preterm birth. Journal of Obstetrics and Gynaecology Research 2015; 41 (7): 1009 - 17.
[23] Sak ME, Sak S, Gül T. Preterm doğumun erken bir belirteci olarak servikovajinal sekresyonlardaki gonadotropin konsantrasyonları. Journal of Clinical and Experimental Investigations 2010; 1 (1): 16 - 20.