Research Article

Study of serum ferritin levels in preterm labor

Nandini M D[1*], H V Shetty[2], B V Rupakala[3], Usha S M R[4], Priyadarshini K S[5], Manjula H S[6], Victoria Ksh[7]

{[1,6,7]II Year Post Graduate-cum-Tutor, [2]Professor and HOD, [4,5]Professor, Department of Biochemistry}
{[3]Professor, Department of Obstetrics and Gynaecology} Rajarajeswari medical college and Hospital, Bangalore, Karnataka, INDIA.
Email: nandinimd29@gmail.com

Abstract

Objectives: To estimate the serum ferritin levels in patients of preterm labor and to compare with normal pregnant women matching with same gestational age. To determine if elevated serum ferritin level is associated with preterm labor. **Methodology:** The study was conducted at Rajarajeswari Medical College and Hospital, Bengaluru. A total of 50 cases preterm labor were taken for the study after satisfying the inclusion and exclusion criteria. Fifty cases of normal pregnant women matching with same gestational age were included in the study under the control group. All patients were evaluated in detail. Serum ferritin level was estimated by particle enhanced immunoturbidimetric method. **Results:** Mean serum ferritin a value of preterm labor is 81.296µg/L and in control subjects is 28.576µg/L. The difference was evaluated by Student's unpaired t-test and was found to be statistically significant (P value=0.0062). Serum ferritin level is significantly high in cases compared to controls. **Conclusion:** Serum ferritin may be considered as a biochemical marker for detecting preterm labor.

Keywords: Serum Ferritin, Preterm labor.

[*]**Address for Correspondence:**
Dr. Nandini M D, Post Graduate-cum-Tutor, Department of Biochemistry, Rajarajeswari medical college and Hospital, Bangalore, Karnataka, INDIA.
Email: nandinimd29@gmail.com
Received Date: 14/03/2015 Revised Date: 22/03/2015 Accepted Date: 25/03/2015

Access this article online	
Quick Response Code:	Website: www.statperson.com
	DOI: 26 March 2015

INTRODUCTION

Preterm labor is defined as regular uterine contractions before 37 completed weeks of gestation with intact membranes with 4cm or more of cervical dilatation observable during a 2hour period. There are sub-catogories based on gestational age:
Extremely preterm (<28 weeks)
Very preterm (28 -32 weeks)
Moderate to late preterm (32- 37 weeks)

Preterm delivery is one of the leading causes of perinatal morbidity and mortality. Every year an estimated 15 million babies are born preterm and the number is raising. An estimated 1 million babies die annually from preterm birth complication. It accounts for nearly 70% of the neonatal deaths and 50% of the long term neurological sequelae. If preterm labor leads to an early delivery, the premature new born is at risk of problems related to incomplete development of its organ systems[1]. Many of the surviving infants suffer serious morbidity such as respiratory distress syndrome, broncho-pulmonary dysplasia, intraventricular haemorrhage, retrolental fibroplasia and developmental problems[2].

In 65% cases of preterm birth, there is always a predisposing cause, however in 35% cases of preterm birth, there is no obvious etiology[3]. Although the pathophysiology of preterm labour remains incompletely defined, a growing body of evidence is emerging that links occult upper genital tract infections with subsequent spontaneous preterm labour[4]. **Predisposing factors are:** Multiple gestations carry one of the highest risks of preterm delivery. A history of a preterm delivery is one of the most significant risk factors. The recurrence risk of preterm birth in women with a history of preterm delivery ranges from 17% to 40%, and appears to depend on the number of prior preterm deliveries. Women younger than 17 and older than 35 carry a higher risk of preterm delivery.Less education and lower socioeconomic status are also risk factors. Various behavioural factors also

How to site this article: Nandini M D *et al.* Study of serum ferritin levels in preterm labor. *International Journal of Recent Trends in Science and Technology* March 2015; 14(2): 477-480 http://www.statperson.com (accessed 28 March 2015).

increase the risk for preterm delivery[5]. Asymptomatic bacteriuria is associated with an increased rate of prematurity. Systemic infections, such as bacterial pneumonia, pyelonephritis, and acute appendicitis, often lead to increased uterine activity, potentially leading to premature delivery[6].

Currently the accepted markers of onset of preterm labor are assessment of fetal fibronectin in cervicovaginal secretions and cervical dilatation[1]. Endotoxins released by microorganisms and cytokines stimulate deciduas responses including the release of prostaglandins which may stimulate uterine contractions. Further the decidual response may include release of matrix-degrading enzymes that weaken fetal membranes leading to premature rupture[7]. Ferritin is released by infiltrating leukocytes, in response to acute and chronic infection. Several previous investigations have indicated an association between elevated serum ferritin concentration and preterm delivery[2]. Ferritin has a central role in iron homeostasis since it binds and sequesters intracellular iron. It is a spheric shell with a central cavity where up to 4,500 atoms of iron are oxidized and stored. Ferritin is a multimer composed of 24 H (heavy) and L (light) subunits in variable proportions in different tissues. The two subunits are highly conserved during evolution, but only the H subunit has ferroxidase activity[8]. Ferritin as an acute phase reactant is well known for its intracellular iron sequestration and storage abilities during immune activation[9]. This function is of high importance for protection of the body against microbial proliferation, oxidative damage, inflammation and cancer. The serum protein differs from intracellular protein is that it is glycated and it contains little or no iron. Tissue ferritin with more heavy chains and serum ferritin with less heavy chains. Ferritin rich in H chains acquire iron more rapidly and ferritin rich in L chains appeared to be more stable and resistant to denaturation[10]. Ferritin is the primary intracellular iron storage protein in both prokaryotes and eukaryotes, keeping iron in soluble and non toxic form and has been identified as a diagnostic marker that its high serum levels is associated with a variety of acute phase reactions, including inflammatory conditions[11]. It has been proposed that extracellular ferritin has an important role in host defence against bacteraemia by stimulating oxidative metabolism. A large proportion of early spontaneous preterm deliveries is associated with upper genital tract infections and most patients show little or no sign of infections[12]. Some mechanisms have been suggested for these evidences. First, the presence of increased levels of ferritin might reflect an acute phase reaction to subclinical genital tract infection or inflammation. In addition, it may be also explained by the covert process of infection associated with preterm delivery that causes tissue damage resulting in increased serum ferritin levels that act as an acute phase reactant[13]. Our purpose in this study is to evaluate the ferritin levels in spontaneous Preterm delivery.

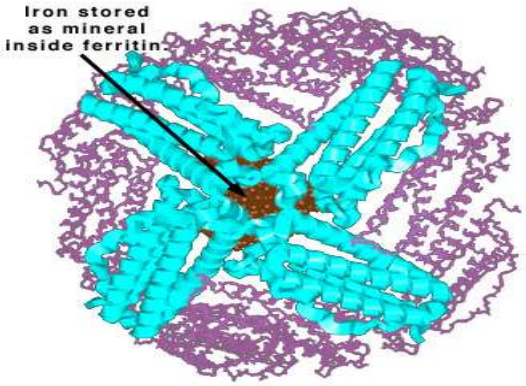

Figure 1: Ferritin

MATERIALS AND METHODS

In a Cross-Sectional Study, we studied the role of serum ferritin in preterm labor in the Department of Biochemistry and Labour room of the department of Obstetrics and Gynaecology, RajaRajeswari Medical College and Hospital, Bengaluru. 100 pregnant women divided into two groups. Group 1(preterm delivery, case group) and group 2 (term delivery, control group). Women with Anemia, Iron over load state, pre-existing chronic infective diseases, Multiple pregnancy, Polyhydromnios, Diabetes Mellitus, Alcoholics and Smokers were excluded. Inclusion criteria was women going into spontaneous preterm labor and Normal pregnant women serving as controls of same gestational age. Ethical clearance has been obtained from the ethical clearance committee of rajarajeswari Medical College and Hospital, Bengaluru. Blood samples were drawn under aseptic condition, after obtaining informed consent and before delivery, venous blood samples were collected by venipuncture and was allowed to clot in iron free tubes at room temperature. Serum was separated within 2 hours and stored at -20^{0}C until final estimation.

Estimation of Serum Ferritin

Serum Ferritin was assayed by particle enhanced immunoturbidimetric method having principle of end point determination of the concentration of ferritin by photometric measurement of antigen-antibody-reaction of latex particles coated with antibodies to ferrtin with ferritin present in the sample. It was done in fully automated analyzer.

Haemoglobin was assayed by spectrophotometric method in fully automated analyser.

STATISTICAL ANALYSIS

All the collected data was tabulated and analyzed using descriptive statistics. The values were expressed as mean ±SD. The significance of difference in means was tested by the student t test. P value less than 0.05 was considered significant.

RESULTS

Table 1: Patient characteristics

Parameter	Preterm(50)	Control(50)
Age in years	23.34 ± 3.10766	22.44 ± 1.71
Gestation in weeks	31.74 ± 1.411	31.78 ± 1.432
Hb (g/dl)	10.6 ± 1.411	10.79 ± 1.323

Table 2: Values of Ferritin(µg/dl) in preterm and control patients

Parameter	Preterm(50)	Control(50)	P value
Ferritin µg/dl	81.29 ± 132.34	28.57 ± 14.48	0.0062*

*P value is Statistically significant

Table 1 exhibits the patient characteristics of study and control groups. All the groups were comparable in terms of age, gestation in weeks and haemoglobin. (P>0.05) Serum ferritin values ranged from 4.4 µg/dl to 841.2 µg/dl and 9.8 µg/dl to 67 µg/dl in preterm and control patients respectively. Mean serum ferritin values was higher in the study groups i.e. 81.29 µg/dl as compared to the control group which was 28.57 µg/dl and the P value was statistically significant(0.0062). (Table 2)

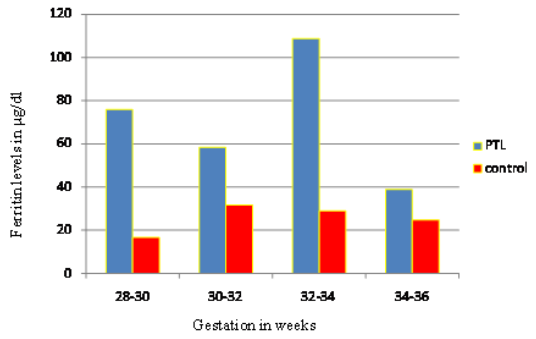

Figure 2: Serum ferritin levels

When pregnancy outcome was assessed in preterm, 31 infants were appropriate for gestational age (AGA) and 13 were small for dates (SFD) in the PTL group. The mean serum ferritin levels in the mothers with AGA infants (97.88 µg/dl) were higher than those with SGA infants (33.59 µg/dl) in preterm patients.

DISCUSSION

The best and most effective prevention of preterm delivery incidence is early identification of pregnant women who belong to a group of high risk[14]. About 65 to 70 % of foetus deaths and the incidence of early neonatal death are in children born before the end of the 37th week of gestation with body weight less than 2500 grams[15]. Pregnancy tends to predispose to vaginocervical infection due to altered vaginal pH. The chorion-decidual interface is infiltrated by macrophages following bacterial colonization and ferritin is produced as an acute phase reactant[16]. Clinical chorioamnionitis complicates 1–5% of term pregnancies, but nearly 25% of preterm deliveries. In a study by Guzick and Winn, histological chorioamnionitis was more common in preterm deliveries than in term ones (32.8% versus 10%)[17]. Watts et al investigated patients in preterm labor and demonstrated that positive amniotic fluid cultures were present in 19% of women with intact membranes with no clinical evidence of intrauterine infection[18]. Organisms that have been associated with histological chorioamnionitis include Ureaplasma urealyticum, Mycoplasma hominis, Gardnerella vaginalis, peptostreptococci, and Bacteroides species[19]. Findings of our study showed serum ferritin levels were significantly higher in preterm labor and it correlates with the similar studies done by Mino Movahedi et al[13], Ayesha Siddika et al[2] that serum ferritin level was significantly higher in preterm delivery. Tamura et al, in their study showed that women with higher serum ferritin concentrations, compared with those women with lower concentrations experienced an almost threefold increased risk of delivering preterm[20]. C.K.Saha et al demonstrated that high serum ferritin level in the study group is most likely a part of 'acute phase reaction' to a subclinical infection[12]. However we did not do various haematological investigations and serum iron levels to know whether serum ferritin is high because of iron overload or subclinical infection. Our results are consistent with C.K.Saha et al, that the mean serum ferritin levels were higher in mothers with AGA infants than with SGA infants in the study group. However, the explanation for these observations needs further evaluation.

CONCLUSION

From the present study it may be concluded that high serum ferritin level is a risk factor for preterm labor, therefore Serum ferritin may be considered as a biochemical marker for detecting preterm labor, as it is *cost effective* and easily done in laboratories. We had some limitations like sample size was too small, we did not correlate the parameters with different gestational age

groups and the mortality of the subjects was not considered. Recommendations are it should be done in larger population and Future research should focus on the development of a risk model with input of individual clinical & biochemical factors to predict preterm with both high sensitivity and specificity.

ACKNOWLEDGEMENTS

I am indebted to pregnant ladies involved in our study for their cooperation. My mother Sumithra Bai and my husband H.S.Vijay Kumar for being a constant support in all my endeavours. I would also like to thank Dr.Rupakala.B.V. Professor, department of Obstetrics & Gynaecology, Rajarajeswari Medical College & Hospital. My special thanks to our beloved Professor and HOD Dr.H.V.Shetty, our professors Dr.Usha.S.M.R., Dr.Priyadarshini.K.S., Associate professor Dr.Bindu.C.M., Assistant professor Dr.Deepti Gupta and Ms.Sowrabhi for all the support and my colleagues ***Department of Biochemistry***, Rajarajeswari Medical College & Hospital.

REFERENCES

1. Bhawna Singh, Binita Goswami, Nikhil Gupta, Archana Dhawan Bajaj, V Mallika.2011."Potential Biochemical Markers for Preterm Labor:A Pilot Study in North India".*Ind J Clin Biochem* 26(1):41-45.
2. Chien PF, Khan KS, Ogsten S, Owen P. The diagnostic accuracy of cervico-vaginal fetal fibronectin in predicting preterm delivery: an overview. BJOG : an international journal of obstetrics and gynaecology 1997; 104:436-444.
3. Ayesha siddika, Begum Nasrin, Shayela Shamim, Nurjahan Begum, N Nahar, Sultana Razia Begum.2009."Serum Ferritin Level in Preterm Labour".*Bangladesh J Obststet Gynaecol*,Vol.24(1):14-17.
4. Leonardo CHB, Cresfor SAA,James SA, Seigel E, Wilson S.1990."Work Related Physical Excretion and Risk of Preterm Low Birth Weight Delivery".*Pediats Perinat Epidemiol* 4:161-174.
5. Robert L. Goldenberg, MD "Management of Preterm Labor" Obstet Gynecol. vol. 100, no. 5, part 1, november 2002.
6. RomeroR,OyarzunE,MazorM,SirtoriM,HobbinsJC, Bracken M. Meta-analysis of the relationship between asymptomatic bacteruria and preterm delivery/birth weight. Obstet Gynecol 1989;73:576–82.
7. Goldenberg RL, Hauth JC, Andrews WW."Intrauterine infection and preterm delivery". New England Journal of Medicine 2000;342(20): 1500-1507.
8. Arosio P, Ingrassia R, Cavadini P. Ferritins: a family of mol- ecules for iron storage, antioxidation and more. Biochim Biophys Acta 2008. doi:10.1016/j.bbagen.2008.09.004.
9. Weiss, G. & Goodnough, L.T. (2005). Anemia of chronic disease. New Engl J Med, 352(10) (2005), pp. (1011-1023).
10. John P. Geer, et al, "Wintrobe's Clinical Hematology" volume-1,2009;810-881.
11. Chen X, Scholl TO, Stein TP.2006."Association of elevated Serum Ferritin levels and the risk of Gestational Diabetes mellitus in Pregnant Women, *The Camden Study Diabetes Care* 29:1077-82.
12. CK Saha, V Jain, I Gupta, N Varma.2000."Ferritin Level as a Marker of Preterm Labor".*International Journal Of Gynecology and Obstetrics* 71,107-111.
13. Movahedi M, Saiedi M, Gharipour M, Aghadavoudi O.2012."Diagnostic Performance of Descriminative Value of the Serum Ferritin Level for Predicting Preterm Labor".*J Res Med Sci*;17(2):164-6.
14. Bittar RE, Yamasaki AA, Sasaki S, Zugaib M. Cervical fetal fibronectin in patients at increased risk for preterm delivery. Am J Obstet Gynecol. 1996;175:178-81.
15. Dražančić A. Perinatal mortality in Republic of Croatia in 2003. Gynaecol Perinatol. 2004;13 (Suppl 3):1-18.
16. Paternoster DM, Stella A, Gerace P, Manganelli F, Plebani M, Snijders D, et al. Biochemical markers for the prediction of spontaneous preterm birth. Int J Gynecol Obs. 2002;79:123–9.
17. Guzick DS, Winn K. The association of chorioamnionitis with preterm delivery. Obstet Gynecol 1985;65:11–6.
18. Watts DH, Krohn MA, Hillier SL, Eschenbach DA. The association of occult amniotic fluid infection with gestational age and neonatal outcome among women in preterm labor. Obstet Gynecol 1992;79:351–7.
19. Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm birth. N Engl J Med 2000;342: 1500–7.
20. Tamura T,Goldenberg RL, Jhonston KE, Cliver SP, Hickey Ca.1996."Serum Ferritin: A Predictor of Early Spontaneous Preterm Delivery".*Obstetrics and Gynaecology*;87:360-365.

Source of Support: None Declared
Conflict of Interest: None Declared