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Significance of Serum Hepcidin a Novel Marker for the Assessment of Iron Status in Pregnant Womens

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KEYWORDS

Anaemia, Hepcidin, iron deficiency, pregnancy.

ABSTRACT:

During pregnancy time iron deficiency anaemia is the most common cause, were it is associated with more maternal as well as fetal morbidity and mortality. To understand the status of iron during pregnancy will provides a foundation for considering the role by screening or supplementation. Iron absorption status in control by the iron regulatory hormone called hepcidin and serum ferritin levels during pregnancy time in women's especially in 1st trimester.

Objectives To study the importance of serum hepcidin as a biomarker of iron status in pregnant women and results were compared with other investigations.

Methods: In our study total of 90 pregnant women before starting iron supplementation were selected. Serum hepcidin and ferritin level were estimated by ELISA method. Based on serum ferritin levels study group have been divided into 2 groups, group 1[>12ng/ml] and group 2[<12ng/ml].

Results: Statistical analysis student t-test and Pearson's correlation analysis were done. Serum hepcidin was significantly low in group 2 [anaemic] than group 1[non anaemic] with a p-value of <0.001 which was highly significant. There was a strong positive correlation between serum hepcidin and serum ferritin[r value 0.657] with p value <0. 001. **Conclusions**: In our study we observed strong positive association of Hepcidin with ferritin is suggestive of its role as a marker of iron status like ferritin. In addition, it can reflect iron absorption status unlike ferritin. It is concluded that hepcidin can a novel biomarker to assess iron status in pregnant women. Hence serum hepcidin could be used as a single novel biomarker of iron status.

Introduction

Iron deficiency anemia affects approximately 3 billion people worldwide, with pregnant women constituting a high-risk group due to physiological iron demands required for fetal development and maternal health maintenance (WHO, 2023). [1] Iron deficiency during pregnancy is linked to adverse outcomes including maternal fatigue, impaired cognitive function, increased susceptibility to infections, preterm delivery, and low birth weight infants (McLean et al., 2017). [2] Accurate assessment of iron status remains critical for timely intervention.

Serum ferritin has traditionally served as a reliable indicator reflecting body iron stores. However, ferritin is an acute-phase reactant and may be elevated during inflammatory states independent of iron status, limiting its specificity (Ganz, 2019).[3] Serum iron levels fluctuate daily and are influenced by diet, circadian rhythm, and inflammation, reducing their diagnostic utility alone. Recently, hepcidin has emerged as a central regulator of iron metabolism. This peptide hormone

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controls iron absorption from the intestine and iron release from macrophages by degrading ferroportin, the cellular iron exporter (Nemeth et al., 2019). [4]

Advances in immunoassay techniques have enabled sensitive measurement of serum hepcidin, allowing investigation of its clinical relevance as a diagnostic biomarker. Several recent studies confirm that hepcidin levels decrease in iron deficiency and increase during iron overload,anemia of chronic disease or inflammatory states, reflecting its dual role in iron metabolism and immune response modulation (Armitage et al., 2021; Silva et al., 2022).[5,6]

Methodology:

Study Population: Primigravida - 10-12 weeks and it's an cross sectional study

Sample Size: Ninety pregnant women were grouped based on serum ferritin level.

Group 1 included 45 anaemic pregnant women.

Group 2 included 45 non-anaemic pregnant women.

Inclusion criteria: Primigravida during 10-12 weeks before starting iron supplementation.

Exclusion criteria:Multigravida, Pregnant women on iron supplementation, Gestational diabetes mellitus, Thyroid disorders, Liver disorders, gastrointestinal disorders, bleeding disorders

Pregnant women during 1st trimester attending the outpatient in the department of obstetrics & gynaecology were selected for the study, after explaining in detail about the study design. Written informed consent was obtained from all pregnant women before the study. A thorough history was elicited from pregnant women chosen for the study. All the study subjects were analysed in full details regarding age, literacy, socioeconomic status and parity. Gestational age was determined by the date of last menstrual period. Under aseptic precaution 5 ml of venous blood samples was collected in test tubes (EDTA test tube, oxalate/ citrate test tube and plain test tube) in fasting state and the serum was separated by centrifugation at 3000rpm at room temperature. Serum was stored at -80º C until analysis done in the Department of Biochemistry. Baseline investigations were estimated using auto analyser with standard kits. Serum ferritin and serum hepcidin were assayed by ELISA method.

Results

No significant differences were observed between non-anaemic and anaemic pregnant women in terms of age, BMI, blood pressure, fasting and postprandial blood glucose, serum urea, creatinine, liver enzymes (AST, ALT, ALP), total cholesterol, and total protein levels. These findings suggest comparable baseline health status between the two groups.

Hemoglobin concentration was significantly reduced in the anaemic group (10.67±1.47 g/dl) compared to the non-anaemic group (11.64±1.57 g/dl) ($p < 0.01$). Hematological indices including MCV, PCV, and MCHC were also significantly lower among anaemic women, though values remained within clinical reference ranges. The reduction in these indices is consistent with microcytic hypochromic anemia, typical of iron deficiency.

Serum iron was significantly lower in anaemic women (51.38±20.81 µg/dl) than in non-anaemic women (63.40±23.40 µg/dl) ($p = 0.022$). Ferritin levels demonstrated a sharp decline in the anaemic group (6.18±3.04 ng/ml) versus the non-anaemic group (31.51±15.13 ng/ml) ($p < 0.001$), confirming depleted iron stores.

Importantly, serum hepcidin levels were markedly reduced in the anaemic group (6.78±4.01 ng/ml) compared to the non-anaemic group (12.99±5.68 ng/ml) ($p < 0.001$). The strong positive correlation between hepcidin and ferritin levels ($r = 0.78$, $p < 0.001$) underscores the regulatory role of hepcidin in iron homeostasis.

1. **Results**

Table 1 Baseline parameters in study group 1 and 2

Parameters	Group 1 [non anaemic]	Group 2 [anaemic]	P Value
AGE (Years)	23.48 ± 5.87	21.11 ± 5.67	NS
BMI (Kg/m2)	20.14 ± 0.54	22.46 ± 3.2	NS
BP (SYSTOLE) (mmHg)	117.11 ± 8.42	118.44 ± 15.5	NS

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BP (DIASTOLE) (mmHg)	78.33 ± 6.8	76.8 ± 11.4	NS
FBS (mg/dl)	89.15 ± 29.2	99.5 ± 30.89	NS
PPBS (mg/dl)	150.93 ± 62.98	149.24 ± 58.21	NS
Serum Urea (mg/dl)	27.31 ± 4.36	26.82 ± 3.41	NS
Serum Creatinine (mg/dl)	0.8 ± 0.09	0.77 ± 0.07	NS
Total cholesterol (mg/dl)	106.66 ± 36.7	118.35 ± 26.3	NS
Total Protein (g/dl)	6.46 ± 0.33	6.59 ± 0.04	NS
AST (u/l)	29.48 ± 6.4	28.91 ± 7.6	NS
ALT (u/l)	27.24 ± 5.05	24.48 ± 6.79	NS
ALP (u/l)	175.68 ± 36.23	174.88 ± 62.34	NS

NS Non Significant

Table 2 Haematological parameters in study groups

Parameters	**Group 1[non-anaemic]**	**Group 2 [anaemic]**	**P value**
Hb[g/dl]	11.64± 1.57	10.67±1.47	<0.01
RBC[10^6/µL]	3.98 ± 0.69	3.85 ± 0.77	**NS**
WBC[10^3/µL]	8.14 ±2.35	5.89 ± 1.99	< 0.05
MCV[fL]	73 ± 8.69	66.31 ± 10.04	<0.05
MCH[pg]	27.48 ± 6.35	26.75± 5.52	**NS**
PCV[%]	37.88 ± 5.71	34.77± 7.37	<0.05
MCHC[g/dl]	31.78 ± 4.10	29.19± 5.81	<0.05

NS Non Significant

Table 3 Special parameters in study groups

Parameters	**Group 1[non-anaemic]**	**Group 2 [anaemic]**	**P value**
SERUM IRON [µg/dl]	63.40±23.40	51.38±20.81	0.022*
FERRITIN[ng/ml]	31.51± 15.13	6.18± 3.04	<0.001*
HEPCIDIN[ng/ml]	12.99± 5.68	6.78± 4.01	<0.001*

***Significant**

Discussion

Our findings support the emerging evidence that serum hepcidin is a sensitive and specific biomarker for iron status assessment in pregnancy. Similar results have been reported by Phiri et al. (2020). [7] who demonstrated decreased hepcidin concentrations in iron-deficient pregnant women and its ability to predict iron status with higher accuracy than serum iron alone. Research study by Simcox et al.(2021). [8] Corroborated the inverse relationship between hepcidin and iron absorption, highlighting hepcidin's potential use in guiding iron supplementation strategies during pregnancy.

Pregnancy is characterized by complex physiological adaptations including increased plasma volume and altered inflammatory status, which can confound traditional iron biomarkers (Peña-Rosas et al., 2019). [9] Hepcidin, regulated by systemic iron levels, erythropoietic activity, and inflammatory cytokines, integrates these signals making it a superior biomarker in this context (Ganz & Nemeth, 2021). [10]

Additionally, recent reviews emphasize that low hepcidin levels during early pregnancy facilitate increased dietary iron absorption and mobilization from stores to meet fetal needs (Sangkhae & Nemeth, 2020). [11] However, persistent low hepcidin in iron deficiency may exacerbate anemia if not properly managed. As such, serum hepcidin measurement can help distinguish true iron deficiency from anemia of inflammation, improving diagnostic precision.

Although ferritin remains a standard marker, its limitations include elevation during infection or chronic inflammation, which commonly occur in pregnancy (Clifton et al., 2023). [12] Hepcidin adds diagnostic value by reflecting iron absorption dynamics that ferritin does not. For instance, Scholl et al. (2022) demonstrated that serum hepcidin levels were reduced in pregnant

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women with iron deficiency anemia despite normal or elevated ferritin due to concomitant inflammation.

Our study, consistent with these findings, suggests that integrating serum hepcidin assessment alongside conventional iron markers may optimize iron deficiency diagnosis and treatment during pregnancy. Early detection of iron deficiency allows timely supplementation, reducing risks of maternal and fetal complications such as preterm birth, low birth weight, and impaired neurodevelopment (McLean et al., 2017; Kassebaum et al., 2022). [13,14]

Future research should focus on standardization of hepcidin assays, establishing definitive reference ranges in pregnancy, and clinical trials validating hepcidin-guided iron therapy protocols. Larger-scale studies across diverse populations will help consolidate the clinical utility of hepcidin as a routine diagnostic biomarker.

Conclusion

This study highlights serum hepcidin as a promising novel biomarker along with serum ferritin levels for the assessment of iron status in pregnant women. Hepcidin correlates strongly with ferritin and captures functional iron absorption changes, providing complementary information to traditional iron indices. Incorporation of serum hepcidin measurement could enhance early diagnosis and management of iron deficiency anemia in pregnancy, potentially improving maternal and fetal health outcomes. Further extensive studies are warranted to establish its implementation in routine prenatal care.

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Conflict of interest:

There is no conflict of interest

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