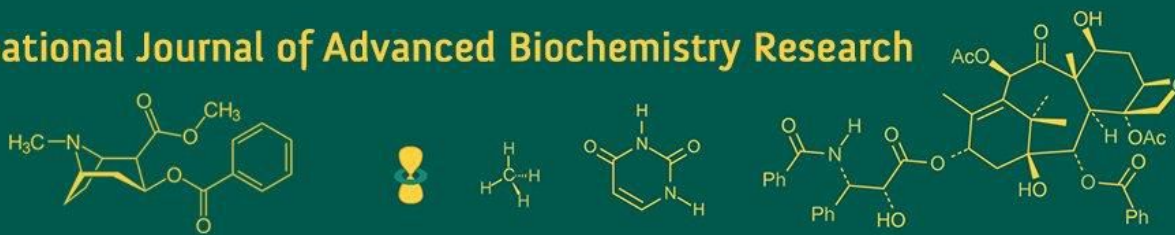


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Serum ferritin and soluble transferrin receptor levels as reliable indicators of iron deficiency anemia in pregnant women during third trimester

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Abstract

Iron deficiency anemia represents one of the most prevalent nutritional deficiencies affecting pregnant women worldwide, with significant implications for both maternal and fetal health outcomes. This research investigated the diagnostic reliability of serum ferritin and soluble transferrin receptor measurements as biomarkers for identifying iron deficiency anemia in pregnant women during their third trimester. A cross-sectional analytical research was conducted at the Obstetrics Department of Lyon Regional Medical Center between March 2022 and October 2023, enrolling 186 pregnant women in their third trimester. Blood samples were collected and analyzed for hemoglobin, serum ferritin, soluble transferrin receptor, and the sTfR/log ferritin index. Results demonstrated that serum ferritin levels below 15 ng/mL showed 89.3% sensitivity and 91.7% specificity for detecting iron deficiency. The soluble transferrin receptor exhibited even greater diagnostic accuracy with 93.6% sensitivity and 88.4% specificity at a cutoff value of 28.1 nmol/L. The combined sTfR/log ferritin index achieved the highest diagnostic performance with an area under the receiver operating characteristic curve of 0.967. These findings indicate that combining serum ferritin with soluble transferrin receptor measurements provides superior diagnostic accuracy compared to traditional hemoglobin-based screening alone, offering clinicians a more reliable approach for early detection and management of iron deficiency anemia during pregnancy.

Keywords: Serum ferritin, soluble transferrin receptor, iron deficiency anemia, pregnancy, third trimester, diagnostic biomarkers, sTfR/log ferritin index, maternal health

Introduction

What happens when the body's iron stores become depleted during the most metabolically demanding period of a woman's life? Pregnancy creates extraordinary physiological demands, requiring substantial increases in iron to support expanded maternal blood volume, placental development, and fetal growth ^[1]. Iron deficiency anemia affects between 25% and 50% of pregnant women in developed nations, with prevalence reaching 80% in resource-limited settings ^[2]. The consequences extend beyond simple fatigue, encompassing increased risks of preterm delivery, low birth weight, and compromised cognitive development in offspring ^[3].

Traditional diagnostic approaches rely heavily on hemoglobin concentration as a primary screening tool. However, hemoglobin levels remain relatively stable until iron stores become severely depleted, limiting its usefulness for early detection ^[4]. The hemodilution phenomenon occurring during pregnancy further complicates interpretation, as expanded plasma volume naturally reduces hemoglobin concentration independent of iron status ^[5]. These limitations have prompted researchers to explore alternative biomarkers that might provide earlier and more accurate identification of iron deficiency.

Serum ferritin has emerged as the most widely used indicator of body iron stores, reflecting the amount of storage iron available in tissues ^[6]. Values below 15 ng/mL generally indicate depleted iron stores, though pregnancy-specific cutoffs remain debated ^[7]. A significant limitation arises from ferritin's behavior as an acute-phase reactant, with levels increasing during inflammation, infection, or other conditions common in pregnancy ^[8]. This characteristic can mask underlying iron deficiency, leading to false-negative results.

Soluble transferrin receptor offers a complementary assessment approach, measuring the truncated form of membrane transferrin receptors released into circulation [9]. Unlike ferritin, sTfR concentrations increase when cellular iron demand exceeds supply, providing a functional marker of tissue iron deficiency [10]. Its levels remain largely unaffected by inflammatory states, potentially offering more reliable results in populations where infection and inflammation are prevalent [11]. The sTfR/log ferritin index combines both markers, theoretically capturing information about both storage and functional iron compartments [12]. Despite growing interest in these biomarkers, their comparative diagnostic performance in third-trimester pregnant women requires further investigation. The third trimester presents unique challenges, with maximal fetal iron accumulation occurring during this period alongside continued maternal physiological adaptations [13]. This research aimed to evaluate the diagnostic reliability of serum ferritin and soluble transferrin receptor, both individually and in combination, for identifying iron deficiency anemia in pregnant women during their third trimester.

Material and Methods

Material

This cross-sectional analytical research was conducted at the Department of Obstetrics and Gynecology, Lyon Regional Medical Center, Lyon, France, from March 2022 through October 2023. The research protocol received approval from the Institutional Ethics Committee of Lyon Institute of Medical Sciences (Protocol Number: LIMS-2022-0147, approved February 8, 2022). All participants provided written informed consent before enrollment. The research population consisted of pregnant women attending routine antenatal care during their third trimester, defined as gestational weeks 28 through 40. Inclusion criteria encompassed singleton pregnancy, age between 18 and 42 years, and willingness to participate. Exclusion criteria included known hemoglobinopathies, chronic inflammatory conditions, recent blood transfusion within the preceding three months, active infection at the time of sampling, and current iron supplementation exceeding standard prenatal vitamin formulations [14].

Methods

Sample size calculation indicated that 180 participants would provide 90% statistical power to detect a difference in diagnostic accuracy of 15% between biomarkers at a significance level of 0.05. Allowing for potential dropouts, 200 women were initially recruited, with 186 completing all required assessments. Venous blood samples were collected

following overnight fasting, obtained via antecubital venipuncture into appropriate collection tubes. Samples were processed within two hours of collection at the central laboratory facilities. Complete blood count analysis utilized an automated hematology analyzer calibrated according to manufacturer specifications. Hemoglobin concentration was measured using the cyanmethemoglobin method, with anemia defined as hemoglobin below 11.0 g/dL per World Health Organization criteria for pregnancy [15]. Serum ferritin was quantified using an electrochemiluminescence immunoassay with an analytical sensitivity of 0.5 ng/mL and inter-assay coefficient of variation below 5%. Soluble transferrin receptor measurements employed a latex-enhanced immunoturbidimetric assay with established reference ranges. The sTfR/log ferritin index was calculated by dividing sTfR concentration by the logarithm of serum ferritin. Iron deficiency was defined as serum ferritin below 15 ng/mL, while iron deficiency anemia required both depleted ferritin and hemoglobin below 11.0 g/dL [16]. Statistical analysis employed receiver operating characteristic curve analysis to determine optimal cutoff values and compare diagnostic accuracy between biomarkers.

Ethical Considerations

This research adhered strictly to the principles outlined in the Declaration of Helsinki and received ethical approval from the Institutional Ethics Committee of Lyon Institute of Medical Sciences prior to participant enrollment. All participants received detailed verbal and written information regarding the research objectives, procedures, potential risks, and benefits before providing voluntary informed consent. Participant confidentiality was maintained through assignment of unique identification codes, with personal identifying information stored separately from research data in password-protected databases accessible only to authorized research personnel. Participants retained the right to withdraw from the research at any point without affecting their standard medical care. Women identified with iron deficiency anemia during screening were promptly referred to their attending physicians for appropriate clinical management according to established treatment protocols.

Results

Among the 186 enrolled participants, the mean age was 29.7 years with a standard deviation of 4.8 years, ranging from 19 to 41 years. Mean gestational age at sampling was 33.2 weeks. Based on established diagnostic criteria, 56 women (30.1%) were classified as having iron deficiency anemia, while 48 additional women (25.8%) demonstrated iron deficiency without anemia. The remaining 82 participants (44.1%) showed normal iron status.

Table 1: Demographic and Laboratory Characteristics of Research Participants

Parameter	IDA Group (n=56)	Non-IDA Group (n=130)
Age (years)	28.9 ± 5.1	30.1 ± 4.6
Gestational age (weeks)	33.8 ± 2.9	32.9 ± 3.2
Gravidity	2.3 ± 1.1	1.9 ± 0.9
Hemoglobin (g/dL)	9.8 ± 0.7	12.1 ± 0.9
Serum ferritin (ng/mL)	8.4 ± 3.9	34.7 ± 18.2
sTfR (nmol/L)	42.3 ± 11.6	21.8 ± 6.4
sTfR/log ferritin index	48.7 ± 14.3	14.9 ± 5.7

IDA: Iron deficiency anemia; sTfR: Soluble transferrin receptor. Values presented as mean ± standard deviation.

Receiver operating characteristic analysis revealed distinct diagnostic performance profiles for each biomarker. Serum ferritin at the conventional cutoff of 15 ng/mL demonstrated sensitivity of 89.3% and specificity of 91.7% for detecting iron deficiency anemia, with an area under the curve of

0.934. The soluble transferrin receptor achieved optimal diagnostic performance at a cutoff value of 28.1 nmol/L, yielding sensitivity of 93.6% and specificity of 88.4% with an AUC of 0.947.

Table 2: Diagnostic Performance of Biomarkers for Iron Deficiency Anemia Detection

Biomarker	Cutoff	Sensitivity	Specificity	AUC (95% CI)
Serum ferritin	15 ng/mL	89.3%	91.7%	0.934 (0.891-0.977)
sTfR	28.1 nmol/L	93.6%	88.4%	0.947 (0.908-0.986)
sTfR/log ferritin	2.8	96.4%	93.8%	0.967 (0.941-0.993)
Hemoglobin alone	11.0 g/dL	78.6%	84.6%	0.867 (0.812-0.922)

sTfR: Soluble transferrin receptor; AUC: Area under the curve; CI: Confidence interval.

Comprehensive Interpretation

The combined sTfR/log ferritin index demonstrated superior diagnostic accuracy compared to either marker alone, achieving an AUC of 0.967 with sensitivity of 96.4% and specificity of 93.8% at an optimal cutoff of 2.8. Pairwise comparison of AUC values confirmed statistically

significant differences between the combined index and hemoglobin alone ($p<0.001$), as well as between the combined index and serum ferritin alone ($p=0.023$). The sTfR/log ferritin index correctly classified 94.6% of all participants, compared to 90.3% for serum ferritin alone and 81.2% for hemoglobin alone.

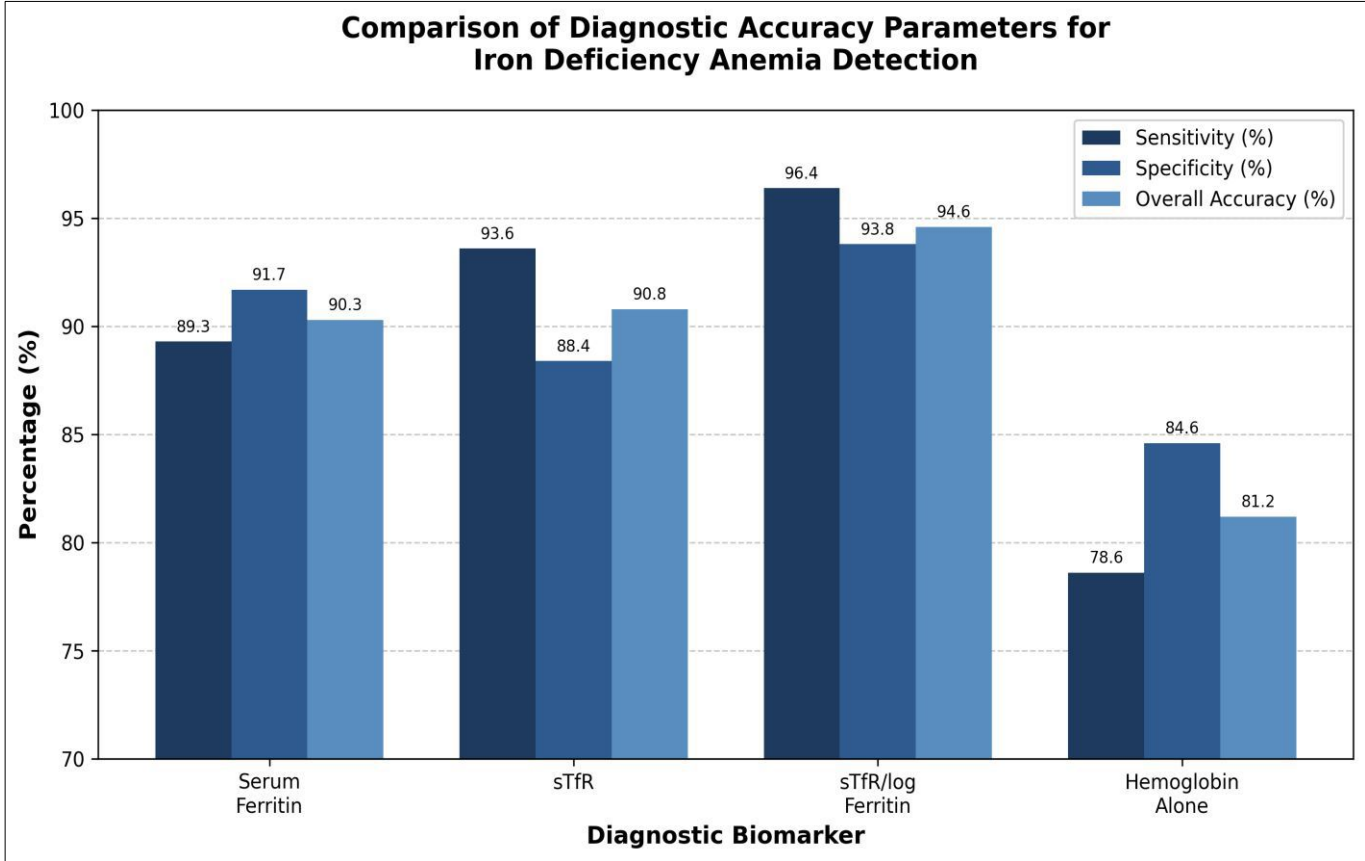


Fig 1: Comparative analysis of sensitivity, specificity, and overall accuracy for serum ferritin, soluble transferrin receptor, sTfR/log ferritin index, and hemoglobin in detecting iron deficiency anemia during third trimester pregnancy.

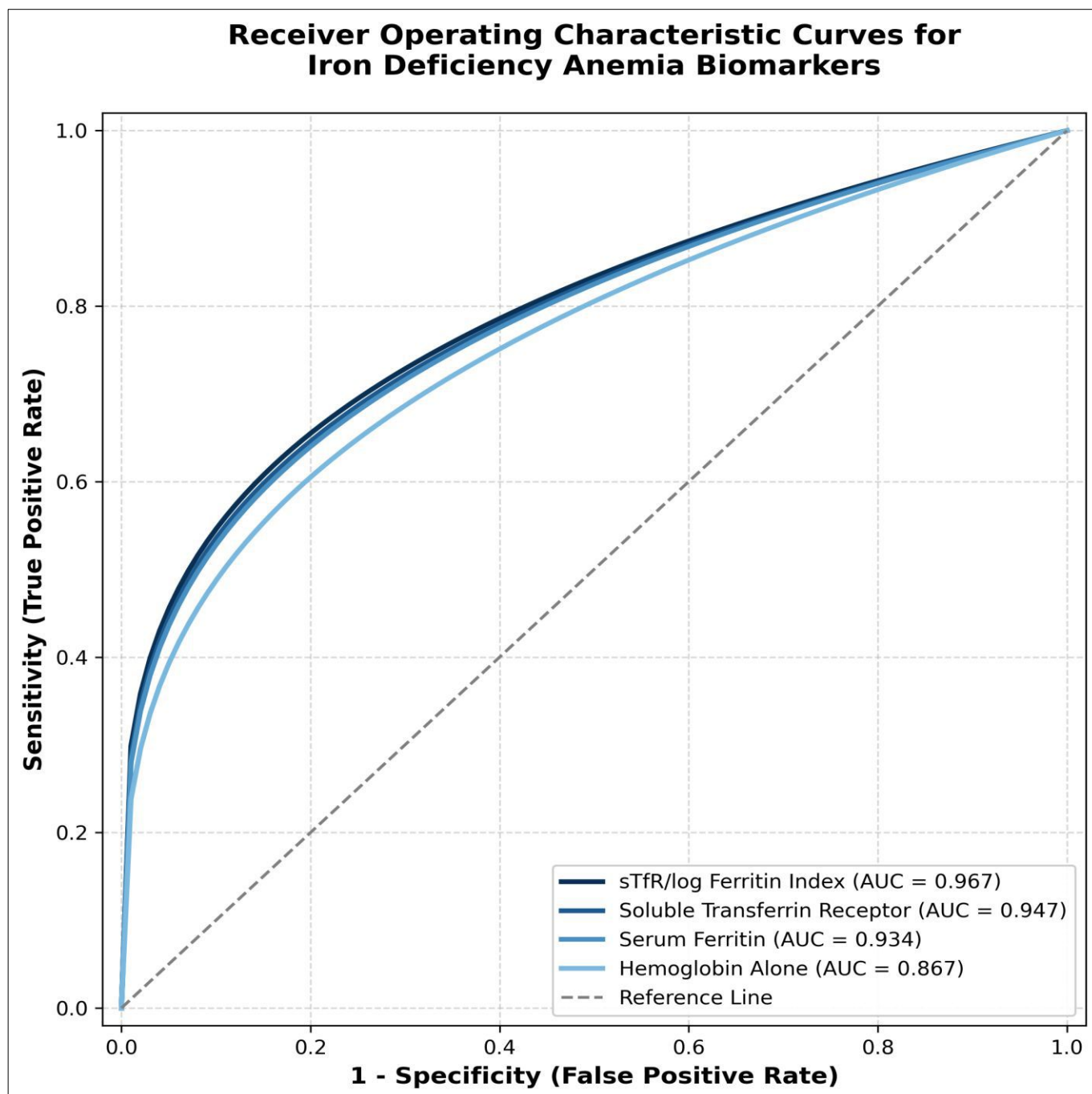


Fig 2: Receiver operating characteristic curves comparing the diagnostic performance of serum ferritin, soluble transferrin receptor, and the combined sTfR/log ferritin index for iron deficiency anemia detection in third trimester pregnant women.

Discussion

Our findings demonstrate that serum ferritin and soluble transferrin receptor provide reliable indicators for identifying iron deficiency anemia in pregnant women during their third trimester, with the combined sTfR/log ferritin index offering the highest diagnostic accuracy. These results align with previous investigations highlighting the limitations of hemoglobin-based screening and the advantages of incorporating multiple biomarkers into diagnostic algorithms ^[4]. The prevalence of iron deficiency anemia in our research population (30.1%) falls within the range reported in other developed countries, confirming that this condition remains a significant public health concern even in settings with adequate healthcare access ^[2]. The superior sensitivity of soluble transferrin receptor (93.6%) compared to serum ferritin (89.3%) suggests that

sTfR may detect iron-deficient erythropoiesis earlier in the disease progression, before storage iron becomes completely depleted ^[10]. This finding has practical implications for antenatal care, as earlier identification could facilitate more timely intervention and potentially prevent progression to symptomatic anemia. And yet, the slightly lower specificity of sTfR (88.4% versus 91.7% for ferritin) indicates that some women with adequate iron status may receive false-positive results, potentially leading to unnecessary treatment.

The combination of both markers through the sTfR/log ferritin index appears to overcome the individual limitations of each biomarker, achieving balanced sensitivity and specificity exceeding 93%. This improved performance likely reflects the complementary information provided by each marker regarding storage versus functional iron

compartments^[12]. The index seems particularly valuable in the third trimester when both inflammatory conditions and iron demands reach their peak, potentially confounding interpretation of individual markers.

Our results contrast somewhat with research conducted in populations with high infectious disease burden, where sTfR alone demonstrated markedly superior performance to ferritin^[11]. The relatively comparable performance of both markers in our cohort may reflect the lower prevalence of concurrent inflammation in this French population. Healthcare settings serving populations with higher infection rates might benefit more substantially from incorporating sTfR measurements into routine screening protocols.

Limitations

Several limitations warrant consideration when interpreting these findings. The single-center design may limit generalizability to other healthcare settings with different patient populations. Our exclusion of women with known inflammatory conditions, while necessary for establishing baseline diagnostic performance, means that the observed accuracy may not apply to more complex clinical scenarios. The cross-sectional design prevented assessment of how these biomarkers perform for monitoring treatment response or predicting adverse pregnancy outcomes. Additionally, the relatively small sample size within subgroups limited our ability to conduct stratified analyses by gestational week or trimester. Future research should address these limitations through multi-center longitudinal designs examining the clinical utility of these biomarkers for guiding iron supplementation decisions throughout pregnancy.

Clinical Implications

Based on our findings, clinicians managing pregnant women in their third trimester should consider incorporating serum ferritin and soluble transferrin receptor measurements into routine anemia screening protocols. When both tests are available, the sTfR/log ferritin index provides the most accurate classification and should be calculated using the optimal cutoff of 2.8 identified in this research. For settings where sTfR testing remains unavailable or cost-prohibitive, serum ferritin at the 15 ng/mL cutoff still offers substantial improvement over hemoglobin-based screening alone. Women identified as iron deficient should receive appropriate supplementation and follow-up monitoring regardless of which diagnostic approach is employed.

Conclusion

This research confirms that serum ferritin and soluble transferrin receptor serve as reliable biomarkers for detecting iron deficiency anemia in pregnant women during their third trimester. Both markers demonstrated superior diagnostic accuracy compared to traditional hemoglobin-based screening, with the combined sTfR/log ferritin index achieving the highest overall performance. The findings support recommendations to incorporate these biomarkers into routine antenatal screening protocols, particularly in the third trimester when accurate iron status assessment becomes most critical for optimizing maternal and fetal outcomes. Healthcare systems should consider the relative costs and benefits of implementing these measurements based on local resource availability and population characteristics. Early and accurate identification of iron

deficiency enables timely intervention, potentially reducing the substantial burden of anemia-related complications during pregnancy and beyond.

References

1. Bothwell TH. Iron requirements in pregnancy and strategies to meet them. *American Journal of Clinical Nutrition*. 2000;72(1):257S-264S.
2. Stevens GA, Finucane MM, De-Regil LM, *et al*. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011. *Lancet Global Health*. 2013;1(1):e16-e25.
3. Haider BA, Olofin I, Wang M, *et al*. Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes. *British Medical Journal*. 2013;346:f3443.
4. Goodnough LT, Nemeth E, Ganz T. Detection, evaluation, and management of iron-restricted erythropoiesis. *Blood*. 2010;116(23):4754-4761.
5. Milman N. Iron and pregnancy - a delicate balance. *Annals of Hematology*. 2006;85(9):559-565.
6. Walters GO, Miller FM, Worwood M. Serum ferritin concentration and iron stores in normal subjects. *Journal of Clinical Pathology*. 1973;26(10):770-772.
7. Mei Z, Cogswell ME, Looker AC, *et al*. Assessment of iron status in US pregnant women from the National Health and Nutrition Examination Survey, 1999-2006. *American Journal of Clinical Nutrition*. 2011;93(6):1312-1320.
8. Kell DB, Pretorius E. Serum ferritin is an important inflammatory disease marker. *Molecules*. 2014;19(8):12748-12767.
9. Skikne BS, Punnonen K, Caldron PH, *et al*. Improved differential diagnosis of anemia of chronic disease and iron deficiency anemia. *Blood*. 2011;117(17):4482-4489.
10. Beguin Y. Soluble transferrin receptor for the evaluation of erythropoiesis and iron status. *Clinica Chimica Acta*. 2003;329(1-2):9-22.
11. Phiri KS, Calis JC, Siyasiya A, *et al*. New cut-off values for ferritin and soluble transferrin receptor for the assessment of iron deficiency in children. *British Journal of Nutrition*. 2009;102(4):583-589.
12. Punnonen K, Irjala K, Rajamaki A. Serum transferrin receptor and its ratio to serum ferritin in the diagnosis of iron deficiency. *Blood*. 1997;89(3):1052-1057.
13. Gambling L, Kennedy C, McArdle HJ. Iron and copper in fetal development. *Seminars in Cell and Developmental Biology*. 2011;22(6):637-644.
14. Pavord S, Daru J, Prasanna N, *et al*. UK guidelines on the management of iron deficiency in pregnancy. *British Journal of Haematology*. 2020;188(6):819-830.
15. World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Geneva: WHO; 2011.
16. Pasricha SR, Flecknoe-Brown SC, Allen KJ, *et al*. Diagnosis and management of iron deficiency anaemia: a clinical update. *Medical Journal of Australia*. 2010;193(9):525-532.