

Original Research Article

Soluble transferrin receptor levels among pregnant women in Port Harcourt, Nigeria

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ABSTRACT

Background: Anaemia in pregnancy is one of the medical problems that affect pregnant women in developing countries. It contributes considerably to the morbidity and mortality in pregnancy especially in areas where malaria is endemic. The concentration of soluble transferrin receptor is a reflection of body iron status. It is therefore, a valuable tool for assessing bone marrow erythropoietic activity and can also be a marker of iron deficiency.

Methods: This study evaluated the levels of soluble transferrin receptor in pregnant subjects. A total of 275 pregnant subjects of age 20 to 45 years and 88 age-matched apparently healthy control subjects were involved in this study. Individuals who had severe anaemia, HIV infection, sickle cell disease or Hookworm infestation were excluded from this study. Five millilitres (5ml) of blood were collected from each consenting subject for the analysis of soluble transferrin receptor, haematological parameters and iron parameters using appropriate methods.

Results: The mean value of parameters for the study subjects were sTfR(21.16±9.11 nmol/L), Hb(9.05±1.22 g/dl), TIBC(332.61±80.87 µg/dl), Serum Iron(97.91±39.44 µg/dl), LIBC(239.36±80.52 µg/dl), TS(30.24±11.00 %) while for control subjects were sTfR(18.21±3.77 nmol/L), Hb(12.19±0.66 g/dl), TIBC(261.94±52.49µg/dl), Serum Iron(107.10±34.77 µg/dl), LIBC(155.52±61.25 µg/dl), TS(42.81±18.03 %). The mean sTfR levels in pregnant women was significantly lower (p<0.001) than in control subjects. The pregnant women also had significantly lower values of Hb (p<0.001), serum iron (p=0.038) and TS (p<0.001) values, and significantly higher values of TIBC(p<0.0001) and LIBC(p<0.0001). There were also increases in soluble transferrin receptor levels from first to third trimesters. The sensitivity of sTfR as against Serum iron parameters from this study was 76% while the specificity was 50%. The positive predictive value was 60% while the negative predictive value was 50%.

Conclusions: sTfR may be a useful supplementary diagnostic tool in the management of anaemia in pregnancy.

Keywords: Anaemia, Port Harcourt, Pregnancy, Soluble transferrin receptor

INTRODUCTION

Anaemia is defined as a reduction in red cell mass in blood resulting in a drop in the amount of oxygen supply to meet in the metabolic needs of the body.¹ It affects about 1.62 billion people (25%), among which, about 56 million are pregnant women.² Anaemia can also be classified in the population, based on the haemoglobin values, into severe, moderate, mild or normal.³ Based on

gender, the cut-off haemoglobin levels for male adults is Hb<13 g/dl, while that of adult females is Hb<11.5g/dl.⁴ Anaemia in pregnancy has been reported to be one of the problems that affect pregnant women in developing countries.⁵ Anaemia in pregnancy is defined as haemoglobin concentration less than 11.0 g/dl or 10.5 g/dl in the second half of pregnancy.⁶ It can be divided into mild anemia (Hb 10.0-10.9 g/dL), moderate anaemia (7.0-9.9 g/dL) and severe anaemia (Hb <7.0 g/dL).

Soluble transferrin receptor (STfR) protein is a single polypeptide chain of 85kDa and is derived from transferrin receptor.⁷ Soluble transferrin receptor is derived from the proteolytic cleavage of the extracellular domain of transferrin receptor.⁸ The concentration of soluble transferrin receptor is a reflection of the receptor density on the cells and also the number of cells that express the receptors. Thus, it is closely related to the cellular iron demands and to erythroid proliferation rate.^{8,9}

Soluble transferrin receptor has been shown to be unaffected by chronic disease and inflammation, unlike serum ferritin and transferrin concentrations.⁷ It is therefore, a valuable quantitative assay of marrow erythropoietic activity and also a marker of tissue iron deficiency.¹⁰ There is also an exponential increase in soluble transferrin receptor in response to the degree of anaemia.¹⁰ Soluble transferrin levels are not influenced by acute phase reactions or hemodilution in pregnancy. High levels of soluble transferrin receptor in pregnancy in the presence of normal haemoglobin can indicate onset of mild iron deficiency.¹¹ The concentration of soluble transferrin receptor rises in iron deficiency anaemia but not in anaemia of chronic disease or iron overload.^{12,13} The concentration of soluble transferrin receptor is a reflection of body iron status and erythropoietic activity.¹⁰

METHODS

Study Population

This study involved 275 pregnant women, of age 20 to 45 years, and 88 age-matched apparently healthy non-pregnant women as control subjects. The bio-data and medical history of the subjects were obtained using questionnaire.

Informed consent

The subjects that participated in this research gave their informed consent to participate in this study. All information was treated with confidentiality.

Inclusion criteria

Pregnant women who were attending clinic in public health facilities in Port Harcourt, Nigeria.

Exclusion criteria

Pregnant women who had sickle cell disease, HIV infection, hookworm infestation or severe malaria.

Study Duration

This study was carried out between March and September, 2017.

Sample collection

Five millilitres (3 ml) of blood was collected from each subject. Three milliliters (3ml) of the sample were put in sample containers with ethylene diethyltetraacetic acid (EDTA) anticoagulated bottles for the assayed of haematological parameters.

Two millimetres (2 ml) of the sample were put in plain containers and centrifuged. The serum obtained was stored at -20°C prior to analysis of biochemical parameters.

Methodology

Soluble Transferrin receptor (using immunoenzymatic methods), Serum Iron and Total iron binding capacity were analyzed using colorimetric methods. Hematological parameters were analyzed using Sysmex hematology autoanalyzer.

Statistical Analysis

The data generated was analyzed using SPSS version 22. p-values less than 0.05 were considered statistically significant.

RESULTS

Table 1 shows the Mean±SD of parameters for the pregnant women and control subjects. The levels of soluble transferrin receptor (p<0.001), total iron binding capacity (p<0.001) and latent iron binding capacity (p<0.001) were significantly higher in the pregnant women than in the control subjects. The levels of haemoglobin (p<0.001), serum iron (p=0.038) and transferrin saturation (p<0.001) were significantly lower in the pregnant women compared to the control subjects.

Table 1: Mean±SD of Parameters for Pregnant Women and Control Subjects.

Subjects/ Parameters	sTfR(mmol/l)	Hb(g/dl)	TIBC(µg/dl)	SI(µg/dl)	LIBC(µg/dl)	TS(%)
Pregnant women (n=275)	22.16±9.11	9.05±1.22	332.61±80.87	97.91±39.44	239.36±80.52	30.24±11.00
Control (n=88)	18.21±3.77	12.19±0.66	261.94±52.49	107.10±34.77	155.52±61.25	42.81±18.03
p-value	<0.001	<0.001	<0.001	0.038	<0.001	<0.001

Key: sTfR- Soluble transferrin receptor, Hb- Haemoglobin, TIBC- Total iron binding capacity, SI- Serum iron, LIBC- Latent iron binding capacity, TS- Transferrin saturation

Table 2 shows the Mean±SD of parameters for the pregnant women according to trimesters. There were significant differences in the levels of soluble transferrin receptor (p=0.002), total iron binding capacity (p<0.006),

serum iron (p=0.02) and latent iron binding capacity (p=0.01) across the trimesters. There were no significant differences in the levels of haemoglobin (p=0.184) and transferrin saturation (p=0.077) respectively.

Table 2: Mean ±SD of Parameters for Pregnant Women according to Trimesters.

Trimesters/Parameters	sTfR(mmol/l)	Hb(g/dl)	TIBC(µg/dl)	SI(µg/dl)	LIBC(µg/dl)	TS(%)
1 st Trimester (n=91)	21.34±12.86 ^a	9.20±0.95	340.90±80.89 ^a	93.56±39.66 ^a	247.34±75.74 ^a	27.90±11.86
2 nd Trimester (n=16)	21.76±6.06 ^a	9.02±1.28	321.97±80.73 ^b	98.15±40.02 ^b	229.25±81.52 ^b	31.43±12.29
3 rd Trimester (n=21)	28.71±6.76 ^b	8.70±1.61	375.17±65.34 ^c	113.21±31.14 ^c	279.35±78.88 ^c	30.99±9.16
p-value	0.002	0.184	0.006	0.02	0.01	0.077

ANOVA, followed by Tukey’s posthoc test. Numbers in the same column with different alphabets are statistically different (p<0.05).

Figure 1 shows the correlation plot of soluble transferrin receptor versus total iron binding capacity. There was a positive, weak correlation between soluble transferrin receptor versus total iron binding capacity. This indicates that soluble transferrin receptor levels increased as the total iron binding capacity increased. Thus, the levels of soluble transferrin receptor reflect the body’s need for iron.

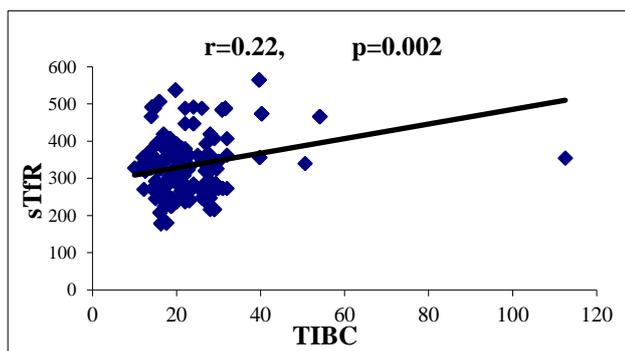


Figure 1: Correlation plot of sTfR vs TIBC.

Figure 2 shows the correlation plot of soluble transferrin receptor versus serum iron. There was a negative, weak correlation between soluble transferrin receptor versus serum iron. Thus, the levels of soluble transferrin receptor decreased as the levels of iron in the serum increased.

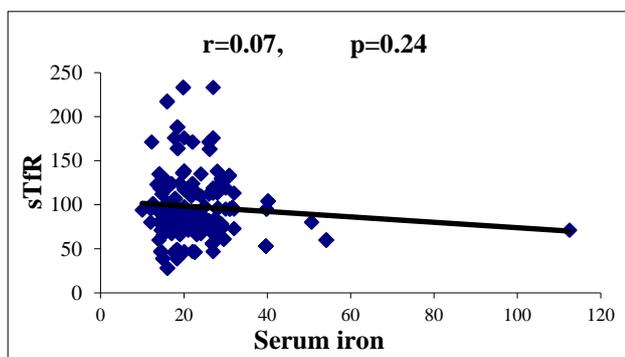


Figure 2: Correlation plot of sTfR vs Serum iron.

Figure 3 shows the correlation plot of soluble transferrin receptor versus latent iron binding capacity. There was a positive, weak correlation between soluble transferrin receptor versus latent iron binding capacity. This correlation indicates that the levels of soluble transferrin receptor increased as latent iron binding capacity of the body cells increased.

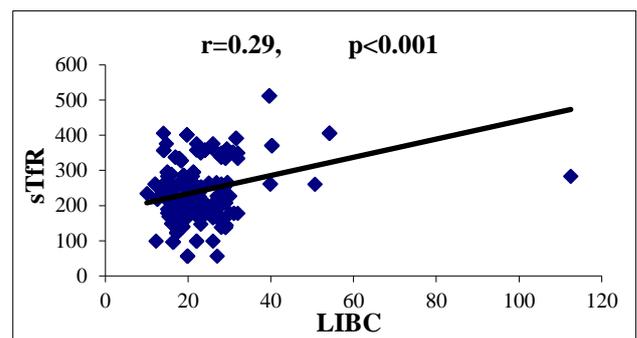


Figure 3: Correlation plot of sTfR vs LIBC.

Figure 4 shows the correlation plot of soluble transferrin receptor versus transferrin saturation. There was a negative, weak correlation between soluble transferrin receptor versus transferrin saturation. This implies that the levels of soluble transferrin receptor reduced as the transferrin saturation levels increased.

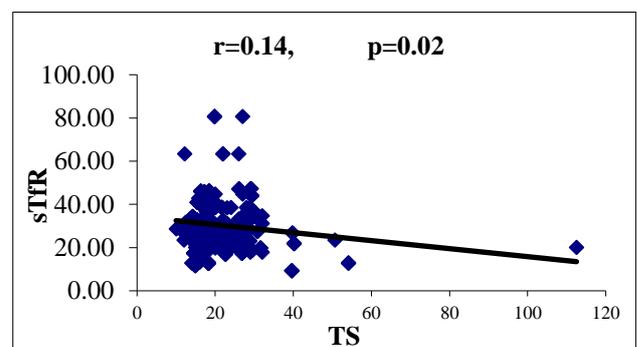


Figure 4: Correlation plot of sTfR vs TS.

DISCUSSION

The haemoglobin level of the pregnant women was significantly lower than control subjects. This is probably because hypochromic red cells are usually released into circulation in cases of anaemia or functional iron deficiency.¹⁴

Soluble transferrin receptor was significantly higher in the pregnant women as well as total iron binding capacity (TIBC) and LIBC. This study also observed a significant decrease in serum iron, transferrin saturation (TS) in the pregnant subjects compared to the control subjects.

This agrees with an earlier finding which indicated that soluble transferrin is not affected by pregnancy unless there is presence of iron deficiency which occurs in pregnancy.¹⁵ Another report indicates that in individuals with iron deficiency anaemia there is an increased level of sTfR compared to control subjects.¹⁶

In this study there was a decrease in haemoglobin and serum iron levels, and an increase in TIBC and LIBC in the pregnant subjects compared to the control. This finding agrees with the work of other studies.¹⁷ Iron deficiency has been reported to be the single micronutrient deficiency that affects 50% of the world population, especially pregnant women. This is probably due to the requirement of iron during pregnancy.¹⁷

Serum iron, TIBC and TS are biochemical parameters that are used for screening and monitoring iron deficiency and iron overload.¹⁸ There was a significant increase in serum transferrin receptor level with the highest level occurring in the third trimester. This finding agrees with an earlier work which reported that there is a gradual increase in sTfR as the age of pregnancy increases.¹³ sTfR is an indicator of iron status in pregnancy.¹³ sTfR has been reported to increase in iron deficiency anaemia and the level is a reflection of the functional iron status of the subjects and also erythropoietic activity.^{20,21}

sTfR generally increases during pregnancy, and the increase reflects the body's attempt at increasing the intracellular iron concentration.^{22,23} It is also an indication of the body's ability to deal with infections.²⁴ sTfR is a useful tool in discriminating and distinguishing iron deficiency anaemia in pregnancy and anaemia of chronic disease.²⁵

sTfR correlated significantly with indicators of iron needs of the body namely TIBC and LIBC. The correlation between sTfR and Serum Iron and Transferrin Saturation was negative. However these correlations were weak. The sensitivity of sTfR as against Serum iron parameters from this study was 76% while the specificity was 50%. The positive predictive value was 60% while the negative predictive value was 50%. Thus, sTfR may be employed as a supplementary diagnostic tool in the management of anaemia in pregnancy.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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