Original Research Article

**Establishing the normal reference range for Serum Ferritin, Percentage Transferrin saturation and Soluble Transferrin Receptor Levels in Nigerian Population.**

**ABSTRACT**

**BACKGROUND:** Iron markers are valuable in assessing iron deficiency and iron deficiency anaemia. Interpretations of iron parameters depend on values obtained from white populations despite variations in mean values of iron markers from region to region, race, age, gender, and disease states.

**OBJECTIVES**: This study aims to establish a normal reference range of Serum Ferritin, Percentage Transferrin saturation, and Soluble Transferrin Receptor Levels in the Nigerian population. It is focused on the notable gap in population-specific hematologic data.

**METHODS**: This is a cross-sectional study involving one hundred and twelve (112) healthy adult persons aged 18-70 years. Full blood count (FBC), and soluble Transferrin receptor assay were done. Percentage transferrin saturation (TSAT) was calculated from the assay of the serum iron and the total iron binding capacity (TIBC) using the colourimetric method. Data was analyzed using SPSS software version 22.0. The level of statistical significance was set at p-value < 0.05.

**RESULTS:** The mean serum ferritin, TSAT and sTfR were 98.38±52.03ng/ml, 32.73±6.86%, and 17.68±6.11nmol/L respectively. The mean serum ferritin for males was 106.94±54.62 while that of females was 73.90±34.02ng/ml. There was no significant statistical difference in the mean TSAT and sTfR among males and females. The reference range of serum ferritin, TSAT, and sTfR among participants was 20.0-218.4ng/ml, 21.5-47.4% and 8.8-26.9nmol/L.

**CONCLUSION:** The mean serum ferritin values in male participants in our study were almost twice that of the female participants. Serum ferritin appears to be higher in blacks than in the white population. There is a wide variation in sTfR levels from one population to another. The findings in this study are important for improving the accuracy of iron deficiency diagnoses, for patient-specific clinical assessments in African diagnostic centres.

Keywords: Ferritin, soluble transferrin receptor, TSAT, reference range, apparently Healthy.

**INTRODUCTION**

Iron deficiency is more prevalent in the developing world with effects more pronounced in infants and women of childbearing age, however, it affects all human populations with men inclusive [1]. Up to 50% of anaemic cases worldwide have been linked to iron deficiency with about 2 billion persons said to be anaemic [2]. Anaemia is associated with diminished cognitive function and increased mortality and morbidity worldwide [3].

Cognitive and motor development are adversely impacted in children with iron deficiency anaemia while adults may suffer from reduced productivity, exhaustion and diminished physical performance. A general increase in mortality and morbidity are common consequences of anaemia in the elderly population [4,5].

Iron status in the human population is best measured using serum ferritin and transferrin receptors. Serum ferritin assesses iron storage. However, serum ferritin an iron marker for assessing iron status is limited in inflammation conditions. Serum ferritin concentration is falsely elevated in conditions of infection and inflammation.

Transferrin receptor concentrations are not affected by inflammation and thus combining serum ferritin and soluble transferrin receptor provides a unique way of differentiating inflammation from iron deficiency [6].

A serum ferritin value of less than <30ng/ml defines absolute iron deficiency in the human population [7]. A study by Jacobs et al in the UK shows a mean serum ferritin of 69.2ng/ml in men and 34.8ng/ml in females [8]. More recent studies on serum ferritin by Beutler et al show a value of 59.15ng/ml among African-American women and 142.20ng/ml among African American Men [9]. The reference value for serum ferritin in a study done by Munoz M among adults shows a value of 30–360 ng/ml [ 10].

Establishing ranges in normal populations is essential to interpreting serum transferrin receptor levels in clinical settings due to the non-availability of international standards and standardized methodology. Ranges in serum transferrin receptor levels in some related human studies range from 2.2 to 5.0 in adult males and 1.9 to 4.4 mg/l in adult females [11, 12]. A transferrin saturation (TSAT) of less than 15% has been demonstrated to be insufficient for erythropoiesis [13].

Iron markers are valuable in the assessment of iron deficiency as well as iron deficiency anaemia. The levels of iron markers are used in evaluating patients with iron deficiency with the hope of making a diagnosis, monitoring patients and for research purposes. There are variations in mean values of most haematological parameters from region to region, age, race, gender and disease states. In most Literature, values from white populations are usually dependent on. There is a paucity of information on serum Ferritin, Percentage Transferrin saturation and Soluble Transferrin Receptor Levels in Apparently Healthy Nigerian Populations, hence the need for this study.

METHODOLOGY:

Study Design

This is a cross-sectional study conducted at the University of Ilorin Teaching Hospital, Ilorin, Kwara state, Nigeria and was carried out

between July 2017 and October 2018.

Study Population

One hundred and twelve (112) healthy adult persons aged 18-70 years were recruited consecutively among hospital staff, Medical and Technologist students and Patient's relatives who gave consenting agreements. The recruitment was carried out using the convenience sampling method. The study included 97 males and 29 females.

Inclusion Criteria

Healthy adult volunteers aged 18-70 who gave consent were also recruited.

Exclusion Criteria

-Those on hematinics

-Volunteers who are blood donor

-Those who had a blood transfusion in the last year

-Volunteer with febrile illness

Methods

Study Tools:

Written and verbal informed consent was taken. The sociodemographic data of the participants were collected using a self-administered structured questionnaire. With an aseptic technique, 4mls of venous blood was collected and dispensed into a well-labelled vacutainer EDTA bottle. Full blood count (FBC) was run the same day using 5 parts automated haematology analyzer, Sysmex KX-21 (Sysmex Corporation, Kobe, Japan) Serum ferritin was measured using ELISA with human Fe (ferritin) Elisa kit ( Elabscience, USA). Soluble Transferrin receptor assay was carried out using the sandwich ELISA methodology as per the manufacturer's insert in the kit (Monobind Inc Lake Forest, CA USA) The procedure was done according to the manufacturer's instruction.

Blood samples of participants with normal haemoglobin levels and normal red blood indices and those with serum ferritin ≥12ng/ml were subsequently stored at -200C for soluble transferrin receptor levels. Percentage transferrin saturation was calculated from an assay of the serum iron and TIBC using the colourimetric method (POINTE SCIENTIFIC, INC iron/TIBC test kit, USA).

ETHICAL CONSIDERATION

Ethical approval for this study was obtained from the Committee on Ethics Research of the University of Ilorin Teaching Hospital, Ilorin.

An informed written and verbal consent was obtained from the participants using a consent form.

STATISTICAL ANALYSIS

The Reference range and the mean values of the serum ferritin, TSAT and sTfR were analysed using descriptive and inferential statistics on SPSS software version 22.0. The reference limits of 95% proportion were determined from the 2.5th percentile and the 97.5th percentile

The level of statistical significance was set at p-value < 0.05.

**RESULTS**

The study population 112 participants including 83(74.1%) males and 29(25.9%) females. The majority of the participants are between the ages of 46-65yrs. See Table 1.

The mean Serum ferritin, TSAT and sTfR were 98.38±52.03ng/ml, 32.73±6.86% and 17.68±6.11nmol/L respectively. The mean serum ferritin for males was 106.94±54.62 while that of females was 73.90±34.02ng/ml with a higher statistically significant difference, a p-value of 0.007. There was no significant statistical difference in the mean TSAT and sTfR among males and females. Tables 2 and 3.

The reference range of serum ferritin, TSAT, and sTfR among participants was 20.0-218.4ng/ml, 21.5-47.4% and 8.8-26.9nmol/L. See Table 4.

**DISCUSSION**

The mean serum ferritin for males in our study was 106.94±54.62 ng/ml while that of females was 73.90±34.02ng/ml. This result is similar to the report of Odunukwe in Lagos, Nigeria where the mean ferritin among adult males and female participants was 99.6±50.5ng/ml and 66.5±44ng/ml respectively [14].

The result of our findings is higher than that of Oluboyede et al done at Lagos with a mean value of 72.4ng/ml and 34ng/ml in males and females respectively. This observed difference could be because anaemic and patients with low red cell indices were not excluded from the later study [15].However, the mean serum ferritin values in the male participant in our study were almost twice that of the female participant similar to the report of Oluboyede et al. Jacob et al recorded a lower mean serum ferritin of 69.2ng/ml in men and 34.8ng/ml in women [8]. This is not surprising as serum ferritin appears to be higher in blacks than in white populations as reported by Beutler et al [16].The reference range of serum ferritin in our study was 20.0-218.4ng/ml.

The mean soluble transferrin receptor in our study was 17.68±6.86ng/ml. Reference range of 8.8-26.9nmol/L. The mean sTfR in males was 17.76±6.17nmol/L while for females 17.47±6.03nmol/L was recorded among the female participants. Allen et al in the USA reported a mean value of 19.6 ±5.0nmol/L among the healthy adult population. The mean value in Males was 20.1 ±4.8nmol/L and in premenopausal females, 19.0 ±4.9nmol/L [17]. A similar study done among the Arabs and non-whites by Knox-Macaulay shows a mean value of 21.8±7.7nmol/L with a reference range of 10.7-38.7nmol/L [18].A study done by Efobi R et al in PortHarcourt reported a lower mean value of 10.4706±5.4118nmol/L with Males, 10.8nmol/L±5.76nmol/L and females, 9.6471±4.35nmol/L [19]. Van den Bosch et al reported a lower mean value of 13.53 ± 3.06nmol/L with a reference interval of 10.12-20.71nmol/L [20].Higher values of mean serum sTfR compared to our findings were reported by Simek et al and Flower et al with a mean value of 21.65±9.4nmol/L and 66.24±1.12nmol/L [21,22].There appears to be a wide variation in sTfR levels from one population to another. Factors responsible for these variations may be the assay methodology and racial and genetic differences. Other factors may be attributable to environmental and dietary differences.

There was no significant difference in the mean values of serum sTfR among genders in our study as reported in some earlier studies done by Efobi et al, van den Bosch et al and Allen et al [17, 19, 21].

In healthy subjects, the concentration of sTfR concentrations offers a useful assessment of iron-deficient erythropoiesis [23].

The variations in the reference values in different sTfR assay kits limit its utilization. Standardization of the methodology used for the measurement of sTfR will enhance its usefulness.

The mean value of TSAT in our study was 32.73±6.86%. Male-32.74±6.72 and females- 32.70±7.37. The reference range of TSAT was 21.5-47.4%. The mean value of TSAT among males in our study is similar to the report of previous findings by Oluboyede et al in Nigeria and that of Jacobs et al in Wales where values of 29.4% and 30.6% were reported respectively [8, 15]. The mean value of TSAT among females in our study is similar to that of Cook et al with a value of 31.2% but in contrast to that of Oluboyede and Jacobs where values of 23.8% and 22.0% were reported [8, 15, 24]. The discrepancy in the findings of these two studies may be because Cook used a selected group in whom anaemia and iron-deficient erythropoiesis were excluded. There is no significant difference in the mean TSAT among the genders in our study and this is similar to the findings done by Milman et al [25].

The interpretation of iron markers in the presence of inflammatory disease requires careful evaluation. Serum transferrin receptor is a useful marker of iron deficiency in the presence of inflammatory disease. However, a study by Krawiec P et al shows that the diagnostic accuracy of soluble transferrin receptor/log ferritin index was superior to soluble transferrin receptor in iron deficiency anaemia recognition [26].

More studies on the diagnostic relevance of soluble transferrin receptor/log ferritin index in the diagnosis of iron deficiency anaemia in inflammatory diseases are expected.

**Conclusion:** The mean serum ferritin values of a male participant in our study were almost twice that of the female participant. Serum ferritin appears to be higher in blacks than in the white population. There was no significant difference in the mean values of serum sTfR and TSAT among genders in our study. There appears to be a wide variation in sTfR levels from one population to another.

This study provides information on the reference range of serum ferritin, serum sTfR and TSAT and the racial variations. However, studies with large sample sizes will be valuable in arriving at an acceptable reference range for serum ferritin among blacks.

**Declaration Section**

**Ethical considerations**: Approval from the ethical committee of the University of Ilorin Teaching Hospital.

**Availability of data and material:** Data and material for the research work are available

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

**REFERENCES**

1. Hurrell, R. F., (1997). Preventing iron deficiency through food fortification. *Nutrition Reviews* 55(6):210-22.

2. WHO/UNICEF/UNU. (2001). Iron deficiency anaemia: assessment, prevention, and control. Geneva: World Health Organization.

3. Graça, C., Wilson, A., and Ershler, W. B., (2004). Prevalence and outcomes of anaemia in geriatrics: a systematic Literature review. *The American Journal of Medicine*, 116(7), 3–10.

4. World Health Organization. (2015). The Global Prevalence of Anaemia in 2011, World Health Organization, Geneva, Switzerland.

5. World Bank.(2004). Public health at a glance.

6. Assessing the iron status of populations: including literature reviews: report of a Joint World Health Organization/Centers for Disease Control and Prevention Technical Consultation on the Assessment of Iron Status at the Population Level, Geneva, Switzerland. (2004). 2nd ed.

7. Camaschella, C., (2015). Iron-deficiency anaemia. *The New England Journal of Medicine*. 372(19):1832–1843.

8. Jacobs, A., Miller, F., Worwood, M.  [Beamish](https://pubmed.ncbi.nlm.nih.gov/?term=Beamish+MR&cauthor_id=5082548), M, R.,  [C A Wardrop](https://pubmed.ncbi.nlm.nih.gov/?term=Wardrop+CA&cauthor_id=5082548), C, A., (1972). Ferritin in the serum of normal subjects and patients with iron overload. *British Medical Journal,* 4(5834):206-208.

9. Beutler, E., West, C., (2005). Hematologic differences between African-Americans and whites: the roles of iron deficiency and alpha-thalassemia on haemoglobin levels and mean corpuscular volume. *Blood*, 106(2):740-745.

10. Munoz, M., Villar, I., and García-Erce, J, A., (2009). An update on iron physiology, *World Journal of Gastroenterology*, 15,(37):4617–4626.

11. Kolbe-Busch, S., Lotz, J., Hafner , G., Blanckaert, N, J, C., Claeys, G., Togni, G., Carlsen, J.,Roddiger, R., Thomas, L. (2002). Multicenter evaluation of a fully mechanized soluble transferrin receptor assay on the Hitachi and Cobasintegra analyzers. The determination of reference ranges. *Clinical Chemistry and Laboratory Medicine*, 40(5):529–536

12. Kratovil, T. DeBerardinis, J. Gallagher, N., Luban, N, L, C., Soldin, S, J., Wong, E, C, C. (2007). Age speciﬁc reference intervals for soluble transferrin receptor (sTfR). *Clinical Chimica Acta,* 380(1-2 ):222–224

13. Bothwell, T, H., Charlton, R, W., Cook J D., Funch, C, A. (1979). Iron metabolism in man. Oxford, Blackwell Scientific Publications.

14. Odunukwe, N, N., Salako, L, A., Okanny, C., Ahmed, O, A., Mafe, A, G., Efinemokwu, C., Raheem, T, Y. (2001) Serum ferritin and other haematological measurements in apparently healthy children with malaria parasitaemia in Lagos, Nigeria. *West African Journal of Medicine*. 20(1):42-5.

15. Oluboyede, O, A., Usanga, E, A., Lukanmbi, E, A.(1983) Evaluation of serum ferritin levels and other Hematological parameters in a Nigerian population. *Nigerian Medical Journal*.. 75(9):885-889.

16**.** Beutler, E., West, C. (2005). Hematologic differences between African-Americans and whites: the roles of iron deficiency and alpha-thalassemia on haemoglobin levels and mean corpuscular volume. *Blood.* 106(2):740-745.

17. Allen, J., Backstrom, K, R., Cooper, J .A., [Cooper](https://pubmed.ncbi.nlm.nih.gov/?term=Cooper+MC&cauthor_id=9550555), M, C.,  [Detwiler](https://pubmed.ncbi.nlm.nih.gov/?term=Detwiler+TC&cauthor_id=9550555), T, C.,  [Essex](https://pubmed.ncbi.nlm.nih.gov/?term=Essex+DW&cauthor_id=9550555) , D, W.,  [Fritz](https://pubmed.ncbi.nlm.nih.gov/?term=Fritz+RP&cauthor_id=9550555), R, P., [Means Jr](https://pubmed.ncbi.nlm.nih.gov/?term=Means+RT+Jr&cauthor_id=9550555), R, T.,  [Meier](https://pubmed.ncbi.nlm.nih.gov/?term=Meier+PB&cauthor_id=9550555), P, B.,  [Pearlman](https://pubmed.ncbi.nlm.nih.gov/?term=Pearlman+SR&cauthor_id=9550555), S, R.,  [Roitman-Johnson](https://pubmed.ncbi.nlm.nih.gov/?term=Roitman-Johnson+B&cauthor_id=9550555) , B, [Seligman](https://pubmed.ncbi.nlm.nih.gov/?term=Seligman+PA&cauthor_id=9550555) P, A. (1998). Measurement of the soluble transferrin receptor in the serum of healthy adults. *Clinical Chemistry*, 44 (1):35-39

18. Knox-Macaulay, H., Gravell, D., Elender, F. (2007) Serum Transferrin Receptor Status of Healthy Adult Arabs. *Annals of Clinical Laboratory Science*, 37(1):57-62.

19. Efobi, C. C., Nwogoh, B., Onyiaorah, I. V., Ejele, O, A. (2017) Soluble Transferrin Receptor levels of Apparently Healthy Adults in Port Harcourt, Nigeria. *Annals of Pathology And Laboratory Medicine*, 4(3):225-229.

20. Van den Bosch, G., Van den Bossche, J., Wagner, C. (2001). Determination of Iron Metabolism-related Reference Values in a Healthy Adult Population. *Clinical Chemistry*, 47(8):1465-1467.

21. Flowers, C. H., Skikne, B. S., Covell, A.M., Cook, J, D. (1989). The clinical measurement of serum transferrin receptor. *The Journal of Laboratory and Clinical Medicine*, 114(4):368-77.

22. Simek, M., Remkova, A., Kratochvilova, H., (2002). Serum transferrin receptor in the diagnosis of iron deficiency. *Bratislava Medical Journal*. 103(1):449-53.

23. Worwood, M. (2002). Serum transferrin receptor assays and their application. *Annals of Clinical Biochemistry*. 9 (39):21- 230.

24. Cook, J, D., Lipschitz, D, ., Miles, L, E, M.(1974). Serum ferritin is a measure of iron stores in normal subjects. *American Journal of Clinical Nutrition*, 27(7):681-687.

25. Milman, N., Ingerslev, J., Graudal, N. (1990) Serum ferritin and iron status in a population of ‘healthy’ 85-year-old individuals, *Scandinavian Journal of Clinical and Laboratory* *Investigation*, 50(1):77-83.

26. Krawiec P, Pac-Kożuchowska E. (2019) Soluble transferrin receptor and soluble transferrin receptor/log ferritin index in iron deficiency anaemia in pediatric inflammatory bowel disease. *Digestive and Liver Disease*, 51(3):352-357.

**Table 1: The Summary of Demographic Characteristics**

|  |  |  |  |
| --- | --- | --- | --- |
| N=112 | | Frequency | Per cent |
| SEX | Male | 83 | 74.1 |
| Female | 29 | 25.9 |
|  |  |  |  |
| Age\_group | </= 25 | 7 | 6.3 |
| 26 – 35 | 8 | 7.1 |
| 36 – 45 | 13 | 11.6 |
| 46 – 55 | 31 | 27.7 |
| 56 – 65 | 33 | 29.5 |
| > 65 | 20 | 17.9 |
|  |  |  |  |
| Occupation | Trader | 15 | 13.4 |
| Civil servant | 64 | 57.1 |
| Teacher | 5 | 4.5 |
| Student | 3 | 2.7 |
| Retired | 2 | 1.8 |
| Others | 23 | 20.5 |
|  |  |  |  |
| EDUCATION | None | 14 | 12.5 |
| Primary | 16 | 14.3 |
| Secondary | 81 | 72.3 |
| Tertiary | 1 | .9 |
|  |  |  |  |
| RELIGION | Christianity | 41 | 36.6 |
| Islam | 71 | 63.4 |

**Table 2: Mean values of Serum Ferritin. TSAT and sTfR**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **N=112** |  |  | **Shapiro-Wilk** | |
| **Mean** | **SD** | **Statistic** | **pValue** |
| **Ferritin (ng/ml)** | 98.38 | 52.03 | .928 | .000 |
| **TSAT (%)** | 32.73 | 6.86 | .954 | .001 |
| **sTFR (nmol/L)** | 17.68 | 6.11 | .922 | .000 |
| \* Normal Distribution p>0.05 | | | | |

\*Shapiro-Wilk Test of Normality (Shapiro-Wilk Test is greater than 0.05, the data is normal. Below 0.05, the data significantly deviates from a normal distribution

**Table 3: The Mean Values of Iron Markers among Gender**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SEX** | | N | Mean | PValue | Test |
| **TSAT** | **Male** | 83 | 32.74(6.72) |  |  |
| **Female** | 29 | 32.70(7.37) | 0.915 | Mann-Whitney U |
| **sTFr** | **Male** | 83 | 17.76(6.17) |  |  |
| **Female** | 29 | 17.47(6.03) | 0.897 | Mann-Whitney U |
| **FERRITIN** | **Male** | 83 | 106.94(54.62)\* |  |  |
| **Female** | 29 | 73.90(34.02)\* | 0.007 | Mann-Whitney U |
| **Table** | | | |  |  |

**Table 4: Reference Range of serum ferritin, TSAT and sTFR among studied Participants**

|  |  |  |  |
| --- | --- | --- | --- |
| **Percentile** | **FERRITIN** | **TSAT** | **sTfR** |
| **2.5** | 20.0 | 21.5 | 8.8 |
| **5** | 22.6 | 23.5 | 8.9 |
| **10** | 35.0 | 24.4 | 9.8 |
| **25** | 64.0 | 27.4 | 13.0 |
| **50** | 88.0 | 32.0 | 16.8 |
| **75** | 122.0 | 37.3 | 23.8 |
| **90** | 186.0 | 43.9 | 26.2 |
| **95** | 215.4 | 46.4 | 26.3 |
| **97.5** | 218.4 | 47.4 | 26.9 |