African Journal of Laboratory Haematology and Transfusion Science

Vol 2, issue 1, page 15-22 | March 2023 | Article ID : 2023-AJLHTS-0002
www.hbtssn.org/ajlhts | ISSN (Print): 2814-0591; (Online): 2814-0605

ORIGINAL ARTICLE

Serum Ferritin and Asymptomatic Malaria: A study in Calabar, Nigeria

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Submitted 10-01-2023.
Accepted: 24-02-2023
Published: 31-03-2023
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ABSTRACT

Introduction

Ferritin is a blood cell protein that contains iron. The serum ferritin level is widely accepted as an accurate indicator of body iron store being the only factor that can give a semi-quantitative indication of the levels of Iron storage. Increased serum ferritin has been reported in asymptomatic malaria infection. This study was done to determine the serum ferritin levels in asymptomatic malaria individuals in Calabar, Cross River State, Nigeria. Ninety (90) apparently healthy subjects were recruited, both male and female within the age of 18 to 65 years.

Materials and Method

The serum ferritin level was assayed using ELISA quantitative method. The Hb and PCV were also assayed using the automated cellular counter Sysmex Kx-21N. Malaria parasite detection was through examination of peripheral blood smears using 2% Giemsa.

Results

The mean serum ferritin levels for the malaria infected subjects was (25.11±1.27ng/ml), and this was significantly higher than the uninfected subjects (16.81±4.66ng/ml) ($P<0.05$). Mean serum ferritin level for infected males was (20.95±8.79ng/ml) which is slightly higher than uninfected males (16.01±3.53ng/ml) ($P>0.05$). The results also show mean serum ferritin for infected females to be (30.57±3.42ng/ml) which is higher than the uninfected females (18.65±1.98ng/ml). This result likewise shows significantly low level of Hb(12.97±1.5g/dl) and PCV (0.38±2.18L/L) in apparently healthy malaria infected individuals while high level of Hb(15.20±1.73g/dl) and PCV (0.44±1.58L/L) were observed among the uninfected subjects. There was also significant difference seen in infected male and infected female subjects, likewise the aparasitaemic males and females had significant difference ($P<0.05$).

Conclusion
This study has shown that asymptomatic malaria parasitaemia increases serum ferritin level, hence serum ferritin estimation without examination for malaria parasitaemia in malaria endemic area such as Calabar, Nigeria may not be reliable. The study also shows that asymptomatic malaria parasitaemia constitutes a significant disease burden and a challenge that should be of global health concern.

Key words: Asymptomatic malaria, serum ferritin, Calabar, Anaemia

INTRODUCTION

Malaria presents enormous health problems in Africa. Possibly over 90% of the 200 million estimated Malaria infected people in the world are in Africa [1]. About 300-400 million acute attacks per year are estimated to occur worldwide [2]. With about 50% of the case and deaths in the world occurring in tropical Africa [1]. An estimated 250 million people in Africa are carriers of malaria parasite [3,4]. This is majorly because the Malaria vectoral system in Africa, south of the Sahara is probably the most powerful available anywhere to human plasmodia [1].

Mild Iron deficiency is frequently not detected by simple haematological measurements in community surveys because of overlap in the values of the Iron deficient and normal subjects. In an iron-deficient state, the Iron store is depleted first before significant changes are noticed in serum as serum ferritin and erythrocyte Iron concentration [4, 5].

The serum ferritin level is widely accepted as an accurate indicator of body iron store [6, 7], being the only factor that can give a semi-quantitative indication of the levels of Iron storage. Its measurement is thus useful in the diagnosis of Iron deficiency anaemia and Iron overload [8, 9]. Serum ferritin increases as Iron accumulates in the Iron store and decreases as storage Iron level drops. Increased serum ferritin has been reported in symptomatic malaria infection. Liver diseases, malignancies [10,11], haemolysis and ineffective erythropoiesis [8,11].The haematological parameters commonly used for the diagnosis of Iron deficiency anaemia-mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), haematocrit and heamoglobin levels only became abnormal after Iron stores have been measurably reduced [12].

In parts of Africa where malaria is highly endemic people are infected and re-infected so frequently that they develop a degree of acquired immunity. These subjects may become asymptomic or mildly symptomatic carriers [1]. The population develops and maintains a high degree of immune response while at the same time there is a nearly permanent presence of very small numbers of malaria parasite in many subjects mostly adults [13]. Bruce-chwatt [14] had described resistance which builds up in previously infected host in the presence of asymptomatic parasitaemia as premonition.

In malaria-endemic countries of Africa, for instance Nigeria, asymptomatic malaria infection is common, and it has always been a

subject of debate as to if this constitutes a significant disease burden that should be treated. The indicator for health risk by asymptomatic parasitaemia has always been whether these infected persons have lower or higher serum ferritin, packed cell volume and hemoglobin concentration than uninfected persons. But since Haemoglobin(Hb) concentration is not the most sensitive measure of blood loss through low grade haemolysis, a false notion of the Iron balance status may be obtained in such individuals hence the need for serum ferritin assay, PCV and Hb estimation in these individuals in order to fully access any hazard Asymptomatic malaria parasitaemia may have on them.

Several studies have reported alteration or changes in the levels of serum ferritin, packed cell volume and haemoglobin caused by asymptomatic malaria infection. However, there have been discrepancies in published literatures with respect to these changes. Therefore, this study was designed to determine and ascertain the serum ferritin level in asymptomatic malaria individuals in Calabar, Cross River State, Nigeria.

MATERIALS AND METHOD

This study was conducted in Calabar, Cross River State Nigeria. Ninety (90) apparently healthy adult male and female subjects within the ages of 18 – 65 years were recruited for this study. Informed consent was obtained from all subjects and none was clinically ill at the time of this study. Their body temperature was taken, those with fever, Genotype SS were excluded. The participants were given structured questionnaires to fill and this provided useful and valid information for this study. Ethical clearance for this study was obtained from Cross River State Ministry of Health Ethical Committee

Seven (7ml) of venous blood (4ml in adult EDTA bottle and 3ml in plain bottle) were aseptically collected from each participant. Haematocrit and Haemoglobin level were determined using blood in EDTA bottle by automated cellular counter sysmex KX-21N. The sera were stored frozen and analyzed in batches for serum ferritin using the ELISA quantitative method. The ferritin standard was supplied by National institute for biological standard and control. Thick blood films were 2% giemsa stained and examined for malaria parasites by a single microscopist using a ×100 oil immersion lens and one eyepiece. One hundred fields were examined before a slide was declared negative [15]. Then thin blood films were stained with leishman stain and examined for malaria parasite species identification.

Statistical analysis was done using Chi-square to show association and comparison between the discrete variables, student T-test was used for variation of the parameters. Level of statistical significance was designated at p-values less than or equal to 0.05 ($P \leq 0.05$).

RESULTS

Table 1 shows the serum ferritin levels of 90 subjects in Calabar screened for malaria infection. The mean serum ferritin levels of aparasitaemic (uninfected) subjects was (16.81±4.66ng/ml). ferritin levels for the parasitaemic subjects was (25.11±1.77ng/ml), with significance difference ($p<0.05$). The Hb and PCV of parasitaemic subjects were (12.97g/dl) and (0.38L/L), which is significantly lower than the aparasitaemic subjects with Hb (15.20g/dl) and PCV (0.44L/L) respectively. The prevalence of malaria parasites among the 90 subjects examined are shown on table 2. The prevalence of the malaria parasite in the male subjects was (56.8%), which was significantly higher than the female subjects (43.2%).Table 3 also shows the comparison of serum ferritin levels, Hb and PCV values of 90 asymptomatic subjects based on gender. The mean serum ferritin level of malaria parasitaemic male was

seen to be (20.95ng/ml), which was seen higher than the aparasitaemic male (16.01ng/ml). Ferritin levels of parasitaemic female was (30.57ng/ml) and higher than the aparasitaemic female (18.65ng/ml) more so, the PCV and Hb of parasitaemic male were (0.39L/L) and (13.39g/dl). And aparasitaemic male were (0.46L/L), and (15.73g/dl). Likewise, the PCV and Hb of parasitaemic female were (0.36L/L), and (12.43g/dl). Aparasitaemic females were (0.40L/L), and (13.98g/dl) respectively.

TABLE 1: Serum ferritin levels of subjects screened for malaria infection.

Number of Subject	PCV L/L	Hb (g/dl)	Ferritin (ng/ml)
Infected (37)	0.38±2.18	12.97 ± 1.05	25.11± 1.27
Un-infected (53)	0.44±1.58	15.20± 1.37	16.81±4.66
p-value	0.001	0.002	0.001
Remark	S	S	S

TABLE 2. Prevalence of malaria parasite amongst the asymptomatic subjects.

Sex	No. Examined	No. Positive for Malaria Parasite
Males	58 (64.4%)	21 (56.8%)
Females	32 (35.6%)	16 (43.2%)
Total	90 (100%)	37 (33.30%)

$x^2 = 0.034$

TABLE 3: Comparison of serum ferritin levels, Hb and PCV values of asymptomatic subjects based on gender

	PCV L/L	Hb (g/dl)	Ferritin (ng/ml)
Infected			
Male	0.39.±2.69	13.39±0.93	20.95±8.79
Female	0.36.±2.50	12.43±0.97	30.57±3.42
p-value	0.002	0.043	0.001
Remark	S	S	S
Uninfected			
Male	0.46.± 2.57	15.73± 099	16.01± 3.53
Female	0.40.± 1.96	13.98±1.37	18.65± 1.98
p-value	0.001	0.002	0.0675
Remark	S	S	NS

DISCUSSION

Ferritin is a blood cell protein that contains iron. The serum ferritin level is widely accepted as an accurate indicator of body iron store being the only factor that can give a semi-quantitative indication of the levels of Iron storage. Its measurement is thus useful in the diagnosis of Iron deficiency anaemia and Iron overload. Serum ferritin increases as Iron accumulates in the Iron store and decreases as storage Iron level drop. Increased serum ferritin has been reported in asymptomatic and symptomatic malaria infection [16].

The result of this study reveals that the level of serum ferritin in apparently healthy subjects who were infected with the malaria parasitaemia was found to be significantly higher than the healthy subjects without malaria parasitaemia. Likewise, there is also significant difference in parasitaemic males and females but not between aparasitaemic men and women. This insignificant differences is mostly in relation with malaria parasitaemia. The malaria parasite present, has probably distorted the normal gender differences in serum ferritin levels. Asymptomatic malaria parasitaemia increases serum ferritin level as shown in this study, hence serum ferritin estimation without examination for malaria parasitaemia in malaria endemic area such as Calabar, Nigeria may not be reliable.

Our findings in this study therefore,

support previous reports [17,18,19] that serum ferritin is elevated in asymptomatic malaria infection. These views are however not different from Adelekan and Thurnham [20] who reported very high serum ferritin ranging from 170 to 1000g/l in children with acute malaria. A study by Odunukwe et al., [21] conducted in Lagos, Nigeria reports a strong positive correlation between serum ferritin level and parasitaemia level, which he further reported resulted in increase in serum ferritin level in subjects with malaria parasitaemia. Although, several mechanisms have been accessed and made available to explain the elevation of serum ferritin in malaria infection. As a known acute phase reactant protein, its concentration in the serum is also known to increase during acute inflammatory reactions. High serum ferritin as earlier stated, has also been reported in liver diseases, folic acid deficiency, likewise haemolytic processes which are reported to be common in malaria infection [18,22]. This malaria parasite infection is majorly of P. falciparum, which invades red cells of all ages thereby causing severe haemolysis [7,23]. This influence of malaria infection on the serum ferritin level has triggered some researchers like Oluboyede and Topley [17] to actually proffer or suggest that direct examination of the bone marrow for iron might be preferable to serum ferritin estimation as a method of assessing iron stores in malaria prone areas. However, a major challenge to this is the traumatic procedure associated with bone marrow aspiration.

A study conducted in Assam in Northeastern India [24] contrary reports decreased levels of serum ferritin in malaria positive subjects when compared to uninfected individuals. Although the mechanism for this consequence was not defined. However, acute erythropoietin deficiency or suppression of marrow response to erythropoietin could lead to decreased erythropoiesis and thus low serum ferritin concentration [25].

More so, it was also observed in this study that the levels of Hb and PCV in the apparently healthy malaria infected individuals are significantly lower than the uninfected healthy individuals. Likewise, significant differences were seen in infected males and females when compared to aparasitaemic males and females. This significant difference is highly associated with the malaria infection. Ordinarily, there are normal values for Hb and PCV by gender. P. falciparum which invades chiefly the Red Cells causing haemolysis and reduce the level of Hb and PCV of the subjects. This supports similar works by [8, 12, 24, 26] who reported significant decrease in Hb and PCV in malaria infected individuals. Malaria parasite feeds majorly on RBC thereby destroying and causing lysis to the cells resulting in reduced PCV and Hb. Many studies revealed that anaemia is one of the most common complications in malaria [16, 27]. Our present study also supports this hypothesis.

In conclusion, a good number of subjects in this study who were majorly asymptomatic had malaria parasitaemia. This study also exposes the dilemma of measuring the serum ferritin levels in a malaria endemic area like Calabar Nigeria without first determining the malaria parasitaemia status. Nevertheless, the significant differences between the serum ferritin levels, Hb and PCV of subjects enrolled for this study shows that asymptomatic malaria parasitaemia constitutes a significant disease burden and challenge that should be of global health concern.

Limitation of the study- Quantification of Parasite was not done in this study , this may have helped to further highlight the relationship between ferritin and malaria burden. This will be done in future study.

ACKNOWLEDGEMENT

We heartily and sincerely appreciate supports

of the University of Calabar Teaching Hospital in which the practical aspect of this research was carried out, and also all members of Calabar community at various levels for accepting to willingly participate in this study.

CONFLICT OF INTEREST

The authors declare that they have no competing interest

FUNDING

There was no external source of funding

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How to cite this paper:
Okafor IM, Ogar CO, Okoroiwu HU. Serum Ferritin and Asymptomatic Malaria: A study in Calabar, Nigeria... *Afr J Lab Haem Transf Sci 2023;* 2(1): 15 - 22.