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Ferritin and serum iron levels in adult patients with sickle cell anaemia at Ibadan, Nigeria

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Summary

The ferritin and serum iron levels in 100 adult patients with sickle cell anaemia (SCA) and in ten pregnant (SCA) females were measured. All the adult sickle cell anaemia patients had serum ferritin levels ranging between 325 ng/dl and > 1500 ng/dl. These levels are within and above the normal range. The same trend was observed in the pregnant adult females with SCA. However, in the pregnant women, significantly lower ferritin levels than in the non-pregnant women were recorded. There is, therefore, a reduction in ferritin levels in pregnancy. This could be due to the increased iron requirements and demand by the developing foetus. Serum iron was below normal in 30% of the pregnant women, only 6% of all the adult patients had serum iron levels below the normal levels. Given the adequacy of ferritin levels in the patients studied and the very low incidence of below normal serum iron levels, it is concluded that the sickle cell anaemia patients in the area of study have adequate levels of iron and ferritin in their serum. Iron should therefore be given only in proven cases of iron deficiency anaemia.

Résumé

Le taux fer du serum, et du ferritinin chez 100 patients adulte soffrant de l'anemie drepanocitaire (SCA) et 10 femmes enceinte (SCA) a été estimé à Ibadan au sud-ouest du Nigeria. Tous les patients adulte souffrant d'anemie drepanocitaire ont tous le taux de ferritin rangé entre 325 g/dl et 1,500 ng/dl. Les taux sont equivalent et au dessus du taux normale. La même tendance a été observé chez les femmes enceintes souffrant de l'anemie drepanocitaire. Cependant, chez les femmes enceintes un taux significativement faible de fernitinin comparé aux femmes non enceinte a été encregiste. II ya cependant eu une réduction du taux de ferritinin pendant la grossesse. Ceci pourrait Etre dû, à l'augementation de la demande en fer par le foetus qui normalement se developpe. Le taux de fer du serum a été en dessous du taux normal chez 30% des femmes enceintes et seulement de 6% chez tous les patients adultes. Le restant des 94% des patients adultes ont ell un taux de fer dans le serum equivalent et au dessas du taux normal. Etant donné les taux adequate de ferritinin au cours de l'étude, et de la très faible incidence de taux de fer du serum en dessous de la normale, il est conclut que l'anemie drepanocitaire chez les patients de cet environement, ont un taux adequat de fer et feritinin dans leur serum. Le fer devrait par consequent être donné ou couseillé aux patients quen cas prouvé d'anemie ferrique.

Introduction

Patients with sickle cell anaemia (SCA) undergo chronic haemolysis of red blood cells throughout their life. This chronic haemolysis results in an anaemic state with a haemoglobin level of 5-10 gm/dl [1]. Presently, there is no effective method to obviate this pathology. However, it is believed that by raising the haemoglobin level, these patients can attain a better quality of life [1].

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Megaloblastic anaemia is a frequent occurrence in patients with SCA for which a prophylactic folic acid supplement is often given [1]. The iron released because of the chronic haemolysis in patients with SCA is incorporated into the tissue iron stores hence the deliberate omission of iron in routine supplemental daily requirements.

In southern Nigeria, studies of iron status in pregnant women with SCA have shown that there are lower levels of serum iron, serum ferritin, and scanty or no iron in the bone marrow [1]. Serjeant [2] conducted a similar study on SCA patients in Jamaica and found normochromia and hypochromia. Anderson [3], Peterson [4] and Roopnarinesingh [5] found iron deficiency in patients with sickle cell anaemia. Fleming [6], on the other hand, observed adequate iron stores in pregnant patients with sickle cell anaemia.

In view of the discrepancies regarding iron status in these patients, it was decided to estimate ferritin and serum iron levels in adult SCA patients, including pregnant women since ferritin level correlate with total body iron stores while serum iron reflects the iron status of the patients. Ferritin can distinguish between iron deficiency anaemia and anaemia of chronic infection and inflammation.

Materials and methods

One hundred adult patients with the diagnosis of SCA were recruited into the study at the University College Hospital, (UCH), Ibadan, Nigeria. Pregnant SCA patients were also studied. All patients recruited confirmed that they had never been on any form of iron therapy prior to sampling. Venous blood (5 ml) was withdrawn by venepuncture from the anterior cubital vein after the skin had been cleaned with methylated spirit. Blood was later transferred to heparinized tubes. Samples were spun and plasma separated into de-ionized tubes and were stored at 4°C until analysis.

Analysis of serum ferritin

A radio immunoassay kit (Amerlex, Kodak Clinical Diagnostics, Amersham UK) was used, while appropriate précautions for handling radioactive materials were taken.

Test protocol for ferritin

All assay tubes were labelled and arranged in an assay rack. 200 μl of the standards and unknowns were pipetted into appropriate tubes. Four hundred μl of 125_I-labelled ferritin solution was pipetted into all tubes and the tubes were stopped. One hundred μl of anti-ferritin serum solution was pipetted into all tubes and this produced a purple colour. All tubes were vortex mixed and covered with plastic film and incubated in a water bath at 37°C for 2 hrs. One thousand μl of the second antibody reagent was pipetted into all tubes. All tubes were mixed for 2 seconds and left to stand for at least 10 min at room temperature. All tubes were centrifuged for 15 min at 2,000 g at room temperature. The tubes were placed in decantation racks and the supernatant discharged. The tubes were gently inverted and care was taken not to tap or shake the tubes. The tubes were kept inverted to drain on tissue papers for 5-10 min. All tubes were counted in a suitable gamma counter for time sufficient to accumulate 10,000 counts.

Calculations

A curve was plotted of the 125_I counts for the standards against the ferritin concentration by the computer system attached to the counter. Values for individual samples were automatically read off the standard curve.

Serum iron analysis

One ml of serum was diluted in 1 ml de-ionized water and read against a reference standard using an automated Atomic Absorption Spectrophotometer (AAS) model 4000. This analysis was based on the procedure described in the AAS manual (model 4000).

Results

Of the 100 patients studied, 43 were males and 57 were females. The age range was 14 years to 37 years with a median of 19 years. The ferritin levels in these patients are shown in Table 1. Thus all the patients had ferritin levels which were within and beyond the normal range for the area of study where the normal range is between 16 and 336 ng/dl. (Adeyefa, personal communication).

Table 1: Ferritin levels in patients with sickle cell anaemia

Ferritin level	Proportion of patients (n = 100)
- ng/dl	%
< 250	0
251 - 500	22
501 - 1,000	23
1,001 - 1,500	11
> 1,500	44

In the 10 pregnant female patients with sickle cell anaemia, the ferritin levels ranged between 83 ng/dl and 450 ng/dl, which were also within and above the normal range. However, ferritin levels among the pregnant patients were on average lower than the levels among non-pregnant female patients. The ferritin and serum iron levels in the pregnant women studied as shown in Tables 2 and 3.

Table 2: Serum ferritin in 10 pregnant patients with sickle cell anaemia

Serum ferritin	Proportion of patients
- ng/dl	%
< 50	0
51 - 100	10
101 - 150	20
151 - 200	10
201 - 250	10
251 - 300	30
351 - 400	10
401 - 450	10

Table 3: Serum iron in 10 pregnant patients with sickle cell anaemia

Serum iron	Proportion of patients
- ng/dl	%
0 - 50	30
51 - 100	50
101 - 150	20

The serum iron in these patients are shown in Table 4. Normal serum iron level is 50 ng/dl. Six patients had serum iron levels below normal. This would explain the hypochromia sometimes seen inspite of the fact that the ferritin level in all patients was adequate.

Table 4: Serum iron levels in patients with sickle cell anaemia

Serum iron level	Proportion of patients (n = 100)
- ng/dl	%
0 - 50	6
51 - 100	34
101 - 150	23
151 - 200	21
201 - 250	9
251 - 300	3
> 300	4

Discussion

In other studies [3,4,5] iron deficiency anaemia was diagnosed in SCA patients in the non-pregnant state. The patients had low levels of serum iron, serum ferritin, and scanty or no iron stores in the bone marrow. It would, however, not be appropriate to equate results obtained in other environments with that in the Nigerian patients as there are various biological, racial, and dietary differences among these groups.

Oluboyede [1] studying a group of pregnant Nigerian women with SCA, found significantly lower than normal levels of serum ferritin and transferrin saturation in this group of patients and concluded that iron deficiency anaemia existed amongst them.

In the present study, non-pregnant adult female SCA patients had ferritin levels within and above the normal range. The same trend was observed in pregnant adult female patients with SCA. However, the pregnant women recorded lower ferritin levels than the non-pregnant women. There is, therefore, a reduction in ferritin levels in pregnancy and this may have resulted from the increased iron requirement and demand by the developing foetus thereby lowering the maternal level. Serum iron was found to be below normal in only three (30%) of the ten pregnant patients.

There was no statistical difference between the mean level of ferritin in adult males and females.

Since ferritin level in all the categories of patients with SCA studied was adequate, the probable causes of anaemia in this group of patients could be megaloblastic due to folate deficiency [1]. However, when Thalassaemia coexists with sickle cell anaemia, the blood film shows a hypochromic and microcytic picture which could be interpreted as a state of iron deficiency anaemia inspite of adequate tissue stores of iron.

Given the adequacy of serum iron levels in the study, the reported inadequacy of serum iron levels [1], low ferritin, and hypochromia [2] suggest a defect in the primary iron storage protein used in haem synthesis when required. The mechanism by which ferritin iron is mobilized is poorly understood, though the process by which the entire ferritin molecule is degraded within lysosomes prior to iron release has been suggested [7]. Iron in hemosiderin is also considered not to be available [7]. Hence, it is not unlikely that most of the storage iron is in the haemosiderin form and this is not easily available for haem synthesis, hence the microcytic and hypochromic blood picture sometimes seen inspite of adequate serum ferritin and serum iron. The adequacy of serum iron and ferritin in this study may also reflect improved nutrition among Nigerian patients in the decade since Oluboyede's [1] study. We therefore conclude that sickle cell anaemia patients in our environment have adequate levels of iron stores. This is independent of their transfusion states.

Finally, given the present results, we advise that patients with sickle cell anaemia in our environment should not be given iron supplements routinely as they tend to have adequate levels in their serum. Iron supplements should only be given in proven cases of iron deficiency anaemia in SCA.

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