



A DETAILED STUDY OF THE ROLE OF SERUM FERRITIN AS THE INDICATOR OF IRON STORES IN SEVERE HOOKWORM INFECTION DIAGNOSED BY DOING ENDOSCOPY

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ABSTRACT

Objective: Severe anaemia is reported to occur in severe hookworm infection in many studies. But so far detailed study of the role of serum ferritin as the indicator of iron stores and iron status in patients with severe anaemia due to hookworm infection diagnosed by doing upper gastro intestinal endoscopy was not done. Hence a detailed study of the role of serum ferritin as the indicator of iron stores and iron status in patients with severe anaemia due to hookworm infection diagnosed by doing upper gastro intestinal endoscopy was done in our institute.

Methods: A study of 1259 patients who had undergone upper gastro-intestinal endoscopy for a period of 5 years from May 2009 to April 2014 was carried out in our institute. In each of these 1259 patients, the first and second part of duodenum were carefully examined to find out the presence of hookworms. In all the patients found to have hookworms in duodenum, investigations were done to know about the presence of anaemia except in the very few patients who were lost for follow up. In patients with severe anaemia [haemoglobin <7g/dl or g%] peripheral smear examination was also done in addition to haemoglobin estimation. But in one patient with severe anaemia, measurement of serum ferritin which indicate the iron stores and iron status was also done in addition to haemoglobin estimation and peripheral smear examination. The results were found as given below.

Results: Of these 1259 patients, as many as 18 patients were found to have hookworms in duodenum while doing upper gastro-intestinal endoscopy. Of these 18 patients, 4 patients were lost for follow up and full details about their investigations were not available. The remaining 14 patients were taken into consideration for our study. Of these 14 patients, 9 patients had anaemia and 2 of these 9 patients were found to have severe anaemia [haemoglobin 3.2g%, 2.1 g%.] The peripheral smear of both the patients showed severe hypochromic anaemia. In one patient with severe anaemia [haemoglobin 3.2g%] in whom serum ferritin which indicate the iron status and iron stores was also done, serum ferritin was extremely low.

Conclusion: Hence measurement of serum ferritin could reveal iron stores and deteriorating iron status in patients with severe anaemia due to hookworm infection.

Key Words: Severe anaemia, Hookworm infection, Serum ferritin, Iron stores, Upper gastro intestinal endoscopy

INTRODUCTION

Severe anaemia is reported to occur in severe hookworm infection in many studies (1to17). But so far detailed study of the role of serum ferritin as the indicator of iron stores and iron status in patients with severe anaemia due to hookworm infection diagnosed by doing upper gastro intestinal endoscopy was not done. Hence a detailed study of the role of serum ferritin as the indicator of iron stores and iron status in patients with severe anaemia due to hookworm infection diagnosed by doing upper gastro intestinal endoscopy was done in our institute.

MATERIALS AND METHODS

This study was conducted in the department of general surgery, Aarupadai Veedu Medical College and Hospital, Puducherry. A study of 1259 patients who had undergone upper gastro-intestinal endoscopy in our institute for a period of 5 years from May 2009 to April 2014 was carried out. In each of these 1259 patients, the first and second part of duodenum were carefully examined to find out the presence of single or multiple hookworms. In all the patients found to have hookworms in duodenum, investigations were done to know about the presence of anaemia except in the very few

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patients who were lost for follow up. Anaemia is defined as haemoglobin < 12g/dl or 12g% in women and haemoglobin < 13g/dl or 13g% in men. Severe anaemia is taken as haemoglobin <7g/dl or g% . In patients with severe anaemia [haemoglobin <7g/dl or g%] peripheral smear examination was also done in addition to haemoglobin estimation . But in one patient with severe anaemia, measurement of serum ferritin which indicate the iron stores and iron status was also done in addition to haemoglobin estimation and peripheral smear examination . The results were found as given below.

RESULTS

Of these 1259 patients, as many as 18 patients were found to have hookworms in duodenum while doing upper gastro-intestinal endoscopy. Of these 18 patients, 4 patients were lost for follow up and full details about their investigations were not available. The remaining 14 patients were taken into consideration for our study. Of these 14 patients, 9 patients had anaemia and 2 of these 9 patients were found to have severe anaemia [haemoglobin 3.2g%, 2.1 g%].

a. Investigations done in the patient with haemoglobin 2.1 g%.

In addition to haemoglobin estimation, peripheral smear examination was also done in the patient with haemoglobin 2.1 g% which showed severe hypochromic anaemia.

b. Measurement of serum ferritin which indicate the iron stores and iron status in the patient with haemoglobin 3.2g%

In this patient with severe anaemia (haemoglobin 3.2g%) , serum ferritin which indicate the iron status and iron stores was also done in addition to haemoglobin estimation and peripheral smear examination.

Serum ferritin[stored iron].

Normally much of the stored iron in the body (about 1 g in men and less in pre-menstrual women and children) is present as ferritin. When iron is present in adequate amounts, ferritin synthesis is promoted and iron storage occurs. Ferritin concentration is an important indicator of total body iron stores.

The function of ferritin

Ferritin is an iron storage protein that keeps iron in a soluble and non-toxic form. The major function of ferritin is clearly to provide a store of iron which may be used for haem synthesis when required. The range of normal serum ferritin is 18-160 ng/ ml or µg/l and a concentration of <12-15 ng/ml or µg/l is taken to indicate deficient iron stores.

Decreased serum ferritin[deficient iron stores] in hookworm infection.

Since serum ferritin level measures the total amount of iron stored in the body, low level of serum ferritin [serum ferritin <12 µg/L or ng/ml] indicates exhausted iron stores (21). Thus iron stores and iron status is assessed by serum ferritin concentration and hookworm infection is associated with the worst iron status (21). Many studies have also shown low level of serum ferritin indicating exhausted and low iron stores due to depletion of iron resulting from loss of blood in severe hookworm infection (18-22).

Decreased serum ferritin [deficient iron stores] in our patient.

In our patient also with severe anaemia due to severe hookworm infection diagnosed by doing upper gastro intestinal endoscopy, serum ferritin is very low-1.4 ng/ ml [normal range 18-160 ng/ ml] indicating exhausted iron stores and very poor iron status. Other studies have also shown low level of serum ferritin in patients with severe anaemia due to severe hookworm infection diagnosed by doing endoscopy (1, 10).

Decreased serum ferritin [indicator of deteriorating iron status].

Measurement of serum ferritin concentration could reveal deteriorating iron status even before the haemoglobin concentration had fallen below the normal value (20). In a very important study, among patients with hookworm infection as many as 42 patients had low level of serum ferritin but with normal blood haemoglobin concentration (20).

DISCUSSION

Iron has the capacity to accept and donate electrons readily, interconverting between ferric (Fe³⁺) and ferrous(Fe²⁺) forms. This capability makes it a useful component of cytochromes, oxygen-binding molecules (ie, hemoglobin and myoglobin), and many enzymes.

Total body iron and stored iron

Total body iron is about 3.5 gm in healthy men and 2.5 gm in women. About 1.5 to 2 gm of this total iron is found in red blood cells as heme in hemoglobin and 0.5 to 1 gm occur as storage iron [mainly ferritin], in bone marrow, spleen, and liver mainly, with the remainder in myoglobin and in enzymes that require iron. Normally much of the stored iron in the body (about 1 gm in men and less in pre-menstrual women and children) is present as ferritin. Thus in pre-menstrual women body iron stores or body iron of >or=500 mg is normal. This is shown in many studies conducted by Milman in Scandinavia.

Studies conducted by Milman in Scandinavia.

These studies have shown that

1. The recommended dietary iron intake is 15 mg/day (12- 18 mg/day) . But majority of women have an intake below this level .
2. Serum ferritin levels >70 microg/l corresponds to body iron of ≥ 500 mg.
3. Serum ferritin levels ≤ 30 microg/l corresponds to small or depleted iron stores or reserves and unfavorable iron status.

First study conducted by Milman in Scandinavia.

More than 90% of Scandinavian women of reproductive age have a dietary iron intake below the recommended 15 mg/day (23). An adequate iron status during pregnancy implies body iron stores or reserves ≥ 500 mg at conception, but only 15-20% of Scandinavian women have iron reserves of such a magnitude in a study conducted by Milman in Scandinavia (23). Among nonpregnant women of reproductive age, ~40% have plasma ferritin ≤ 30 $\mu\text{g/l}$, i.e. an unfavorable iron status with respect to pregnancy (23).

Second study conducted by Milman in Scandinavia.

Dietary iron intake in fertile women is median 9 mg/day. i.e. the majority of women have an intake below the estimated allowance of 12- 18 mg/day(24) . Among fertile women, 20% have iron reserves of >500 mg, which is the required minimum during pregnancy; 40% have iron stores of 100-500 mg, and 40% have virtually no iron stores in another study conducted by Milman et al. in Scandinavia (24).

Third study conducted by Milman in Scandinavia.

42% of non-pregnant women have serum ferritin levels ≤ 30 microg/l, i.e. small or depleted iron reserves in another study conducted by Milman in Scandinavia (25). Only 14-20% have ferritin levels >70 microg/l corresponding to body iron of ≥ 500 mg. Non-pregnant women have a low iron status (25). Thus iron status and body iron can be monitored using serum ferritin(25) .

Fourth study conducted by Milman in Scandinavia.

Iron deficiency was defined by serum ferritin <12 microg/l in pregnancy and <15 microg/l postpartum in another study conducted by Milman in Scandinavia (26).

Study conducted by Hallberg et al.

In clinical practice the gold standard to estimate iron stores is to stain a bone marrow aspirate for iron, but this is not practical to do during population surveys, so alternative methods have been sought(27). Hallberg et al. determined the serum

ferritin concentration of 203 women aged 38 years who had undergone bone marrow examination(27) .They concluded that a value of <15 $\mu\text{g/l}$ was the best predictor of iron deficiency (confirmed by an absence of stainable iron in the bone marrow) (27).

Serum ferritin levels closely correlate with total body iron stores.

Ferritin concentration is an important indicator of total body iron stores and a concentration of <15 $\mu\text{g/l}$ indicates the absence of storage iron while concentrations >100 $\mu\text{g/l}$ indicate the presence of storage iron (27).

World Health Organization recommendation

The range of normal serum ferritin is 30–300 ng/mL ($=\mu\text{g/L}$) for males, and 15–200 ng/mL ($=\mu\text{g/L}$) for females and the mean is 88 ng/mL($=\mu\text{g/L}$) in men and 49 ng/mL($=\mu\text{g/L}$) in women. The World Health Organization recommends that a serum ferritin concentration <12 $\mu\text{g/l}$ indicates depleted iron stores in children <5 years of age, while a concentration <15 $\mu\text{g/l}$ indicates depleted iron stores in those >5 years of age (27).

Decreased serum ferritin in hookworm infection in 3 studies.

Serum ferritin was a valuable indicator of iron stores in populations infected with the helminths(27). Iron deficiency has generally been defined as an absence of iron stores [ferritin]. In many regions where iron deficiency is of great public health importance malaria, hookworm and other parasitic infections are endemic (27). In adults with hookworm infection serum ferritin concentrations is inversely correlated with the intensity of infection (27).

First study conducted by Albonico M et al

In the study conducted by Albonico M et al, 492 children with hookworm positive faecal cultures, ferritin concentrations decreased with increasing proportions of *Ancylostoma duodenale*. Among children with only *Necator americanus* larvae, the prevalence of ferritin <12 microg/l was 33.1%, while in children with $>$ or $=50\%$ *Ancylostoma duodenale* larvae, the prevalence of ferritin <12 microg/l was 58.9 % (28).

Second study conducted by Bakta I. M et al

In the study conducted by Bakta I. M et al, there was a significant negative correlation between serum ferritin level and hookworm egg count(28).

Third study conducted by Pritchard DI et al

There was also a significant negative correlation between plasma ferritin level and hookworm burden in the study conducted by Pritchard DI et al (19).

Decreased serum ferritin in relation to number of hookworms

Up to a burden of 100-200 worms there is rather little effect on blood iron or serum iron, whereas there is a much larger effect on the stored iron (serum ferritin) in the study conducted by Crompton DW et al (20).

Decreased serum ferritin associated with worse iron status in hookworm infection.

Infection with malaria, *Trichuris trichiura*, *Ascaris lumbricoides*, and hookworms were all associated with worse iron status; the association with hookworms was strongest by far. In multivariate analyses, hookworm infection intensity was the strongest explanatory variable for serum ferritin (21).

CONCLUSION

Hence measurement of serum ferritin could reveal iron stores and deteriorating iron status in patients with severe anaemia due to hookworm infection.

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