



# ROLE OF TRANSFERRIN SATURATION, SERUM IRON AND TOTAL IRON BINDING CAPACITY INDICATING IRON-DEFICIENT ERYTHROPOIESIS IN SEVERE HOOKWORM INFECTION

**Govindarajalu Ganesan**

Associate professor, Department of General Surgery, Aarupadai Veedu Medical College and Hospital, Puducherry.- 607402, India.

## ABSTRACT

**Objective:** Severe anaemia is reported to occur in severe hookworm infection in many studies. But so far detailed study of the role of percent transferrin saturation, serum iron and total iron binding capacity which indicate iron-deficient erythropoiesis 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 percent transferrin saturation, serum iron and total iron binding capacity which indicate iron-deficient erythropoiesis 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 various investigations which indicate iron-deficient erythropoiesis and iron status were also done namely transferrin saturation, serum iron and total iron binding capacity [TIBC] 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%, haemoglobin 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 various investigations which indicate iron-deficient erythropoiesis and iron status were also done, transferrin saturation and serum iron were extremely low but total iron binding capacity [TIBC] was normal.

**Conclusion:** Hence measurement of transferrin saturation, serum iron and total iron binding capacity could reveal iron-deficient erythropoiesis and deteriorating iron status in patients with severe anaemia due to hookworm infection.

**Key Words:** Severe anaemia, Hookworm infection, Transferrin saturation, Serum iron, Total iron binding capacity, Upper gastro intestinal endoscopy

## INTRODUCTION

Severe anaemia is reported to occur in severe hookworm infection in many studies (1 to 17). But so far detailed study of the role of percent transferrin saturation, serum iron and total iron binding capacity which indicate iron-

deficient erythropoiesis and iron status was not done in patients with severe anaemia due to hookworm infection diagnosed by doing upper gastro intestinal endoscopy. Hence a detailed study of the role of percent transferrin saturation, serum iron and total iron binding capacity which indicate iron-deficient erythropoiesis and iron

Corresponding Author:

Govindarajalu Ganesan, Associate professor, Department of General Surgery, Aarupadai Veedu Medical College and Hospital, Puducherry.- 607402, India; E-mail: drganesan@gmail.com

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status was done in patients with severe anaemia due to hookworm infection diagnosed by doing upper gastro-intestinal 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 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, various investigations which indicate iron-deficient erythropoiesis and iron status were also done namely transferrin saturation, serum iron and total iron binding capacity [TIBC]. 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%, haemoglobin 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. Detailed investigations which indicate iron-deficient erythropoiesis and iron status in the patient with haemoglobin 3.2g%.

In this patient with severe anaemia with haemoglobin 3.2g%, various investigations which indicate iron-deficient erythropoiesis and iron status were also done

namely transferrin saturation, serum iron and total iron binding capacity [TIBC] in addition to haemoglobin estimation and peripheral smear examination. In this patient with severe anaemia with haemoglobin 3.2g%, transferrin saturation is very low and is only 5% [normal range is 20-50%] and serum iron is very low-20  $\mu\text{g} / \text{dL}$  [normal range 50 to 170  $\mu\text{g} / \text{dL}$ ]. Total iron binding capacity or TIBC is however normal in this patient- 434  $\mu\text{g} / \text{dL}$  [normal range 240-450  $\mu\text{g} / \text{dL}$ ].

These three tests- serum iron, percent transferrin saturation and total iron binding capacity are generally done at the same time to diagnose iron deficiency. Iron deficiency results in a reduction in serum iron (SI) levels, an elevation in transferrin (total iron-binding capacity [TIBC]) levels, and hence a net reduction in transferrin saturation (i.e. serum iron/ total iron binding capacity). Transferrin saturation is calculated from serum iron and total iron binding capacity and gives a measure of iron availability for erythropoiesis. Transferrin saturation = serum iron/ total iron binding capacity.

### Transferrin[iron transport]

Iron absorbed from intestinal mucosal cells is transferred to transferrin, an iron-transport protein synthesized in the liver. Transferrin contains two specific high-affinity ferric (III) binding sites and each molecule of transferrin binds with similar affinity two molecules of iron (18). Serum ferritin measures the stored iron, but only transferrin binds the iron ions or ferric ions and is essential if stored iron is to be moved and used.

### Decreased transferrin saturation[indicator of impaired erythropoiesis].

The extent to which sites on transferrin molecules are filled by iron ions is known as percent transferrin saturation and its normal range is 20-50%. Transferrin saturation identifies iron-deficient erythropoiesis and erythropoiesis is impaired when transferrin saturation falls to < 16%(19). In our patient, transferrin saturation is very low and is only 5% indicating iron-deficient erythropoiesis.

### Decreased transferrin saturation[indicator of deteriorating iron status].

Measurement of transferrin saturation 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 16 patients had low percentage of transferrin saturation but with normal blood haemoglobin concentration(20).

### Decreased serum iron

Serum iron measures the iron molecules that are bound to transferrin and circulating in the blood. But in our pa-

tient, serum iron is very low-20  $\mu\text{g}/\text{dL}$  [normal range 50 to 170  $\mu\text{g}/\text{dL}$ ] which indicates that only very low amount of iron molecules are bound to transferrin and are circulating in the blood of our patient. In one important study also, patients with hookworm infection had very low levels of serum iron (21).

### Decreased serum iron as indicator of impaired erythropoiesis

In addition to transferrin saturation, measurement of serum iron level is also the other important indicator of iron-deficient erythropoiesis (21). Erythropoiesis is impaired when serum iron falls to  $< 50 \mu\text{g}/\text{dL}$  ( $< 9 \mu\text{mol}/\text{L}$ ) and transferrin saturation falls to  $< 16\%$ . Our patient also had very low levels of serum iron -20  $\mu\text{g}/\text{dL}$  and very low levels of transferrin saturation- only 5% indicating the severity of her iron-deficient erythropoiesis.

### Total iron binding capacity or TIBC [normal in iron deficiency] .

Measurement of the total amount of transferrin is called total iron binding capacity [TIBC] which is however normal in our patient- 434  $\mu\text{g}/\text{dL}$ [normal range 240-450 $\mu\text{g}/\text{dL}$ ] . The total amount of transferrin which is produced by the liver is normal. Only the extent to which the sites on transferrin molecules are filled by iron ions [transferrin saturation] has become very low in our patient.

## DISCUSSION

### Transferrin [iron transport]

Transferrin, is the specific transport protein for iron in the plasma pool, and each molecule binds with two molecules of iron (18). The protein circulates throughout the plasma pool and delivers iron to cells via the transferrin receptor pathway (18).

### Percent transferrin saturation

65% of iron in the body is bound up in haemoglobin. 30% of iron in the body is stored as ferritin in the spleen, bone marrow and the liver. Transferrin is a molecule produced by the liver that binds one or two ferric ions and transferrin is essential if stored iron is to be moved and used. Usually 30% [ 20 -50 %] of the available sites on the transferrin molecule are filled. But in our patient, transferrin saturation is very low and is only 5% . Hence only 5% [normal range 20-50%] of the available sites on the transferrin molecule are filled indicating the severity of her iron deficient erythropoiesis.

### Serum iron

In our patient, serum iron is very low-20  $\mu\text{g}/\text{dL}$  [normal range 50 to 170  $\mu\text{g}/\text{dL}$ ]. In one important study also,

patients with hookworm infection had very low levels of serum iron (22) .

### Decreased percent transferrin and serum iron as indicators of impaired erythropoiesis.

Concurrent helminth infections have harmful effects on erythropoiesis in young children. Decreased percent transferrin saturation and serum iron reveal impaired erythropoiesis and deteriorating iron status as shown by many studies.

### Study conducted by Ahmed F et al

In a study conducted by Ahmed F et al 15% of adolescent schoolgirls in urban Bangladesh had subnormal serum iron ( $< 7.16 \mu\text{mol}/\text{l}$ ) and about 25% were iron deficient judged by decreased serum transferrin saturation (Transferrin saturation  $< 15\%$ ). (22).

### Study conducted by Chelchowska M et al

The lowest values of iron were observed in a group of urban middle-class non-pregnant women in a study conducted by Chelchowska M et al. (23). Saturation of transferrin lower than 15%, which indicated deficiency of iron for erythropoiesis, was also observed in this group of urban middle-class non-pregnant women (23) . Hence this study has demonstrated that a transferrin saturation of  $< 15\%$  is insufficient to meet normal daily requirements for erythropoiesis.

### Total iron binding capacity (TIBC) [ normal or increased in iron deficiency] .

Total iron binding capacity or TIBC is normal or increased in people with iron deficiency. Early stage of iron deficiency is characterized by decreased bone marrow iron stores and serum ferritin level falls to  $< 15 \text{ ng}/\text{mL}$ . The compensatory increase in iron absorption causes an increase in total iron-binding capacity (transferrin level).

### Study conducted by Kaneshige E

Serum ferritin concentration and transferrin level or total iron binding capacity were measured simultaneously in a study conducted by Kaneshige E during pregnancy. During the second and third trimesters, serum ferritin level decreased significantly. However, transferrin level or total iron binding capacity increased(24) . Hence total iron binding capacity[TIBC] is not decreased in iron deficiency.

Hookworm infection is the most common cause of iron deficiency in developing nations.

### Decreased serum iron 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 in the study conducted

by Crompton DW et al(20). At worm burdens of about 500 there is a very large reduction in blood iron or serum iron (20).

### Decreased serum iron in hookworm infection

People of aboriginal community in north-west Australia over 14 years of age who had hookworm (number = 82) had significantly lower levels of serum iron than uninfected Aborigines (number = 38) and non-Aborigines (number = 19) in the same age group (21).

### Decreased transferrin saturation in hookworm infection

Measurements of transferrin saturation could reveal deteriorating iron status among patients with hookworm infection in the study conducted by Crompton DW et al (20).

### Decreased transferrin saturation and serum iron in hookworm infection

In a study conducted by Bakta I. M et al Herberg's criteria of iron deficiency (serum iron < 50 mg/dl, transferrin saturation < 16% and serum ferritin < 20 ng/dl) was used. Hookworm infection causes chronic blood loss which lead to iron depletion. This is shown in the iron status of the patients. All patients were iron depleted as shown by low transferrin saturation. Low serum iron was found in 75% of cases (25).

## CONCLUSION

Hence measurement of transferrin saturation, serum iron and total iron binding capacity could reveal iron-deficient erythropoiesis and deteriorating iron status in patients with severe anaemia due to hookworm infection.

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