بسم الله الرحمن الرحيم

University of Khartoum
The Graduate College
Medical and Health Studies Board

IRON STATUS IN NON HAEMOLYTIC ANAEMIC CHILDREN IN KHARTOUM

By:

Dr: Sirag El Nour Mohamed Ahmed

MBBS (U. of Gezira 1993)

A thesis
submitted in partial fulfillment for the requirement of the clinical M.D in Paediatrics and Child Health.

Supervisor:

Dr. Mohamed Sir El Khatim Hashim

(FRCPCH,FRCP, FRCPI, DTCH, DCH.)
Associate Professor, Department of Paediatrics and Child Health, Faculty of Medicine U. of K.

Co-supervisor**:**

Dr. Anwaar . A. Y. Kordofaani

(MBBS, DCP Lon. , FRCPath.UK)
Associate Professor, Department of Pathology, Faculty of Medicine U. of K.

October 2005

DEDICATION

To the soul of my father

To my mother who encouraged me since infancy

To my wife who stood beside me at every step

قال الله تعالى :

(لقد أرسلنا رسلنا بالبينات وأنزلنا معهم الكتاب والميزان ليقوم الناس بالقسط وأنزلنا الحديد فيه بأس شديد ومنافع للناس وليعلم الله من ينصره ورسله بالغيب ان الله قوى عزيز)

سورة الحديد الاية (25)

Contents

ACKNOWLEDGMENT

I would like to express my thanks to those who have contributed so much to this thesis. I am most grateful to my supervisors Dr. M. Sir K. Hashim and Dr. Anwaar A. Y. Kordofani. I owe them an enormous debt for their keen and challenging supervision. They deserve special thanks not only for the advice and priceless comments, which appear on every page of this study, but also for their kind and supportive manner and encouragement.

Grateful appreciation is also extended to the technical staff in Gaafar Ibn Aouf Hospital and the staff at Sudan Atomic Energy Corporation (SAEC). Special regards to Dr. Abdel Moniem, Sief Alyazal and Abdal Aziz for their help in carring out the investigations. Sincere gratitude to Dr. Safaa, from The Community Medicine Department, for her much appreciated assistance and Mr. Hassan Ali for performing the statistical analysis.

I would like to express my gratitude to all paediatric registrars for their great help and encouragement. Special appreciation and thanks to my wife for her support and

encouragement which enabled me to complete this study. At last I pay great thanks to Mrs. Fadia and Miss Widad for their unlimited help in printing this thesis.

ABSTRACT

This was a cross-sectional, hospital based, case study conducted at Khartoum Children's Emergency Hospital (KCEH) during the period from July 2004 to February 2005. The aim of the study was to assess iron status in patients who had anaemia not attributed to haemolysis between the age 6 months and 16 years.

Hundred anaemic patients were included in the study. Thirty one children (31%) had history of pica, (04%) had history of bilharziasis as well as worms infestation and none had history of dysphagia. On examination (93%) were pale, (50%) had smooth tongue, (24%) had splenomegaly and (26%) had signs of other vitamins deficiency.

Haematological assessment showed (98%) had low Hb level, (44%) had low (MCV), (24%) with low (PCV), (27%) low (MCH) and (26%) with low (MCHC). There was no difference between gender and haemoglobin level. Iron study results showed that (66%) with low serum iron and (33%) with normal iron level. Only (21%) had low ferritin and (50%) with normal ferritin. All the results of (TIBC) were either normal or high. Serum iron results were related to (MCH), (MCV), history of worms, bilharziasis and history of pica, but not to spelnomegaly and smooth tongue. Also

iron level is related to cow's and goat's milk as supplements. Ferritin results showed the majority of ferritin levels were either normal (50%) or elevated (29%). This may be attributed to its elevation during inflammation even in patients with low iron stores.

The study concluded that iron deficiency is the commonest cause of anaemia in the studied group particularly the lower social class. Iron evaluation should not depend on a single test like ferritin level. The study recommended that further studies for evaluation of other causes of anaemia beside the etiological causes of iron deficiency are needed. Routine investigations of iron for anaemic patients and fortification of supplementary food with iron are also essential.

ملخص الأطروحة

هذه الدراسة اجريت فى مستشفى حوادث الأطفال الخرطوم فى الفترة ما بين سبتمبر 2004م وحتى فبراير 2005م. كان الهدف من الدراسة هو الوقوف على حالة مستوى عنصر الحديد فى الدم فى الأطفال الذين لديهم فقر فى الدم غير معزى لأمراض فقر الدم الانحلالى فى الأطفال من عمر 6 أشهر وحتى 16 سنة.

وقد شملت الدراسة 100 مريض تم حجزهم بالمستشفى. ثلاثون بالمائة منهم لديهم تاريخ سابق بأكل الطين، (04%) لديهم تاريخ إصابة بداء المنشقات وعدد مماثل بديدان معوية. لا يوجد أحد لديه أعراض عسر البلع. بعد الكشف السريري وجد أن (93%) لديهم شحوب فى الجسم، (50%) لديهمم ملوسة اللسان، (24%) لديهم تضخم فى الطحال و(26%) لديهم أعراض عوز الفيتامينات.

أوضحت نتاج تحليل الدم أن (98%) منهم خضاب الدم لديهم أقل من الطبيعي (فقر دم) وكانت نسب دالات كريات الدم الحمراء التى كانت أقل من الطبيعي كما يلي: (44%) متوسط حجم الخلية، (24%) حجم الخلية المتراكم، (27%) متوسط خضاب دم الخلية و (26%) متوسط تركيز خضاب دم الخلية. لا يوجد فرق بين الجنسين فى مستوى خضاب الدم. أما نتائج تحليل الحديد فى الدم وضح أن (66%) منهم لديهم مستوى عنصر الحديد أقل من الطبيعي بينما (33%) منهم مستوى عنصر الحديد طبيعي. أما حالة الفيرتين فإن (21%) منه مستواه أقل من الطبيعي و (50%) منه طبيعي. لكن كل حالات سعة ارتباط الحديد الكلية إما طبيعية أو مرتفعة. نتائج عنصر الحديد لها علاقة مع متوسط خضاب دم الخلية، متوسط حجم الخلية وتاريخ أعراض الديدان وداء المنشقات بالإضافة إلى تاريخ أكل

الطين لكنها ليست لها علاقة مع تضخم الطحال وملوسة اللسان. كذلك مستوى عنصر الحديد له علاقة مع تناول لبن البقر والماعز كطعام تكميلي للبن الأم.أما عنصر الفيرتين فمعظم نتائجه أما طبيعية (50%) أو مرتفعة (29%) وذلك يعزى إلى أنه فى حالة وجود حالات التهابية بالجسم فإن مستواه يرتفع حتى عند وجود مستوى منخفض لعنصر الحديد.

استخلصت الدراسة أن عوز الحديد هو أكثر أسباب فقر الدم شيوعاً فى مجموعة البحث وبالأخص أطفال الطبقات الاجتماعية الدنيا ، كما أن تقييم حالة الحديد فى الجسم يجب ألا يعتمد على نتيجة اختبار واحد مثل الفيرتين. لذا نوصى فى الدراسات القادمة ببحث أسباب فقر الدم بجانب أسباب نقصان عنصر الحديد. كذلك فحص عنصر الحديد يجب أن يكون من ضمن الفحوصات الاساسية لمرضى فقر الدم بالإضافة إلى ضرورة تدعيم الأطعمة التكميلية للرضاعة عند الأطفال بعنصر الحديد.

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

CVS	Cardiovascular system
EDTA	Ethylene diamine tetra-acetic acid
ELIZA	Enzyme-linked immunosorbant assay
FEP	Free erythrocyte protoporphyrin
Hb	Haemoglobin
IDA	Iron deficiency anaemia
KCEH	Khartoum Children Emergency Hospital
L.L	Lower limb
MCH	Mean corpuscular haemoglobin
MCHC	Mean corpuscular haemoglobin concentration
MCV	Mean corpuscular volume
PCV	Packed cell volume
QC	Quality control
RBC	Red blood cells
RES	Reticulo-endothelial system
RIA	Radioimmunoassay
SAEC	Sudan Atomic Energy Corporation
STD	Standard
StfR	Serum transferrin receptor
TIBC	Total iron binding capacity

UIBC	Unsaturated Iron Binding Capacity
USA	United States of America

1- INTRODUCTION AND LITERATURE REVIEW

1.1 Definition of iron deficiency:

Iron deficiency is a state in which the content of iron in the body is less than the normal range of the patient's age and sex. Iron deficiency anaemia is also defined as presence of low haemoglobin (Hb) concentration, with reduced serum iron and abnormal results from tests of serum ferritin, zinc erythrocyte protoporphyrin and total iron binding capacity [1,2].

After release from a relatively hypoxic intra-uterine environment, mean haemoglobin concentration falls by (30%) to 11 g/dl by the eighth postnatal week, followed by a rise to 12.5 g/dl at the age of 04 months. Mean haemoglobin then increases gradually to reach 13.5 g/dl in preadolescents. The lower (95%) limit of reference range from 6 months to 4 years for haemoglobin is 11 g/dl, with corresponding values of (32%) for packed cell volume (PCV), and 72 fl for Mean Corpuscular Volume [3].

1.2 Classification of iron deficiency:

1.2.1 Iron depletion: is the earliest stage of iron deficiency, in which storage of iron is decreased or absent but serum iron concentration and blood haemoglobin levels are normal[1,4].

1.2.2 Iron deficiency without anaemia: is somewhat more advanced stage of iron deficiency, characterized by decreased or absent storage iron, usually low serum iron concentration and transferrin saturation without frank anaemia [1,4].

1.2.3 Iron deficiency anaemia: is the most advanced stage of iron deficiency. It is characterized by decreased or absent iron storage, low serum iron concentration, low transferrin saturation and low haemoglobin concentration or haematocrit value [1,4,5].

1.3 Iron Metabolism:

1.3.1 Amount and distribution:

The total body iron content of the normal adult varies from 03 to 05 grams, depending on the sex and weight of the individual. It is greater in males than in females [6,7,8,9]. Iron is distributed in the body in several distinct forms:

1.3.1.1 Haemoglobin iron: Constitute approximately (60%-70%) of the total body iron. Aged red blood cells (RBCs) are

phagocytosed in reticulo-endothelial system (RES). Nearly all the iron derived is reutilized by marrow erythroblasts for haemoglobin synthesis.

1.3.1.2 Storage tissue iron:

These are available tissue iron in the form of ferritin and haemosiderin. They can be readily mobilized when needed for haemoglobin synthesis. In adults, it is about 1000 – 2000 mg. Iron stores are slowly accumulated during childhood and adolescence. It is depleted in iron deficiency anaemia and increased in haemosiderosis and haemochromatosis.

1.3.1.3 Essential tissue iron:

These present in the myoglobin of the muscles and in certain enzymes of cellular respiration such as cytochromes, cytochrome oxidase, catalase and peroxidase. It is estimated about 500 mg in adults.

1.3.1.4 Plasma iron:

It is called transport iron. About 03 to 04 mg iron present in the plasma, where it is bound to a specific protein, transferrin. Each molecule of transferrin binds one or two atoms of ferric iron. It's function is transport of iron from the site of absorption or release from destroyed (RBCs) to site of haemoglobin synthesis or iron storage [4,6-8,10,11].

1.3.2 Iron absorption:

Iron absorption depends not only on the amount of iron in the diet, but also, on the bioavailability of that iron, as well as the body needs for iron. A normal balanced diet provides 15 mg from which about 03 mg is taken by the mucosal cells and only about 01 mg (5-10%) of the dietary iron is transferred to the portal blood [7,10,12].

Iron absorption can be influenced at several different stages:

1.3.2.1 Dietary factors:

Most of the dietary iron is non-haem iron derived from cereals. The lesser component is haem iron derived from haemoglobin and myoglobin in meats. Haem iron is more readily absorbed than non-haem iron [6,12,13]. Also the iron that present in the food in the ferrus form is more favourable to absorption than that of the ferric form [6,12].

Iron in breast-milk is present in low concentration, but uniquely well absorbed and utilized. However, the total amount of iron absorbed by breast fed infants is less than that absorbed by those receiving an iron supplemented formula and by 09 months, there is evidence of iron deficiency in some breast fed infants unless additional sources of iron are present in the diet [3].

1.3.2.2 Luminal factors:

Iron is released from protein complexes by acid and proteolytic enzymes in the stomach and small intestine. Iron is maximally absorbed from the duodenum and less well from the jejunum, probably because the increasingly alkaline environment leads to the formation of insoluble ferric hydroxide complexes. Low molecular weight substances such as sugars and ascorbic acid, form soluble iron and facilitate attachment of iron to the mucosa. In contrast, phosphates and phytates in the diet bind to the iron and inhibit its absorption [3,6,7,12,13].

Alkalies and tea also reduce iron absorption. Therapeutic ferrus iron salts are well absorbed on an empty stomach and absorption is reduced if it was given after meals [12].

1.3.2.3 Mucosal factors:

A variety of mechanisms for binding of non-haem iron to the mucosa have been described. Specific, saturable, receptor mediated mechanism and passive diffusion at high doses may occur [12]. Haem iron binds to a specific mucosal receptors, breaking down the porphyrin ring and releasing its iron into intra cellular transit iron pool [12,13].

1.3.3 Iron excretion:

There is probably no control mechanism of iron excretion. The loss of iron from the body depends on the ferritin iron content of the cells lost by desquamation, mostly into the intestinal tract and from the skin. The total daily loss by these routes is about 18 μmol (1mg). Losses can be much higher if there is menorrhagia and may then cause iron deficiency. During pregnancy the mean extra daily loss to the fetus and placenta is about 27μmol (1.5mg).

Normal iron loss is so small and the normal iron stores are so large that it would take about 3 years for the patient to develop iron-deficiency on a completely iron-free diet. Of course, this period is much shorter if there is any abnormal blood loss [14].

1.3.4 Sources of iron:

Iron is obtained from meat especially liver and kidney, egg yolk, cereals, pulses, vegetables and fruit. Red meat contains 2-3 mg/100 gm in the form of haem while White meat contains 0.5-1 mg/100 gm and liver has 07-10 mg/100 gm. Hilba (fenugreek seed) has very high content 22 mg/100 gm of dry seed and pulses have 2-9 mg/100 gm. Milk, particularly cow's milk, has low iron content. Considerable amounts of iron may be added to the food by cooking in iron utensils[6,10].

1.3.5 Iron balance:

Under normal circumstances, iron absorption is slightly exceeding iron excretion. A balanced diet contains 10-20 mg of iron, of which (10%) or less is absorbed; so that uptake varies from 1 to 2 mg per day. Basal losses range from 0.5 to 1.0 mg per day [6].

The daily iron requirement for haemoglobin synthesis is 20–25 mg. It has been pointed out that the body conserves its iron stores by re-utilizing the iron derived from the break down of the haemoglobin from aged red blood cells. In normal individuals, red blood cells destruction and formation take place at almost identical rates. Thus, in the absence of bleeding or increased demand, sufficient iron for haemoglobin synthesis is provided by the breakdown of haemoglobin during the destruction of aged red blood cells [6, 12].

Males normally are in a state of positive iron balance, i.e. the amount of iron liberated by the normal destruction of aged red blood cells together with the amount absorbed, very slightly exceeds the amount required for haemoglobin synthesis and the amount lost by excretion. However, in females of childbearing age, the positive balance is only very slender, because of the additional loss by menstruation. Thus, a moderate increase in the

menstrual loss, especially if associated with impaired intake, can easily induce negative iron balance [6].

1.3.6 Iron Imbalance:

Beside iron deficiency and its causes and presentations mentioned above, a patient can present with complications of increased iron intake. These patients present in two forms:

1.3.6.1 Iron overload:

The absence of a physiological pathway for the excretion of excess iron means that patients with increased iron intake are at risk of iron overload. The patients at risk are:

- Patients with repeated blood transfusions such as congenital and/or acquired refractory anaemias.
- Those who have excess iron absorption: like hereditary haemochromatosis and massive ineffective erythropoiesis.
- Those with excess iron uptake such as sub - Saharan dietary iron overload from traditional beer of high iron content.
- And those with excess parenteral iron therapy.

These patients are at risk of progressive accumulation of iron and potentially lethal tissue damage leading to

haemochromatosis affecting mainly liver, heart and endocrine glands [7, 12].

The iron accumulates initially in the reticulo-endothelial cells of the liver, spleen and bone marrow. There are few harmful effects but under certain circumstances the distribution may progress so that parenchymal damage occurs. Whatever the cause of massive iron overload, there may be parenchymal accumulation and tissue damage. There are two variations:

- *Haemosiderosis*: is defined as an increase in iron stores as haemosiderin and is a histological definition. It does not necessarily mean that there is an increase in the total body iron.
- *Haemochromatosis:* describes the clinical disorders due to parenchymal iron induced damage [9, 14].

Treatment is by chelation therapy using subcutaneous or intravenous deferoxamine. Although some aspects of treatment still controversial for the safety of deferoxamine infusion for more than 24 hours, the maximal infusion rate, the total amount to be given, the serum iron level at which to treat and the end point of treatment [9, 15, 16].

1.3.6.2 Iron poisoning:

Iron poisoning continues to be one of the most common intoxications in children. Preparations available commercially present potential hazards. A toxic potential is related to elemental iron, which is high in all preparations.

A safe lower limit for toxic ingestion has not been clearly established. Ingestion of as low as 30 mg/kg can cause toxicity, which is only 5 times the recommended daily dose [15, 16].

It must be emphasized that, because of the nature of medication, it is rarely known how many pills in a bottle or how many actually were ingested.

Toxic manifestations are due to either the direct caustic effect on the mucosa or the presence of iron with a high level in the circulation. In few hours after ingestion, the patient presents with nausea, vomiting, lethargy and bleeding. Followed by a quiescent period of several hours which can be deceptive. Then the systemic symptoms of free iron in the circulation develop including coma, circulatory collapse, severe metabolic acidosis, cyanosis and fever. Late effect seen days to weeks after ingestion include hepatic necrosis and intestinal obstruction due to scarring [15-18].

Management is through good supportive and symptomatic care. Ipecac-induced emesis can be used to remove the drug from

the stomach; however, it may mask the gastrointestinal symptoms caused by iron. Oral bicarbonate (02%) and magnesium hydroxide (milk of magnesia) react with iron to form less soluble, poorly absorbed iron salts, but they are toxic and of questionable benefit. Activated charcoal does not adsorb iron and should not be used.

Deferoxamine is a specific chelator and an antidote for iron intoxication. It should be administered as an intravenous infusion, and continued till the patient is symptom free [15].

Iron poisoning is most often accidental in paediatric population and intentional in adults. Physicians should instruct parents to keep iron formulation out of the reach of children [16].

1.4 Geographical Distribution of iron deficiency:

1.4.1 Iron deficiency in Sudan:

A study was conducted by El Tohami EA in 1980 about pica and its relation to iron deficiency, showed that in (51.4%) of children aged 0-6 years had pica which is related to anaemia. A subgroup of 120 children were randomly selected and only 62 children of those who were selected attended; all of them had iron deficiency [19].

Whereas Mustafa MI in 1988 evaluated the iron status in patients with sickle cell anaemia, revealing that as high as (86%) of the studied group had iron deficiency [20].

In 2003, Bafakeer SS studied iron status in patients with low red cell indices irrespective of the haemoglobin value and found that (81%) of the anaemic patients had low red cell indices, (72.5%) of them were anaemic and (37.5%) had iron deficiency [21]. A/Elgader EA in 2004 studied the assessment of iron status in Sudanese pregnant ladies and their newborn babies in 80 cases. She found that (10%) of the mothers had low haemoglobin, (60%) had low serum ferritin and only (7.5%) had low serum iron. While (22.5%) of the babies had low haemoglobin, (10%) had low serum ferritin and (05%) had low serum iron. Newborn babies who were anaemic all their mothers had normal haemoglobin and (11.1%) of them had low serum iron [22].

1.4.2 Iron deficiency anaemia worldwide:

Iron deficiency and iron deficiency anaemia are common nutritional and haematologic disorders worldwide [1,23]. An estimated 2.15 billion individuals are anaemic because of iron deficiency [24]. It is being more prevalent and severe in young children (6 – 24 months) and women of reproductive age [25]. It is the most prevalent nutritional problem around the world [23].

Although (IDA) is not a major health problem in developed countries, a specific groups of the population remain endangered. Among these groups are young children and adolescents [26].

In (USA) a study was carried in New York in 1988 through 1994 among 5398 children between the age 6 and 16 years was only (03%) had iron deficiency and (0.3%) had iron deficiency anaemia [27]. However, another study at the same period in 24894 children aged one year and older were evaluated for iron status, the results showed (09%) of toddlers aged one to two years and (09%-11%) of adolescent girls and women of child bearing age were iron deficient; of these, iron deficiency anaemia was found in (03%) and (02%-05%) respectively [28].

In Mexico, a study carried in children 4-6 years in Oaxaca city revealed anaemia in (23.7%) and (IDA) in (11.9%). And (13.6%) with low iron reserve [29]. Another study also was done in Mexico in 1999 in 8111 children aged one to two years, revealed that the prevalence of anaemia is (50%) in infants less than 02 years and varied between (14%) and (22%) in 6 -11 years old, and positively associated with nutritional status, socio-economic status, duration of lactation together with iron and calcium intake [30].

In a study in Brazil, 332 children aged 07 to 15 years were enrolled in the study. Anaemia was found in (36.2%) of which (20%) were iron deficient [31]. Another study carried in Turkey in 1223 children were surveyed. The rate of anaemia was found to be (16.9%) overall with a highest prevalence of (18.3%) in the children

(00 – 02 years) and (16.3%) in 14+ age group. The prevalence of iron deficiency was found to be (17.2%) overall, being (48%) in the infant group, (19.6%) in the children and (14.7%) in the 14+ age group [32].

A screening for iron deficiency was also carried in 485 preschool children in Northern Ireland. The results showed (17%) were iron deficient while (03%) of the total number (18.5% of the iron deficiency) had iron deficiency anaemia [33].

Around Sydney in Australia, iron status was assessed in 678 children aged 09 to 62 months. The results revealed that (10.5%) had iron depletion, (02.8%) had iron deficiency and (01.1%) had iron deficiency anaemia. The 24 to 36 months age group had the highest prevalence (03%) of (IDA). Whereas iron depletion and iron deficiency were highest among 09 - 23 months age group [34].

In Pennsylvania, a screening of 282 children aged 09 to 30 months old for anaemia and (IDA) revealed that the prevalence of anaemia was (35%), iron deficiency without anaemia was (07%) and (08%) had iron deficiency with anaemia [35].

While in Arab Gulf countries, the prevalence of iron deficiency anaemia among preschool children ranged from (20%) to (67%) while that among school children ranged from (12.6%) to (50%). The percentages of pregnant women who suffered from

(IDA) ranged from (22.7%) to (54%) of them [36]. In Al Ain, United Arab Emirates, during 1992 and 1993, 309 children aged 01 to 22 months and their mothers visiting an immunization facility were studied for anaemia and the role of iron deficiency in causing anaemia. Anaemia was detected in (03%) of those aged 1-2 months, (08%) of those aged 3-5 months, and (25%-39%) of those aged more than 06 months. Those who were anaemic, (53%) were iron depleted [37].

In Africa and Asia where most of the developing countries exist, anaemia and iron deficiency seems to be more striking. A nutritional survey was conducted in Tanzania in 660 households of 2320 subject age from 6 months to 65 years, showed (55%) of the subjects had anaemia and (61%) of the anaemia was associated with iron deficiency. And preschool children were the most affected group that (84%) of them were anaemic [32].

Another study done in eight countries in Africa and Asia in school children, anaemia was found to be more than (40%) in the five African countries [38]. Whereas in Zanzibari, a study in 3595 school children showed prevalence of anaemia in (62.3%), of which (82.7%) was associated with iron insufficiency [39].

In Peshawar, Pakistan, a study involving 275 children screened for anaemia. Ninety percent of the children their

haemoglobin was below 11 g/dl, (67%) were iron deficient and (63%) had iron deficiency anaemia [40]. And in Delhi, India, a study was conducted in 406 school children randomly selected and evaluated for anaemia and it was found to be (41.8%). Another subset of 95 anaemic children aged 5 to 10.9 years are studied for the etiology of nutritional anaemia. Pure or mixed (IDA) was found in (68.42%), and pure iron deficiency anaemia occurring in (41.05%) of this group [41].

1.5 Clinical Presentation:

The onset of iron deficiency anaemia is usually insidious. While symptoms are those common to all anaemias, nature and severity vary with the degree of anaemia and the age of the patient [6].

The common manifestations of (IDA) are pallor, irritability, anorexia and decrease in the normal activity. Pallor is usually evident and mild to moderate degree of periorbital or dependant oedema may be present [11]. The patient also may present with palpitation and dyspnea on exertion [1,3,11]. Headache, parathesia and burning sensation of the tongue are symptoms of iron deficiency not related to the degree of anaemia [1].

Pica, the eating of storage items such as coal, earth, or foods in great excess like tomatoes and green vegetables, is more common than generally realized, and may be uncovered only if the patient is specifically asked [2]. But dysphagia is extremely rare and when present should raise the possibility of post cricoid's web; Plummer –Vinson syndrome [2,6,7].

Iron deficiency may have effects on neurologic and intellectual function. A number of reports suggest that iron deficiency anaemia and even iron deficiency without significant anaemia, affects attention span, alertness and learning of both infants and adolescents [42-45].

Physical findings include: pallor, glossitis (smooth, red tongue), stomatitis and angular cheilitis [1,42]. Tachycardia and blowing, apical systolic flow murmur is frequently heard but cardiac enlargement is unusual [6,42]. Koilonychia, loss of cutaneous elasticity and changes of texture of hair may occur in advanced and severe cases [1,6,42]. Splenomegaly is uncommon unless the anaemia is severe and may then reflect other diseases such as portal hypertension in which the iron deficiency is also a feature [2]. Retinal hemorrhage and exudates may be seen in severely anaemic patients [1].

1.6 Diagnosis:

Diagnosis of iron deficiency anaemia based on three steps:

1- Confirmation that anaemia is due to iron deficiency based on assessment of iron status, bone marrow and erythrocyte protoporphyrin.

2- Full blood count and indicices.

3- The cause of iron deficiency.

1.6.1 Iron status

Iron is carried in the plasma bound to protein transferrin. This molecule binds two atoms of Fe^{3+} and delivers iron to the cells by interaction with the membrane transferrin receptor [46]. About (70%) of the total iron is circulating in erythrocyte haemoglobin, and up to (25%) of the body iron is stored in the reticulo-endothelial system in the liver, spleen and bone marrow [14].

Serum iron can be measured directly, and generally decreases and iron stores are depleted. However, serum iron may not reflect iron stores accurately because it is influenced by several factors including iron absorption from meals, infection, inflammation and diurnal variations [40,47]. Circulating iron, bound to the transferrin, comprises only a very small amount of the total body iron (0.01%), and has very high turn over rate of 10-20 times per day in normal subjects, these factors contribute to the

variability of measurement encountered and limit the diagnostic usefulness of an individual serum iron measurement [40,48].

Laboratory assessment of iron status includes serum ferritin, serum iron, total iron binding capacity (TIBC), erythrocyte protoporphyrin and bone marrow:

1.6.1.1 Serum ferritin:

The small quantity of ferritin in the human serum reflects the body iron stores. Measurement of serum ferritin has been widely adopted as a test for iron deficiency and iron over load.

In most normal adults, serum ferritin concentrations lie within the range 15–300 µg/dl. Concentration of less than 15 µg/dl indicates depletion of storage iron. In children, mean levels of storage iron are lower and a threshold of 12 µg/dl has been found to be appropriate, for detecting iron deficiency [46,49].

In patients with acute or chronic diseases, interpretation of serum ferritin concentration is less straight forwards and patients may have serum ferritin concentration of up to 100 µg/dl despite an absence of a stainable iron in the bone marrow [1,6,7,46,49].

1.6.1.2 Serum iron:

The measurement of serum iron concentration alone provides little useful clinical information because; although

methodological variation is low; there is considerable variation from hour to hour and day to day in normal individuals.

In the first month of life, mean concentration of serum iron is higher than in adults (22 µmol/L), falls to about 12 µmol/L by the age of one year and remains at that level throughout the childhood [1,6,7,46].

1.6.1.3 Transferrin and total iron-binding capacity (TIBC):

In the plasma, iron is bound to transferrin and the total iron-binding capacity is a measure of this protein. The additional iron binding transferrin is known as the 'unsaturated iron-binding capacity (UIBC). The sum of iron concentration plus the (UIBC) give the (TIBC).

In health, the serum transferrin is 2-3 g/L, and 1 mg of transferrin binds 1.4 µg/L of iron. The normal serum level of (TIBC) is 68 ± 12.6 µmol/L. The (TIBC) is raised in iron deficiency anaemia and in pregnancy. In pathological iron overload, (TIBC) in the serum is reduced [1,7,46,50]. Serum transferrin receptors level is a sensitive measure of iron deficiency and correlates with haemoglobin and other laboratory parameters of iron status. It is of great value in distinguishing iron deficiency from anaemia of chronic diseases [51].

In iron deficiency, the levels are higher than normal, where as in the anaemia of chronic and inflammatory diseases, levels are slightly but not significantly higher than normal. They can be measured by a sensitive enzyme-linked immunosorbant assay (ELIZA) technique [51].

1.6.1.4 Erythrocyte protoporphyrin:

Protopophyrin represents the stage in the biosynthetic pathway of heme immediately before the incoporation of iron [51]. Protoporphyrin accumulates in the red blood cells in the free form, as there is insufficient iron to combine with it to produce haem. Estimation of red cell protoporphyrin has been used to diagnose iron deficiency before the development of overt hypochromic anaemia [51].

In iron deficiency, red cell protoporphyrin is increased to values ranging from 100-600 µg/dl while the normal range is only 20-40 µg/dl [6,46,49,52]. In both iron deficiency and lead poisoning, the free erythrocyte protopophyrin (FEP) level is elevated. It is much higher in lead poisoning than in iron deficiency. The (FEP) is normal in α & β-thalassemia minor. Its elevation occurs as soon as the body stores of iron are depleted, but before microcytic anaemia develops and therefore an indication for iron therapy even when anaemia and microcytosis have not yet developed [51].

1.6.1.5 Bone marrow staining:

The evaluation of marrow iron stores is a sensitive and usually reliable means for the diagnosis of iron deficiency anaemia. Decreased or absent haemosiderin is characteristic. Haemosiderin appears in the unstained marrow film as golden refractile granules, but it is more readily and more reliably evaluated after staining by *Prussian blue* method. Iron granules which are normally found in the cytoplasm of (10%) or more of erythroblasts become rare but may not be entirely absent.

Marrow examination is seldom necessary for diagnosis, unless there are unusual difficulties in the differentiation of (IDA) from other causes of hypochromic anaemia [1,6,50,53].

1.6.2 Other haematologic changes:

The essential features are diminished concentration of haemoglobin while anaemia is usually of mild to moderate severity. The red blood cell count is reduced together with the mean corpuscular volume (MCV) and the mean corpuscular haemoglobin (MCH). The degree of reduction depends on the severity of the anaemia so that reduction in (MCHC) and (MCV) occur in severe iron deficiency.

In the blood film, the red blood cells are hypochromic and there are microcytosis, anisocytosis and poikilocytosis. In infants and children, hypochromia may occur earlier in the course of iron deficiency. Target cells may sometimes be present [1,6,54,55].

Reticulocyte count is usually normal, but in severe iron deficiency anaemia associated with bleeding, reticulocyte count of (03-04%) may occur [51].

The white cells count and differential are usually normal while the platelets count is usually normal, but it may vary from thrombocytopenia to thrombocytosis. Thrombocytopenia is more common in severe iron deficiency anaemia while thrombocytosis is present when there is an associated bleeding from the gut. [51,54,55].

1.6.3 Causes of iron deficiency:

Iron deficiency anaemia develops when the supply of iron is insufficient for the requirement of the haemoglobin synthesis. There are three major factors for the causes of iron deficiency anaemia:

a- *Increased physiological demand for iron*: This occurs in children during period of growth and women during reproductive period.

b- *Pathological blood loss:* Loss of blood to any extent causes lowering of the total body iron, especially if it is

massive or chronic that can't be restored by diet such as hookworms infestation, bilharsiasis and recurrent bleeding from any site.

c- *Inadequate intake:* Occurs in either nutritional deficiencies or impaired absorption [1,6,7,12,56-61].

1.7 Management:

Once it has been established that a patient is deficient in iron, replacement in therapy should be instituted. Iron may be administered in one of several forms; orally; as simple iron form or parenterally; as an iron-carbohydrate complex or as a blood transfusion. Within 72-96 hours after administration of iron to an anaemic child, peripheral reticulocytosis is noted with a peak occurring after 1-2 weeks [1,7,14].

Reticulocytosis is followed by arise in the haemoglobin level which may increase daily by 0.1-0.2 g/dl, and should attain a normal value within 02-04 months. Iron medication should be continued for 12 weeks after blood values are normal. Body iron is restored in 03 to 06 months.

Failure of iron therapy occurs when a child does not receive the prescribed medication, when iron is given in a form that is poorly absorbed or when there is continuing unrecognized blood loss such as intestinal or pulmonary loss or in the menstruation. An

incorrect original diagnosis of nutritional iron deficiency may be revealed by therapeutic failure of iron medication [14].

1.7.1 Oral iron therapy:

The patient is encouraged to eat a diet containing all nutritional requirements although neither meat nor any other dietary article contains enough iron to be useful therapeutically. Iron preparations in forms of sulphate, fumarate, gluconate and succinate are available in tablets and paediatric mixtures. The daily dose is 150-200 mg/day in adults and 06 mg/kg/day in paediatrics as elemental iron to be given divided doses. Absorption is best in an empty stomach but side effects are less if it was taken after meals. Mild side effects are anticipated such as metallic taste, constipation or loose stool [1,7,12,25,62].

1.7.2 Parenteral iron therapy:

Occasionally it becomes necessary to administer iron by parenteral route as in malabsorption, intolerance to oral iron, iron needed in excess to that taken orally or where follow-up is likely to be inadequate. Iron preparations are available in forms of iron sorbitol (Jectofer) and iron dextran (Imferon). Anaphylaxis, flushing, nausea, fever, pain and staining at injection sites are possible side effects. Response to treatment is the same as the oral medication [1,7,12,25,62,63].

1.7.3 Blood transfusion:

Blood transfusion is preserved to the patients who are severely anaemic or those who have signs of heart failure [1,7,12]. Anaemia that develops slowly, the decision to transfuse these patients with (RBCs) should not be based solely on blood haemoglobin levels because children with chronic anaemias may be asymptomatic despite very low haemoglobin levels.

The (RBCs) product of choice for children and adolescents is the standard suspension of (RBCs) isolated from whole blood by centrifugation and stored in an anticoagulant/preservative medium at a haematocrit value of about (60%). The usual dose is 10-15 ml/kg but transfusion volumes vary greatly depending on clinical circumstances [63].

2 . JUSTIFICATIONS AND OBJECTIVES

2.1. Justifications:

1. Iron deficiency anaemia is the commonest cause of anaemia worldwide.
2. Sudan is one of the developing countries where iron deficiency is one of the major nutritional problems.
3. No study was done among children in Sudan.

2.2. Objectives:

1. To determine the prevalence of iron deficiency in ill anaemic patients between 6 months & 16 years.
2. To study the associated symptoms and signs in patients with iron deficiency anaemia.
3- To study co-relation between iron deficiency and Socio-demographic factors.

3- PATIENTS AND METHODS

3.1. Nature of the study:

This is a descriptive, cross-sectional, hospital-based, case study.

3.2. Study area:

The study was conducted at Khartoum Children Emergency Hospital (KCEH).

3.3. Duration of the study:

The duration of the study was 08 months started from July-2004 and ended at February- 2005.

3.4. Study population:

Children presenting with low haemoglobin to Khartoum Children Emergency Hospital.

3.5. Sample size:

Sample size was determined according to the following formula and was found to be 89 patients.

$$N = \frac{z^2 pq}{d^2}$$ (64).

N: Sample size = 89 patients

Z : Statistical certainty = 1.96 at a 95% confidence interval

P : probability of success

Q : probability of failure (1-p)

D : designed margin of error

3.6. Inclusion criteria:

All admitted children between the age of 6 months and 16 years, with haemoglobin less than 11 grams /dl were enrolled in the study.

3.7. Exclusion criteria:

Children with age less than 6 months or more than 16 years were excluded together with those who refused to be enrolled in the study. Known patients with haemolytic disorders and patients who are already on haematonics for more than 03 weeks were also excluded.

3.8. Research team:

Those who contributed in this study were the author, paediatric registrars and doctors in the casualty, laboratory technicians, biochemists and a statistician.

3.9. Methods

3.9.1. Questionnaire

A well prepared questionnaire sheet was designed including the personal data, along with the nutritional, socio-demographic characteristics, family history, medical history and a detailed review of symptoms of anaemia.

Anthropometric measures along with the clinical signs of anaemia and other associated findings were also included.

2.9.2. Selection of patients:

Three days of the week were randomly selected; every other day, on Sundays, Tuesdays, and Thursdays, excluding Fridays.

All admitted children in different wards were investigated for haemoglobin by calorimetric method, using finger prick sample.

Children satisfying the inclusion criteria with haemoglobin less than 11 grams/ dl were selected for the study. The personal data along with the relevant past and nutritional history beside the clinical examination including anthropometric measurement were performed and registered in a questionnaire by the author.

2.9.3. Investigations:

Five mls of venous blood were drawn from the patient and collected in 2 separate containers. Two mls in the first container which contains anticoagulant, ethylene diamine tetra acetic acid (EDTA) for the measurement of red blood cell (RBC) indices including haemoglobin (Hb) and (ESR). The remaining 3 mls were collected in a plain container, left to clot and centrifuged to obtain 2 mls of serum, which was stored at low temperature (less than 15º C) and used for iron studies namely serum ferritin, serum iron and total iron binding capacity [13].

2.9.3.1 Haematological tests

Haemoglobin and red blood cell (RBC) indices namely packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were measured by automatic

blood counter (Sysmex-Kx-21). Erythrocyte sedimentation rate (ESR) was measured by pipetting 01ml of blood in an (ESR) tube and sedimentation was read after one hour.

2.9.3.2. Iron studies:

- **Serum iron:**

It was done by a photometric calorimetric test with lipid clearing factor. The method uses its own specific kit from “Human” to detect the “end point”. Iron reacts with chromazurol B (CAB) and cetyl-trimethyl-ammonium-bromide (CTMA). It forms a coloured ternary complex with an absorbance maximum at 623 nm. The intensity of the colour produced is directly proportional to the concentration of iron in the sample. Quality control was insured by proper calibration and use of a control sera from the same source Humatrol quality control serum [13].

- **Total iron binding capacity (TIBC):**

Also total iron binding capacity (TIBC) was done by photometric calorimetric test. The iron binding protein transferrin in serum is saturated upon treatment with an excess of Fe^{+3} irons. Unbound (excess) iron is adsorbed onto aluminum oxide and precipitated. The transferrin-bound iron in the supernatant is then

determined. The total iron binding capacity is calculated by multiplying the result of the iron determination in the supernatant by the diluent's factor [13].

- **Serum ferritin:**

Ferritin was measured by sensitive radio-immunoassay (RIA) technique. The specific binding site is provided by immunization of sheep with human ferritin hormone.

Sufficient (polystyrene) test tubes were labeled in duplicates and arranged as racks, and then 25 µl were pipetted into each tube of the standards (STD), quality control (QC) sample and the patient's sample. And 250 µl of anti-ferritin anti body were added to each tube. To the standard, quality control and patients' samples 250 µl of tracer were also added.

After mixing well and incubated at 37º C for 45 minutes, the racks were placed in a magnetic base for 10 minutes, to separate the bound fraction from the free fractions by decant and supernatant. Lastly, each tube was counted in the gamma counter to evaluate the gamma emission per minute, and binding percent was plotted versus the concentration, to get standard calibration curve. From the curve obtained, the concentration of ferritin in

patients' samples were evaluated. This method is bioassay method (radio-immunoassay), using radioactive isotope of iodine (I^{125}) which is gamma emitter.

2.9.4. Case definition:

A patient is defined as either iron sufficient, having iron deficiency without anaemia or having iron deficiency anaemia:

3.9.4.1. Iron sufficient:

The patient is labeled as iron sufficient if his Hb is more than 11gm/dl, serum ferritin is more than or equal to 30µg/dl, serum iron is more than or equal to 60 µg/dl and iron saturation is more than (12%).

3.9.4.2. Iron deficiency without anaemia:

The patient is considered as iron deficient without anaemia if his Hb is more than 11gm/dl, serum ferritin is less than 30µg/dl, serum iron is less than 60 µg/dl and iron saturation is less than (12%).

3.9.4.3. Iron deficiency anaemia:

The patient is defined as having iron deficiency anaemia if his Hb is less than 11gm/dl, serum ferritin is less than 30µg/dl,

serum iron is less than 60 µg/dl and iron saturation is less than (12%).

3.10. Statistical analysis:

The data were analyzed using Statistical Package for Social Sciences (SPSS) computerized program. Chi square test was used to compare the associations between the variables .

3.11. Ethical considerations:

- Written consent was obtained from the director of the hospital.
- Informed consent was taken from doctors of the units working at the casualty.
- Informed consent was also taken from the parents.
- results of the complete blood count (CBC) and iron study results of patients who had low iron levels were handled to the patient.

3.12. Difficulties encountered:

The main problems faced were:

- Samples of the (CBC) and iron study were investigated in two different laboratories which made difficulties in delivering the samples to the 2 laboratories.

- Amount of blood which was needed (05mls) was so much that led some of the patients to refuse taking the sample, although they were fulfilling the inclusion criteria.
- The study was very costly concerning syringes, containers, storing of samples, iron study kits and investigations.

4 . RESULTS

4.1. Socio-demographic characteristics:

The total number of the study population was 100 patients, of whom 52 (52%) were males and 48 (48%) were females, which gave a balanced sample as shown in (**Fig. 1**).

The ages of the study population ranged between 06 months and 16 years. Those below 02 years of age were 36 patients (36%), between 02-<06 years were 29 patients (29%), between 06-10 years were 21 patients (21%) and only 14 patients (14%) were above 10 years, this is shown in (**Fig. 2**).

Most of the patients reside in Khartoum, but those who were originally from the Western Sudan predominated 48 (48%), while those from the Northern regions were 18 (18%), from Central Sudan were 15 (15%), from the South were 11 (11%) and only 08 patients (08%) were from Eastern Sudan (**Fig. 3**).

4.2. History:

4.2.1. Family and social history:

Regarding age of the mothers in the study group; 05 of them (05%) were below 20 years, 57 (57%) were between 20-35 years and 38 (38%) were above 35 years as shown in (**Fig. 4**).

Educational level of mothers was also obtained. The majority 67(67%) were illiterate, 25 (25%) had primary education; and only 08 (08%) had secondary education, none had university or postgraduate education as shown in (**Fig.5**).

Regarding fathers' education, 38 of the fathers (38%) were illiterate, 44 (44%) had primary education, 16 (16%) had secondary school education and only two (02%) were graduated from the university. None had postgraduate education as shown in (**Table1**).

Concerning fathers' occupation, 14 of them (14%) were government employees, 07 (07%) were small scale businessmen, 18 (18%) were skilled labourers, 16 (16%) were unskilled labourers and 45 (45%) were unemployed (**Fig. 6**).

Regarding the siblings of the study group, 40 of them (40%) had 3 or less siblings, 43 (43%) had 4-7 siblings and only 17 (17%) had more than 07 siblings (**Fig. 7**).

Table (1): Educational level of fathers

Educational level	No	%
Illiterate	38	**39%**
Primary	44	**44%**
Secondary	16	**16%**
University	02	**02%**
Post graduate	00	**0.0%**
Total	100	**100%**

About the family income, 40 patients in the study group (40%) were from very low income families, 53 (53%) had low income and only 07 (07%) had average income, none had satisfactory income (**Fig. 8**). As for the housing conditions of the study group, 31 (31%) had very poor housing conditions, 57 (57%) had poor housing conditions and only 12 (12%) had satisfactory housing conditions as shown in (**Fig. 9**).

4.2.2. Past history:

From the study findings, it was noticed that most of the studied population 98 (98%) were born at term, and only two (02%) were born preterm (**Fig. 10**). Ninety-four patients (94%) were singleton whereas 06 (06%) were twin deliveries (**Fig. 11**). The majority of the children 78 (78%) were born with average birth weight, 21 (21%) with low birth weight and only one (01%) was born with large birth weight as shown in (**Fig. 12**).

Only 05 of the studied group (05%) were transfused and 11 (11%) had started haematonics recently. Thirty-one patients (31%) had history of pica, four patients (04%) had positive history of bilharsiasis and four patients (04%) had history of worms infestation. Those who had recurrent epistaxis were 06 (06%) and none had dysphagia as shown in (**Table 2**).

Table (2): Some presenting symptoms of the study group

Symptoms and signs	No.	%
Blood transfusion	05	**05%**
H. of haematonics	11	**11%**
H. of pica	31	**31%**
H. of bilharsiasis	04	**04%**
H. of worms	04	**04%**
Rec. epistaxis	06	**06%**
H. of dysphagia	00	**0.0%**

Regarding vaccination, 66 patients (66%) were vaccinated up to date, 27 (27%) were partially vaccinated and only seven (07%) were not vaccinated (**Fig. 13**).

4.2.3. Nutritional history:

Regarding supplementary feeding of the study group, 36 patients (36%) had started supplementary feeding before the 4th month of age, while 64 (64%) after the 4th month (**Fig. 14**). Types of supplementary feeds that had been received, 65 patients (65%) had received cow's milk, 17 (17%) goat's milk, six (06%) formula milk and 15 (15%) were on breast milk with other types of food as shown in (**Table 3**).

Thirteen patients (13%) had not yet been weaned, three (03%) were weaned before one year of age, 75 (75%) were weaned between 1-2 years while nine (09%) were weaned after 2 years of age as shown in (**Fig. 15**).

Table (3): Types of supplementary feeding in the study group

Type d-food	No	%
Cow's milk	65	**65%**
Goat's milk	17	**17%**
Formula milk	06	**06%**
Breast milk only	12	**12%**
Total	100	**100%**

4.3. Clinical characteristics:

4.3.1. Anthropometric characteristics:

The weight of children in the study group ranged between 03 kg and 45 kg. The majority 59 (59%) had their weight below the 3rd centile, 10 (10%) between the 3rd and 10th centile and 31 (31%) were above the 10th centile (**Fig. 16**). Whereas the height of the children in the study group ranged between 56 cm and 180 cm, 32 patients (32%) heights were below the 3rd centile, 17 (17%) were between the 3rd and the 10th centile while the majority 51 (51%) were above the 10th centile as shown in (**Fig. 17**).

4.3.2. Clinical signs:

Concerning the clinical signs, most of the patients had obvious pallor, 78 patients (78%) were pale, 07 (07%) were very pale and 15 (15%) were clinically not pale (**Fig. 18**).

Regarding the other clinical signs, 36 (36%) look wasted, 26 (26%) had angular stomatitis, 50 (50%) had smooth tongue and 15 (15%) had oral thrush. No patient in the study group had signs of vitamin A deficiency. Five children (05%) were jaundiced, 24 (24%) had splenomegaly, 17 (17%) presented with abnormal respiratory system findings while 10 (10%) had abnormal (CVS) and only one patient (01%) had abnormal neurological signs as shown in (**Table 4**). Nineteen patients (19%) presented with

Table (4): Some clinical signs in the study group

Signs	No	%
Wasting	36	**36%**
Angular stomatitis	26	**26%**
Smooth tongue	50	**50%**
Oral thrush	15	**15%**
Jaundice	05	**05%**
Splenomegaly	24	**24%**
Resp. system	17	**17%**
CVS	10	**10%**
CNS	01	**01%**
Abdominal	36	**36%**

oedema, of whom 14 (73.7%) had lower limb oedema, three (15.8%) had puffiness of the face and only two patients (10.5%) had generalized oedema (**Fig. 19**).

4.4. Results of the investigations:

4.4.1. Haematological results:

All patients, when tested initially had haemoglobin levels below 11 g/dl. When tested by automatic blood counter there were only two patients (02%) who were not anaemic as shown in (**Fig. 20**).

Regarding the relationship between haemoglobin level and gender, Hb level was equally distributed between males and females. Twenty-seven patients had haemoglobin levels below 7 g/dl, of those 15 (55.6%) were females and 12 (44.4%) were males. Among the 71 patients (71%) whose Hb was between 7-11 g/dl, 39 (54.9%) were males and 32 (45.1%) were females. The only two males and 32 (45.1%) were females. The only two patients who had normal Hb, one was a male and the other was a female as shown in (**Table 5**). Concerning history of worms infestation, the four patients (04%) who had worms, 03 of them (75%) their Hb level was between 7-11 g/dl and only one patient (25%) had normal Hb level, whereas all the four patients with bilharsiasis their Hb level was between 7-11 g/dl (**Table 6**).

Table (5): Relationship between haemoglobin level and the gender in the study group

Haemoglobin level	Gender		Total
	Male	Female	
< 7 gm/dl	12 (**44.4%**)	15 (**55.6%**)	27 (**27%**)
7 – 11 gm/dl	39 (**54.9%**)	32 (**45.1%**)	71 (**71%**)
> 11 gm/dl	01 (**50%**)	01 (**50%**)	02 (**02%**)
Total	**52**	**48**	**100**

X2 = 13.9 P = 0.65

Table (6): Relationship between haemoglobin level and history of worms.

Haemoglobin level	History of worms			Total
	Worms	**Bilharzia**	**None**	
< 7 gm/dl	00 **(0.0%)**	00 (**0.0%**)	27(**27**%)	27 (**27%**)
7 – 11 gm/dl	03 (**75.0%**)	04 (**100%**)	64(**64**%)	71 (**71%**)
> 11 gm/dl	01 (**25.0%**)	00 (**0.0%)**	01(**01**%)	02 (**02**%)
Total	04 (**04%**)	04 (**04%**)	92 (**92%**)	100 (**100%**)

X^2 = 13.9 **P. value < 0.01**

Patients who had splenomegally were 24, 11 of them (45.8%) had Hb less than 7 g/dl, 12 (50%) had Hb between 7-11 g/dl and only one child (4.2%) had normal Hb level (**Table 7**). Concerning patients with history of pica, 31 children were found to have such a history. Ten patients (32.3%) had Hb less than 07g/dl, 21 patients (67.7%) had Hb between 07-11 g/dl and no patient had Hb more than 11g/dl as shown in (**Table 8**).

When considering the clinical sign of pallor, patients with Hb less than 7 g/dl, 19 patients (70.4%) were pale, 07 (25.9%) were very pale while only one patient (3.7%) was not pale. Patients whose Hb level was between 7 - 11 g/dl, 59 of them (83.1%) were pale and 12 (16.9%) were not pale. And the only two patients who were not anaemic had no pallor (**Table 9**).

Regarding (MCV) values in the studied group, nearly half of the patients (44%) had low levels, and 55 (55%) had normal values while only one (01%) had high value of (MCV). Twenty-seven patients (27%) had (MCH) below the normal range, 66 (66%) had (MCH) within the normal range while only seven patients (07%) had a level above the normal range. Similarly, 26 patients (26%) had a level of (MCHC) below the normal range, 72 (72%) had normal levels while only two patients (02%) had high

Table (7): Relation between the Hb level and patients with splenomegaly

Haemoglobin level	Splenomegaly		Total
	Yes	No	
< 7 gm/dl	11 (**40.7%**)	16 (**59.3%**)	27 (**27%**)
7 – 11 gm/dl	12 (**16.9%**)	59 (**83.1%**)	71 (**71%**)
> 11 gm/dl	01 (**50%**)	01 (**50%**)	02 (**02%**)
Total	24 (**24%**)	76 (**76%**)	100 (**100%**)

X^2 = 6.85 **P. value < 0.03**

Table (8): Relationship between the haemoglobin level and history of Pica in 31 children

Haemoglobin level	History of Pica		Total
	Yes	No	
< 7 gm/dl	10 (**37%**)	17 (**63%**)	27 (**27%**)
7 – 11 gm/dl	21 (**29.6%**)	50 (**70.4%**)	71 (**71%**)
> 11 gm/dl	00 (**0.0%**)	02 (**100%**)	02 (**02%**)
Total	31 (**31%**)	69 (**69%**)	100 (**100%**)

$X^2 = 6.85$ P. value = 0.49

Table (9): Correlation between haemoglobin and pallor in the study group

Hemoglobin level	Pallor			Total
	Not pale	Pale	Very pale	
< 7 gm/dl	01 (**3.7%**)	19 (**70.4%**)	07 (**25.9%**)	27 (**27%**)
7–11 gm/dl	12 (**16.9%**)	59 (**83.1**%)	00 (**0.0%**)	71 (**71%**)
> 11 gm/dl	02 (**100%**)	00 (**0.0%**)	00 (**0.0%**)	02 (**02%**)
Total	15 **(15%)**	78 **(78%)**	07 **(07%)**	100 **(100%)**

X^2 = 33.03 **P. value < 0.01**

values. About (PCV), the majority of the patients 65 (65%) had normal values, 24 (24%) had low values while only 11 patients (11%) had high values as shown in (**Table 10**).

Thirty-three patients (33%) had normal (ESR), 54 (54%) had high (ESR) while 13 patients (13%) had very high value (>100 mm/hr) as shown in (**Fig. 21**).

4.4.2. Iron study results:

About serum iron results, two third of the patients (66%) had low serum iron, one third (33%) had normal iron level while only one (01%) had high serum iron level. Half of the patients (50%) had normal ferritin level, 21 (21%) had low level and 29 (29%) had high serum ferritin level. Concerning the (TIBC), two third (65%) had normal level, one third (35%) had high level and none had low level of (TIBC) as shown in (**Table 11**).

Concerning the relationship between these iron study results, 18 patients (18%) had low level of both serum iron and serum ferritin while 13 of these patients (72.2%) had high level of (TIBC). Nineteen patients (19%) had both normal serum iron and ferritin, of whom 16 (84.2%) had normal (TIBC) while the only one who had high serum iron, had high serum ferritin and normal (TIBC) as shown in (**Table 12**).

Table (10): The red blood cell indices in the study group

	PCV	MCV	MCH	MCHC
Low	24 (**24%**)	44 (**44%**)	27 (**27%**)	26 (**26%**)
Normal	65(**65%**)	55 (**55%**)	66(**66%**)	72 (**72%**)
High	11(**11%**)	01 (**01%**)	07(**07%**)	02 (**02%**)
Total	100(**100%**)	100(**100%**)	100(**100%**)	100(**100%**)

Table (11): Results of iron studies in the study group

	Serum iron	**Serum ferritin**	**TIBC**
Low	66 (**66%**)	21 (**21%**)	00 (**0.0%**)
Normal	33 (**33%**)	50 (**50%**)	65(**65%**)
High	01 (**01%**)	29 (**29%**)	35(**35%**)
Total	100 (**100%**)	100 (**100%**)	100 (**100%**)

Table (12): Relationship between serum iron, serum ferritin and (TIBC).

Serum iron	Serum ferritin	TIBC		Total
		Normal	High	
Low	Low	05	13	18
	Normal	19	12	31
	High	12	05	17
Normal	Low	02	01	03
	Normal	16	03	19
	High	10	01	11
High	Low	00	00	00
	Normal	00	00	00
	High	01	00	01
Total		**65**	**35**	**100**

Low S. iron $X^2 = 7.54$ **P < 0.02**

Normal S. iron $X^2 = 1.09$ P = 0.58

Regarding the correlation between (MCH) and serum iron, 27 patients (27%) who had low (MCH), 26 of them (96.3%) had low serum iron and only one (3.7%) had normal iron. Patients who had normal (MCH), 38 patients (57.6%) had low serum iron, 28 patients (42.4%) had normal iron level and the only one who had high iron level also had high (MCH) as shown in (**Table 13**).

Regarding the relationship between (MCH) and serum ferritin, Among the 27 patients who had low (MCH), 08 patients (29.6%) had low serum ferritin, 13 (48.1%) had normal ferritin and 06 (22.2%) had high ferritin level. Patients who had normal (MCH) were 66, 13 of them (19.7%) had low ferritin level, 31 (47%) had normal ferritin and 22 (33.3%) had high ferritin level. The seven patients who had high (MCH), 06 patients (85.7%) had normal ferritin while only one patient (14.3%) had high serum ferritin level as shown in (**Table 14**).

About the relationship between (MCV) and serum iron, Among the 44 patients who had low (MCV), 43 of them (97.7%) had low serum iron and only one (2.3%) had normal iron level. Fifty-five patients had normal (MCV), 23 of them (41.8%) had low serum iron and 32 (58.2%) had normal iron level. The only one who had high (MCV), also had high iron level (**Table 15**).

Table (13): Relationship between (MCH) and serum iron in the study group

MCH	Serum iron			Total
	Low	Normal	High	
Low	26 (**96.3%**)	01 (**3.7%**)	00 (**0.0%)**	27 (**27**%)
Normal	38 (**57.6%**)	28 (**42.4%**)	00 (**0.0%**)	66 (**66%**)
High	02 (**28.6%**)	04 (**57.1%**)	01 (**14.3%)**	07 (**07%**)
Total	66 (**66%**)	33 (**33%**)	01 (**01%**)	100 (**100%**)

$X^2 = 29.27$ **P < 0.01**

Table (14): Relationship between (MCH) and ferritin level in the study group

MCH	Serum ferritin			Total
	Low	Normal	High	
Low	08 (**29.6%**)	13 (**48.1%**)	06 (**22.2%**)	27 (**27%**)
Normal	13 (**19.7%**)	31(**47.0%**)	22 (**33.3%**)	66 (**66%**)
High	00 (**0.0%**)	06 (**85.7%**)	01(**14.3%**)	07 (**07%**)
Total	21 (**21%**)	50 (**50%**)	29 (**29%**)	100 (**100%**)

$X^2 = 5.78$ P = 0.22

Table (15): Relationship between (MCV) and iron level in the study group

MCV	Serum iron level			Total
	Low	Normal	High	
Low	43 (**97.7%**)	01(**2.3%**)	00 (**0.0%**)	44 (**44%**)
Normal	23 (**41.8%**)	32 (**58.2%**)	00 (**0.0%**)	55 (**55%**)
High	00 (**0.0%**)	00 (**0.0%**)	01(**100%**)	01 (**01%**)
Total	66 (**66%**)	33 (**33%**)	01 (**01%**)	100 (**100%**)

$X^2 = 134.73$ **P < 0.01**

Regarding the correlation between the (MCV) and ferritin level, 44 patients (44%) had low (MCV), of whom 15 (34.1%) had low ferritin, 18 (40.9%) had normal ferritin and 11 (25%) had high ferritin level. As for the patients with normal (MCV), 06 patients (10.9%) had low ferritin, 32 (58.2%) had normal ferritin and 17 (30.9%) had high ferritin level. The only patient who had high (MCV) also had high ferritin level (**Table 16**).

When we looked into the serum iron status in the four patients who had history of worms infestation, 03 of them (75%) were found to have low serum iron while one (25%) had normal iron. However, in bilharsiasis the reverse is true, three out of the four patients with bilharsiasis (75%) had normal serum iron and only one had low iron level (**Table 17**).

All mothers whose ages were below 20 years, their children had low serum iron, while those with ages between 20-35 years, 39 of them (68.4%) their children had low serum iron and 18 (39.5%) their children had normal iron level. Mothers whose age was above 35 years, 22 (57.9%) of their children had low serum iron, 15 (39.5%) had normal iron and only one (2.6%) had high iron level (**Table 18**).

Table (16): Relationship between (MCV) and ferritin level in the study group

MCV	Serum ferritin level			Total
	Low	Normal	High	
Low	15 (**34.1%**)	18 (**40.9%**)	11 (**25%**)	44 (**44%**)
Normal	06 (**10.9%**)	32 (**58.2%**)	17 (**30.9%**)	55 (**55%**)
High	00 (**0.0%**)	00 (**0.0%**)	01 (**100%**)	01 (**01%**)
Total	21 (**21%**)	50 (**50%**)	29 (**29%**)	100 (**100%**)

$X^2 = 10.48$ **P < 0.03**

Table (17): Relationship between serum iron level and history of worms.

Serum iron	History of worms			Total
	Worms	Bilharsiasis	None	
Low	03 (**4.5%**)	01 (**1.5%**)	62 (**93.9%**)	66 (**66%**)
Normal	01 (**3.0%**)	03 (**9.1%**)	29 (**87.9%**)	33 (**33%**)
High	00 (**0.0%**)	00 (**0.0%**)	01 (**100%**)	01 (**01%**)
Total	04 (**04%**)	04 (**04%**)	92 **(92%**)	100 (**100%**)

$X^2 = 3.26$ P = 0.48

Table (18): Relationship between mothers' age and serum iron level in the study group.

Mother age in years	Serum iron level			Total
	Low	Normal	High	
< 20 yrs	05 (**100%**)	00 (**0.0%**)	00 (**0.0%**)	05 (**05%**)
20 – 35 yrs	39 (**68.4%**)	18 (**31.6%**)	00 (**0.0%**)	57 (**57%**)
> 35 yrs	22 (**57.9%**)	15 (**39.5%**)	01 (**2.6%**)	38 (**38%**)
Total	66 (**66%**)	33 (**33%**)	01 (**01%**)	100 (**100%**)

$X^2 = 5.10$ P = 0.28

About the 24 patients who had splenomegaly, 18 patients (75%) had low serum iron, 05 (20.8%) had normal serum iron while only one patient (4.2%) had high iron level as shown in (**Table 19**). Patients who had history of pica were 31, of whom 27 (87.1%) had low serum iron and only four (12.9%) had normal iron level. None had high serum iron level (**Table 20**).

Regarding ferritin level, 07 patients (22.6%) had low ferritin, 14 (45.2%) had normal ferritin and 10 patients (32.3%) had high ferritin level (**Table 21**). In co-relating serum iron with the type of supplementary feeds given to those children, it was found that patients who were supplemented with cow's milk, 38 of them (58.5%) had low serum iron, 27 (41.5%) had normal iron level (**Table 22**). While those who were supplemented with goat's milk, 15 of them (88.2%) had low serum iron and only two (11.8%) had normal iron level (**Table 23**).

When considering the clinical sign of pallor, patients with low serum iron, 53 (80.3%) were pale, 06 (9.1%) were very pale and only seven (10.6%) were not pale. Patients with normal serum iron, 25 of them (75.8%) were pale and 08 (24.2%) had no pallor, while only one patient who had high iron level appeared very pale (**Table 24**).

Table (19): Relationship between serum iron level and splenomegaly

Serum iron	Splenomegaly		Total
	Yes	No	
Low	18 (**27.3%**)	48 (**72.7%**)	66 (**66%**)
Normal	05 (**15.2%**)	28 (**84.8%**)	33 (**33%**)
High	01 (**100%**)	00 (**0.0%**)	01 (**01**%)
Total	24 (**24%**)	76 (**76%**)	100 (**100%**)

$X^2 = 4.97$ P = 0.08

Table (20): Relationship between serum iron level and history of pica in the study group

Serum iron level	History of pica		Total
	Yes	No	
Low	27 (**40.9%**)	39 (**59.1%**)	66 (**66%**)
Normal	04 (**12.1%**)	29 (**87.9%**)	33 (**33%**)
High	00 (**0.0%**)	01 (**100%**)	01 (**01%**)
Total	31 (**31%**)	69 (**69%**)	100 (**100%**)

X^2 = 8.98 **P < 0.01**

Table (21): Correlation between serum ferritin and history of pica in the study group

History of pica	Serum ferritin level			Total
	Low	Normal	High	
Yes	07 (**22.6%**)	14 (**45.2%**)	10 (**32.3%**)	31 (**31%**)
No	14 (**20.3%**)	36 (**52.2%**)	19 (**27.5%**)	69 (**69%**)
Total	21 (**21%**)	50 (**50%**)	29 (**29%**)	100 (**100%**)

$X^2 = 0.43$ P = 0.81

Table (22): Relationship between supplements with cow's milk and serum iron level

Cow's milks supplements	**Serum Iron**			**Total**
	Low	Normal	High	
Yes	38 (**58.5%**)	27 (**41.5%**)	00 (**0.0%**)	65 (**65%**)
No	28 (**80%**)	06 (**17.1%**)	01 (**2.9%**)	35 (**35%**)
Total	66 (**66%**)	33 (**33%**)	01 (**01%**)	100 (**100%**)

$X^2 = 7.56$ **P < 0.02**

Table (23): Relationship between serum iron level and supplements with goat's milk

Supplements with goat's milk	Serum iron level			Total
	Low	Normal	High	
Yes	15 (**88.2%**)	02 (**11.8%**)	00 (**0.0%**)	17 (**17%**)
No	51 (**61.4%**)	31 (**37.3%**)	01(**1.2%**)	83 (**83%**)
Total	66 (**66%**)	33 (**33%**)	01 (**01%**)	100 (**100%**)

$X^2 = 4.54$ **P < 0.01**

Table (24): Correlation between serum iron and the clinical signs of pallor in the study group

Serum iron level	Pallor			Total
	Not pale	Pale	Very pale	
Low	07(**10.6%**)	53 (**80.3%**)	06 (**9.1%**)	66 (**66%**)
Normal	08 (**24.2%**)	25 (**75.8%**)	00 (**0.0%**)	33 (**33%**)
High	00 (**0.0%**)	00 (**0.0%**)	01(**100%**)	01 (**01%**)
Total	15 (**15%**)	78 (**78%**)	07 (**07%**)	100 (**100%**)

$X^2 = 18.08$ **P < 0.01**

Regarding smooth tongue, patients with low iron level, 37 (56.1%) had smooth tongue and 29 (43.9%) had not, while those with normal iron level, 13 (39.4%) had smooth tongue and 20 (60.4%) had no smooth tongue. The only one who had high iron level had no smooth tongue (**Table 25**).

Table (25): Correlation between serum iron level and smooth tongue

Serum iron level	Smooth tongue		Total
	Yes	No	
Low	37 (**56.1%**)	29 (**43.9%**)	66 (**66%**)
Normal	13 (**39.4%**)	20 (**60.6%**)	33 (**33%**)
High	00 (**0.0%**)	01 (**100%**)	01 (**01%**)
Total	50 (**50%**)	50 (**50%**)	100 (**100%**)

$X^2 = 3.46$ P = 0.18

5 . DISCUSSION

5.1. Socio-demographic characteristics:

The total number of the studied population was 100 children, 52 of them were males (52%) and 48 were females (48%). This finding was different from a study done in India in which females predominated (77%), however, it was similar to that which was done in (USA) in which females were (53%) of the studied group [31,37].

Age group ranged between 06 months and 16 years with peak age below 02 years. Younger infants were not enrolled, to avoid the physiological anaemia.

Majority of patients (59%) were originally from West or South Sudan and lived mainly in the outskirts of Khartoum town. This could be explained by the fact that the free resources of the hospitals are mainly utilized by the lower social class. Most of these people being recent immigrants or displaced by war, drought and famine are more prone to have a higher prevalence of anaemia.

5.2 History:

5.2.1 Family and social history:

Only five of the mothers (05%) were below 20 years of age and 38 (38%) were above 35 years. This indicate that children of elderly mothers are more susceptible to anaemia. This difference may be due to the fact that mothers with multiple deliveries are more prone to depletion of body iron stores which can be reflected in their children.

Regarding mothers' education, the majority (67%) were illiterate, which plays an important role in child's nutritional adequacy. As Sudan is a developing country, this percentage of high illiteracy is well understood, but to be living in the capital and be illiterate is quite unfair. However, they could have migrated recently from rural areas as shown above, the majority were from regions of conflicts.

Fathers' occupation reflects the economical status and the social class. Nearly half of the fathers (45%) were unemployed. This reflects the instability of the child's nutritional status. This was clearly reflected in the family income, which showed that (93%) of the patients' families had low or very low income. Moreover, (88%) of the study group had poor or very poor housing condition.

5.2.2 Past history:

From the history of birth, most of these patients were born normally, (98%) were term, (94%) were singleton and (78%) with average birth weight. This indicates that most of these patients' anaemia was acquired later in life and that it was mainly nutritional in origin.

Patients who had a history of pica were (31%). This is similar to a study which was done by El Tohami EA in 1980, that showed (40.3%) of the patients had history of pica [38].

Very few patients who had history of worms infestation or bilharziasis, accounting for only (04%) each. This is may be due the fact that Khartoum State is not an endemic area of bilharziasis or other worms. The majority of the studied group (65%) were below 05 years of age and consequently they were not expected to be exposed to the sources of bilharzia transmission at this age. So worms and bilharziasis were not major causes of iron deficiency in this study group. This is similar to a study carried in Ethiopia in 230 anaemic patients showed that the incidence of hookworms were (0.4%) and contributed little in their anaemia [65]. However, it is not similar to the findings in other countries such as Zanzibar where hookworms accounting for (33.8%), were one of the major causes of iron deficiency in children below 05 years of age [66]. Another

study conducted in Delhi (India) in 406 children and found that (47.5%) of the children studied had history of worm infestations [37]. Moreover, in north-west Australia, the prevalence of hookworms in children aged 05-14 years was (93%) with iron deficiency (79%) in this age group [70].

None of the patients had history of dysphagia that may suggest Plummer-Vinson syndrome. This is consistent with the literature that denoted: “Plummer-Vinson syndrome usually occurs in adults, rarely in adolescents, however, there have been no previous reports in the English-language literature of the syndrome occurring in childhood". The first case that was reported in the year 2000 was in 6 years old child in United Leeds Teaching Hospital, England [71].

The majority of the patients (66%) were vaccinated up to date, (27%) were incompletely vaccinated while only (07%) were not vaccinated. This reflects the awareness of the families about the importance of vaccination, and also could be explained by the efforts of the team of the National Programme of Immunization (EPI).

5.2.3 Nutritional history:

Regarding supplementary feeding, about two thirds of the patients (64%) started supplementary feeding after the fourth

month. The majority (65%) were supplemented with cow's milk which also, like breast milk, contains small amount of iron while only (10%) of its iron content is absorbed [71]. This goes with a study conducted in Dublin (England) showing that at age 12 months, cows' milk consumption was negatively associated with iron status [72].

As mentioned above; most of the families were of low social class, the other supplementary feeds could also be deficient in iron. All these factors could predispose to the development of anaemia and iron deficiency in those children at earlier stages of their lives.

Concerning weaning, it was found to be adequate for (75%) of the patients who were weaned between age 1-2 years, with only (03%) who were weaned before one year of age. This reflects that breast milk was the main source of feeding in early infancy in our study population.

5.3. Clinical characteristics:

5.3.1 Anthropometric characteristics:

The weight of the majority of the patients (59%) was below the 3rd centile while almost half of them (51%) had normal height. This reflects that their problems were acute affecting weight loss together with anaemia without affecting height so much.

5.3.2 Clinical signs:

Regarding the clinical sign of pallor, (85%) of the patients looked pale or very pale. This indicates that the clinical sign of pallor can give a clue about the amount of haemoglobin in the blood and directs the doctor towards investigating the patient for anaemia.

Other clinical signs such as wasting (36%) angular stomatitis (26%), oral thrush (15%), jaundice (05%) as well as (CVS), respiratory and neurological signs were not related to iron deficiency. They could be due to an underlying illness that led to anaemia or a concomitant complication of the underlying illness such as oral thrush and angular stomatitis. Whereas other signs like smooth tongue, which was in (50%) of study group and splenomegaly in (24%), were features of chronic iron deficiency. As splenomegaly is an uncommon feature in iron deficiency, this high percentage (24%) could be due to other underlying problems and not due to iron deficiency.

Nineteen percent of the patients had oedema and it was not a presenting feature of iron deficiency. Although it might be due to anaemic heart failure, yet it may be due to many other diseases which present affecting various parts of the body.

5.4 Results of the investigations:

5.4.1 Haematological results:

All patients were anaemic by calorimetric method. When automatic blood counter was used, (98%) of them were still anaemic, indicating the high sensitivity of calorimetric method for checking the haemoglobin level.

Haemoglobin level was equally distributed between males and females and there was no significant difference between them (P=0.65). Females, during reproductive age, are more prone to develop anaemia and iron deficiency than males [21]. However, this was not observed in the study group as they were all below this age.

Anaemic patients who had lower haemoglobin level had a higher percentage value of splenomegaly. That (40.7%) their Hb below 07 gm/dl with (16.9%) had Hb of 7-11gm/dl, with significant association between haemoglobin level and splenomegaly (P=0.03). This could be explained by the fact that, the severity of the disease leading to a reduced haemoglobin level, may cause more other detectable features which splenomegaly is one of them. Moreover, it could be a secondary site for red blood cells destruction (hypersplenism), leading to much lower haemoglobin.

There was no significant correlation between haemoglobin level and history of pica (P=0.49). This is true for anaemia which has different etiological factors while pica is related to iron deficiency only and not associated with other causes of anaemia. However, there was significant correlation between haemoglobin level and clinical pallor (P=0.01). This means that clinical pallor reflects the haemoglobin level of the patients.

Most of the results of the red blood cell indicies were either low or normal such as (PCV) values (24%) were low and (65%) were normal. While (44%) of the (MCV) values were low and (55%) were normal. Moreover, (27%) of the (MCH) results were low and (66%) were normal. These results reflect the high sensitivity of the red blood cell indicies to change by different haematological effects and they can be used as a clue for the underlying deficiency. In these results, (44%) of the patients had low (MCV) which is indicative of microcytic cells and this is related to iron deficiency which is one of the causes of microcytosis. This goes with a study conducted in Ohio (USA) in 305 children revealed that the prevalence of microcytic anaemia was (08%) and was associated with iron deficiency [(73)]. However, it was not similar to another study carried in Texas (USA) in 321 infants between 09-12 months showing that haematocrit was not an adequate

screening test for iron deficiency [74]. This could be explained by the fact that haematocrit is related to both red cell count and (MCV). Moreover, the study used a younger age group with a narrow range that can not be applied for all children.

Only (13%) of the studied group had normal erythrocyte sedimentation rate (ESR). These elevated (ESR) results could be either due to the underlying illnesses, as these children were admitted to the hospital for medical problems or due to the anaemia itself which could raise the (ESR).

5.4.2 Iron study results:

Concerning serum iron, the majority of the patients (66%) were having low serum iron. This is different from the results of a study carried in (USA) which reported iron deficiency in only (15%) of the study population, they were (08%) with anaemia and (07%) without anaemia [13]. However, it is similar to the findings of the studies conducted in India showing iron deficiency anaemia in (68.42%), and in Tanzania which showed that (61%) of the anaemic patients had iron deficiency [37,28]. While in Sudan, Mustafa MI showed that (86%) of the patients with sickle cell anaemia had iron deficiency [39]. Moreover, Bafakeer SS in his study showed that (63.6%) of the children's group had low serum iron [40]. From the data mentioned above, having a far higher

percentage of iron deficiency in these children than in (USA) is expected, as it is a developed country. However, the results were similar to the studies from Delhi (India) and Tanzania as they were developing countries along with the study carried in Sudan by Bafakeer SS.

About the results of the study of the sicklers conducted by Mustfa MI, they were a group of haemolytic anaemia not included in my study. It is unlikely that children with sickle cell anaemia to have high prevalence of iron deficiency .

Regarding serum ferritin, half of the patients 50 (50%) had normal ferritin, 29 (29%) had high ferritin level and only 21 of study group (21%) had low serum ferritin level. Although it was measured by a very sensitive radio-immunoassay technique, this low percentage of low level could be attributed to the fact that serum ferritin is an acute phase reactant protein that can be normal or elevated during inflammation [(65)]. Moreover, all patients were admitted to hospitals with medical problems, so serum ferritin can not be taken alone in ill patients in such a situation for evaluation of iron status.

About the total iron binding capacity (TIBC), all of the results were either normal (65%) or high (35%) reflecting the low level of serum iron mentioned above. This differs from the study

which was conducted by Bafakeer SS that showing the results of children's group in whom the majority (45.5%) were having low (TIBC) level [40].

Regarding the association between serum iron and (MCV), the 44 patients who had low serum iron (44%), 43 of them (97.7%) had low serum iron and only one (02.3%) had normal iron level. While the 55 patients who had normal serum iron (55%), 23 of them (41.8%) had low serum iron and 32 (58.2%) had normal iron level. The only one who had high (MCV) also had high ferritin level. This association statistically is very significant (**P < 0.01**).

Considering the relationship between serum ferritin and the (MCV), 44 patients (44%) who had low (MCV), 15 of whom (34.1%) had low serum ferritin, 18 (40.9%) had normal ferritin and 11 (25%) had high ferritin level. While the 55 patients who had normal (MCV). 06 patients (10.9%) had low serum ferritin, 32 (58.2%) had normal ferritin and 17 (30.9%) had high ferritin level. The only one who had high (MCV) also had high serum ferritin. This relationship was also statistically significant (**P<0.03**), indicating that the reduction in serum iron and ferritin has thier effect on reducing (MCV) level.

Concerning the correlation between serum iron and history of worms infestation, it was not significant (P=0.48), as well as the

relationship between the serum iron and splenomegaly ($p<0.08$). Whereas the association between iron level and history of pica, the 31 patients who had history of pica, 27 of them (87.1%) had low serum iron and only four (12.9) had normal iron level. This association is very significant (**P < 0.01**). However, it was not statistically significant when the history of pica was compared with ferritin level (P = 0.81).

More than half of the patients who were supplemented with cow's milk (58.5%) had low serum iron while (41.5%) had normal serum iron and non had high iron level. This association is statistically significant (**P<0.02**). This is also similar to the association between goat's milk and serum iron of the children in whom (88.2%) had low serum iron while (11.8%) had normal iron level (**P < 0.01**). From these results, cow's milk and goat's milk seem to have a role in developing iron deficiency if given as a supplementary feeds without supplying the infant with iron or iron rich food.

Regarding pallor, (80.3) of the Patients who had low serum iron, (80.3%) of them appeared pale, (09.1%) very pale and only (10.6%) looked normal. This correlation between iron level and clinical sign of pallor seems to be significant (**P = 0.01**). While these patients with such level of serum iron, (56.1%) of them had

smooth tongue and (43.9%) had not, and this relationship was found to be statistically not significant (P = 0.81).

6- CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

Iron deficiency is the commonest cause of anaemia, which is mainly nutritional.

Anaemia and iron deficiency anaemia are more common among people of lower social class, who have recently migrated to Khartoum State.

In iron deficiency, it is difficult to differentiate between splenomegaly due to iron deficiency from that due to other causes. However, it is a common finding in ill patients, although it is a rare sign in iron deficiency in apparently healthy children.

Pica is one of the common presenting symptoms of iron deficiency.

Child's nutrition, mother's education and father's economical status play a major role in iron deficiency anaemia among children.

Cow's milk and goat's milk have a great effect in reducing serum iron if used as supplement food during infancy without iron supplementation.

Worms and bilharziasis were not major problems in Khartoum State.

Serum ferritin is a single sensitive test which reflects iron stores. However, during infection it is not useful alone for evaluation of iron status.

Other red blood cell indices are sensitive to changes due to iron deficiency such as packed cell volume (PCV), mean corpuscular volume(MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC).

6.2 RECOMMENDATIONS

More studies involving large numbers from different clusters are needed.

Further studies for evaluation of other causes of anaemia are important and will be valuable.

Etiological causes of iron deficiency anaemia should be included in future studies.

Detection of haemolytic anaemia using reticulocyte count must be considered in the future researches.

Reference values for haemoglobin and iron study parameters need to be studied in the future researches and studies.

Peripheral blood picture should be included in the future studies.

Patients who are anaemic, need evaluation of their anaemia and should be started on iron supplement if they are iron deficient.

Iron fortification of supplementary food should be adopted in our country.

Formula milk should be substituted for cow's milk and goat's milk as supplementary food in infants together with iron rich foodstuffs such as Hilba (fenugreek seed), cereals and pulses.

Iron studies should be included in the routine investigations of the patients with anaemia.

Education schools for illiterate women together with health education sessions should be established in the outskirts of Khartoum town.

REFERENCES

(1) Fairbeaks VF, Beuller E. Iron deficiency. In: Boutler E, Lichtman MA, Coller BS, Kipps TJ, Seligsohn U, (editors). Williams Haematology, 6th ed. Massachusetts**:** McGraw-Hill; 2001.p. 447-465.

(2) Edwards CRW, Bouchier IAD, Haslett C, Chilvers ER. Diseases of the blood. In: Mackie MJ, Ludtam CA, (editors). Davidson's Principles and Practice of Medicine, 17th ed. Edinburgh: Churchill Livingstone; 1995. p. 775-842.

(3) Booth IW, Aukett MA. Iron deficiency Anaemia in infancy and early childhood. Arch Dis Child. 1997 Jun; 76:549-54.

(4) Fleming AF. Haematological diseases in the tropic. In: Cook GC, (editor). Manson's Tropical Diseases, 20th ed. London: W.B. Saunders Company Ltd; 1996.p. 101-173.

(5) Talbptt JH. Haematologic disorders. In: Berkow R, Bondy DC, Ormsby JW, Bondy PK, Petersdorf RG, (editors). The merk manual of diagnosis and therapy. 14th ed. Rahway (USA). Merk & Company inc; 1982.p.705-69.

(6) Rush B. Iron deficiency and sideroblastic anaemia. In: Firkin F, Chesterman C, Penington D, Rush B. (editor). deGruchy's Clinical Haematology in Medical Practice,

5th ed. London: Blackwell Scientific Publications 1989; p. 37-61.

(7) Pippard MJ. Iron metabolism and its disorders. In: Weatherall DJ, Ledingham THH, Warrell DA, (editors). Oxford Textbook of Medicine, 3rd ed. New York: Oxford University Press; 1996.p. 3471-3483.

(8) Hall JE. Red cells anaemia and polycythaemia. In: Guyton AC, Hall JE, (editor). Textbook of Medical Physiology, 9th ed. Philadelphia: W.B. Saunders Company; 1996.p. 425-434.

(9) Bondy DC, Schreiner GE. Nutrition and metabolic disorders. In: Berkow R, Bondy DC, Ormsby JW, Bondy PK, Petersdorf RG,(editors). The merk manual of diagnosis and therapy. 14th ed. Rahway (USA). Merk & Company inc; 1982.p.575-656.

(10) Abdul Gader AM. The blood.In: Sukkar MY, El-Munshid HA, Ardawi MSA. Concise Human Physiology, 2nd ed. London: Blackwell Science Ltd; 2000.p. 15-38.

(11) Rowan RM. The blood and bone marrow. In: MacSween RNM, Whaley K, (editors). Muir's Text Book of Pathology, 13th ed. London: Arnold; 1992.p. 585-644.

(12) Pippard MJ, Hoffbrand AV. Iron. In: Hoffbrand AV, Lewis SM, Tuddenham EGS, (editors). Postgraduate Haematology, 4th ed. Wolburn: Butterworth-Heinemann; 1999.p. 23-46.

(13) Ganong WF. Digestion and absorption.In: Ganong WF, (editor). Review of Medical Physiology; 18th ed. Connecticut: Appleton & Lange; 1997.p. 437-447.

(14) Pannall PR Iron metabolism. In: Zilva JF, Pannall PR, Mayne PD,(editors). Clinical Chemistry in Diagnosis and Treatment, 5th ed. London: Edward Arnold; 1988.p. 388-401.

(15) Mettler FA, Williams SL. Environmental health hazards. In: Behrman RE, Kliegman RM, Jenson HB, (editors). Nelson Textbook of Pediatrics. 16th ed. Philadelphia. W.B.Saunders Company; 2000.p.2148-178.

(16) Sing K.Toxicologic disorders: Iron. In: Aghababian RV, Allison EJ, Richard BG,Fleisher GR, McCabe JB, Moorhead JC, (editors). Emergency medicine the core curriculum. 1st ed. Philadelphia. Lippincott-Raven Publishers; 1998.p.1139-143.

(17) Henretig FM, Lavelle JM, Ditmar MF. Emergency Medicine. In: Polin RA, Ditmar MF,(editors). Pediatric Secrets. 2nd ed. Philadelphia. Hanley & Belfus Inc; 1997.p.99-127.

(18) Nechout RC. Iron poisoning. In: Gellis SS, Kagan BM. Current Paediatric Therapy, 9th ed. Philadelphia: McGrowth Hill Companies; 1980.p. 685-686.

(19) El Tohami EA. Nutritional aspects of pica and its relation to iron deficiency**.** 1980; (Thesis) U. of K**.**

(20) Mustafa MI. Iron deficiency in Sudanese children with sickle cell anaemia. 1988; (Thesis). U. of K.

(21) Bafakeer SS. Assessment of iron status in Sudanese patients presenting to SUH with low red cell indices irrespective of their Hb values. 2003; (Thesis) U. of K.

(22) A/Elbager EA, Assesment of iron status in Sudanese pregnant ladies and their newborn babies, 2004; (Thesis). U of K.

(23) Yip HKR, Schultink W, Dillon DHS. World Health Organization: Cut-off points for the detection of anaemia are valid for an Indonesian population. Am J Nutr Sci 1999; 129: 1669-674.

(24) Couper RTL, Simmer KN. Iron deficiency in children: food for thought. Med J Aust 2001; 174: 162-63.

(25) Kapur D, Sharma S, Agarwal KN. Effectiveness of nutrition education, iron supplementation or both or iron status in children. Indian Paediatr 2003; 40(12): 1131-144.

(26) Marx JJ. Iron deficiency in developed countries: prevalence, influence of lifestyle factors and hazards of prevention. Eur J Clin Nutr 1997; 51(8): 491-94.

(27) Halterman JS, Kaczorowski JM, Aligne CA, Auinger P, Szilagyi PG. Iron deficiency and cognitive achievement among school age children and adolescent in the United States. Pediatrics 2001; 107: 1381-386.

(28) Looker AC, Dallman PR, Carroll MD, Gunter EW, Johnson CL. Prevalence of Iron deficiency in the United States. JAMA 1997; 277(12): 973-76.

(29) Tejas AR, Wyatt CJ, Ramirez MJ. Prevalence of undernutrition and Iron deficiency in re-school children from different socio-economic regions in the city of Oaxaca, Oaxaca, Mexico. J Nutr Sci Vitaminol 2001; 47(1): 47-51.

(30) Villalpando S, Shamah-Levy T, Ramirez-Silva CI, Mejia-Rodriguez F, Rivera JA. Prevalence of anaemia in children 1 to 12 years of age. Results from a nationwide probabilistic survey in Mexico. Salud Pub Mex 2003; 45(suppl 4): S490-98.

(31) Norton RC, Figueiredo RC, Diamante R, Goulart EM, Mota JA, et al. Prevalence of anaemia among school children from Rio-Acima (State of Minas Gerais, Brazil): Use of the standardized prevalence method and evaluation of Iron deficiency. Braz J Med Biol Res 1996; 29(12): 1617-624.

(32) Kocak R, Alpraslan ZN, Agridog G, Baslamisli F, Aksungur PD, et al. The frequency of anaemia iron deficiency, haemoglobin S and beta thalassemia in the south of Turkey. Eur J Epidemiol 1995; 11(2): 181-84.

(33) Grant GA. Prevalence of iron deficiency in rural pre-school children in Northern Ireland. Br J Gen Pract 1990; 40 (332): 112-13.

(34) Karr M, Alpertein G, Causer J, Mira M, Lammi A, Fett MJ. Iron status and anaemia in pre school children in Sydney. Aust J Pub Hlth 1996; 20(6): 618-22.

(35) Bogen DL, Duggan AK, Dover GJ, Wilson MH. Screening for iron deficiency anaemia by dietary history in a high risk population. Pediatrics 2000; 105(6): 1254-259.

(36) Musaiger AO. iron deficiency anaemia among children and pregnant women in the Arab Gulf countries: the need for action. Nutr Hlth 2002; 16(3): 161-71.

(37) Hossain MM, Bakir M, Pugh RN, Sheekh-Hussen M, Bin Ishaq SA, et al. The prevalence and correlates of anaemia among young children and women of child bearing age in Al Ain, United Arab Emirates. Ann Trop Paediatr 1995; 15(3): 227-35.

(38) Hall A, Babrow E, Brooker S, Jukes K, Lambo J, et al. Anaemia in school children in eight countries in Africa and Asia. Pub Hlth Nutr 2001; 4(3): 749-56.

(39) Stoltzfus RJ, Chwaya HM, Tielsch JM, Schulze KJ, Albonico M, et al. Epidemiology of Iron deficiency anaemia in Zanzibari school children: The importance of hookworms. Am J Clin Nutr 1997; 65(1): 153-59.

(40) Paracha PI, Hameed A, Simon J, Jamil A, Nawab G. Prevalence of anaemia in semi-urban areas of Peshawar, Pakistan: a challenge for health professionals and policy makers. J Pak Med Assoc 1997; 47(2): 49-53.

(41) Gomber S, Bhawna, Madan N,Lal A,Kala K. Prevalence and etiology of nutritional anaemia among school children of urban slums. Indian J Med res. 2003 Oct; 118: 167-71.

(42) Schwartz E. Anaemia of inadequate production. In: Behrman RE, Kliegman RM, Jenson HB, (editors). Nelson

Text Book of Paediatrics, 16th ed. Philadelphia: W.B. Saunders Company; 2000.p. 1463-1472.

(43) Lane PA, Nuss R, Ambruso DR. Haematologic disorders. In: Hay WW, Hayward AR, Levin MJ, Sondheimer JM, (editors). Current Paediatric Diagnosis & Treatment, 15th ed. New York: McGraw-Hill Companies; 2001.p. 741-792.

(44) Lozoff B, Klein NK, Nelson EC, McClish DK, Manuel M, et al. Behaviour of infants with Iron deficiency anaemia. Child Dev 1998; 69(1): 24-36.

(45) Oti-Boateng P, Sestiadri R, Petrick S, Gibson RA, Simmer K. Iron status and dietary iron intake of 6-24 month-old children in Adelaide. J Paediatr Child Hlth 1998; 34(3): 250-53.

(46) Mark W. Iron deficiency anaemia and iron overload. In: Lewis SM, Bain BJ, Bates I, (editors). Dacie and Lewis Practical Haematology, 9th ed. Lodnon: Churchill-Livingstone; 2001.p. 115-128.

(47) Annchen WV, Lesperance L, Bernstean H. Screening for iron deficiency. Pediatr Rev 2001; 23: 171-78.

(48) Walters HM, Seal LH. Systematic approach to the assessment of erythropoiesis. Clin Lab Haematol 2001; 23: 271-283.

(49) Serdar MA, Sarici SU, Kurt I, Alpay F, Okutan V, et al. The role of erythrocyte protoporphyrin in the diagnosis or iron deficiency anaemia of children. J Trop Paediatr 2000; 46 (6): 323-26.

(50) Choi JW, Pai SH. Association between serum transferring receptor concentration and erythropoietic activities according to body iron status. Ann Clin Lab Sci 2003; 33(3): 279- 84.

(51) Paley C, Iron deficiency anaemia. In: Lanzkowsky P (editor). Manual of paediatric haematology and oncology, 3rd ed. San Diego, California. Academic press. 2000.p.33-49.

(52) Mei Z, Parvanta I, Cogswell ME, Gunter EW, Grummer-Strawn LM. Erythrocyte protoporphyrin or haemoglobin: which is a better screening test for iron deficiency in children and women. Am J Clin Nut 2003; 77(5): 1229- 33.

(53) Ganti AK, Moazzam N, Laroia S, Tendulkar K, Potti A, et al. Predictive value of absent bone marrow iron stores in the clinical diagnosis of iron deficiency anaemia. Vivo 2003; 17(5): 389-92.

(54) Nuchprayoon I, Sukthawee B, Nuchprayoon T. Red indices and therapeutic trial of iron in diagnostic work-up for

anaemic Thai females. J Med Assoc Thai 2003; 86 (supp 2): S160-69.

(55) Brugnara C. Iron deficiency and erythropoiesis: new diagnostic approaches. Clin Chem 2003; 49(10): 1573-578.

(56) Stollzfus RJ, Chwaya HM, Montresor A, Albonico M, Savioli L, et al. Malaria, hookworms and recent fever are related to anaemia and iron status indicators in 0 to 5 years old Zanibari children and these relationships change with age. J Nutr 2000; 130(7): 1724-733.

(57) Sultan AN, Zuberi RW. Late weaning: The most significant risk factor in the development of iron deficiency anaemia at 1-2 years of age. J Ayub Med Coll Abbottabad 2003; 15(2): 3-7.

(58) Adish AA, Esrey SA, Gyorkos TW, Johns T. Risk factors for iron deficiency anaemia in preschool children in northern Ethiopia. Pub Hlth Nutr 1999; 2(3): 243-52.

(59) Tatala S, Svanberg U, Mduma B. Low dietary iron availability is a major cause of anaemia: a nutrition survey in the Lindi district of Tanzania. Am J Clin Nutr 1998; 68(1): 171-78.

(60) Oslen A, Magnussen P, Ouma JH, Andreassen J, Friis H. The contribution of hookworm and other parasitic infections

to haemoglobin and iron status among children and adults in western Kenya. Trans R Soc Trop Med Hyg 1998; 92(6): 643-49.

(61) Prual A, Daouda H, Develoux M, Sellin B, Galan P, Hercberg S. Consequences of schistosoma haematobium infection on the iron status of school children in Nigar. Am J Trop Med Hyg 1992; 47(3): 291-97.

(62) Viteri FE. Iron supplementation as a strategy for the control of iron deficiency and ferropenic anaemia. Arch Latinoan Nutr 1999; 49 (3 suppl 2): 15 S-22 S.

(63) Surico G, Muggeo P, Muggeo V, Lucarelli A, Martucci T, Daniele M, Rigillo N. Parenteral iron supplementation for the treatment of iron deficiency anaemia in children. Ann Haematol 2002; 81(3): 154-57.

(64) Triola FM. Determining sample size in: Elementary statistics. 7th ed. New York: RR Donnely & Scns press; 1998. P:319-21.

(65) Adish AA, Esrey SA, Gyorkos TW, Johns T. Risk factors for iron deficiency anaemia in preschool children in Northern Ethiopia. Public Health Nutr. 1999; 2(3):243-52.

(66) Staltzfus RJ, Chwaya HM, Montresor A, Albonico M, Savioli L, Tielsch JM. Malaria, hook worms and recent fever are

related to anaemia and iron status indicators in 0 to 5 years old Zanzibari children and these relationships change with age. J Nutr 2000; 130(7): 1724-33.

(67) Strauss RG. Blood and blood component transfusions. In: Behrman RE, Kliegman RM, Jenson HB, (editors). Nelson Textbook of Pediatrics. 16th ed. Philadelphia. W.B.Saunders Company; 2000.p.1499-503.

(68) O´Neil R, The blood. In: Emslie-Smith D, Paterson CR, Scratcherd T, Read NW (editors). Textbook ofphysiology. 11th ed. Edinburph. Churchill Livingstone; 1988. p.23-41.

(69) Taylor PG, Martinez-Torres C, Mendez-Castellano H, Bosch V, Leets I, et al. The relationship between Iron deficiency and anaemia in Venezuelan children. Am J Clin Nutr 1993; 58(2): 215-18.

(70) Hopkins RM, Gracey MS, Hobbs RP, Spargo RM, Yates M, Thompson RC. The prevalence of hookworm infection, iron deficiency and anaemia in an aboriginal community in north-west Australia. Med J Aust. 1997; 166(5): 241-44.

(71) Antony R, Sood S, Strachan DR, Fenwick JD. Acase of Plummer-Vinson syndrome in childhood. J paediatr Surg 2000; 35(6): 1015.

(72) Freeman VE, Mulder J, van't Hof MA, Hoey HM, Gibney MJ. A longitudinal study of iron status in children at 12, 24 and 36 months. Public Health Nutr. 1998; 1(2): 93-100.

(73) Boutry M, Needlman R. Use of diet history in the screening of iron deficiency. Pediatrics. 1996; 98(6): 1138-42.

(74) Kazal LA. Failure of hematocrit to detect iron deficiency in infants. J Fam Pract. 1996; 42(3): 237-40.