iJRASET
International Journal For Research in Applied Science and Engineering Technology



INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Volume: 6 **Issue:** XII **Month of publication:** December 2018

DOI:

www.ijraset.com

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International Journal for Research in Applied Science & Engineering Technology (IJRASET)
ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 6.887
Volume 6 Issue XII, Dec 2018- Available at www.ijraset.com

Ferritin and Hepcidin Levels among Iron Deficient Children in Khartoum

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Abstract: Introduction: Iron deficiency anemia is one of the global issues the world concerns about, as iron importance extended to many functions in human body, in addition to the oxygen content provided with it. Children can't tolerate iron deficiency as it affects their growth in many ways. Always iron deficiency anemia based diagnosis, the outcome of complete blood count considering the red cell count, hemoglobin concentration and red cell indices, but it not enough sometimes, if there an infection presents, ferritin level would be increased in response, therefore blocking other diagnosis tool for iron deficiency anemia when measuring iron profile. So this study aimed to assess iron deficiency anemia though measuring ferritin and hepcidin considering the findings of complete blood count. This study was approved by the ethical committee of Alneelain University-faculty of medical laboratory science and children's parents also gave a permission for enroll their children in the study after acknowledged them with its importance.
Material and method: one hundred and fifty children were recruited to be evaluated for iron deficiency anemia through complete blood count, which conducted via full automated hematology analyzer Mindray BC 200. Ferritin level was measured using a Tohoso analyzer and hepcidin assessed by enzyme linked immunosorbent assay using BTS 350 device as a tool for the measurement.
Result: 55 children were fount having iron deficiency anemia, considering red cell count, hemoglobin concentration red cell indices and low or normal count of white blood cell. Those children were assessed further for ferritin and hepcidin. Low levels for both parameters were found among males and females in comparison to the reference ranges.
Keyword: hepcidin, ferritin, complete blood count

I. INTRODUCTION

Iron is a vital element in many metabolic processes in the human body, but in excess it is toxic, with the result that both iron deficiency and overload have severe consequences. Iron deficiency is the most prevalent nutritional problem in the world, affecting an estimated 500 million people. The majority (85%) of the iron in the body is contained in functional iron compounds, mainly in circulating hemoglobin and in myoglobin, which acts as a reservoir of oxygen in muscles. Only a small proportion (0.2%) of body iron is available in the circulation for immediate erythroid cell uptake and is bound to the transport protein transferrin. Once in the plasma the iron is transported by transferrin to the bone marrow for synthesis of hemoglobin and incorporation into the erythrocytes[1]. The uptake, transport, and storage of iron are closely regulated in the body, with ferritin playing an important role. Dietary iron in the form of inorganic Fe (III) is absorbed from the intestinal lumen across the brush border of duodenal enterocytes via active uptake mechanisms that reduce Fe (III) to Fe (II). This uptake of iron from the lumen occurs via the divalent metal transporter-1 (DMT1), which is expressed on the apical membrane of the duodenal enterocytes and is closely associated with the membrane ferrireductase DCYT-B that is responsible for the reduction of Fe (III) [2]. Once within the enterocyte, Fe (II) is then exported across the basolateral membrane by the Fe (II) transporter ferroportin [3]. After export, it is reoxidized from Fe (II) to Fe (III) by the membrane-bound ferroxidase hephaestin and possibly by intestinal ceruloplasmin [4]. Fe (III) is then released into the circulation, where it binds to the iron transport glycoprotein transferrin. Transferrin has two high-affinity binding sites for Fe(III) which maintain the iron in a redox-inert state [5].
Hepcidin is a peptide hormone that is synthesized in the liver [6]; it inhibits iron entry into the plasma compartment from the three main sources of iron: dietary absorption in the duodenum, the release of recycled iron from macrophages and the release of stored iron from hepatocytes. Multiple signals reflecting systemic iron stores and concentrations, erythropoietic activity and host defense converge to regulate hepcidin production and thereby affect iron homeostasis; hepcidin is regulated by iron, so that more hepcidin is

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produced by hepatocytes when iron is abundant, limiting further iron absorption and release from stores. When iron is deficient, hepatocytes produce less or no hepcidin, allowing more iron to enter plasma. Both diferric plasma transferrin and stored iron in hepatocytes can stimulate hepcidin synthesis, by distinct mechanisms [7.] Iron deficiency anemia in young children is recognized as a major public health issue and the most prevalent form of micronutrient deficiency worldwide [8-9]. The global prevalence of anemia (defined as hemoglobin level of <11.0 g/dl in children aged 6–59 months is 43% and half is attributable to iron deficiency anemia (IDA) which is defined as hemoglobin level of <11.0g/dl and ferritin level of < 12 µg/L [8-10]. IDA contributes substantially to childhood mortality and morbidity and is linked to impaired brain development and cognitive functions [11-12]. IDA is also ranked as the third leading cause of disability worldwide and the 13th leading risk factor for the global disability adjusted life years [13]. Most of the burden of IDA is in the resource poor settings of Africa and Asia[10-14].

II. MATERIAL AND METHOD

This cross sectional study conducted among children in Khartoum state, in order to evaluate the levels of Ferritin and hepcidin among iron deficient children, to evaluate body response to decreased iron level in their bodies. 150 of children were recruited for such reason. Hemoglobin and red cell indices were measured in whole blood samples collected in ethylene diamin tetra acetic acid anticoagulant as parts of complete blood count, which conducted with hematology auto-analyzer BC 200 Mindray trade mark. Plasma collected from blood samples collected in heparinized containers contributed in the measurement of ferritin, which assessed via Tohos 311 full automated chemical analyzer provided with suitable reagents same brand, it works with principle of immune based analysis and hepcidin, which measured with enzyme linked immune sorbent assay (ELISA) using BTS350 plus device. Laboratory work was conducted at Elgaily Khalid Musa medical laboratory-Omdurman. Data obtained was analyzed using the statistical package of social science program (SPSS) version 22.

III. RESULT

Children involved in this study were identified as iron deficient anemia diagnosed by means of readings of complete blood count, red cell count, hemoglobin concentration and red cell indices, which were low levels than reference ranges, they were 87 (58%), then white blood cell count was also taken under consideration, to define absolute anemia, it was either low or normal, as its bound to infection and that leading to increased ferritin level, which plays as acute phase reactant. They were 150 children, 55 out of the 87 (63%) were having iron deficiency anemia, their age (mean±SD) was (6.4+4.3) years; they were 27 (49%) males and 28 (51%) females. Statistical analysis for the data, by conducting independent T-test among males and females, ferritin and hepcidin levels showed decreased measurement in comparison to reference values, providing significant difference as p value was 0.000 for each as in table 1and table 2 respectively.

Table 1: ferritin and hepcidin among IDA males

Parameters	Case Mean±SD	Reference value	*P value*
Ferritin	15.37±13.83	82.5 (15-150)	0.000
hepcidin	20.81±12.86	70 (46-94)	0.000

Significant difference p value 0.05

Table 3-: Table 1: ferritin and hepcidin among IDA females

Parameters	Case Mean±SD	Reference value	*P value*
Ferritin	11.12±11.61	187.5 (25-350)	0.000
hepcidin	25.18±18.44	60 (46-74)	0.000

Significant difference p value 0.05

Considering age of the children, Pearson correlation with ferritin and hepcidin levels showed positive correlation for ferritin and negative correlation for the hepcidin as in table 3.

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Table 3-6: Correlation of iron profile and hepcidin with age of IDA subjects.

Parameter	R value	*P value*
Ferritin	0.058	0.685
hepcidin	-0.046	0.744

IV. DISCUSSION

Hepcidin expression increases in response to high circulating and tissue levels of iron and in persons with systemic inflammation or infection. Its production is inhibited by the expansion of erythropoiesis, iron deficiency, and tissue hypoxia in response to signals originating in the bone marrow, the liver, and probably muscle tissue and adipocytes [15-16]. Increases in hepcidin levels that are induced by inflammatory cytokines, especially interleukin-6, explain the iron sequestration and reduced supply of erythropoietic iron that occurs in the anemia of chronic disease [17]. In the general population, hepcidin levels are low in girls[18-19].

In this study concerning about children with iron deficiency anemia, to see how response to the deficiency children bodies acted, decreased levels of both ferritin and hepcidin in iron deficient children reflect that no infection the children were under. Out of the 150 children recruited, 55 (36.7) % were anemic, considering red cell count, red cell indices and white blood cell count. At the same manner directed toward children, a community based cross-sectional study was conducted in Southwest Ethiopia from April to July 2013. A total of 616 school children aged 6 to 12 years were included. They tested each child for hematological examinations. Anemia was defined as a hemoglobin level lower than 11.5 g/dl and 12 g/dl, ferritin levels were below reference values. Overall, prevalence of anemia was 43.7%, and that of IDA was 37.4%, due to low families incomes and infection with intestinal parasites and malaria [20]. An agreement obtained with other study in U K an evaluation study conducted as searching for strategies to evaluate iron deficiency anemia among pregnant women and infants, it revealed that studies evaluated hematological outcomes of anemia, but few analyzed clinical consequences. Hemoglobin and ferritin appeared the most suitable screening tests [21]. Also other study suggested that anemia is usually observed in chronic disease states such as non-specific anemia, which may cause diagnostic difficulties. It is important to rule out iron deficiency and other causes of anemia as misdiagnosis will in most cases lead to refractoriness to standard therapy. The cytokines and acute-phase proteins play important roles in the pathogenesis of anemia of chronic disease. Alterations in the metabolism of iron via the molecule hepcidin and ferritin are largely responsible for the consequent anemia. Concomitant iron deficiency might be present and could affect the diagnosis and therapeutic protocol [22].

V. CONCLUSION

In this study complete blood count enabled to sort iron deficiency anemia according to hemoglobin concentration and related parameter, then confirmation of the anemia by means of iferritin and hepcidin levels assessment. Comparing to finding around our country and the percentage of children with IDA, it seem to be a decline frequency of IDA, mostly due to substitution of feeding hygiene and raised awareness find way to overcome anemia among residents' children. Children presented low hepcidin levels, probably have chronic disorders not detected yet or some sort insufficient hepcidin gene expression.

VI. RECOMMENDATION

Hepcidin can be used to identify children with iron deficiency anemia due to chronic disease to treat the causative agent, which mostly neglected or missed diagnosed. Substitute feeding program should be distributed to encourage local people to participate in community survey to detect or follow up health status of children. Genetic studies should be expanded to include hepcidin, which apparently has un- used specification in our community.

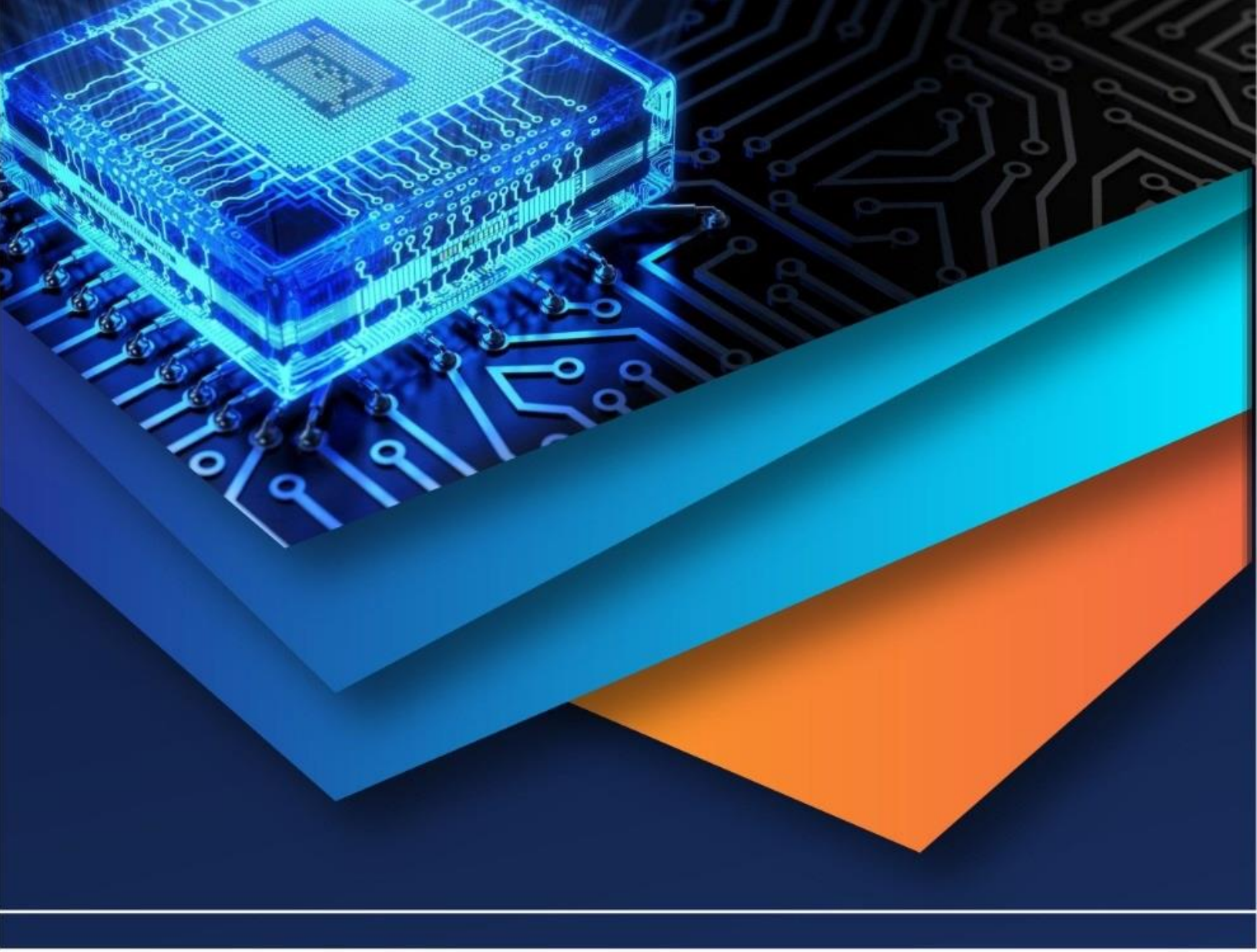
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