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A REVIEW ON IRON DEFICIENCY ANEMIA

Safia Mengal[1], Rahman Gul[1, 2]*, Abdullah Khan[3], Ghulam Farooq Baloch[1], Kashmala Khan[4] and Muhammad Zaman Khethran[1] and Dawood Khan[1]

[1]Institute of Public Health Quetta, Pakistan.
[2]Faculty of Pharmacy & Health Sciences University of Balochistan, Quetta.
[3]Civil Secretariat of Balochistan, Pakistan.
[4]Fatima Jinnah Medical University, Lahore, Pakistan.

***Corresponding Author: Rahman Gul**

Institute of Public Health Quetta, Pakistan.

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ABSTRACT

Anaemia is a clinical condition in which body does not have sufficient health red blood corpuscles or hemoglobin level in the blood to meet the body's physiological requirements. Comparatively female are exposed to be at high risk as compared to children due to physiological resigns. Anaemia one of the widespread cause of iron deficiency anaemia at worldwide. In literature paper multiple determinants of iron deficiency anemia has acknowledged as well as environmental and inherited factors. There are numbers of factors that lack of poor socio-economic status, suitable diet and elevated parity of women that access to poor health hereditary etc. Among women of reproductive age group iron deficiency anemia characteristically is one of the imperative public health dilemmas in developing countries. This literature paper will primarily focus on extent of crisis, causes, solutions and role of iron studies in the diagnosis of iron deficiency anaemia. There are several factors that might expect anemia which in turn leads to different unfavorable outcome.

KEYWORDS: Iron deficiency, anemia, CBC, Fortification, Nutrients, Vitamins, IDA.

INTRODUCTION

Anemia with < 80 µm3 therefore microcytic anemia's resulted due to abridged production of hemoglobin including siderobalstic anemia, anemia of chronic disease, iron deficiency anemia and thalassemia.[1] Such as ↓ iron → ↓ heme → ↓ hemoglobin → microcytic anemia This microcytic anemia is known as iron deficiency anemia. Iron deficiency anaemia remains amongst the five leading causes of lives with disability in humans particularly in women. Iron consists just about *5% of earth's outer layer*. Iron's redox (*oxido-reduction*) states formulate iron constructive for developing biological processes.[2]

Hemoglobin is the main source of iron present in the *erythrocytes*.,a molecule composed of four units. Each unit comprising one heme group and one protein chain. Hemoglobin structure allows copious oxygen loaded within lungs and partially unloaded in tissues (e.g. muscles).[3] Myoglobin having iron-containing oxygen storage protein in muscle that is similar in structure with hemoglobin but having just one heme unit and one globin chain.[4] Several iron-containing enzymes as cytochromes which also have one heme group and one globin protein chain. significant meanings of iron-containing enzymes such as *cytochrome P450 (Cpy)* enzymes are membrane- bound hemo-proteins that plays a pivotal role in detoxification of foreign materials in the liver, synthesis and metabolism of steroid hormones,,bile acids and neurotransmitters signal controlling abilities such as the serotonin and dopamine arrangement in brain.[5]

Iron having capability as reversible storage within the liver as *hemosiderin* and *ferritin* while it is transported between various sections of body by protein *transferring*.[6]

Erythrocytes are biconcave cells that filled with hemoglobin that transport O2 and CO2 between the lungs and tissues.[7] Hemoglobin enclosed in erythrocytes containing iron that pick up oxygen from air deliver it every-where in the body.

During adulthood oxygen requirements for tissues and erythrocyte production usually remain stable by lack of hemorrhage, disease or altered substantial bustle.

Aging senescent erythrocytes are cleared just about 20 ML on daily basis and about 20 Mg of iron in those cells which recycled the production of latest erythrocytes.[8]

Iron deficiency anemia having shorter half-life of circulating erythrocytes then iron is recovered earlier in those patients but amount of iron in every microcytic erythrocyte is abridged**.**

During hemorrhage diet is used to meet the extra iron absorbed from the body to maintain the blood sustainsibility.[9]

Maximum amounts of iron require for the production of heme from erythrocytes, hemoglobin and erythrocytes precursors. Therefore iron may be the essential component of hemoglobin structure and function.[10]

Iron deficiency anemia events.

- Serum iron is depleted or − ↓serum iron ↓ % saturation.
- Storage iron is depleted − ↓ ferritin ↑ TIBC.
- Microcytic, hypochromic anemia – Bone marrow makes smaller and fewer RBCs.
- Normocytic anemia – Bone marrow makes fewer but normal size RBCs.1

Anemia outline	
Inclusions in Blood cells	
Red Blood Corpuscles	**(RBCs)**
Reticulocytes	Residual rRNA
Howell Jolly Bodies	Nuclear residua
Heinz Bodies	Denatured Hb
Oppenheim Bodies	Iron
White Blood Corpuscles	(WBCs)
Toxic granules	Azurophil granules
Dohle Bodies	Ribosome rich + Endoplasmic reticulum
Reticulocyte production less than 2 indicated	Hypo-proliferative anemia or maturation disorders

Plummer-vinson syndrome or *(Paterson-brown-kelly)* is a web linked with iron deficiency anemia, inflammation of the tongue and inflammation of the mucous membrane of the mouth. This syndrome most commonly affects the women and cause of this disease not understood.[11]

The web may be difficult to see at endoscopy and may be ruptured accidentally durining the transition of endoscope.

Appearance of inexplicable contradiction of elevated prevalence disdains the effective treatment that represents the major challenge to public health attempts.[12]

Several impediments linking such as cultural barriers, economics and infectious diseases converge and make eradication more complicated.

AETIOLOGY

Numerous etiological agents involved as pathologic, physiologic, environmental and genetic causes of iron deficiency that leads to iron deficiency anemia.[13]

- Lack of iron in your diet.
- Blood Loss because blood contain iron within red blood cells.
- Inability to absorb iron especially in diet foodstuff.
- Pregnancy.

CAUSES OF IRON DEFICIENCY ANEMIA

Iron deficiency anemia is the most common cause of anemia in the World, affecting 30% of international population.[14]

- Deprived or poor intake of iron
- Decreased absorption of iron e.g. (Post-gastrectomy)
- Dietetic erythrocyte iron is not usually sufficient to compensate the acute blood loss when iron storage depleted or decreased.[15]
- Durining iron deficiency anemia loss of blood in each and every case should be measured.
- Hemorrhage is the most common mechanism for acute iron loss and anemia in a adolescence and pregnant women.
- Chronic blood loss during menstruation or hookworm infection has maximum impact internationally.
- Bleeding causes loss of blood from multiple sites of intestinal tract and colon and also blood donation and nosebleeds etc.[16]
- Intravascular destruction of red blood cells or hemolysis results iron loss in malaria. Sweat and physical execration results significant iron loses that contribute to deficient iron.

Iron studies distinctive Features	
Unique features	**Evaluation**
Low ferritin	iron deficiency anemia (IDE)
High iron	sideroblastic anemia
Normal iron studies	Thalassemia

EPIDEMIOLOGY

Iron deficiency anemia affects one-third of inhabitants of the world. Anemia concerned 27% of the international population and iron deficiency anemia as 60% relatively.[17]

- Micronutrient deficiencies are widespread in Pakistan regarding anemia which is more common in non-pregnant women of reproductive age as 43% and among children 53.7%, 54.2% respectively.
- WHO recognized 30% iron deficiency anemia in the population due to nutritional deficiencies at international level.
- Percentage of iron deficiency anemia 45% in Pakistan which is somewhat high realizing the failure of public health measures (actions) to control it.
- Iron deficiency anemia is further difficult in the elderly population to treat and merely represents approximately 30% of anaemia cases at country level in the population.
- Iron deficiency anemia cause by inadequately documented recurrent blood donation.[18]

- Anemia and iron deficiency anemia have also been documented in 42.6% and 33% of cancer patients respectively.
- A documented report of iron deficiency anemia prevalence in chronic inflammatory circumstances varies at a great extent among different studies depending on thresholds of iron parameters used to identify iron deficiency anemias.
- In surgical cases preoperative anaemia is present in just about 1/3 of patients undergoing major surgery more than 2/3rd cases having iron deficiency anemia.[19]
- Prevalence of postoperative anaemia can attain up to 90%. These data attentive the alarming figures of iron deficiency anemia prevalence across high-risk populations.

DAILY IRON REQUIREMENTS

Iron is a basic mineral that need for growth and development of every individual. The body uses iron to make hemoglobin.[20] A red blood corpuscle having a protein that carries oxygen from lungs to all parts of the body and myoglobin is a protein that provides oxygen to muscles.

DAILY RECOMMENDED DIETARY INTAKE OF IRON	
AGE GROUPS	**DAILY RDI VALUE OF IRON**
All Individual	
1 to 3 years	9 daily
4 to 8 years	8 to 10 mg daily
9 to 13 years	8 mg daily
Boys	
14 to 18 years	11 mg daily
Girls	
14 to 18 years	12 to 15 mg daily
Men	
19 to 50 years	8 mg daily
Women	
19 to 50 years	15 to 18 mg daily
50 on-ward	
Pregnant And Lactating Women	
All pregnant women	25 to 27 mg daily
Lactating women	8 to 9 mg daily

ABSORPTION OF IRON

Regarding the initial step of iron absorption *duodenal cytochrom b* reductase (*DCYTB*) is also known as cytochrome b reductase in human encoded by a CYBRD1 gene which catalyzes the the (Fe+3) into (Fe+2) form.[21] It is necessary because duodenal metal transporter 1 (DMT1) allows just divalent metals (mainly iron but also Copper (Cu), Plumbum (Pb) and Mananese (Mn)) through apical membrane of duodenal enterocytes. However *Divalent metal transporter 1 (DMT1)* is not only a molecule but also it facilitates the transport of iron through enterocyte-membrane. A carrier protein of heme is one more significant molecule that transports iron inside the heme from apical surface into the enterocytes (intestinal absorptive cells).[22] Iron substraction from heme requires a multistep metabolic pathway in enterocytes and macrophages. In multistep metabolic pathway. *Heme oxigenase 1(HO-1)* is a decisive enzyme. Ferroportin is known as iron exporter in which ferrous iron is transported from enterocyte to blood. Ferroportin situated at baso-lateral surface of enterocyte and macrophage membranes. Due to high level of iron in the body hepatic synthesis of *hepcidin* increases.[23] Binding of ferroportin to hepcidin in its outside segment causes ubiquitylation, internalization, and degradation of ferroportin. While resulting iron transfer to blood is decreased. Ferroportin as divalent metal transporter1 *(DMT1)* is a permeable merely for ferrous iron.[24] As a result transferrin can bind iron into ferric form.

Therefore hephaestin is necessary for oxidation of ferrous iron (Fe+2) into ferric (Fe+3) form for absorption. *Ceruloplasmin (CP)* is liver protein homologs as hephaestin stores and carries copper around the whole body. *Ceruloplasmin (CP)* carries 65% - 90% copper in the blood and plays a neuroprotective role in cerebral ischemia of brain.[25]

TRANSPORT OF IRON

The transferrin *(Tf)* is a main protein that involved in the transport of iron to tissues. Each transferrin molecule is able to convey two ferrous iron molecules.[26]

Transferrin receptor (TfR) binds to transferrin on the cell membrane; such as transferring receptor (TfR1) or transferring receptor2 (TfR2). Transferrin receptor 1 is uttered in all tissues except of mature erythrocytes. It is an important molecule in embryogenesis.[27]

Due to neurological mal-development and defective erythropoiesis the TfR1 could not survive. Transferrin receptor 2 *(TfR2)* is mainly expressed in the liver. Therefore protein structures level of TfR1 and TfR2 contain high degree of homology but functions and

regulation are not the identical. Hereditary hemochromathosis *(HFE)* express the TfR1 that regulate the cellular iron levels. Therefore there is no effect on the regulation of TfR2 due to cellular iron levels.[28]

Transferrin receptor2 having sentience of transferring saturation of the body iron status and regulates hepcidin expression appropriately.[29] Acidification process occurred by means of ATPase proton pump *(PH 5.5)* that helps to dissociate iron from transferrin inside the endosomes. A Six transmembrane epithelial antigen of prostate 3 (STEAP3) protein having capability to convert Fe+3 to Fe+2 in erythroid precursor cells.[30] The convertion of ferric ions is necessary since DMT1 allows only divalent metals from endosome to cytoplasm in the enterocytes.

Transferrin and transferring receptors are iron scavenging system where as transferring freely circulate Fe- binding protein and *TfR* is a membrane destined protein and associated with DMT-1 in endosomes for divalent metal transport.[31]

FACTORS INFLUENCING IRON ABSORPTION

Iron is readily absorbed in inorganic form and ferrous state. HCL and vitamin-c helps in iron absorption by converting ferric into ferrous state.[32] Absorption occurs in the duodenum and jejunum.[22] After absorption iron is carried in the blood in ferric state joined to globulin called as iron binding protein (transferring).

FACTORS INCREASE THE IRON ABSORPTION

- Ascorbic acid and vitamin-c (e.g certain fruit juices, fruits, potatoes and certain vegetables) Meat, chicken, fish and other sea-food.[33]
- Other organic acids (e.g.. citric acid) alcohol and fermented food also enhance non-heme iron absorption.

FACTORS INHIBIT THE IRON ABSORPTION

- There are certain inhibitors that inhibits iron absorption Dietary inhibitors such as phytates, calcium, poly-phenols that enhanced Ascorbic acid and proteins efficiently influence the bio-availability.[34]
- Iron-binding phenolics compounds (e.g coffee, tea, cocoa, certain spices specified Vegetables and essential red wines), Calcium (e.g. Milk, cheese)[35] etc.
- Phytates found in all kinds of grains, seeds, nuts, vegetables, roots (e.g. potatoes) and fruits. Chemically phytates are inositol hexa-phosphate salts that are storage form of Phosphates and minerals.[36]

PREVALENCE OF IORN DEFICIENCY ANEMIA

- Anemia affects 33% of world's population which is 1/3 of the world population.
- Prevalence criteria for iron deficiency anemia shows that diagnostic studies results as.
- Low hemoglobin (HB) (< 7.7 mmol/l in men and <7.5 mmol/l in women).
- Low serum level iron (< 7.2 µ g/l).
- Low transferring (<30ng/l).
- Low transferrin saturation (<15%).[37]

Iron deficiency anemia diagnostic laboratory criteria

- low valuation of hemoglobin (Hb) and hematocrit (Hct)
- low valuation of iron saturation.[38]
- low valuation of ferritin
- low valuation of serum iron
- low mean cellular volume
- high transferring or total iron binding capacity (TIBC)

Country-wide iron deficiency anemia prevalence

Countries	Children	Non pregnant women	Pregnant women
Pakistan	49.1%	43.0%	53.0%
Indonesia	38.0%	46.6%	48.9%
Turkey	40.0%	30.0%	37.0%
Saudi Arabia	40.0%	37.0%	30.0%
India	58.6%	53.2%	50.4%
Afghanistan	60.5%	40.0%	44.0%

OUTCOMES OF IRON DEFICIENCY ANEMIA

Main outcome of iron deficiency outcome resulted risky causes such as fatigue, decreased motor abilities, impaired memory and delays in mental development.[39]

- In pregnancy anemia can enhance the risk of pre-term delivery and pre-term babies having health concerns like low birth weight and neural tube defects that leads to death. Infant mortality is the major cause in developing countries.[40]
- Iron supplementation throughout pregnancies might helps in reduction of pre-term birth.

- Menarche juvenile girl's shows iron deficient in developing countries since not treated due to lack of awareness or resources.[41]
- Durining pregnancies iron deficiency anemia may leads to natal and post-natal complication.
- Iron-deficient mother's children and Infants born with poor cognitive development of brain function leading intelligence failure.
- Iron deficiency is also carried out in multiple pregnancies and therefore compromise health and increased hazard of complication.[42]
- Anemia common signs and symptoms include slow development, feeling lethargy, reduced immune function, inflamed tongue, palpitations, dizziness, emotional un-stability, depression and rest-lessness. Studies designate increased incidence of stress fractures interconnected with anemia.[43]

INTERVENTION PLAN

Realistic plan for deficiencies and iron importance in government of Pakistan a five year plan has committed to control the crisis.[44]

- Encourage the iron deficient patient to ask for help for self care and house-hold responsibilities support.[45]
- Provide instruction plan for activities and exertion.
- Provision of medications indicated by health professional.
- A specific diet plan for iron deficiency anemia such as green leafy-vegetables, beans, meat, poultry, and moreover exact foods for iron absorption.[46]
- Provision of iron supplements or oral iron that help to increase the iron requirements for the body needs.
- Implement a plan to encourage adequate rest periods for iron deficient patient.
- Numerous intervention plans exist at country level working efficiently but we need to keep evaluation of these interventions in order to make interventions more effective.
- An extraordinary need to expand the interventions programs that are already working effectively and efficiently for the whole population.[47]
- Implement the empowerment strategies for women empowerment at national level.
- National resources should be mobilized for each and every patient on an equitable basis. Finally government and private agencies should join together for the benefit of local population of country.[48]

EVALUATION PLAN

Evaluation plan is essentially written document that describes how we will monitor and evaluate our program. Iron deficiency anemia resulted with decreased oxygen delivery to entire body and includes symptoms such as pale-skin, fatigue, lack of energy and shortness of breath.[49]

- Evaluation needs a physical examinations and history of each and every patient.
- Assessment of risk factors for underlying conditions.[50]
- A special evaluation plan to evaluate a anemic patient such as complete blood count(CBC), reticulocyte count, iron profile, liver function test and serum creatinine.[51]

CONCLUSION

Iron deficiency anemia is a main public health problem now-a-days. National and regional synchronized efforts should be made to manage anaemia. International recognized risk factors should be calculated during prevention and control strategies of anemia and iron deficiency anemia. Therefore predisposing factors of anaemia were documented at huge scale. There is a specific strategic plan need to identify specific aetiologies and indispensable causes of anemia among affected population.

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