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Anemia- Still a Significant and Challenging Health Problem Review

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ABSTRACT

Anemia is the inability of the blood to carry enough oxygen to meet body needs. It can result from inadequate Red blood cell (RBC) production or low levels of hemoglobin in the blood, but in sometimes it is due to the production of faulty hemoglobin, production of insufficient or defective erythrocytes and blood loss or excessive erythrocytes breakdown (Hemolysis). Anemia can have caused by abnormal changes in red cell size or color. Anemia associated with a normal RBC count and no abnormalities of erythrocytes structure is may be due to normochromic, normocytic Anemia. As per WHO, the severity anemia follows mild, moderate, severe and very severe. The mainly three major groups because anemia are; Blood loss, Hemolysis, Decreased production of RBC's. Genetic factors may include Haemoglobinopathies (thalassemia), enzyme abnormalities of the glycolytic pathways, defect of the RBC cytoskeleton, congenital dyserythropoietic Anemia, and Rh null disease, hereditary exocytosis, a beta lipoproteinemia and Fanconi Anemia. Nutritional etiologies include Iron deficiency, Vitamin B_{12}, folate deficiency, starvation and generalized malnutrition. Physical causes include trauma, burns, frostbite. The major problem in developing countries is Iron deficiency anemia, majorly preschool children, school children, and women are more affected. Pregnant women's 1 in every 3 is affected with IDA.

INTRODUCTION

Anemia is the in the ability of the blood to carry enough oxygen to meet body needs. It can result in adequate Red blood cell (RBC) production or low levels of hemoglobin in the blood, but at sometimes it is due to the production of faulty hemoglobin [1,2]. Production of insufficient or defective erythrocytes, blood loss or excessive erythrocytes breakdown (Hemolysis). Anemia can have caused by abnormal changes in red cell size or color. Anemia associated with a normal RBC count and no abnormalities of erythrocytes structure is may be due to normochromic, normocytic Anemia [1]. According to WHO the severity anemia is as follows given in Table No. 01 [3].

Table No. 01: Severity Anemia as per WHO.

Category	Anemia severity	Hemoglobin level (gm/dl)
1	Mild	10.0-10.9
2	Moderate	7.0-10.2
3	Severe	<7.0
4	Very severe	<4.0

Stimulation of Erythropoiesis Production and Hemoglobin Synthesis:

EPO, 90% produced by the kidney, initiate production of RBC's, EPO release into plasma, which stimulate the steam cell to differentiate pro-erythroblasts, in case the rate of reticulocyte from marrow and induce the Hb formation. Hb consists of a protein compartment with two alfas and two beta chains, each chain linked to a homegroup consist of porphyrin ring structure with iron atom chelates at center, which capable of binding oxygen [2].

Etiology of Anemia:

There are 400 types of Anemia are there in that mainly three major groups. Blood loss, Hemolysis, decreased the production of RBC's [4]. Genetic factors may include Haemoglobinopathies (thalassemia), enzyme abnormalities of the glycolytic pathways, defect of the RBC cytoskeleton, congenital dyserythropoietic Anemia, Rh null disease, Hereditary exocytosis, a beta lipoproteinemia and Fanconi Anemia. Nutritional etiologies include Iron deficiency, Vitamin B_{12}, folate deficiency, starvation and generalized malnutrition. Physical causes include trauma, burns, frostbite. Chronic diseases and malignant etiologies include renal diseases, hepatic diseases, chronic infections, neoplasm's, collagen vascular disease,

gram-negative sepsis, malaria dengue, thrombotic thrombocytopenic purpura, hemolytic uremic, drug-induced Anemia include inorganic arsenic, benzene, radiation or chemotherapy [5]. Anemia due to blood loss may be due to Gastrointestinal bleeding like gastritis, ulcers, hemorrhoids, and cancers, use of NASID's, menstrual and childbirth bleeding [6].

Clinical Manifestations:

Anemia relates to the inability of blood to supply body cells with enough oxygen and may represents adaptive measures like tachycardia, palpitations, angina pectoris this is due to increased effort of the overworked heart muscle, dyspnea [1]. In iron deficiency anemia (IDA) symptoms are fatigue, emotional instability, depression, stress, impaired physical performance, uncomfortable tingling or crawling feeding in the face, increase susceptibility to infections, headache, vertigo, sensitivity to cold, loss of skin tone in women's reproductive age, causing impaired congenital abilities. In pregnancy condition, it shows negative complications like impaired brain development, premature birth, low birth weight [7].

Diagnosis of Anemia:

Complete blood picture, including RBC indices, a reticulocyte index, examination of peripheral blood smear, examination of a stool sample for occult blood [3, 7].

Hemoglobin:

Highest values seen in males are due to stimulation of RBC production by androgen steroids and decrease Hb in female's causes by the loss of blood during menstruation. The levels of Hb can be used as the rough estimate of oxygen-carrying capacity of blood It can be reduced because of a decreased quantity of Hb per Abnormal Hb in males is 13.5-17.5 g/dL, females 12-16 g/dL [3].

Hematocrit (Hct):

Expressed as a percentage, Hct is the actual volume of RBCs in unit volume of whole blood. In general, it is about three times Hb volume, Normal adult males 41-53% females 36-46% [3].

RBC count:

An actual count of RBC per unit of blood, the RBC count is an indirect estimate of Hb content of blood. Normal adult 4.5-5.9 million/mm^3 [3].

Mean Corpuscular Volume (MCV) (Hct/RBC count):

MCV represents the average volume of RBCs, cells are said to be macrocytic if they are larger than normal, microcytic if they are smaller than normal, and normocytic if their size falls within normal limits. Folic acid and Vitamin B_{12} deficiency, Anemia yield macrocytic morphology, whereas iron deficiency and thalassemia are examples of microcytic Anemia [3].

Mean Corpuscular Hemoglobin (MCH) (Hgb/RBC count):

The percentage of Hb in RBC is the MCH. Two morphologic changes, microcytosis or hypochromic, can reduce the MCH. Cells can be both microcytic and hypochromic, as seen in with IDA, and MCH alone cannot alone distinguish between microcytotic and hypochromic [3].

Mean Corpuscular Hemoglobin Concentration (MCHC) (Hgb/Hot):

The weight of Hb per volume of the cell is the average MCHC. Because the MCHC is independent of cell size, it is more useful than MCH in distinguishing between microcytotic and hypochromic. Low MCHC always indicates hypochondrial microcyte with a normal Hb concentration will have a low MCH, but normal MCHC [3].

Total reticulocyte count:

Although indirect assessment, the total reticulocyte count is an indication of new RBC production. In the normal situation, 1% of RBCs are replaced daily; this represents a reticulocyte count of 1%. The reticulocyte count in normocytic Anemia can differentiate hypo-proliferative marrow from a compensatory response to an Anemia. Multiplying the percentage of reticulocyte by the patient's hematocrit and then dividing the product by an average normal hematocrit is produces a percentage of reticulocyte [3].

Red blood cell distribution width (RDW):

The highest RBC distribution width, the more variables the size of the RBCs. The distribution width increases in early IDA, but this change is not specific to the disease. The distribution width can also be helpful in the diagnosis of mixed Anemia [3].

Serum Iron:

The level of serum iron is the concentration of iron bound to transferrin. Normally, transferrin is about one third bound (saturated) to iron. Unfortunately, the serum iron levels of many patients with IDA remains within the lower limits of normal, giving false negative test results [3].

Percentage of Transferrin Saturation:

The ratio of the serum iron levels to the total iron binding capacity (TIBC) indicates transferrin saturation. It expressed as a percentage. Normally transferrin is 20-50% saturation with iron [3].

Transferrin saturation=serum iron /TIBC) ×100

Folic acid:

The results of folic acid measurements may vary, depending on the ASSY method used. Decrease serum folic acid levels indicates a folate deficiency megaloblastic Anemia that may coexist with Vitamin B_{12} deficiency anemia [3].

Vitamin B_{12}:

The levels of vitamin B_{12} (cyanocobalamin) may vary according to assay method used. Low levels indicate Vitamin B_{12} deficiency Anemia [3].

Schilling test:

The purpose of the Schilling test is diagnosing Vitamin B_{12} deficiency anemia caused by a B_{12} absorption defect resulting from a lack of intrinsic factor (pernicious Anemia). The patient first receives an oral dose of radiolabeled Vitamin B_{12}. Two hours later, the patient receives a large intramuscular dose of nonlabelled Vitamin B_{12} to saturate plasma transport protein. Any excess Vitamin B_{12} that is not taken up by the transport protein or stored in the

liver will be excreted in the urine. A 24 hours urine collection is then measured for radioactivity. If sufficient gastrointestinal intrinsic factor is being produced, the B_{12} will be absorbed. Normally 7% of absorbed radiolabeled B_{12} appears in urine over 24 hours. Patient with pernicious Anemia excretes less than 7% of original oral radiolabeled dose [3].

Coombs test:

Antiglobulin tests, also called as Coombs test, indicate hemolytic anemia caused by the immune response. A direct Coombs test detects antibodies bound erythrocytes, whereas indirect Coombs test measure antibodies present in serum. A positive finding indirect antiglobulin tests is usually indicative of immune hemolysis [3].

Erythropoietin levels:

The healthy individual requires 10-30mU/mL of EPO to maintain normal Hb and hematocrit concentration. Endogenous EPO levels can increase up to 100 to 1000 folds during hypoxia or anemia. This marked increase does not occur in end-stage renal disease, the patient receiving chemotherapy and patients with AIDS, especially those taking azidothymidine (AZT) [3].

IRON DEFICIENCY ANEMIA (IDA):

Iron deficiency anemia is ascertained by the presence of low serum ferritin <12-15 microgram/Litre, usually with a low serum transferrin saturation <15-16. The human body operates several hundred irons contain metallo-enzymes in which iron is indispensable, iron containing protein is Hb {8}. In IDA, the RBC count is often normal but the cells are small, pale, of variables size and contain less Hb than normal. Hb in each cell regard below the normal when MCH is less than 27pg/cell (27-32pg/cell) [1,8].

Etiology of IDA:

IDA solely or partly responsible for 75-80% of all Anemia in women of reproductive age. Daily diet is restricted some way, as in poorly planned vegetarian diet, weight reducing diets, in women's mainly due to monthly menstrual blood loss (menorrhagia), 3-4 pregnancies or child delivery's, chronic blood loss, peptic ulcers, hemorrhoids, poor absorption from alimentary tract. Malabsorption like acid environment in the stomach, gastric pH may reduce absorption, excessive use of antacids, removal part of the stomach, chromes disease. Anemia

is regarded as severe when the Hb is below 9g/dL, reproductive age <11 g/dL in 1st and 3rd trimester, 10.5 g/dL in 2nd trimester [1,3, 8]. Colorectal cancer causes IDA [9].

Treatment for IDA:

Dietary iron comes mainly from red meat, highly colored vegetables. Take iron supplements like ferrous caliphate, along with food or shortly after eating helps reduce the side effects. Alternate for ferrous caliphate is ferrous gluconate, this includes dark green leafy vegetables, iron-fortified bread and cereals, beans, nuts, apricots, prunes, dates etc. Ferric iron sucrose IV 200 mg, low molecular weight iron dextrose can give iv dose of 500-1000mg, ferric iron carboxylases, given as the total dose of 500-1000mg elemental iron. Tea, coffee, calcium found in dairy products such as milk, antacid set. They reduce the iron absorption from the guy and they should be aviated. Vitamin C supplements help in absorption iron better absorption [1,3,4].

IDA in pregnant women, consequences for the fetus and newborn:

In pregnancy, iron requirements are incised both for fetal growth and to support the additional load on the mother's cardiovascular system. Iron is essential for the normal demand of brain contain iron contain metalloenzymes are involved in the metabolic process in the brain [1,7]. In pregnancy80-100 microgram /liter no iron supplements required, 15-30 microgram/ liter required by oral or iv route. Oral ferrous salts up to 200 mg daily given. Check Hb after 2 weeks after treatment if Hb does not increase >≈10/dL, switch second-line treatment, IV iron 500-1000 mg total dose infusion more than 13 weeks gestation. The significant correlation between maternal mortality rate and the prevalence of anemia. Post-partum Anemia depends on two main factors they include the women peripartum iron status, the presence of ID or IDA at delivery another one is magnitude of blood losses in associated with delivery, a good peripartum iron status and moderate blood losses of 200-400 mL will reduce the risk of peripartum Anemia thus maternal death [1,4,7]. Iron consists of different salts given in the Table No. 02. [10]

Table No. 02: Different Salts of Iron.

Salt	The dose of Salt (mg)	Elemental Iron (mg)
Ferrous Fumarate	200	65
Ferrous Gluconate	300	335
Ferrous Glycine Sulphate	225	45
Ferrous Succinate	100	35
Ferrous Sulphate	300	60
Ferrous Sulphate Dried	200	65

Vitamin B_{12} and Folic Acid Deficiency Anemia:

Deficiency of Vitamin B_{12} and /or folic acid impaired erythrocytes maturation and abnormally large erythrocytes (megaloblasts) found in blood circulation. When deficiency of Vitamin B_{12} and folic acid occurs, the rate of DNA and RNA synthesis is reduced, delaying cell division, therefore grow larger than normal between divisions. Hb content of each cell in normal or raised, the cells are fragile and their lifespan is reduced to 40-50 days [1].

Vitamin B_{12} (Hydroxocobalamin) Deficiency Anemia:

Pernicious anemia is commented in females over 50 years, it is an autoimmune disease which autoantibodies destroy intrinsic factor and parental cells in the stomach. Dietary deficiency of vitamin B_{12} is available in animal-derived foodstuff, include dairy products, meat, and eggs deficiency is rare except vegetarian may need supplementation as tablets or fortified cereals or soya [1, 4]. Other causes of vitamin B_{12} deficiency is gastrectomy, chronic gastritis, malignant diseases and ionizing radiation this damage the gastric mucosa including partial cells that produce intrinsic factor, malabsorption by removal of terminal ileum or inflamed, chromes disease, intestinal parasite infections or infections of HIV, alcohol abuse etc. Complications of vitamin B_{12} deficiency these may appear before sings of Anemia because vitamin B_{12} is used in myelin production, deficiency leads to irreversible neurological damage, common in the spinal cord, mucosal abnormalities like glossitis. Vitamin B_{12} 5-25 microgram available. The digestive system has trouble absorbing vitamin B_{12} from the food eat, may need vitamin B_{12} shoots for one month. Vitamin B12 in plasma is <90 microgram/L [1,2,7].

Folic acid Deficiency Anemia:

Deficiency of folic acid causes a form of megaloblastic anemia identical to vitamin B_{12} deficiency, but not associated with neurological damage, it may be due to dietary deficiency and Malabsorption from the jejunum caused by coeliac diseases, anticonvulsant drugs, and interference with folate metabolism by cytotoxic drugs. Folic acid 5 mg is administered. During early pregnancy, sufficient folic acid can help prevent the fetus from developing neural tube defects such as spinal Bifida. Folate found in broccoli, green cabbage, wheat grains, pulses, nuts, green leafy vegetables [1,4,7].

Types of Anemias:

Aplastic anemia:

Aplastic (hypoplastic) Anemia results from bone marrow failure since the bone marrow produced leukocytes and platelets, red blood cells all three low condition pancytopenia. Blood transfusion required to boost levels of red blood cell count may need marrow transplantation if the bone marrow is diseased [1,2,4].

Hemolytic Anemia:

These are occurring when circulating RBC are destroyed or removed permanently from the blood because the cells are abnormal or the spleen is overactive. Managing hemolytic anemia include avoid suspect medication, treating related infections; removal of the spleen can be helpful. In this disease, genetic abnormalities lead to the synthesis of abnormal hemoglobin and increase red cell membrane fragility, reducing their oxygen carrying capacity and lifespan [1,2,4].

Sickle cell Anemia:

The abnormal hemoglobin molecule become misshapen when deoxygenated, making the erythrocytes sickle-shaped, if cells contain the high proportion of abnormal Hb, sickling is permanent. The lifespan of cells is reduced by early hemolysis, which causes Anemia. Sickle cell does not move smoothly through the circulation, they obstruct blood flow, leading to iv blood clotting, tissue ischemia. Acute episode can blockage of small vessels causes acute pain in the affected area, often the hand and feet, long time lead to cardiac disease, kidney failure, retinopathy, poor tissue healing and slow growth in children [1].

Administration of oxygen, pain-reliving drugs, oral and IV fluids to reduce the pain and prevent complications, the physician may recommend blood transfusion, folic acid supplements. Bone marrow transplantation may be an effective treatment in some circumstances. Cancer drug hydroxyurea used [2,3]. Complications of sickle cell Anemia infections, dehydration, excessive hemolysis results in high levels of circulating bilirubin. This frequently leads to cholelithiasis and cholecystitis.

Thalassemia:

Thalassemia is the genetic disorder, which an autosomal recessive inherited, which cause the impaired production of Hb molecule. The most prevalent are alfa thalassemia, beta thalassemia, which in turn reduce Erythropoiesis and stimulate Hemolysis, the resultant Anemia may prevent in range of focus from mild and asymptomatic to profound and life threatening. Homozygous and beta-thalassemia major produce severe Anemia and patient required blood transfusion in order to survive. Prevention and control of thalassemia are should include population screening for heterozygote, genetic counseling and condition can range in severity from mild to life-threatening, the most severe form called Cooley's Anemia. Lead exposure is toxic to bone marrow, leading fewer red blood cell, in children who eat paint chips cause lead poisoning [1,2,7].

Prophylaxis of Anemia:

In pregnant women:

Prevent ID and IDA, ensure adequate iron stores at the delivery time, reduce the birth complications, reduce the frequency post-partum anemia thereby reducing mortality, reduce the number of blood transfusion, reduce the side effects of oral iron treatment.

In fetus/newborn infants:

Ensure the adequate iron supply to the fetus, normal brain development, ensure adequate iron stores at birth, reduce premature and low birth weight. Folic acid 5 mg, Vitamin B_{12} 5-25 mg, ascorbic acid 100 mg are given for prophylaxis of Anemia [7]. Prophylaxis starts on basis of Serum Ferritin in plasma given in Table No. 03.

Table No. 03: Showing Prophylactic Treatment for decreased Serum Ferritin

Serum Ferritin (microgram/lit)	Iron supplements
>70-80	No supplements
≥30-70	40-50mg ferrous iron/day
<30	100mg ferrous iron /day

Iron overload may cause dysfunction of organs, especially the heart, necessitate treatment with Iron chelators [1,7].

Prevention of Anemia and Patient Counseling:

Infants and preschool children Anemia prevented by encouraging exclusive breastfeeding of infants without supplementation (without supplementary liquids, forms of solid food) for 4-6 months after birth. During the weaning from the breastfeeding, no other iron supplements required, in breastfeeding infants have IDA iron deficiency diet 1 mg per kg per day iron drops are recommended. Since milk hampers the absorption of iron from the gut, it should be suggesting that children age is 1-5 years need no more 24 oz. of cow's milk, soy milk, goat milk per day. Food rich in Vitamin C like citrus fruits vegetables and juices are recommended beyond six months to increase iron absorption. For adolescent girls and women's prevention of iron deficiency include healthy iron-rich diet. In pregnancy condition oral, low dose 30 mg per day supplements of iron at the first parental visit may be started to prevent Anemia[4].

Epidemiology:

POPULATION GROUP	PREVALANCE OF ANEMIA		POPULATION AFFECTED	
	PERCENT	95% CI	NUMBERS (MILLIONS)	95% CI
Pre-school age children	47.4	45.7-49.1	293	283-303
School-age children	25.4	19.9-30.9	305	239-371
Pregnant women	41.8	39.9-43.8	56	54-59
Non-Pregnant women	30.2	28.7-31.6	468	446-491
Men	12.7	8.62-16.9	260	175-345
Elderly	239	18.3-29.4	164	126-202
Total population	24.8	22.9-26.7	1620	1500-1740

Globally, Anemia affects 1.62 billion people (95% CI: 1.50-1.74 billion) which corresponds to 24.8% of population (95% CI: 22.9-26.7%). The highest prevalence is in preschool-age children (47.4%, 95% CI; 45.7-49.1) and lowest prevalence in men (12.7%,95%CI;8.6-16.9%). However, the population group with the great number of individual affected in non-pregnant women (468.4 million,95%CI; 446.2-590.6) [6]

Table No. 5: WHO, Global Prevalence of Anemia in 2011.

Country	**Mean hemoglobin concentration (g/l)**		**Percentage of non-pregnant women with blood Hb concentration<120g\l**		**Percentage of non-pregnant women with blood Hb concentration<80g\l**		**Level of public health screening**
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	
INDIA	119	113-125	48	29-63	2.5	0.8-5.4	SEVERE

CI=Credibility Interval

Levels of public health significance are severe in India [11]{10}.

According to WHO estimates up to 56% of all women's leave in developing countries are anemic. In India, national family health survey-2 in 1998-1999 shows that 54% of women's in rural and 46% in urban are anemic.

SUMMARY

In India, most patients attending outpatient clinics had anemia. The highest prevalence of anemia was seen in children <10 years followed by women and older adults, the vast majority of anemia were in microcytic, suggesting that iron deficiency main cause of anemia. However, the prevalence of normocytic anemia increases with age, so further studies are needed to clarify the anemia cause of anemia among the older adults. The results of can are used by the public health programmes to design target interventions aimed at reducing the huge burden of anemia in India.

REFERENCES

1. Ross and Wilson. Anatomy and Physiology in Health and Illness. Churchill Livingstone, 12th edition; pp.73-75
2. Joseph T. Dipiro, Robert L Talbert, Gary C. Yee, Gary R. Matzke, Barbara G. Wells, L. Michael Posey. Pharmacotherapy: A Pathological Approach. The McGraw-Hill Companies, Inc. 5th edition; pp.1729-34.
3. J.B. Sharma, Meenakshi Shankar. Anemia in Pregnancy. *JIMSA*,2010; 23:4:253-60
4. www.news-medical.net
5. www.medscape.com
6. www.webmd.com
7. Bruno de Benoist, Erin McLean, Ines Egli and Mary Cogswell. Worldwide prevalence of anemia1993-2005. WHO 2008; 1-51
8. Nils Mailman. Iron deficiency anemia in pregnant women in Malaysia still significant and challenging health problems. J Preg Child Health, 2015; 2: 168.
9. Nawal S Faris. Prevalence of IRON DEFICIENCY ANEMIA Etiological and Prevention. European Journal of Biology and Medical Science Research. 2014; 2:2: 55-60
10. Masatsugu OHTA. Management of Anemia in Elderly. JMAJ. 2009; 52:4: 219-23 ,2009.
11. WHO. The global prevalence of anemia in 2011. Geneva: World Health Organization; 2015: 1-48 (www.who.int)