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Prevalence of Anemia: A comprehensive review

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Abstract
Anemia is a prevalent condition associated with inadequate nutrition and global health concerns that impact both emerging and wealthy nations. It presents significant health hazards and poses challenges to social and economic progress. The World Health Organization (WHO) reports that around one-third of the global population is affected by anemia, primarily attributed to inadequate consumption of nutrient-rich diet. The objective of this review is to acquire a deeper understanding of anemia, encompassing its various classifications, etiology, clinical manifestations, and therapeutic interventions, with the intention of disseminating knowledge to the general population on this pathological condition. Anemia, a prevalent public health issue, is known to result in compromised cognitive and psychomotor development, diminished work productivity, and stunted growth in children. The primary etiological factors can be attributed to inadequacies in nutrition and infestations by parasites. The primary etiologies of anemia are nutritional deficiencies; specifically iron deficiency anemia, vitamin B12 deficiency anemia, and folate deficiency anemia.

Keywords: Prevalence, anemia, deficiency, iron, vitamin B12, RBC

Introduction
The presence of anemia results in a visibly pallid complexion in individuals. Individuals who have a blood condition are more susceptible to need blood transfusions following surgical procedures. Anemia, dietary factors affecting red blood cell (RBC) production, and an elevated prevalence of RBC insufficiency are often seen etiologies of anemia. The most prevalent factors leading to blood loss include trauma and internal bleeding. The augmented degradation of red blood cells (RBCs) can be attributed to genetic disorders, such as sickle cell anemia, as well as illnesses like malaria and autoimmune disorders. Anaemia can be further categorized based on the dimensions of red blood cells and the quantity of haemoglobin contained within each individual cell [1-3].

Anemia is a prevalent public health issue that is widely observed across the globe. The prevalence of this phenomenon is significantly higher in underdeveloped nations, when individuals experience both starvation and helminthic diseases. Conversely, it is noteworthy that in developed nations, the primary etiology of anemia is the insufficient presence of iron in the diet. Anemia is a medical disorder characterized by a deficiency of red blood cells, which impairs the transportation of oxygen from the lungs to the body's cells [4, 5]. The condition described is characterized by a hemoglobin (Hb) concentration level below 11g/dl for pregnant women and children aged six months to five years, below 12g/dl for children aged 6-14, and below 13g/dl for men. Anemia is associated with significant health consequences, including impaired cognitive and motor development, decreased job productivity, heightened vulnerability to parasite infections, stunted growth in children, and in severe instances, elevated rates of child and mother mortality [6-8] (figure 1).

The World Health Organization (WHO) has reported that over two billion individuals worldwide are afflicted with anemia, with a significant component of this population originating from South Asia. On a global scale, it is observed that about 50% of children in the preschool age group and 41.8% of pregnant women experience the condition of anemia. Currently, there is a dearth of comprehensive information regarding the primary causes of anemia and its most straightforward preventive measures. Hence, the objective of this study is to examine the primary factors contributing to the occurrence of anemia and provide an optimal approach for preventing anemia [9-11] (figure 2).

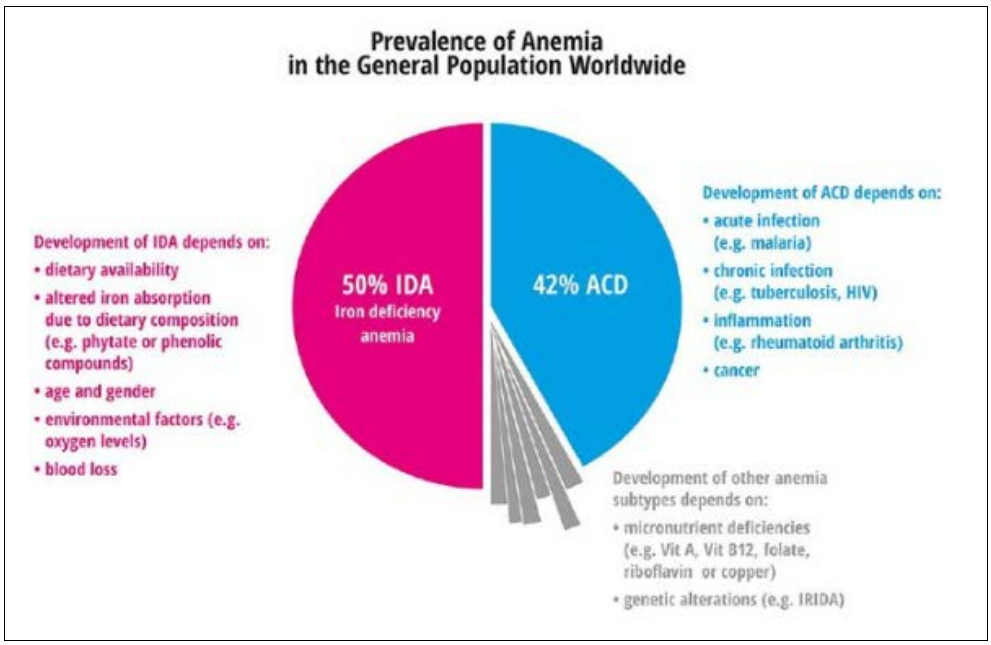

Fig 1: Prevalence of Anaemia in the general population worldwise

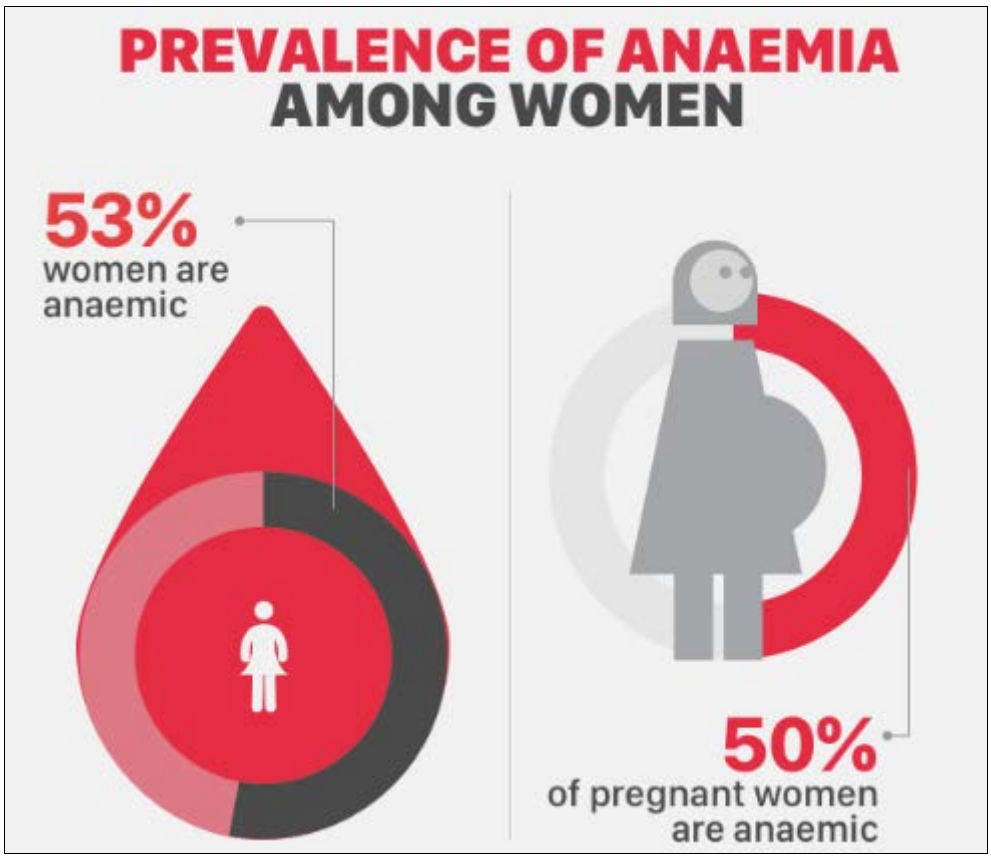

Fig 2: Prevalence of Anaemia among women

Anaemia is a medical condition characterized by a lower than normal count of haemoglobin. The range of values considered normal is contingent upon an individual's sex and age. The typical range for haemoglobin levels in adult males is between 13 and 14 grams per deciliter (gm/dL). If the individual's haemoglobin count falls below this specified range, they are diagnosed with anaemia. In the female population, the established standard range for hemoglobin levels typically falls between 12 and 13 grams per deciliter (gm/dL). Any value below this range is indicative of anemia. The cause is subsequently discovered following additional testing [12, 13]. Iron supplements are commonly provided to specific populations, such as pregnant women, as a preventive measure. The administration of blood transfusion is considered the established therapeutic approach in instances of severe illness. The administration of medications that promote the generation of red blood cells is typically limited to individuals diagnosed with severe anemia. The severity of anaemia can be assessed by grading it according to the haemoglobin count, providing insight into the extent of the problem [14, 15] (figure 3).

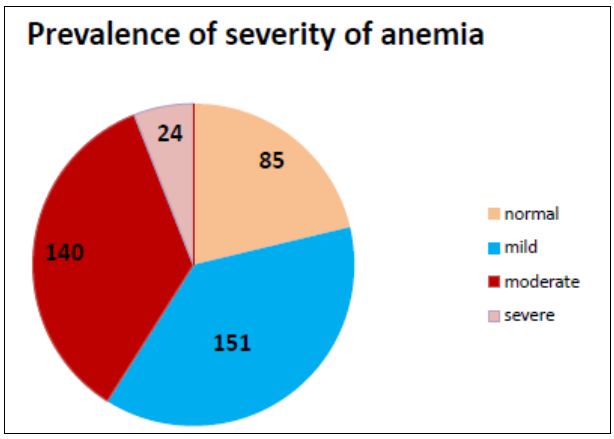

Fig 3: Prevalence of anemia severity

Types of Anaemia

Anemia occurs due to various abnormalities in red blood cells (RBCs), including impaired production observed in aplastic anemia, deficient maturation in megaloblastic anemia, errors in hemoglobin synthesis resulting in iron deficiency anemia, genetic defects in hemoglobin maturation evident in thalassemia, synthesis of abnormal hemoglobin detected in hemoglobinopathies such as sickle cell anemia and thalassemia, and loss of RBCs through hemolytic anemias [16, 17].

Anemia can be attributed to various variables, encompassing low socioeconomic level, nutritional inadequacies, helminth infections, other infectious diseases, illiteracy, and blood disorders such as sickle cell anemia. Iron deficiency, hookworm infection, folate insufficiency, and malaria are identified as the primary factors contributing to the prevalence of health issues within societies. The present review aims to elucidate the primary etiological factors contributing to the development of anemia [18].

Iron-Deficiency Anaemia

IDA, also known as iron deficiency anaemia, is a prevalent kind of anaemia that is widely observed both globally and within the country of India. Iron deficiency is a medical disorder characterized by a lack of iron in the circulatory system. Haemoglobin, an essential protein, is found within red blood cells (RBCs) and serves the crucial function of transporting oxygen throughout the entirety of the human body. Iron is an essential element required by the human body for the synthesis of hemoglobin. Insufficient iron levels result in a decrease in the production of haemoglobin and red blood cells, ultimately resulting in the condition known as anaemia. Iron is a vital element for the diverse physiological processes within the human body, particularly in the biosynthesis of hemoglobin. There is a higher propensity for anemia to manifest in adolescents and women [19, 20].

Moreover, vitamin C has a crucial role in facilitating the absorption of iron within the human body. The administration of an iron-rich diet and the utilization of iron supplements have been observed to ameliorate the condition of anemia. In the event that an individual is prescribed iron supplements, it is common for medical professionals to advise concurrent use of a vitamin C source, such as a glass of orange juice or an orange fruit [21].

Pernicious Anaemia

The term "pernicious" denotes a quality of being highly detrimental or harmful. Historically, this particular kind of anemia was erroneously believed to be a fatal illness, leading to its designation as "dangerous." The utilization of Vitamin B-12 injections or oral supplements has become a viable option for therapeutic intervention. The term "pernicious" refers to something that is harmful, destructive, or having the prevention and treatment of anaemia resulting from insufficient dietary intake can be achieved through the consumption of a vitamin B-12-rich diet. Food items such as meat, fish, eggs, milk, yogurt, and cheese are considered to be abundant sources of Vitamin B-12. Specific medications are administered to enhance the assimilation of vitamin B-12 [22, 23].

Haemolytic Anaemia

Haemolytic anemia is a pathological condition characterized by the premature removal of red blood cells (RBCs) from circulation prior to the completion of their normal lifespan. Individuals across many age groups, ethnicities, and sexes experience the impact of this particular form of anemia. Sickle cell anemia, Thalassemias, and hereditary spherocytosis are representative instances of the hereditary variant of anemia. Red blood cells (RBCs) can also undergo damage as a result of specific diseases and chemical agents, ultimately resulting in the occurrence of hemolytic anemia. The most severe manifestation of haemolytic anemia arises from the administration of red blood cells that are incompatible with the recipient's blood type. Various therapeutic interventions are employed in the management of haemolytic anemia, including blood transfusions, pharmacological agents, blood and bone marrow transplantation, modifications to one's lifestyle, as well as surgical procedures. In severe circumstances, it may be necessary to perform a splenectomy to remove the spleen. Indeed, red blood cells (RBCs) are absent. The removal of the canopy has the potential to mitigate the deleterious effects on red blood cells [24, 25].

Sickle cell Anaemia

In individuals with Sickle Cell Anemia, the red blood cells exhibit a characteristic morphology resembling that of scissors. The presence of atypical hemoglobin within the blood cells results in a distinctive scissor-like configuration, hence impeding its smooth transit through the vascular system. There is evidence to suggest that outbreaks tend to be intensified in both pregnant individuals and youngsters. The occlusion of blood vessels results in the manifestation of discomfort, hence potentially precipitating severe infections and organ impairment. Cells that are in a diseased state exhibit a limited duration of existence, often ranging from 10 to 20 days. Consequently, the human body is unable to generate a sufficient quantity of red blood cells (RBCs) to replenish those that undergo cellular death, resulting in a loss of blood [26, 27].

Thalassemia

Thalassemia is a hematological condition characterized by the production of abnormal red blood cells and reduced levels of hemoglobin. Alpha and beta thalassemia represent the prevailing forms of thalassemia. Alpha thalassemia major, often referred to as hydrops fetalis, is a mild manifestation of alpha thalassemia, whereas beta thalassemia major, also known as Cooley's anemia, denotes a severe form of beta thalassemia. Both males and females are equally impacted by thalassaemias, a condition that

exhibits a higher prevalence in regions such as Italy, Greece, the Middle East, Asia, and Africa. The composition of RBC hemoglobin consists of two distinct protein chains, namely alpha and beta globin. Red blood cells (RBCs) exhibit reduced production in instances where the body fails to generate an adequate quantity of protein chains, hence resulting in insufficient oxygen storage capacity. The regulation of hemoglobin chain synthesis is governed by genetic factors. Thalassemia manifests when these genes are either lacking or modified. Thalassemia is an inherited genetic condition that is transmitted over successive generations [28, 29].

Aplastic Anaemia

Aplastic anemia is a hematological ailment characterized by insufficient hematopoiesis in the bone marrow, resulting in a range of health complications including arrhythmias, cardiac hypertrophy, cardiac insufficiency, susceptibility to infections, and hemorrhaging. The treatment regimen encompasses the administration of blood transfusions, bone marrow stem cell transplants, and pharmacological interventions. These interventions are efficacious in the prevention or mitigation of problems, alleviation of symptoms, and enhancement of quality of life. A balanced and nutritious diet is essential for meeting the physiological requirements of the human body. Hence, the consumption of a well-rounded food is enough in mitigating the occurrence of anemia. The primary etiology of anemia is attributed to deficiencies in essential nutrients such as anemia, folic acid, and iron-rich dietary sources. Anemia is a prevalent condition observed in children, primarily because to diminished iron levels present at birth, inadequate iron content in breast milk, and insufficient iron consumption during the stages of infancy and adolescence [30, 31].

Pathogenesis

The pathogenetic mechanisms exhibit variability, as each pathway is heavily influenced by the specific etiological cause. Nevertheless, each of the various causes contributes to the ultimate etiology of anemia.

Reduced Erythropoiesis

Interleukin-6 (IL-6) has been suggested as the primary cytokine responsible for the development of allergic contact dermatitis (ACD). This compound demonstrates strong inhibitory effects on TNF-α and stimulates the transcription of ferritin, resulting in enhanced retention and storage of iron inside the reticulo-endothelial cells. Prior research has indicated the presence of alternative mechanisms for inducing anemia in animal species with chronic illnesses, wherein the inhibition of TNF increase did not effectively mitigate the development of anemia. In addition to its role in inhibiting the absorption and uptake of iron, IL-6 has inhibitory effects on erythropoiesis through other mechanisms. The expression of the SLC4a1 gene is downregulated in late erythroid precursors, resulting in a reduction in haemoglobin production [32, 33]. Furthermore, it has been observed that it leads to a decrease in both the mitochondrial mass and function within the budding erythroid progenitors. It elicits an elevation in the hepatic production of the acute-phase protein known as hepcidin. It appears that IL-6 may induce anemia via mechanisms that do not rely on hepcidin, implying either direct suppression of erythropoiesis or the presence of unidentified pathways. The production of Activin B by hepatic cells is significantly enhanced in the presence of inflammation, leading to its binding to the receptor type 1 of the bone morphogenetic protein (BMP). The activation of this receptor induces the elevation of hepcidin expression through the involvement of transmembrane proteins, including SMAD and JAK-STAT. The expression of both IL-6 and hepatic hepcidin has been observed to exhibit considerable increases in diverse cancers [34, 35].

Diminished Response to Erythropoietin

In certain instances of anemia of chronic disease (ACD), the level of erythropoietin response may not be proportional to the severity of anemia, leading to the designation of a "blunted erythropoietin response." The aforementioned occurrence has been documented in individuals with sickle cell disease who also suffer from chronic kidney disease (CKD), wherein the administration of erythropoiesis-stimulating agents (ESAs) fails to rectify the condition of anemia. The observed phenomenon can be partially elucidated by the influence of cytokines, bacterial lipopolysaccharides, and IFN-γ on the production of nitric oxide and oxygen free radicals. These molecules have been shown to directly impede the expression of erythropoietin in laboratory settings. It is hypothesized that these reactive oxygen species also possess the ability to impede the transcription factors responsible for triggering erythropoietin production, in addition to causing harm to the cells responsible for manufacturing erythropoietin. The capacity of silymarin to reverse this tendency is attributed to its modulation of immune cells through the inhibition of prostaglandin and prostacyclin synthesis, as well as the suppression of neutrophil and monocyte activation and mobilization [36, 37].

Approximately 25% of patients diagnosed with end-stage renal disease had a diminished response to erythropoietin, hence requiring the administration of greater dosages. Multiple inflammatory proteins, including the inflammatory cytokine IL-6, have been associated with the reduced efficacy of erythropoietin. In certain individuals diagnosed with chronic kidney disease (CKD) who exhibit inadequate response to erythropoietin, the administration of vitamin D therapy has been observed to result in enhanced management of anemia, accompanied by a decreased need for erythropoietin. The observed occurrence of this response has been documented in patients who did not exhibit a decrease in parathyroid hormone levels. The direct enhancement of erythroid precursor proliferation through the activation of 1α-hydroxylase has been seen in the presence of calcitriol. The use of vitamin A, D, and E supplements has been found to result in improvements in anaemia and enhanced responsiveness to erythropoiesis-stimulating agents (ESAs). The activation of vitamin D receptors on immune cells results in the secretion of interleukin-10 (IL-10) by the stromal and accessory cells present in the bone marrow. Recent research has indicated that the presence of 1, 25-dihydroxyvitamin D 3 in lipopolysaccharide-stimulated THP-1 cells leads to the downregulation of hepcidin and an increase in ferroportin expression. In a dose-dependent way, it has been observed that high levels of vitamin D can lead to a reduction in the prohepcidin cytokines IL-6 and IL-1β [38, 39].

Hypoferraemia and Reduced Erythrocyte Survival

The expression of DMT-1 is increased in a dose-dependent way by IFN-γ and bacterial lipopolysaccharides. This leads

to an enhanced uptake of unbound iron into the enterocytes and the monocyte/macrophages. Additionally, it results in the retention of iron within the monocytes by downregulating the expression of ferroportin mRNA. Previous studies have indicated a correlation between elevated levels of TNF-α and IL-6 and decreased serum iron levels in patients with chronic illnesses. This association leads to a state of hypoferremia and subsequently reduces the erythropoietic capacity. This phenomenon could potentially be attributed to an elevated erythrophagocytosis rate, which is a physiological mechanism aimed at eliminating old and impaired red blood cells under normal circumstances [40, 41].

The impairment of these cells can be induced by several factors such as cytokines, endotoxins, and reactive oxygen species. Several animal tests have demonstrated that the administration of sublethal levels of TNF-α can result in the phagocytosis of erythrocytes by macrophages. The condition of hypoxia results in an upregulation of transcription of hepcidin messenger RNA (mRNA). It is widely believed that this process is facilitated by platelet-derived growth factor. Conversely, the generation of reactive oxygen species during the inflammatory response leads to the secretion of pro-inflammatory cytokines, such as hepcidin. Additional pro-inflammatory cytokines, such as IFN-γ, have been found to induce an upregulation in the expression of inducible nitric oxide mRNA, leading to the subsequent synthesis of nitric oxide. The concurrent occurrence of superoxide molecule generation during inflammation has the potential to induce a reversal of the impact of hypoxia on hepcidin synthesis. The aforementioned process triggers death of red cell precursors through the mediation of nitric oxide, thereby exacerbating the condition of anaemia [42, 43].

Bone Marrow Infiltration

Anaemia that arises as a result of cancer can be attributed to three fundamental mechanisms: (a) diminished production of red blood cells, which can be caused by tumor infiltration, the impact of cytotoxic medications, inadequate nutrition, or inhibition due to cytokines; (b) heightened loss of red blood cells by either haemolysis or haemorrhage; and (c) several other causes. In the majority of instances, there exist notable intersections among these pathways; nevertheless, the primary mechanism at play is inflammation induced by malignancy. This observation suggests that alternative pathways may play a significant role in the pathogenic mechanisms that contribute to the development of anemia in cancer patients. Tumors induce the release of several substances, including cyclo-oxygenase-2, vascular endothelial growth factor, granulocyte-monocyte colony-stimulating factor, interleukin-6, and tumor necrosis factor-alpha. These substances contribute to the development of cancer cachexia and anemia [44, 45].

The cyclo-oxygenase-2 inhibitor, celecoxib, has been observed to exhibit a mitigating effect on the anemia and cachexia commonly associated with anemia of chronic disease (ACD). The present study has detected a new chemical that exhibits an inverse correlation with serum hepcidin levels in cancer patients suffering from erythropoiesis-stimulating agent (ESA)-resistant anaemia. An increase in the expression of GDF-15 leads to a decrease in the levels of hepcidin and is linked to the metastasis, angiogenesis, progression, and hematopoiesis of tumors. The presented hypothesis suggests that cancer-driven inflammation plays a significant role in the development of anaemia, with the serum concentration of GDF-15 showing a strong correlation with the severity of anaemia in individuals with cancer. In the context of infective agents such as Plasmodium and HIV, it has been observed that the toxic byproducts produced by these parasites have a direct inhibitory effect on the process of erythropoiesis. Furthermore, these organisms and malignant cells engage in competitive interactions that result in the deprivation of iron for erythroid precursors. The microbial cells that engage in invasion necessitate iron as a crucial constituent of many iron-containing enzymes that are essential for the processes of protein synthesis and proliferation [46, 47].

Laboratory Diagnosis

The initial assessment encompasses a comprehensive evaluation of the patient's medical history pertaining to the condition, along with conducting general investigations to exclude alternative etiologies of anemia. An examination of the morphology of the blood film and bone marrow, determination of reticulocyte count, analysis of stool samples, measurement of serum bilirubin and lactate dehydrogenase levels, and evaluation of renal function are necessary. Differentiating anemia of chronic disease (ACD) from iron deficiency anemia (IDA) and other potential causes of hypochromic, microcytic anemia is a crucial factor in its diagnosis. A comprehensive comprehension of the stimuli and regulatory mechanisms involved in the generation of the molecules typically subjected to test is necessary for this task [48, 49].

Blood Film Morphology

The initial morphology of the red blood cells exhibits a normochromic and normocytic appearance, which then transitions over time to a hypochromic and microcytic state. The typical range for haemoglobin concentration is 8-9.5 g/dL, indicating mild to moderate anaemia, with few occurrences of levels falling below 6 g/dL. When there is a suspicion of ACD accompanied by severe anaemia, it is imperative to thoroughly evaluate other factors that may contribute to the loss or destruction of red blood cells. The reticulocyte count, or alternatively referred to as the reticulocyte index, is often diminished in both anemia of chronic disease (ACD) and iron deficiency anemia (IDA). The blood film has the potential to yield valuable insights into the etiology of anemia of chronic disease (ACD). For instance, thrombocytosis may indicate chronic hemorrhage, while the presence of toxic granules in neutrophils may suggest severe sepsis. Additionally, the identification of hypersegmented neutrophils may point towards a mixed nutritional shortage or deficiencies in folate/B12, which are commonly observed in malignant situations [50, 51].

Ferrokinetic Studies

One notable distinction between ACD and IDA is in the contrasting iron status observed in each condition. In IDA, there is a complete absence of iron, as indicated by serum ferritin levels below 30 ng/mL. On the other hand, the etiology of ACD is multifactorial, involving various factors, and although iron is present, it is not effectively utilized by the immature erythroid precursors. In the context of anemia of chronic disease (ACD), it has been observed that levels of transferrin are elevated, although serum iron and transferrin saturation are diminished. Additionally, there is an increase in erythrocyte-free protoporphyrin, serum ferritin, and

marrow-stainable iron [52]. In the context of anemia of chronic disease (ACD), the diminished transferrin saturation might be attributed not alone to iron deficiency, but also to an augmented production of transferrin. Hypoferraemia occurs as a result of the sequestration of iron inside the cells of the reticulo-endothelial system. Consequently, the reduced levels of iron in the serum lead to a decrease in transferrin saturation. The concentration of the transport protein transferrin is thus elevated in individuals with iron deficiency anemia (IDA), but it is diminished or within the normal range in those with anemia of chronic disease (ACD) [53, 54].

Serum Ferritin/Ferritin Receptor

Ferritin is classified as an acute-phase protein, and its concentrations are elevated in cases of chronic inflammatory conditions. Once underlying inflammation has been excluded, assessing body iron status can serve as a reliable indicator. Typically, the serum ferritin levels fall within the range of 15 to 300 µg/L. Consequently, individuals diagnosed with anemia of chronic disease (ACD) typically exhibit elevated levels of serum ferritin. This can be attributed to the accumulation of iron by the reticulo-endothelial cells and heightened production resulting from inflammation. The soluble transferrin receptor (sTfR) is a cleaved portion of the membrane-bound transferrin receptor (TfR), and there appears to be a correlation between the amounts of sTfR and TfR. The regulation of both molecules' production is contingent upon the intracellular iron's availability through the interaction between the iron regulatory element and protein. Consequently, diminished iron availability results in elevated levels of transferrin receptor (TfR) and soluble transferrin receptor (sTfR). While inflammatory cytokines might impact the level of soluble transferrin receptor (sTfR), it is often valuable in distinguishing between anemia of chronic disease (ACD) and iron deficiency anemia (IDA). The reciprocal effects of pro-inflammatory cytokines and erythroid iron shortage on sTfR contribute to the equilibrium of their respective influences. The outcome demonstrates that the soluble transferrin receptor (sTfR) levels in anemia of chronic disease (ACD) tend to be lower compared to iron deficiency anemia (IDA), and are comparable to the levels observed in non-anaemic individuals [55, 56].

Hepcidin

The protein in question is a 25-amino acid chain that exhibits a structural resemblance to a hairpin. It is synthesized within the hepatic parenchymal cells. The integrity of this structure is sustained by the presence of disulfide bonds that link the four cysteine amino acid residues within the chain. Additionally, it is generated to a certain degree by active neutrophils and macrophages. The synthesis of hepcidin is stimulated by excessive iron levels and inflammation, whereas it is suppressed by conditions such as anemia and hypoxia. The mechanism of action involves the inhibition of iron export from iron-containing cells, specifically duodenal endothelial cells and macrophages. The aforementioned process is facilitated through the modulation of ferroportin, leading to its subsequent deterioration. Ferroportin serves as the exclusive transporter of iron in cells that contain iron. The main pathogenetic mechanism of allergic contact dermatitis (ACD) is believed to be this. The utilization of serum hepcidin is currently being suggested as the most precise serological indicator for distinguishing between anemia of chronic disease (ACD) and iron deficiency anemia (IDA). This academic discussion focuses on the notable laboratory distinctions between ACD (anemia of chronic disease) and IDA (iron deficiency anemia), as well as the anticipated outcomes when both conditions coexist [57, 58].

Erythropoietin Assay

Erythropoietin is synthesized by the cells located in the renal medulla in response to the presence of anemia and a decrease in oxygen levels. Caution should be exercised when interpreting the assay results in ACD, as its primary utility may lie in its ability to predict the likelihood of a positive response to erythropoietin therapy. In the context of a two-week treatment with recombinant human erythropoietin, it has been observed that an erythropoietin level exceeding 100 U/L or a ferritin level surpassing 400 ng/mL can serve as indicators of an unfavorable response to erythropoietin in 88% of patients who are not concurrently receiving anticancer medications. The replication of this phenomenon has not been observed in individuals undergoing cancer chemotherapy [59, 60].

Treatment

Treatment for ACD aims to do two things: increase the blood's ability to carry oxygen, and find and treat the condition's underlying cause. Urgent treatment eliminates the poor prognosis associated with anemia in most illness states, especially when end organ destruction is imminent and overactive cardiac compensatory mechanisms may lead to adverse effects. Patients with chronic kidney disease, cancer, and heart failure who also suffer from anemia have a worse prognosis. In haemodialysis patients with CKD, the risk of death doubles when the patient's hemoglobin level falls below 8 g/dL compared to when it's between 10 and 11 g/dL. Patients whose haemoglobin levels were optimized to between 10 and 11 g/dL also fared better in terms of survival and response to treatment.

Iron Therapy

Considering that the etiology of ACD involves a relative deficiency in the availability of iron to the red cell precursors rather than an absolute deficiency, iron therapy may not be very helpful in ACD. There are a number of microorganisms and cancer cells that can use the extra iron to grow and spread. The immune system is known to be suppressed by iron because of its ability to block IFN-mediated pathways. It also increases hydroxyl radical generation, which damages tissues and endothelium. However, parenteral iron may be utilized in cases of insufficient oral consumption or absorption. Except for rare, serious cases of malabsorption, iron taken orally is well absorbed, has good bio-availability in its reduced form, and should be used. Parenteral iron administration includes intravenous (IV) and intramuscular (IM) injections. Loading doses of intravenous iron are typically given as a steady infusion of iron dextran. Because of the potential for a life-threatening anaphylactic response, an emergency tray should always be on hand. Sometimes a deep intramuscular injection utilizing the Z (zig zag) method is used to administer the injectable iron brand Jectofer. This is done to prevent the unsightly result of a black spot surrounding the injection site, which is especially noticeable in those with lighter skin [61, 62].

Red Cell Transfusion

The utilization of blood transfusion continues to be a significant intervention for the immediate care of persons experiencing severe anemia accompanied by cardiac decompensation. Nevertheless, the extended utilization of red blood cell transfusion has been linked to heightened death rates, primarily attributed to the accumulation of iron and the activation of the immune system through HLA antigens in individuals who may ultimately undergo transplantation [63].

Erythropoiesis-Stimulating Agents

By activating the bone morphogenetic protein and the JAK-STAT5 pathway, erythropoietin promotes the proliferation of erythroid precursor burst-forming unit erythroid in the marrow. SMAD is involved in the transduction of signals from BMP, which is a member of the transforming growth factor- family and binds to serine-threonine kinase receptors. Binding of bone morphogenetic protein (BMP) to haemojuvelin, a signaling component of BMP, causes hepatocytes to produce hepcidin and reduce iron absorption. By reducing monocyte IL-6 synthesis, hepcidin's pro-inflammatory effects can be mitigated through activation of the JAK-STAT pathway. In addition to individuals with CKD and HIV infection, those with ACD caused by malignancies or anticancer chemotherapy may also benefit from erythropoietic medications. Iron absorption and haem production in erythroid precursors are stimulated, and the antiproliferative effects of proinflammatory cytokines are mitigated. Haemoglobin levels above 12 g/dL have been associated with a worse treatment outcome, hence it is recommended that these drugs be taken with iron to achieve this goal. Elevated blood pressure, cerebral convulsion/hypertensive encephalopathy, thrombo-embolic problems, iron deficiency, and influenza-like syndrome are just few of the prevalent adverse effects of erythropoietin that need to be evaluated for each individual patient [64, 65].

Targeting the Cytokines

There is clinical evidence that omega-3 polyunsaturated fatty acids reduce TNF- and IL-6 production. Their activity on nuclear factor-B suggests that they may be useful in treating autoimmune inflammatory diseases such rheumatoid arthritis and type 2 diabetes. In contrast to saturated fats, polyunsaturated fatty acids have few, if any, negative side effects. Inhibitors of the mitogen-activated protein kinase pathway, which have shown some promise in patients with myelodysplastic syndrome, warrant further study because of their role in mediating myelosuppression [66, 67].

Hepcidin's pivotal role in the etiology of ACD makes it a promising therapeutic target. Studies have shown that elevated hepcidin levels are associated with ESA failure, suggesting that blocking this protein could enhance the body's response to erythropoietin. In animal experiments, the anemia has been cured thanks to a novel antihepcidin drug (NOX-H94). In animal studies, treatment with a combination of hepcidin inhibitors and ESAs was more effective than treatment with ESAs alone. Due to its essential function in mutagenesis, angiogenesis, metastasis, and ACD in different cancers, GDF-15 has also been recommended as a viable target. The discovery of a hepcidin-independent pathogenetic pathway underlying the onset of ACD has bolstered the case for combination therapy [68].

Anemia Prevention and Control

Due to the significant public health implications associated with anemia, there is a global imperative to prioritize its cost-effective prevention and management measures. Numerous economically viable strategies targeting anemia, which have been well documented, encompass addressing the root causes, restoring hemoglobin concentration to optimal levels, and implementing measures to avoid and cure associated consequences. Various tactics are employed for the purpose of providing supplementary iron to individuals [69]. However, among these strategies, the most promising in terms of preventing iron deficiency anemia are food fortification and dietary diversification with iron. In contrast, within regions where vitamin A insufficiency is prevalent, the World Health Organization (WHO) advocates for the regular administration of vitamin A supplements during pregnancy or at any stage of lactation [70].

The iron content of red teff has been found to reach levels of up to 150mg per 100g. Furthermore, it has been observed that consuming one cup of raw grain teff might potentially fulfill as much as 82% of the needed daily intake of iron. Consequently, those residing in regions of Ethiopia where red teff intake is more widespread had elevated hemoglobin levels, thereby reducing the likelihood of developing anemia [70]. Furthermore, teff is not only a source of iron but also contains B-complex vitamins, which play a crucial role in the production of red blood cells and the facilitation of food metabolism. A single cup of uncooked teff provides around 47% of the recommended daily intake for vitamin B6, 50% for vitamin B1, 31% for vitamin B2, 32% for vitamin B3, and 18% for vitamin B5. Moreover, teff is rich in vitamin C, which plays a crucial role in facilitating iron absorption, but it contains a relatively low quantity of vitamin A. Presently, there has been an increasing worldwide fascination in the utilization of teff as a dietary staple. The primary reason for this interest is from teff's gluten-free nature and its comparatively high nutrient content, making it a viable ingredient for food products intended for individuals with celiac disease [71].

Conclusion

Anemia is a common blood disorder that can have multiple root causes, including genetics, the immune system, and nutritional deficiencies. However, if further safety measures are performed, this won't be an issue. Seek quick medical treatment and advice from a doctor if you suffer any of the aforementioned symptoms. In order to raise a healthy generation, it is crucial that anemia be detected and treated without delay. That example, the prevalence of anemia might go down if everyone makes an effort. To rephrase, taking precautions helps ensure a more joyful existence. Children with anemia have delayed mental and psychomotor development, poorer work performance, and shorter statures. Anemia is the most common public health issue. Malnutrition and parasite diseases are major contributors. Iron deficiency anemia, vitamin B12 deficiency anemia, and foliate deficiency anemia are the most common forms of nutritional deficit-related anemia.

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