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Anemia Epizootiology, Physiopathology and Analysis in Middle- and Low-income Countries

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Abstract

Anemia influences 33% of the total populace and adds expanded dreariness and mortality, diminished work usefulness and disabled neurological turn of events. Comprehension of anemia's altered, and multifarious analysis is urgent for creating viable intercessions that report the setting explicit reasons for iron deficiency and for checking anemia control programs. We elaborated definitions and orders of anemia, designate systems through which it creates, and survey the assortment of conditions that add to its advancement. We accentuate the danger factors generally pervasive in the low and center pay nations, including wholesome lacks, disease/irritation, and hereditary hemoglobin issues. Ongoing work has encouraged how we might interpret anemia perplexing etiology, including the extent of anemia brought about by lack of iron and the job of aggravation and contamination. Collecting proof demonstrates that the extent of anemia because of iron deficiency varies by populace bunch, topographical setting, irresistible infection trouble, and the predominance of other iron insufficiency causes. Further research should be focused to examine malnutrition and the commitment of infections, just as the significance of hereditary hemoglobin issues in specific populaces.



SCAN ME



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Introduction

Anemia is a disorder in which hemoglobin (Hb) focus or red blood cell (RBC) records are more minor than typical and lacking to come across a person's physiological needs-influences about 33% of the earth's populace [1, 2]. Anemia is related to expanded impermanence in children and ladies, helpless birth consequences, diminished labor usefulness in adults, and debilitated mental and social improvement in children. Women of reproductive age (WRA) and preschool children (PSC) are especially impacted [3-8]. Anemia is on the other hand characterized as a diminished outright figure of flowing RBCs or a state where the quantity of RBCs (thusly their oxygen-conveying limit) is inadequate to encounter physiologic requirements [1, 12]. Nevertheless, most generally analyzed by short Hb fixation or a little hematocrit, pallor can likewise be analyzed utilizing RBC amount, Hb electrophoresis, mean corpuscular volume, blood film investigation or the blood reticulocyte calculation [12, 13]. At the populace level and in clinical practice, Hb focus is the most well-known hematological appraisal technique used and the supreme well-known marker used to characterize anemia [14]. The basic job of Hb to convey oxygen to the cells clarifies the chief well-known proven manifestations of anemia, which incorporate proven exhaustion, windedness, palpitations or bouncing heartbeats, palmar pallor and conjunctival [15]. Medical indications and clinical history are utilized to analyze anemia when hematological information is inaccessible; however, they are restricted in their capacity to recognize anemia [16, 17]. Severe anemia is of specific significance clinically, as it can bring about elevated-yield cardiovascular breakdown and expiry [1, 12].

Characterizing a strangely small amount of Hb fixation involves seeing how Hb normally changes by sex, age, natural pregnancy position, hereditary, race and conceivably. Hb shifts with age, most drastically in the primary long stretches of life [18]. Typical Hb fixations in the infant are somewhere in the range of 17 and 21 g/L, their most noteworthy opinion throughout life [18, 19]. Hb focuses then, at that point, diminishes through the main 2–3 long stretches of life in childhood before expanding again, and afterward intensities of all through maturity before deteriorating again in more seasoned age [18, 20, 21]. Gender contrasts in Hb fixations start in adolescence and proceed all

through the conceptive years [21]. Throughout gestation, on account of the development of blood capacity and ensuing weakening impact, Hb fixation normally decreases through the first and second trimesters, climbing up steadily again in the third period [24]. Separately from biological elements, conduct and natural circumstances, like smoking and height can likewise influence Hb statistics [1].

The WHO Hb shorts for anemia are generally realistic worldwide and are pregnancy, sex, and age particular. These shorts were principally settled in 1968 by dietary anemia concentrate on a bunch at WHO utilizing factual shorts rather than limits connected to significant wellbeing outcomes [15]. Hb shorts were changed marginally from that point forward to consider extra age partitions among youngsters, change for kids in the 5–11 age bunch considering the information of noniron-insufficient kids from America, and formation of the classes of "mild," "moderate," and "severe" anemia [24, 27]. Cutoffs were additionally upheld by discoveries amid associates of the Second National Health and Nutrition Examination Survey (NHANES II) who were not iron requiring [14]. The requirement for independent shorts in view of identity has been anticipated, as have updates to the shorts for specific age gatherings [28-32].

The purpose of this paper is to set up proper limits to characterize that anemia is accurately recognized, and its adverse consequences forestalled. As significant, understanding the differences and the multiplex etiology of anemia is critical for creating suitable mediations that report the setting explicit reasons for anemia and for checking the accomplishment of anemia control programs. With that in mind, the essential points of this paper are to clarify definitions and arrangements of anemia; portray the organic instruments through which anemia creates; audit the assortment of variables and conditions that add to iron deficiency improvement, stressing those generally common in the low-to-middle-income country (LMICs) and distinguish research needs.

Worldwide scale of anemia

Around 33% of the total populace was assessed to experience the ill effects of anemia in 2010 [2]. The populace bunches generally helpless against anemia incorporate (1) kids below 5 years old (42% with pallor in 2016), especially babies and kids below 2 years old; (2) pregnant ladies (46% with anemia in 2016); and (3) women of reproductive

age (WRA) (39% with anemia in 2016) [33, 34]. Women were reliably at more danger of iron deficiency than men in practically all environmental districts and most age groups [2]. Other in danger bunches incorporate the old, as the predominance of iron deficiency among adults over 50 years old ascends with progressing age; however, information is restricted [35]. The pervasiveness of anemia additionally fluctuates via geographic district; South Asia, the Caribbean, Oceanic and Sub-Saharan Africa had the most noteworthy anemia predominance across all age gatherings and two genders in 2010 [2]. On the nation scale, anemia amid WRA and kids below 5 years old are average-to-extreme general victims in most of World Health Organization (WHO) portion countries [9, 10]. Development of diminishing anemia has been generally speaking sluggish and lopsided. For all age gatherings and the two genders, anemia is assessed to have diminished approximately seven percent somewhere from 40% to 33%, in the range between 1990 and 2016 [2]. The WHO Global Nutrition Target 2025 on anemia means to decrease anemia in WRA by half by 2025 [36]. Based on a worldwide predominance of 29-38% iron deficiency amid WRA starting in 2011, a decrease of 1.8-2.4% each year would be needed to encounter this objective.

Physiopathology of anemia: concerns for advancement, growth and birth results

Anemia has critical ramifications for human wellbeing, just as for the financial and social turn of events. In 2010, anemia represented 68.4 million years of everyday routine experienced with incapacity, or 9% of the entire globe's incapability suffering from all situations [2]. Anemia has been interconnected with destructive comfort and advancement results, containing neonatal and perinatal impermanence, untimely birth, low birth weight and deferred kid growth [37, 39]. The adverse consequences of welfare and progression result from anemia ascent from the effects of lessened oxygen transportation to tissues, just as footprints connected with the basic details for anemia, which are hard to undo. For illustration, in iron deficiency anemia (IDA), reduced iron accessibility has grounded adverse consequences on mental fitness and working even earlier anemia growth [40].

Etiology of anemia: conjectured models and characterizations

At the natural level, anemia creates in light of an abnormality in erythrocyte calamity compared with formation; this can be because of lacking or inadequate erythropoiesis and additionally inordinate erythrocytes' loss (because of blood misfortune). Maximum anemias have a trademark RBC appearance, which can give bits of knowledge to the conclusion of anemia. Numerous variables can root a comparable kind of RBC morphology [41]. Moreover, as iron deficiency might have different roots, even in similar individuals, hematological indications of a specific reason can be covered by another. For instance, the sign of anemia brought about by folate or cobalamin insufficiencies is macrocytic anemia. Associative ID, which originates in microcytosis, may veil completely the impacts of the folate or B12 inadequacy. Although lists exist in medical practice for recognizing anemia analysis given RBC boundaries, their dependability for segregating between bases differs [42,43].

A theoretical example of the examination of anemia recognizing how distal elements add to supplementary general elements of anemia, like food instability, sterilization microcytosis at last, the supreme quick reasons for anemia (e.g., dietary lacks, sickness, Hb disorders and irritation) [13, 44, 45]. Many of these factors are interconnected. Destitution, for instance, is a significant cause of wellbeing and nourishment, and poor financial situation is connected to a serious danger of iron deficiency among ladies and kids [13, 46]. Correspondingly, a little training level is likewise connected with a serious danger of anemia [13]. A new examination of 53 demographic and health studies with Hb information tracked down that anemia amid PSC (was firmly connected with maternal pallor, family riches, motherly schooling, and small birth weight [47]. It is essential to take a reminder that the essential drivers of gentle and direct anemia will generally contrast with the chief reasons for serious anemia. However, there are restricted examinations on the etiology of serious anemia, jungle fever is often distinguished as a chief reason for extreme anemia, especially in African youngsters [48]. The supreme steady indicators of serious anemia in populace-based overviews of the PSC were jungle fever, helpless sterilization, underweight, and aggravation (in African nations); hindering, vitamin A and

provincial area were likewise huge determinants in great or extremely great contamination in the biomarkers reflecting inflammation and nutritional determinants of anemia (BRINDA) project [49]. In an investigation of Malawian PSC, influences related to serious pallor comprised intestinal sickness, hookworm disease, human immunodeficiency virus (HIV) disease, bacteremia, favism lack, B12 deficiencies and vitamin A (VA) [48]. In this populace, iron deficiency (ID) was defensive of serious anemia, possible because of the connection between iron and disease. Extreme pallor was related to jungle fever, aggravation, and hindering, while indicators of more adequate types of anemia were ID, intestinal sickness, and α -thalassemia in Kenyan PSC [50]. Drastic anemia is likewise a co-morbidity of serious unhealthiness; for instance, in India, of hospices that found youngsters with SAM, 67% additionally had serious anemia [51]. It is distinguished and reflected in worldwide examinations of anemia trouble somewhere in the range between 1990 and 2010, the most proximal danger factors for anemia incorporate nourishing lacks, illness/contamination, and hereditary Hb syndromes [52]. These conditions and a few others, which are likewise common reasons for pallor in LMIC, will be talked about in further features underneath.

Dietary anemia

Nourishing anemias outcome when absorptions of hematopoietic supplements those engaged with RBC creation or upkeep are deficient to encounter those demands [13]. Reasons for supplement lack incorporate expanded supplement misfortunes, insufficient dietary admission, impeded ingestion or modified supplement digestion While supplement augmentation is a typical precautionary and handling procedure for nourishing anemias-for instance, iron augmentation for the anticipation of IDA-the bio-accessibility and in this manner assimilation from various supplement arrangements can differ, possibly restricting their impact [53]. The most common and widely recognized dietary lack prompting anemia is the deficiency of vitamin A, iron deficiency and lack of vitamin B (riboflavin, folate and B12 [54]. Numerous of these supplements like vitamin A, B12 and B6, riboflavin and folic corrosive are required for the ordinary creation of RBCs; different supplements, like nutrients E and C, may secure RBCs through their cell reinforcement purpose [55]. Minute amounts like zinc and copper are originated in the designs of

catalysts that follow up on iron digestion [56]. Copper may likewise add to anemia improvement through decreases in erythropoietin (EPO) and cancer prevention agent proteins that require copper, in this manner, expanding oxidative pressure and diminishing RBC lifespan the systems through which zinc inadequacy is related to anemia are not also characterized [57]. The degree to which every one of these inadequacies adds to the worldwide anemia trouble is as yet a matter of examining. While a portion of these supplements lacks are uncommon and may contribute essentially nothing to the weight of anemia universally, a lack of numerous trace minerals probably has a synergistically effect on anemia advancement [58].

Iron deficiency

ID creates when nutritional iron admission can't address iron issues throughout some time, particularly through times of life when iron necessities are especially extraordinary or when iron misfortunes surpass iron admission. ID regularly advances in three phases: loading iron exhaustion, iron-insufficient erythropoiesis, and IDA [59]. The WHO suggests serum ferritin or soluble transferrin receptor (sTfR); serum ferritin, a proportion of physique stockpiling iron and a delicate proportion of ID, is raised by the intense stage reaction and sTfR levels when great show tissue ID, yet sTfR may likewise be impacted by irritation and different causes for erythropoiesis [60, 61]. As of the impact of aggravation on numerous biomarkers of iron status, intense stage proteins ought to be evaluated when probable [60]. A full audit of iron grade pointers, external to the extent of the paper at this time, is also accessible in another place [61]. Gauges from the last part of the 1990s set the number of people impacted by iron deficiency (ID) at 2 billion, and ID has for some time been accepted to add to around half of the pallor cases internationally [62, 63]. A new examination of worldwide anemia information that determined reason explicit acknowledgment for 17 circumstances connected with anemia positioned ID as the most well-known reason in practically all worldwide areas checked. The WHO involved the adjustment of Hb focus from iron augmentation studies to appraise the "proportion of all anemia amenable to iron" as half of anemia among pregnant and nonpregnant ladies, and 42% of anemia in kids [9]. Modern investigations from the BRINDA project demonstrated that alongside jungle fever and age, ID was unique of the elements connected

with anemia; however, the extent of pallid kids and ladies with ID shifted by irresistible infection load [46, 49]. Additional review that surveyed the job of ID in anemia trouble among nonpregnant WRA and PSC across a scope of nations with changing statuses on the human development index, exhibited that between roughly a quarter to 33% of iron deficiency amid WRA and PSC was related to ID [64]. In nations where the commonness of anemia is more prominent than 40% and in nations where irritation ranks are high, ID plays a lot more modest role [64]. Thus, while ID stays an essential driver in numerous settings, the extent of anemic people with ID differs by context-oriented elements, and helpless iron sustenance can't be thought to be the essential driver in all circumstances. However, iron mediations are fundamental to supreme pallor control projects, and WHO at present has 17 rules on iron augmentation [65]. Known for the multifaceted analysis of anemia, the degree to which ID represents the anemia trouble keeps on being explored.

Vitamin A deficiency

Vitamin A deficiency (VAD) is common in numerous LMICs, especially amid expectant ladies, WRA and PSC. WHO assessed in 2005 that 9.1 million pregnant ladies and 190 million PSC from locales in danger of VAD were VA lacking (in light of serum retinol focuses), which addresses 33% of PSC and 15% of expecting ladies from these countries [66]. Anemia and VAD have been seen to happen in similar populaces for quite a long time, and huge connections between Hb and VA rank biomarkers have been depicted in different nations and populaces comprising preschool and young youngsters, youths, and adults [67]. VA augmentation has been displayed to build Hb focuses, some iron grade files and hematocrit, and in any event, when directed without iron additives [55, 67]. VAD is remembered to cause anemia through numerous components, containing the job of retinoids in erythropoiesis, VA's significance for invulnerable capacity, just as VA's grounded job in iron breakdown rather than IDA, which is set apart by consumption of iron supplies, anemia because of VAD is set apart by an increment in iron supplies in spleen and the liver and expanded serum ferritin engrossment [67, 68]. The pallor of VAD has then again been portrayed as microcytic, hypochromic or hypochromic, however different variables comprising other wholesome lacks and contaminations happening all the while may root

irregularities in RBC limitations [67]. BRINDA examinations showed that amid PSC, VAD was related to anemia in the near portion of the studies (5/12) and diagonally ranks as an irresistible sickness problem [49]. In the BRINDA task amid WRS where VAD and ID were together evaluated, ID and VAD were related to anemia in all overviews (5/5 reviews) in both low-and high-disease trouble groups [46]. Approximations regarding how much anemia would be diminished by tending to VAD authorizations extra exploration. Likewise, similar to press status files, VA biomarkers are impacted by aggravation, in this manner confounding the appraisal of anemia because of VAD in situations where the irresistible infection is prevailing [69].

Insufficiencies of B vitamins

A few B nutrients are associated with Hb amalgamation or iron digestion, containing pyridoxine (B6), B2 (lactoflavin), folic acid and B12 Lack of these supplements has been related to anemia; in any case, the degree to which they add to the worldwide weight of anemia differs and sometimes is muddled. Lack of vitamin B6 is rare and won't be tended now [55]. Both folate and vitamin B12 inadequacy can prompt macrocytic anemia. The lack of these supplements influences megaloblastic changes and DNA combination, for example, on the fringe blood smear; hyper-segmented neutrophils [70]. Folic acid inadequacy can likewise prompt diminished erythrocyte life length. Lack of vitamin B12 in LMIC supreme ordinarily outcomes from less dietary admission of the supplement. Bioavailability is just in natural source food varieties; however, cobalamin lack can likewise outcome from malabsorption, especially in the older amid whom digestive decay is customary, in instances of vindictive pallor, an immune system sickness in which autoantibodies are framed contrary to inherent element fundamental for B12 retention, and in one parasitic and bacteria coinfections [13, 71, 72]. Folic acid inadequacy will in general be more normal in populaces depending on unfortified rice or wheat as a chief food and that devour small measures of vegetables and green verdant vegetables [71]. Preterm babies, expectant ladies, and people living in jungle fever widespread locales are in high danger of folate deficiency [55, 73]. For ladies during gestation, folic acid requests increment; and beginning pregnancy with a helpless folic acid grade can prompt megaloblastic anemia, which is additionally aggravated by the extra folic acid essentials for lactation [13].

Information on the pervasiveness of folic acid and cobalamin insufficiencies at the public scale is inadequate [74]. Out of seven nations with public information on the grade of B12 (estimated utilizing various markers, including methylmalonic corrosive or homocysteine serum vitamin B12) principally from Europe and America, five had degrees of lack more noteworthy than 5% [74]. Among the 10 studies of WRA, in the BRINDA project, four estimated cobalamin rank; amid these, the inadequacy of cobalamin was exceptionally low (<3%) in the United States and Mexico, yet greater (around 15%) in Colombia and Côte d'Ivoire [46]. In the worldwide audit of folate and vitamin B12 rank by McLean et al., folic acid lack was assessed to be of general wellbeing importance (>5% insufficient) in 6 out of 8 nations with public information, and especially impacted gatherings remembered PSC for Venezuela (33.8%), expectant ladies in Venezuela (25.5%), Costa Rica (48.8%) and the old in England (15%) [74]. The predominance of folic acid inadequacy was <3% in Mexico and the United States, but >80% in both Georgia and Côte d'Ivoire, according to the BRINDA project summaries of WRA [46].

The commitment of folic acid and B12 lacks to the worldwide pervasiveness of anemia is obscure; however, information proposes that it very well might be insignificant. One audit demonstrated that a great pervasiveness of folate or B12 inadequacy didn't relate to a high predominance of anemia aside from potentially for ladies (and their babies and kids) consuming veggie-lover slims down who were B12 deficient [43]. The folate and vitamin B12 insufficiencies were not essentially connected with pallor, the BRINDA project showed; however, test sizes for concentrates on that deliberate these lacks were inadequate [46]. Vitamin that acts as a cofactor in redox responses is riboflavin, which is a significant piece of digestion of iron, and riboflavin lack in creatures can diminish the synthesis of iron from stocks, increment iron sufferers, decline iron assimilation and disable globin manufacture [55, 75]. Riboflavin inadequacy is believed to be normal in numerous populations and has been reported in expectant and nurturing ladies, babies, young kids, juvenile young ladies, and the old in both major league salary and LMICs, particularly where utilization of milk/dairy items and meat (essential sources of riboflavin) is less [75]. If riboflavin inadequacy is an essential contributing variable to pallor in people stays indistinct. Riboflavin complements given along iron enhancements have

been displayed to greatly affect Hb focus than iron enhancements alone among youngsters and expectant ladies in certain investigations, but not all [76]. In a longitudinal investigation of Chinese grownups, deficient riboflavin admission was related to pallor at the gauge and expanded danger of anemia during a 5-year follow-up duration [77]. Yet, in Côte d'Ivoire students, Hb fixation was not related to riboflavin inadequacy or anemia notwithstanding a pervasiveness of riboflavin lack of 65%, however, it was related to ID [76].

Overweight and undernutrition

Hindering, wasting and being underweight have been related to anemia in certain revisions; however, not all [49, 78-80]. In investigations of the BRINDA project, hindering and below weight were related to anemia in PSC in the greater part of the review for which these factors were accessible [49]. These appearances of deprived wholesome position are related to anemia because of comparable variables, including poor motherly sustenance, insufficient home and local area conditions, lack correlative taking care of works on prompting helpless micronutrient and creature source food consumption, tainted water and helpless sterilization, imperfect breastfeeding rehearses, subclinical and clinical infections [81]. While further connected with ID than anemia essentially, weighty and large people have an expanded danger for ID, as information from different nations shows [82]. The essential connection between these circumstances is believed to be via hepcidin-a peptide chemical delivered overwhelmingly by the liver and answerable for iron homeostasis and raised within the sight of irritation [83]. The persistent subclinical aggravation present in weighty and stout people increments hepcidin ranks, bringing about decreased iron immersion [82]. But Hb focus will quite often be in the typical variety [82, 83].

Anemia of irritation and contagion, and related major maladies

Through different systems, numerous infections are related to anemia, comprising sickness explicit consequences for blood misfortune, erythropoiesis, or hemolysis, and through the impacts of aggravation on iron digestion. The existence of an improperly low quantity of reticulocytes for the level of anemia is utilized clinically to demonstrate situations because of healthful lacks, aplastic

anemia, diminished erythropoietin levels, or acquired bone marrow disappointment disorders [70]. Somewhere in the range of 1990 and 2010, worldwide examinations of anemia trouble, schistosomiasis, hookworm, and intestinal sickness established three essential drivers of anemia [2]. Underneath, in LMICs, we portray AI just as the particular systems for quite a long-time infection related with pallor and pervasive.

Anemia of inflammation

Anemia of inflammation (AI) is by a low reticulocyte count with large normocytic and is described to be gentle to direct (Hb fixations 8–10 g/L) [84]. In AI, cytokines are delivered in the host safeguard reaction to disease, pro-inflammatory (IL-6 specifically; however, different cytokines are likewise intricate) and adjust iron digestion so that iron is concealed inside cells of the reticuloendothelial framework and gastrointestinal enterocytes, and RBC creation and lifespan expectancy is condensed [84]. The consequences for iron digestion are interceded by hepcidin to alike an extent that incendiary cytokines increment its creation, which downregulates the statement of ferroportin in digestive enterocytes, hepatocytes and macrophages accordingly hindering iron ingestion and preparation of iron from stocks into exchange [82, 85]. Erythrogenic cytokines additionally add to the abbreviated RBC life cycle range, just as debilitating the creation and capacity of EPO and restraining typical erythroid forebear cell differentiation and multiplication [84, 86]. Artificial intelligence has been known as the succeeding best normal reason for anemia after IDA and keeping in mind that illness/contaminations are the top reasons for anemia, the extent of worldwide anemia because of irritation isn't known, and logical changes by siting and sickness trouble [84, 86]. Amid PSC in the BRINDA project, aggravation was for the most part connected with anemia across nations. Be that as it may, in a pooled investigation of nations by contamination trouble, irritation was related to pallor in the high-and extremely high-disease trouble gatherings, yet not in the high-and very high-disease burden groups. Among iron-deficient PSC in moderate-, less-, high-, and exceptionally elevated-contamination trouble nations 13.7%, 9.1%, 37.4%, and 70.3%, separately, additionally had aggravation (any level) [49]. Thus, in nations with complex irresistible sickness trouble, the job of irritation is probably bigger than in nations with

lower irresistible illness trouble. Among WRA, aggravation was altogether connected with pallor in nations with low and high (not in moderate) irresistible illness trouble; the chances of anemia among WRA with irritation were 90% and a half more than the chances among WRA without aggravation in extraordinary- and little-contamination nations, individually. In the older, generally, 10–32% of anemia is believed to be because of aggravation, as flowing IL-6 levels ascend with expanding age; however, there are various reasons for iron deficiency comprising ID and different pathologies that develop more normal with progressing age [87].

Soil-sent helminth sicknesses

Hookworm (*Ancylostoma duodenale* and *Necator americanus*) is the essential soil-sent helminth related to anemia. *Ancylostomiasis* appends to and nourishes from the digestive mucosa initiating blood (and iron) misfortune and, contingent upon hidden iron grade just as the existence of other dangerous aspects, can prompt iron deficiency anemia (IDA). Bloodsucking worms are normal in sub-Saharan Africa, Southeast Asia and, especially in regions with neediness, underprivileged water, sterilization, cleanliness, and framework, initiating an expected 576–740 million contaminations [88]. The seriousness of blood misfortune and ensuing anemia hazard from bloodsucking worms is not entirely set in stone by a few variables: (1) the power of contamination, (2) regardless of whether there is coinfection with numerous parasites, and (3) the types of hookworm. Weighty power and Moderate hookworm contaminations are related to lower Hb in children, while in grownups, some degree of disease is related to lower Hb [89]. Children may be adversely impacted by even light hookworm infections due to insufficient iron position in the first place [89]. *A. duodenale* contamination is related to a danger of ID and anemia on account of a fivefold more noteworthy blood misfortune [90]. Although the two sorts cross over topographically, and both are indigenous to numerous areas [90]. Coinfection with various bloodsuckers, for example, *Ascaris lumbricoides* (roundworm), *Schistosoma* sp., *Plasmodium* or *Trichuris trichiura* has been displayed to additively affect anemia hazard, with a more prominent impact than would be expected [79,90]. Anthelmintic therapy, especially albendazole and albendazole directed with praziquantel, has positive effect on Hb [90].

In a deliberate investigation that positioned the reasons for worldwide anemia trouble in 2010 by commonness, ancylostomiasis disease was positioned as the third and fourth supreme pervasive root among guys and females, separately, however iron deficiency because of hookworm diminished somewhere in the range of 1990 and 2010, especially for males [2]. Because of bloodsucking worm contamination, Anemia was a prevalent reason for anemia in Oceania and East Asia [2]. Bloodsucking worm diseases will more often than not be more uncommon amid PSC and may not add fundamentally to pallor amid this best defenseless group. Though in an investigation of reasons for extreme anemia in Malawian kids, hookworm contaminations were normal and further serious in youngsters with serious anemia, and three-fourths of tainted kids were below 2 years old [48]. The authors guessed that more youthful kids may be additional helpless against extreme hematologic entanglements from weighty hookworm contaminations.

Schistosomiasis

It is a flunky sickness conveyed by freshwater escargot contaminated with one of five assortments of the bloodsucker of Schistosoma and essentially happens in sub-Saharan Africa. It influences an expected 240 million individuals in up to 78 nations and arrives at top power and pervasiveness in 10–15-year-olds [91]. The specific systems of bilharzia-actuated pallor are not surely known, and the affiliation may likewise rely upon the types of bilharzia bloodsucker triggering the contamination. Information is generally steady for a causal connection between *S. japonicum* and anemia; however, anemia has been related to the other two essential species-*S. haematobium* and *S. mansoni*-as well [96]. Schistosomiasis, likewise to ancylostomiasis, has been displayed to prompt blood misfortune, especially assuming the force of contamination is extraordinary, which can add to IDA. Indeed, mental anemia is connected to Schistosomiasis, which might be essential to some extent because of the subsequent ID [92]. Schistosome disease may likewise add to iron deficiency via splenic segregation of erythrocytes, expired RBC life length, immune system hemolysis, or AI [96]. Bilharzia is an essential driver of anemia in sub-Saharan Africa, especially among females [2]. Schistosomiasis as a reason for anemia expanded for the two genders, somewhere

in the range of 1990 and 2010, however somewhat more among females.

Malaria

Malaria (Jungle fever) brought about by *Plasmodium* parasites can cause extreme anemia, notwithstanding different complexities, including demise. *P. falciparum* is the peak common in Africa and liable for the utmost jungle fever-related passings, and *P. vivax* is transcendent exterior to sub-Saharan Africa. Almost 50% of the total populace are in danger of jungle fever; however, the WHO African locale bears a lopsidedly high weight of intestinal sickness, representing 90% of jungle fever cases and 92% of intestinal sickness passings (as of 2015) [93]. Human beings at an expanded danger of contracting malaria and creating extreme infection incorporate babies, PSC, and pregnant ladies; more than 66% of jungle fever passings happen among youngsters below 5 years of age [94]. It largely occurs in regions where ID is additionally exists; ID might ensure in contrast to extreme malaria in individuals, and the connection between intestinal sickness and iron is complicated [95]. The parasite necessitates iron for development, and jungle fever altogether upsets iron digestion and circulation in more ways than one, comprising hemolysis, the arrival of heme, expanded iron in macrophages, deficient erythropoiesis and diminished iron absorption [96]. The system for intestinal sickness-related pallor is multifactorial, comprising expanded hemolysis of parasitized RBCs; however, more critically, expanded obliteration of non-parasitized RBCs, which is the essential supporter of anemia advancement in malaria [95]. Lessened RBC creation (smothered erythropoiesis) during and for weeks after intense intestinal sickness additionally adds to anemia, as do expand red cell freedom and abbreviated erythrocyte existence [13,94]. Blood misfortune isn't a reason for anemia because of jungle fever. Hepcidin is upregulated in intestinal sickness contamination, which additionally probable adds to anemia. Malaria control in indigenous regions can lessen anemia and serious anemia among kids beneath 5 by 27% and 60%, respectively [96]. Jungle fever is one of the essential drivers of anemia extensively and is an essential driver of extreme anemia. Jungle fever is a much more normal reason for anemia in Africa, especially in West sub-Saharan Africa, where intestinal sickness represented 25% of anemia prevalence [2]. Among PSC broke down in the

BRINDA project, intestinal sickness was reliably connected with iron deficiency in all the overviews led prevalent regions (5/5) [49].

HIV

Anemia is quite possibly the supreme well-known hematological irregularity among individuals contaminated with HIV. It is commonly described as normocytic and normochromic anemia with a little reticulocyte count, ordinary iron supplies, and a debilitated EPO reaction [97]. Anemia predominance in HIV-positive people increments with propelling movement of the infection and is remembered to upshot from a few elements, mutually in a roundabout way and straightforwardly connected with the infection. HIV contamination causes a constant intense stage reaction, raised hepcidin and AI, and changed iron metabolism [97, 98]. Opportunistic contaminations normal among HIV-positive patients can likewise prompt anemia (*e.g.*, jungle fever and hookworm) as do wholesome inadequacies coming about because of the virus [99]. The HIV infection additionally seems to affect anemia by influencing hematopoietic forebear cells and diminishing receptiveness to EPO [99]. Antiretrovirals have been displayed to lessen the rate of anemia and increment Hb levels [100]. In conclusion, anemia amid HIV victims is an indicator of the movement to AIDS, as the level of pallor relates to sickness advancement and is freely connected with impermanence [98,100].

Tuberculosis

Anemia is normal among tuberculosis (TB) patients and might be more normal among people who are concomitant with HIV and TB [104]. 88% of TB patients concomitant with HIV were anemic in one review from Malawi, 60% of famished TB victims were anemic in Indonesia while, 71% of TB/HIV concomitant victims were anemic, in Uganda [100]. Anemia amid aspiratory TB victims is remembered to result from AI, just as expanded blood misfortune from hemoptysis (blood in sputum), diminished RBC creation, and helpless hunger and food admission, prompting helpless supplement status (of iron yet additionally of different supplements, remembering selenium for one analysis) [88, 99]. In South Africa, the Gambia and Tanzania, AI was the essential driver of anemia in victims affected by TB [101].

Hereditary HB maladies

Internationally, 330,000 children are assessed to be conceived every year with a genuine acquired Hb problem and around 80% of these deliveries happen in LMICs [102]. Crudely, 5% of the worldwide populace is assessed to convey a huge Hb variation; the rate is a lot higher in Asia (7%) and Africa (18%) [31]. Sick Cell Disorders (SCDs), which are related to chronic hemolytic anemia, are the most widely recognized hereditary Hb issues tracked down prevalently in sub-Saharan Africa, trailed by α - and β -thalassemia, moved in Southeast Asia predominantly [102]. Although not examined exhaustively here, favism lack is perhaps the most well-known acquired enzyme anomaly in humans, and its appropriation will in general cover regions where jungle fever is endemic [100]. Because of specific activators-for instance, consumption of fava beans and openness to the antimalarial primaquine-acute hemolytic anemia can outcome; Favism inadequacy is assessed to be among the main 35 reasons for anemia internationally [2, 112]. The extent of anemia because of hereditary Hb issues, which are right now unchanging reasons for anemia in LMICs is simply expected to ascend as different causes are better precise. This requires expanded comprehension of the commitment of acquired blood problems to anemia trouble; a new report from Malawi viewed that 60% of examined tests for acquired blood issues amid PSC in the Malawian Demographic and Health Survey had somewhere around one strange result [102].

Sickle cell disorders

In sickle cell sickness, sickle-molded RBCs are delivered because of an inadequate β -globin chain and block small blood vessels, damaging large vessels. They also cause serious agony and remaining organ harm, and have a much-abbreviated life expectancy, leading to hemolytic anemia [28, 103]. SCD affected kids have an expanded danger of diseases and unhealthiness, which can have adverse well-being ramifications, comprising painful episodes and increased hemolysis, which can prompt severe acute anemia [103]. SCDs were among the top reasons for anemia among females and guys, separately, in 2010 [2]. Moreover, the sickle cell attribute is generally pervasive in Africa [31], sickle cell illness represents a difficult extent of cases in North America, Western Europe and other big-time

salary locales because of the longer future in these nations, just as few other causes [2].

Thalassemia

A gathering of acquired situations where there are surrenders in the combination of at least one of the globin chains that comprise Hb; a diminished union of the α -globin chain causes α -thalassemia while β -thalassemia is brought about by missing/decreased amalgamation of the β -globin chain [104]. This gathering of autosomal passive issues is portrayed by hemolytic anemia and disabled erythropoiesis, amid different difficulties relying upon the severity of the genetic defect. [104]. Internationally, around 1.7% of the total populace is assessed to convey α -or β -thalassemia characteristics (*e.g.*, asymptomatic transporters), however inside specific ethnic gatherings α -thalassemia is generally normal in people from Southeast Asia and Africa while β -thalassemia is utmost frequently originate in people from Africa, the Mediterranean and Southeast Asia-the degree can be somewhere in the range of 5% and 30% [105]. Thalassemia was assessed as the 6th and ninth most pervasive reason for anemia worldwide among females and guys [2].

Prospective guidelines

Notwithstanding progress in the comprehension of anemia etiology, for the study of disease transmission, and pathophysiology, significant research gaps remain. For instance, studies to advance the evaluation of iron deficiency utilizing Hb would advance aptitude to assess anemia burden. Questions additionally stay on understanding the involvement of nourishment in the analysis of anemia, just as non-nourishing reasons, like diseases and ecological variables, and non-modifiable roots such as acquired Hb issues. A test for series is deciding how to carry out anemia government programs that all the while reporting the setting explicit reasons for anemia. Without addressing these gaps in information and implementation science, the worldwide objectives to decrease anemia trouble are probably going to fail.

Summary and conclusions

Anemia endures being a widespread and critical international medical issue that remains to be satisfactorily tended to, especially in LMICs where advancement has been sluggish and lopsided.

However, ID stays an essential driver of anemia in many locales, ongoing work proposes that anemia etiology is perplexing and setting explicit. Endeavors are expected to additionally see the primary roots of anemia, containing ID and other healthful inadequacies, infection, and Hb problems, add to anemia so that suitable mediations in explicit settings can be carried out. This work will demand containing biochemical proportions of micronutrient status (VA and iron fundamentally) and indicators of inflammation, in addition to hematological files while evaluating anemia clinically and in populaces.

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Competing interests

The authors declare no competing interests

References

- [1] Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, et al. A systematic analysis of global anemia burden from 1990 to 2010. *J Am Soci Hemat* 2014; 123(5):615-24.
- [2] Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, De Onis M, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *The lancet* 2013; 382:427-51.
- [3] Scott SP, Chen-Edinboro LP, Caulfield LE, Murray-Kolb LE. The impact of anemia on child mortality. *Nutrients* 2014; 6(12):5915-32.
- [4] Haider BA, Olofin I, Wang M, Spiegelman D, Ezzati M, Fawzi WW. Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes. *Bmj* 2013; 346:f3443.
- [5] Rasmussen KM. Is there a causal relationship between iron deficiency or iron-deficiency anemia and weight at birth, length of gestation and perinatal mortality? *J Nutri* 2001; 131:590-603.
- [6] Haas JD, Brownlie IV T. Iron deficiency and reduced work capacity. *J Nutri* 2001; 131:676S-90S.
- [7] Walker SP, Wachs TD, Gardner JM, Lozoff B, Wasserman GA, Pollitt E, et al. International Child Development Steering Group. Child development: risk factors for adverse outcomes in developing countries. *The lancet* 2007; 369:145-57.
- [8] Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F, et al. Nutrition Impact Model Study Group. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant

- and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. *Lancet Glob Health* 2013; 1:16-25.
- [9] Suchdev PS, Namaste SM, Aaron GJ, Raiten DJ, Brown KH, Flores-Ayala R. Overview of the biomarkers reflecting inflammation and nutritional determinants of anemia project. *Adv Nutr* 2016; 7:349-56.
 - [10] Schrier SL, Mentzer WC, Landaw SA. Approach to the adult patient with anemia. *UpToDate* 2016; 2016:1-33.
 - [11] Balarajan Y, Ramakrishnan U, Özaltin E, Shankar AH, Subramanian SV. Anaemia in low-income and middle-income countries. *The Lancet* 2011; 378:2123-35.
 - [12] Centers for Disease Control (CDC). CDC criteria for anemia in children and childbearing-aged women. *Morbidity and Mortality Weekly Report* 1989; 38:400-4.
 - [13] Chalco JP, Huicho L, Alamo C, Carreazo NY, Bada CA. Accuracy of clinical pallor in the diagnosis of anaemia in children: a meta-analysis. *BMC Pediatrics* 2005; 5:1-3.
 - [14] Dewey KG, Chaparro CM. Session 4: Mineral metabolism and body composition Iron status of breast-fed infants: Symposium on 'Nutrition in early life: new horizons in a new century'. *Proceedings of the Nutrition Society* 2007; 66:412-22.
 - [15] Jopling J, Henry E, Wiedmeier SE, Christensen RD. Reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period: data from a multihospital health care system. *Pediatrics* 2009; 123(2):333-7.
 - [16] Nilsson-Ehle H, Jagenburg R, Landahl S, Svanborg A. Blood haemoglobin declines in the elderly: implications for reference intervals from age 70 to 88. *Eur J Haematol* 2000; 65:297-305.
 - [17] Miller EM. Iron status and reproduction in US women: National Health and Nutrition Examination Survey, 1999-2006. *PLoS One* 2014; 9(11):e112216.
 - [18] Milman N, Clausen J, Byg KE. Iron status in 268 Danish women aged 18–30 years: influence of menstruation, contraceptive method, and iron supplementation. *Annals of Hematology* 1998; 77:13-9.
 - [19] Blanc B. Nutritional anemias. Report of a WHO scientific group. *WHO Technical Report Series* 1968; 405:1-40.
 - [20] Beutler E, Waalen J. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? *Blood* 2006; 107(5):1747-50.
 - [21] Johnson-Spear MA, Yip R. Hemoglobin difference between black and white women with comparable iron status: justification for race-specific anemia criteria. *Am J Clin Nutr* 1994; 60:117-21.
 - [22] Domellof M, Dewey KG, Lonnerdal B, Cohen RJ, Hernell O. The diagnostic criteria for iron deficiency in infants should be reevaluated. *J Nutr* 2002; 132(12):3680-6.
 - [23] Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. *Bulletin of the World Health Organization* 2008; 86:480-7.
 - [24] Patel KV. Epidemiology of anemia in older adults. *Seminars in Hematology* 2008; 45:210-217.
 - [25] Figueiredo AC, Gomes-Filho IS, Silva RB, Pereira PP, Da Mata FA, Lyrio AO et al. Maternal anemia and low birth weight: a systematic review and meta-analysis. *Nutrition* 2018; 10(5):601.
 - [26] Rahman MM, Abe SK, Rahman MS, Kanda M, Narita S, Bilano V, Ota E, et al. Maternal anemia and risk of adverse birth and health outcomes in low-and middle-income countries: systematic review and meta-analysis. *Am J Clin Nutr* 2016; 103:495-504.
 - [27] McCann JC, Ames BN. An overview of evidence for a causal relation between iron deficiency during development and deficits in cognitive or behavioral function. *Am J Clin Nutr* 2007; 85:931-45.
 - [28] Beard J. Iron deficiency alters brain development and functioning. *J Nutri* 2003; 133:1468-72.
 - [29] Hoffmann JJ, Urrechaga E, Aguirre U. Discriminant indices for distinguishing thalassemia and iron deficiency in patients with microcytic anemia: a meta-analysis. *Clin Chem Lab Med* 2015; 53:1883-94.
 - [30] Metz J. A high prevalence of biochemical evidence of vitamin B12 or folate deficiency does not translate into a comparable prevalence of anemia. *Food Nutrition Bulletin* 2008; 29:74-85.
 - [31] Namaste SM, Aaron GJ, Varadhan R, Pearson JM, Suchdev PS. Methodologic approach for the biomarkers reflecting inflammation and nutritional determinants of anemia project. *Am J Clin Nutrition* 2017; 106:333-47.
 - [32] Pasricha SR, Drakesmith H, Black J, Hipgrave D, Biggs BA. Control of iron deficiency anemia in low- and middle-income countries. *J Am Soc Hematol* 2013; 121:2607-17.
 - [33] Wirth JP, Woodruff BA, Engle-Stone R, Namaste SM, Temple VJ, Petry N, et al. Predictors of anemia in women of reproductive age: biomarkers reflecting inflammation and nutritional determinants of anemia project. *Am J Clinical Nutrition* 2017; 106:416-27.
 - [34] Prieto-Patron A, Van der Horst K, Hutton ZV, Detzel P. Association between anaemia in children 6 to 23 months old and child, mother, household and feeding indicators. *Nutrition* 2018; 10(9):1269.
 - [35] Calis JC, Phiri KS, Faragher EB, Brabin BJ, Bates I, Cuevas LE et al. Research Article (New England Journal of Medicine) Severe anemia in Malawian children. *Malaw Med J* 2016; 28:99-107.
 - [36] Engle-Stone R, Aaron GJ, Huang J, Wirth JP, Namaste SM, Williams AM, et al. Predictors of anemia in preschool children: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia project. *Am J Clin Nutr* 2017; 106:402-15.
 - [37] Foote EM, Sullivan KM, Ruth LJ, Oremo J, Sadumah I, Williams TN, et al. Determinants of anemia among preschool children in rural, western Kenya. *Am J Trop Med Hyg* 2013; 88(4):757.
 - [38] Thakur N, Chandra J, Pemde H, Singh V. Anemia in severe acute malnutrition. *Nutrition* 2014; 30:440-2.
 - [39] Kassebaum NJ, GBD 2013 Anemia Collaborators. The global burden of anemia. *Hematol Oncol Clin North Am* 2016; 30:247-308.
 - [40] Zariwala MG, Somavarapu S, Farnaud S, Renshaw D. Comparison study of oral iron preparations using a

- human intestinal model. *Sci Pharm* 2013; 81:1123-40.
- [41] Wieringa FT, Dahl M, Chamnan C, Poirot E, Kuong K, Sophonneary P, et al. The high prevalence of anemia in Cambodian children and women cannot be satisfactorily explained by nutritional deficiencies or hemoglobin disorders. *Nutrition* 2016; 8(6):348.
- [42] Fishman SM, Christian P, West KP. The role of vitamins in the prevention and control of anaemia. *Pub Healt Nutr* 2000; 3:125-50.
- [43] Hacibekiroglu T, Basturk A, Akinci S, Bakanay SM, Ulas T, Guney T, et al. Evaluation of serum levels of zinc, copper, and Helicobacter pylori IgG and IgA in iron deficiency anemia cases. *Eur Rev Med pharmacol Sci* 2015; 19:4835-40.
- [44] Jafari SM, Heidari G, Nabipour I, Amirinejad R, Assadi M, Bargahi A, et al. Serum retinol levels are positively correlated with hemoglobin concentrations, independent of iron homeostasis: a population-based study. *Nutri Re* 2013; 33:279-85.
- [45] Bothwell TH, Charlton RW, Cook JD, Finch CA. Iron metabolism in man. *AGRIC* 1979; 34:451-555.
- [46] Suchdev PS, Williams AM, Mei Z, Flores-Ayala R, Pasricha SR, Rogers LM, et al. Assessment of iron status in settings of inflammation: challenges and potential approaches. *Am J Clin Nutr* 2017; 106:1626-33.
- [47] Lynch S, Pfeiffer CM, Georgieff MK, Brittenham G, Fairweather-Tait S, Hurrell RF, et al. Biomarkers of Nutrition for Development (BOND)—iron review. *J Nutr* 2018; 148:1001-67.
- [48] Vázquez LI, Valera E, Villalobos M, Tous M, Arija V. Prevalence of anemia in children from Latin America and the Caribbean and effectiveness of nutritional interventions: systematic review and meta-analysis. *Nutrition* 2019; 11(1):183.
- [49] Petry N, Olofin I, Hurrell RF, Boy E, Wirth JP, Moursi M, et al. The proportion of anemia associated with iron deficiency in low, medium, and high human development index countries: a systematic analysis of national surveys. *Nutrition* 2016; 8(11):693.
- [50] Semba RD, Bloem MW. The anemia of vitamin A deficiency: epidemiology and pathogenesis. *Euro J Clin Nutr* 2002; 56:271-81.
- [51] Michelazzo FB, Oliveira JM, Stefanello J, Luzia LA, Rondó PH. The influence of vitamin A supplementation on iron status. *Nutrition* 2013; 5(11):4399-413.
- [52] Larson LM, Namaste SM, Williams AM, Engle-Stone R, Addo OY, Suchdev PS, et al. Adjusting retinol-binding protein concentrations for inflammation: biomarkers reflecting inflammation and nutritional determinants of anemia (BRINDA) project. *Am J Clin Nutr* 2017; 106:390-401.
- [53] Allen LH. Causes of vitamin B12 and folate deficiency. *Food Nutr Bull* 2008; 29:20-34.
- [54] Green R, Allen LH, Björke-Monsen AL, Brito A, Guéant JL, Miller JW, et al. Vitamin B12 deficiency. *Nat Rev Dis Primer* 2017; 3:1-20.
- [55] Chango A, Abdennebi-Najar L. Folate metabolism pathway and Plasmodium falciparum malaria infection in pregnancy. *Nutr Rev* 2011; 69:34-40.
- [56] McLean E, de Benoist B, Allen LH. Review of the magnitude of folate and vitamin B12 deficiencies worldwide. *Food Nutr bullet* 2008; 29:38-51.
- [57] Powers HJ. Riboflavin (vitamin B-2) and health. *The Am J Clin Nutr* 2003; 77(6):1352-60.
- [58] Rohner F, Zimmermann MB, Wegmueller R, Tschannen AB, Hurrell RF. Mild riboflavin deficiency is highly prevalent in school-age children but does not increase risk for anaemia in Cote d'Ivoire. *Br J Nutr* 2007; 97(5):970-6.
- [59] Shi Z, Zhen S, Wittert GA, Yuan B, Zuo H, Taylor AW. Inadequate riboflavin intake and anemia risk in a Chinese population: five-year follow up of the Jiangsu Nutrition Study. *PLoS One* 2014; 9(2):e88862.
- [60] Ehrhardt S, Burchard GD, Mantel C, Cramer JP, Kaiser S, Kubo M, et al. Malaria, anemia, and malnutrition in African children—defining intervention priorities. *J infect dis* 2006; 194:108-14.
- [61] Soares Magalhães RJ, Clements AC. Mapping the risk of anaemia in preschool-age children: the contribution of malnutrition, malaria, and helminth infections in West Africa. *PLoS Med* 2011; 8(6):e1000438.
- [62] McCuskee S, Brickley EB, Wood A, Mossialos E. Malaria and macronutrient deficiency as correlates of anemia in young children: a systematic review of observational studies. *Annal Glob Healt* 2014; 80:458-65.
- [63] Tussing-Humphreys L, Pustacioglu C, Nemeth E, Braunschweig C. Rethinking iron regulation and assessment in iron deficiency, anemia of chronic disease, and obesity: introducing hepcidin. *J Acad Nutr Diet* 2012; 112:391-400.
- [64] Cepeda-Lopez AC, Aeberli I, Zimmermann MB. Does obesity increase risk for iron deficiency? A review of the literature and the potential mechanisms. *Inter J Vitam Nutr Res* 2010; 80:256-263.
- [65] Weiss G, Goodnough LT. Anemia of chronic disease. *New Eng J Med* 2005; 352:1011-23.
- [66] Nairz M, Theurl I, Wolf D, Weiss G. Iron deficiency or anemia of inflammation? *Wiener Medizinische Wochens* 2016; 166:411-23.
- [67] Wang CY, Babitt JL. Hepcidin regulation in the anemia of inflammation. *Curr Opin Hematol* 2016; 23:189-197.
- [68] McCranor BJ, Langdon JM, Prince OD, Femnou LK, Berger AE, Cheadle C, et al. Investigation of the role of interleukin-6 and hepcidin antimicrobial peptide in the development of anemia with age. *Haematologica* 2013; 98:1633-1640.
- [69] Smith JL, Brooker S. Impact of hookworm infection and deworming on anaemia in non-pregnant populations: a systematic review. *Trop Med Int Health* 2010; 15:776-95.
- [70] Albonjco M, Stoltzfus RJ, Savioli L, Tielsch JM, Chwaya HM, Ercole E, et al. Epidemiological evidence for a differential effect of hookworm species, Ancylostoma duodenale or Necator americanus, on iron status of children. *Int J Epidemiol* 1998; 27:530-7.

- [71] Ezeamama AE, McGarvey ST, Acosta LP, Zierler S, Manalo DL, Wu HW, et al. The synergistic effect of concomitant schistosomiasis, hookworm, and trichuris infections on children's anemia burden. *PLoS Negl Trop Dis* 2008; 2(6):e245.
- [72] Brooker S, Akhwale W, Pullan R, Estambale B, Clarke SE, Snow RW, et al. Epidemiology of plasmodium-helminth co-infection in Africa: populations at risk, potential impact on anemia, and prospects for combining control. *Am J Trop Med Hyg* 2007; 77:88-98.
- [73] Stoltzfus RJ, Chwaya HM, Montresor A, Albonico M, Savioli L, Tielsch JM. Malaria, hookworms and recent fever are related to anemia and iron status indicators in 0-to 5-y old Zanzibari children and these relationships change with age. *J Nutri* 2000; 130:1724-33.
- [74] Friedman JF, Kanzaria HK, McGarvey ST. Human schistosomiasis and anemia: the relationship and potential mechanisms. *Trend Parasitol* 2005; 21:386-92.
- [75] Spottiswoode N, Duffy PE, Drakesmith H. Iron, anemia and hepcidin in malaria. *Front Pharmacol* 2014; 5:125.
- [76] White NJ. Anaemia and malaria. *Mala J* 2018; 17:1-7.
- [77] Korenromp EL, Armstrong-Schellenberg JR, Williams BG, Nahlen BL, Snow RW. Impact of malaria control on childhood anaemia in Africa—a quantitative review. *Tropi Medi Int Healt* 2004; 9:1050-65.
- [78] Minchella PA, Armitage AE, Darboe B, Jallow MW, Drakesmith H, Jaye A, et al. Elevated hepcidin is part of a complex relation that links mortality with iron homeostasis and anemia in men and women with HIV infection. *J Nutr* 2015; 145:1194-201.
- [79] Belperio PS, Rhew DC. Prevalence and outcomes of anemia in individuals with human immunodeficiency virus: a systematic review of the literature. *Am J Med* 2004; 116:27-43.
- [80] Van Lettow M, West CE, van der Meer JW, Wieringa FT, Semba RD. Low plasma selenium concentrations, high plasma human immunodeficiency virus load and high interleukin-6 concentrations are risk factors associated with anemia in adults presenting with pulmonary tuberculosis in Zomba district, Malawi. *Eur J Clin Nutr* 2005; 59:526-32.
- [81] Karyadi E, Schultink W, Nelwan RH, Gross R, Amin Z, Dolmans WM, et al. Poor micronutrient status of active pulmonary tuberculosis patients in Indonesia. *J Nutr* 2000; 130:2953-8.
- [82] Shah S, Whalen C, Kotler DP, Mayanja H, Namale A, Melikian G, et al. Severity of human immunodeficiency virus infection is associated with decreased phase angle, fat mass and body cell mass in adults with pulmonary tuberculosis infection in Uganda. *J Nutr* 2001; 131:2843-7.
- [83] Hella J, Cercamondi CI, Mhimbira F, Sasamalo M, Stoffel N, Zwahlen M, et al. Anemia in tuberculosis cases and household controls from Tanzania: contribution of disease, coinfections, and the role of hepcidin. *PloS one* 2018; 13(4):e0195985.
- [84] Minchella PA, Donkor S, Owolabi O, Sutherland JS, McDermid JM. Complex anemia in tuberculosis: the need to consider causes and timing when designing interventions. *Clin Infect Dis* 2015; 60:764-72.
- [85] Kerkhoff AD, Meintjes G, Opie J, Vogt M, Jhilmeet N, Wood R, et al. Anaemia in patients with HIV-associated TB: relative contributions of anaemia of chronic disease and iron deficiency. *Int J Tuberc Lung dis* 2016; 20:193-201.
- [86] Weatherall DJ. The inherited diseases of hemoglobin are an emerging global health burden. *The J of the Am Soc Hematol* 2010; 115:4331-6.
- [87] Howes RE, Battle KE, Satyagraha AW, Baird JK, Hay SI. G6PD deficiency: global distribution, genetic variants and primaquine therapy. *Adv Parasit* 2013; 81:133-201.
- [88] Yoshimi A, Kojima S, Taniguchi S, Hara J, Matsui T, Takahashi Y, et al. Unrelated cord blood transplantation for severe aplastic anemia. *Biol Blood Marrow Transp* 2008; 14:1057-63.
- [89] Young NS, Calado RT, Scheinberg P. Current concepts in the pathophysiology and treatment of aplastic anemia. *Blood* 2006; 108:2509-19.
- [90] Dhar N, Agarwal KN, Taneja PN, Gupta S. Iron deficiency anemia in children. *Ind J Pediatr* 1969; 36:436-441.
- [91] Fleming AF, Ghatoura GB, Harrison KA, Briggs ND, Dunn DT. The prevention of anaemia in pregnancy in primigravidae in the guinea savanna of Nigeria. *Ann Trop Med Parasitol* 1986; 80:211-33.
- [92] Baker SJ, DeMaeyer EM. Nutritional anemia: its understanding and control with special reference to the work of the World Health Organization. *Am J Clin Nutr* 1979; 32:368-417.
- [93] Wolide AD, Mossie A, Gedefaw L. Correction: nutritional iron deficiency anemia: magnitude and its predictors among school age children, southwest Ethiopia: a community based cross-sectional study. *PLoS one* 2018; 13(8):e0202380.
- [94] Brabin BJ, Premji Z, Verhoeff F. An analysis of anemia and child mortality. *J Nutr* 2001; 131:636-648.
- [95] McGann PT, Williams AM, Ellis G, McElhinney KE, Romano L, Woodall J, et al. Prevalence of inherited blood disorders and associations with malaria and anemia in Malawian children. *Blood Adva* 2018; 2:3035-44.
- [96] Ansong D, Akoto AO, Ocloo D, Ohene-Frempong K. Sickle cell disease: management options and challenges in developing countries. *Mediterr J Hematol Infect Dis* 2013; 5(1):e2013062.
- [97] Muncie Jr HL, Campbell JS. Alpha and beta thalassemia. *Am family Physi* 2009; 80:339-44.
- [98] Ekvall H. Malaria and anemia. *Cur Opin Hematol* 2003; 10:108-14.
- [99] Kreuzer KA, Rockstroh JK. Pathogenesis and pathophysiology of anemia in HIV infection. *Annal Hematol* 1997; 75:179-87.
- [100] Lee SW, Kang YA, Yoon YS, Um SW, Lee SM, Yoo CG, et al. The prevalence and evolution of anemia

- associated with tuberculosis. J Korea Med Sci 2006; 21:1028-32.
- [101] Kuo PH, Yang PC, Kuo SS, Luh KT. Severe immune hemolytic anemia in disseminated tuberculosis with response to antituberculosis therapy. Chest 2001; 119(6):1961-3.
- [102] Kearney SL, Nemeth E, Neufeld EJ, Thapa D, Ganz T, Weinstein DA, et al. Urinary hepcidin in congenital chronic anemias. Pedia blood cancer 2007; 48:57-63.
- [103] Smith JA, Espeland M, Bellevue R, Bonds D, Brown AK, Koshy M. Pregnancy in sickle cell disease: experience of the Cooperative Study of Sickle Cell Disease. Obstet Gyneco 1996; 87:199-204.
- [104] Muncie Jr HL, Campbell JS. Alpha and beta thalassemia. Am Fami Physi 2009; 80:339-44.
- [105] Sanchaisuriya K, Fucharoen S, Ratanasiri T, Sanchaisuriya P, Fucharoen G, Dietz E, et al. Thalassemia and hemoglobinopathies rather than iron deficiency are major causes of pregnancy-related anemia in northeast Thailand. Blood Cells, Mole Disea 2006; 37:8-11.