



Review Article

PREVALENCE OF ANEMIA AMONG PREGNANT WOMEN IN ETHIOPIA AND ITS MANAGEMENT: A REVIEW

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ABSTRACT

Anemia is a major global health problem, especially in developing countries and is a common and serious problem in pregnancy. It has serious short- and long-term consequences during pregnancy and beyond. This fundamental health issue has not still been solved but continues to exist affecting the health, quality of life and working capacity in billions of people all over the world.

The anemic condition is often worsened by the presence of other chronic diseases such as malaria, tuberculosis, HIV, and diabetes. Untreated anemia also leads to increased morbidity and mortality from these chronic conditions as well. Current knowledge indicates that iron deficiency anemia in pregnancy is a risk factor for preterm delivery and subsequent low birth weight, and possibly for inferior neonatal health. Even for women who enter pregnancy with reasonable iron stores, iron supplements improve iron status during pregnancy and for a considerable length of time postpartum, thus providing some protection against iron deficiency in the subsequent pregnancy.

This literature review focuses on the prevalence and major causes of anemia seen on a global & Ethiopian scale. Most cases of anemia are due to iron deficiency, which often work in combination with folate deficiency and/or vitamin B12 deficiency as well as with infections. More efforts should be dedicated to tackle this massive problem- we have the tools and we know the ways. Iron fortification of appropriate food items combined with iron supplements in specific population groups has proved to be efficient. Initially, the efforts should be centered on the specific risk groups for iron deficiency anemia, i.e. pregnant women.

Key Words: Anemia, Pregnancy, Iron deficiency anemia, Vitamin B12 deficiency, Ethiopia

INTRODUCTION

Anemia is one of the most widespread public health problems, especially in developing countries. It impairs cognitive development, reduced physical work capacity and in severe cases increased risk of mortality particularly during prenatal period. During pregnancy, approximately 75% of all anemias diagnosed are due to iron deficiency. Furthermore, WHO considers that women in developing countries may be pregnant for as much as one half of their reproductive lives and therefore are at increased risk of anemia during this time¹.

Globally, anemia has been found to be the most common complication in pregnancy. The World Health Organization (WHO) estimates that more than 40% of non-pregnant and over 50% of pregnant women in developing countries are affected. The majority of the cases occur in sub-Saharan Africa and South East Asia. In 1993, the World Bank ranked anemia as the 8th leading cause of disease in girls and women in the developing world. Apart from maternal morbidity and mortality, neonatal mortality is high among the babies of anemic mothers².

Women go through a variety of physiological changes during pregnancy. Changes in the blood circulatory system are particularly notable, permitting normal fetal growth. Even in normal pregnant women, the hemoglobin concentration decreases with dilution according to the increase in the volume of circulating blood. Because of hemodilution and increasing needs of iron and other nutrients for both the mother and the fetus, hemoglobin (Hb) levels decrease progressively in pregnancy, whereas in the third trimester,

hemoconcentration results in higher Hb levels. Since iron and folic acid in amounts necessary to the fetus are preferentially transported to the fetus, the mother is likely to develop iron deficiency anemia and folic acid deficiency anemia. About 20% of pregnant women suffer anemia, and most of the cases are iron deficiency, folic acid deficiency, or both. The administration of iron and folic acid to pregnant women is a controversial issue, and the policy regarding this therapy varies among countries³.

METHODS FOR THIS REVIEW

The literature search for this document was carried out by accessing Pub Med, HINARI and Medline using the search terms 'anemia, prevalence, pregnancy, developing countries, Ethiopia'.

In addition, helpful documents were found and downloaded from Google Scholars. The WHO Reproductive Health Library and Cochrane Library web sites were also helpful especially for systematic reviews. Finally the Google Scholars access to health research collection of articles and books related to the topic were very useful for successful completion of this review.

MATERNAL AND HEMATOLOGICAL CHANGES DURING PREGNANCY

During pregnancy, the circulating plasma volume increases linearly to reach a plateau in the 8th or 9th month of pregnancy. The increment is about 1,000 ml, which corresponds to 45% of the circulating plasma volume in non-pregnancy. The plasma volume decreases rapidly after

delivery and is then restored to the non-pregnancy level at about 3 puerperal weeks. Because of hemodilution and increasing needs of iron and other nutrients for both the mother and the fetus, hemoglobin (Hb) levels decrease progressively in pregnancy, whereas in the third trimester, hemoconcentration results in higher Hb levels. Although erythrocytes and hemoglobin also increase during pregnancy, their increases are slow in the initial half of the pregnancy period, causing relative hydremia, and the hemoglobin concentration and hematocrit are lowest in the 5th to 7th month of pregnancy. In the latter half of the pregnancy period, erythrocytes and hemoglobin increase markedly, and the hemoglobin concentration and hematocrit tend to increase and finally reach normal levels at 6 puerperal weeks³.

Pregnancy is associated with normal physiological changes that assist fetal survival and prepares the mother for labour, delivery and breastfeeding. The changes start as early as 4 weeks of gestation and are largely as a result of progesterone and estrogen. The total blood volume increases steadily from as early as 4 weeks of pregnancy to reach a maximum of 35-45 % above the non-pregnant level at 28 to 32 weeks. The plasma volume increases by 40-45 % (1000mls). Red blood cell mass increases by 30- 33 % (approximately 300mg) as a result of the increase in the production of erythropoietin. Thus women who enter pregnancy in an iron deficient state are then unable to meet the demands of pregnancy by diet alone and require supplementation. It takes approximately 2-3 weeks after delivery for these hematologic changes to revert to pre-pregnancy status².

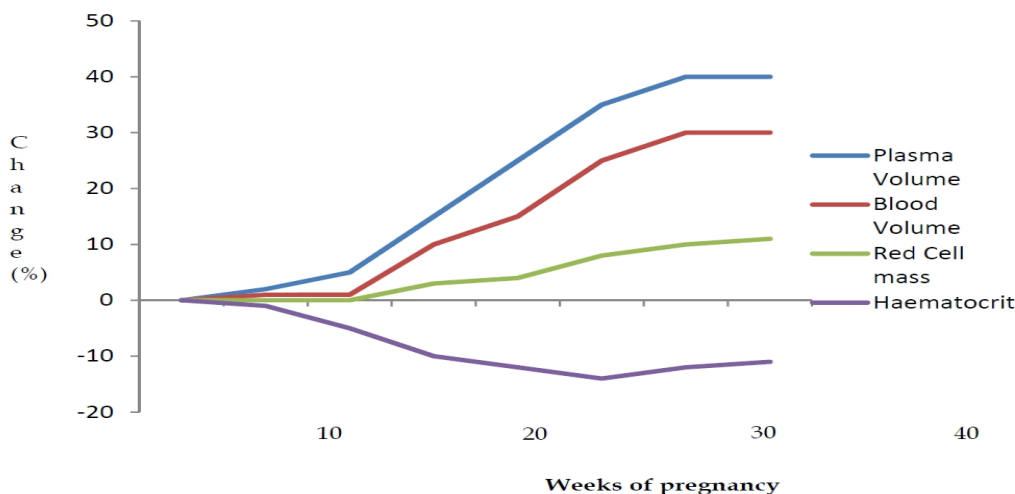


Figure 1: Graphical representation of hematological changes in pregnancy

BACKGROUND OF ANEMIA

Anemia is defined as a condition in which there is less than the normal hemoglobin (Hb) level in the body, which decreases oxygen-carrying capacity of red blood cells to tissues. World Health Organization (WHO) definitions for anemia differ by age, sex and pregnancy status as follows: children 6 months to 5 year anemia is defined as a Hb level <11g/dl, children 5–11 years Hb < 11.5 g/dl, adult males Hb < 13 g/dl; non pregnant women Hb <12g/dl and pregnant women Hb < 11g/dl⁴. Anemia could be classified as mild, moderate and severe. The Hb level for each class of anemia in pregnancy are 10.0–10.9g/dl (mild), 7– 9.9g/dl (moderate) and <7g/ dl (severe)⁵.

Anemia is also considered as an indicator of both poor nutrition and health status. The most dramatic health effects of anemia, increased risk of maternal and child mortality due to severe anemia, have been well documented^{4,6}. Patients with anemia have similar clinical symptoms irrespective of the cause. Fatigue, breathlessness, dizziness, lethargy, pallor of the skin and inner eyelid and headache are some of the common complaints. Examination of a stained blood smear using a microscope for morphology of red blood cell is helpful in diagnosing anemia in areas where automated analysis is less accessible⁷.

Food based approaches to increase iron intake through food fortification and dietary diversification are important, sustainable strategies for preventing iron deficiency anemia in the general population. In settings where iron deficiency is not the only cause of anemia, approaches that combine iron interventions with other measures are needed. Strategies

should include addressing other causes of anemia, and should be built into the primary health care system and existing programs^{8,9}. It is estimated that approximately 1.3 billion individuals in the world suffer from anemia, making it one of the most important public health issues on the international agenda^{10,11}. The knowledge of the prevalence of anemia in pregnant women is fundamental for the planning and execution of effective interventions by health authorities¹². Prevalence of anemia among pregnant women in developing countries at average reported as 56% with a range of 35% to 100% among various region of the world. It is more common in developing countries because of poor nutritional status and high prevalence parasitic infestation¹³. It has been reported that close to 500,000 maternal deaths occur every year, vast majority of them taking place in developing world^{14,14}. Worldwide, anemia contributes to 20% of all maternal deaths. Anemia in pregnancy also leads to premature births, low birth weight, fetal impairment and infant deaths. The reduction in women's productivity places an economic burden on the families, communities and the societies. Recently, mental impairment in children who were anemic in the very beginning of their life has been reported. All of those showed the necessity of special control program for anemia in vulnerable population^{15,16}. Given the multi-factorial nature of this disease, correcting anemia often requires an integrated approach. In order to effectively combat anemia, the contributing factors must be identified and addressed^{11,17}. In Ethiopia anemia is one of the serious health problems among pregnant women. Prevalence rates of 40.5% in the general population and 47.2% in the children were reported from

southwest Ethiopia¹⁸. Higher rates about 57% have also been reported in pregnant women in Jimma¹⁹.

Anemia in pregnancy

As a result of normal physiological changes in pregnancy, plasma volume expands by 46-55%, whereas red cell volume expands by 18-25%. The resulting hemodilution has, perhaps wrongly, been termed ‘physiological anemia of pregnancy’²⁰.

Cut-off points for defining anemia and severe anemia in pregnancy

In most published studies, the mean minimum hemoglobin in healthy pregnant women living at sea level is 11-12g/dl. The mean minimum acceptable hemoglobin level during pregnancy by WHO criteria is taken to be 11g/dl in the first half of pregnancy and 10.5 g/dl in the second half of pregnancy²¹. The World Health Organization further divide

anemia in pregnancy into: mild anemia (hemoglobin 10-10.9g/dl), moderate anemia (Hb 7.0- 9.9g/dl) and severe anemia (hemoglobin < 7g/dl)²².

Due to lack of resources and lack of staff motivation, screening of anemia is often done solely by clinical examination of the conjunctivae or is not carried out at all. For example, one study carried out in Malawi showed that the sensitivity using the color scale was consistently better than for conjunctiva inspection alone and intra observer agreement and agreement with coulter counter measurement was good. The hemoglobin color scale is simple to use, well accepted, cheap and gives immediate results²³. In Ethiopia Physical screening methods for anemia include pallor of fingernails, eyelids, or palms; low blood pressure; headaches; low mid-arm upper circumference (MUAC) and weight loss²⁴. Table 1 shows the public health significance of anemia²⁴ and table 2 shows the classification of anemia by degree of severity.

Table 1: Public health significance of anemia²⁵

Anemia Prevalence	Public Health Significance
>40%	Severe
20-39%	Moderate
5-19%	Moderate
0-4.9%	Normal

Table 2: Classification of anemia by degree of severity²

Degree of Severity	Hemoglobin level
Normal hemoglobin level	>11 g/dl
Mild Anemia	9-11 g/dl
Moderate	7-9 g/dl
Severe	4-7 g/dl
Very severe	<4 g/dl

EPIDEMIOLOGY OF ANEMIA

Global estimates of prevalence of anemia in pregnancy

The anemia estimates are provided by region for all population groups, based on data collected from 1993 to 2005 by WHO (Figure 2). The data coverage is about 70% or more for preschool-age children (76.1%), pregnant (69%) and non-pregnant (73.5%). Coverage for the remaining population groups is much lower; 33% for school-age children, 40.2% for men and 39.1% for elderly. Overall, the coverage for the general population is 48.8%. The global prevalence of

anemia for the general population is 24.8% and it is estimated that 1620 million people are affected by anemia. For pregnant women the prevalence is slightly lower; however, its distribution by region follows the same trend as the one observed for preschool-age children. The highest prevalence is in Africa (57.1%) and in South-East Asia (48.2%), followed by the Eastern Mediterranean (44.2%), Western Pacific (30.7%), and the European Americas regions, 25% and 24.1% respectively. Overall, 56.4 million pregnant women are anemic (41.8% prevalence globally)²⁶.

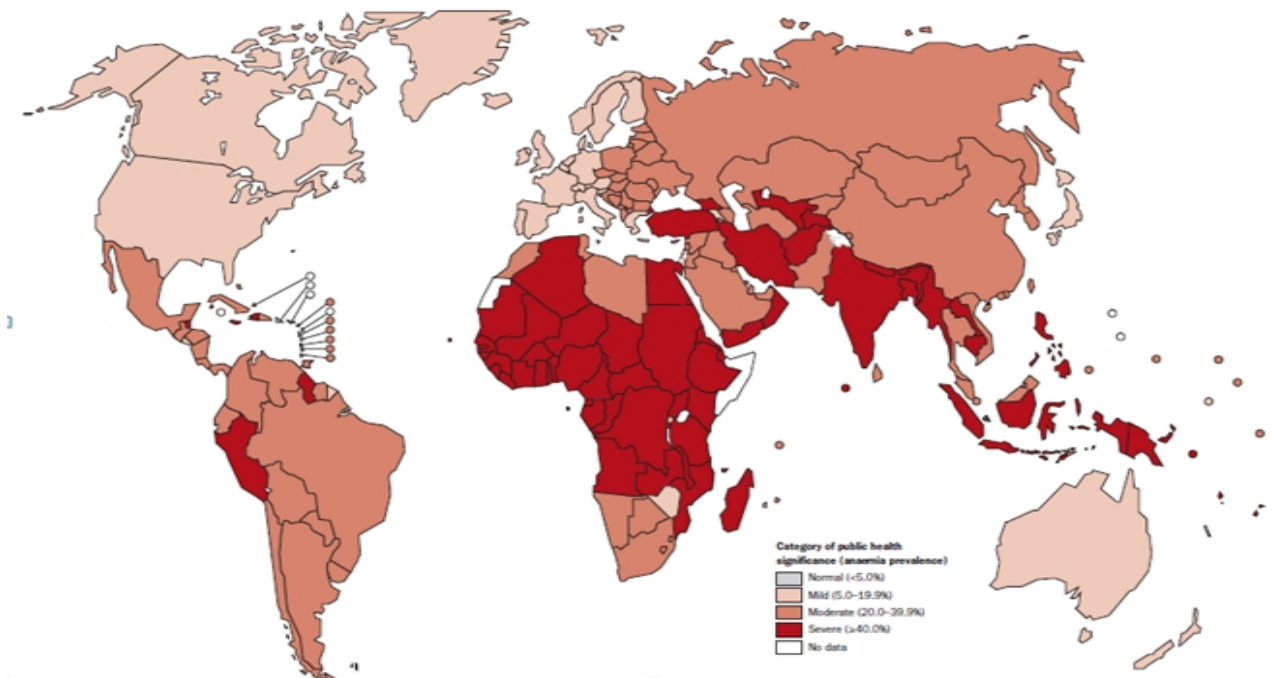


Figure 2: Anemia as a public health problem by country: pregnant women. Source: Worldwide prevalence of anemia 1993–2005; WHO Global Database on Anemia (2008)

Prevalence of anemia during pregnancy in Ethiopia

One cross-sectional study explicitly measured the prevalence of anemia and associated risk factors among pregnant women attending antenatal care in Azezo Health Center Gondar town, Northwest Ethiopia, from February to May 2011. Among the 384 study participants, the prevalence of anemia was 83 (21.6%). Over half (64.8%) of the pregnant women attended antenatal care in the second trimester (between 13 and 28 weeks of gestation). Majority, 373 (97.1%) of the pregnant women had normocytic normochromic red cell morphology. The majority of anemic cases 49 % (41/83) were of the mild type (Hb 10.0–10.9g/dl) followed by 46% cases of moderate anemia (7–9.9g/dl) and 5% severe anemia (Hb < 7g/ dl)²⁷.

There is also a need to design strategies that help to diagnose pregnant women for malaria and Soil Transmitted Helminth (STH) infections during their antenatal care (ANC) visit instead of testing for only hemoglobin (Hb) levels and blood group²⁸.

Another cross-sectional community-based study with analytic component was conducted among Ethiopian women during June-July 2005 to assess the magnitude of anemia and deficiencies of iron and folic acid and to compare the factors responsible for anemia among anemic and non-anemic cases. In total, (n= 970) women, aged 15-19 years, were selected systematically for hematological and other important parameters. The overall prevalence of anemia, iron deficiency, iron-deficiency anemia, deficiency of folic acid, and parasitic infestations was 30.4%, 50.1%, 18.1%, 31.3%, and 13.7% respectively²⁹.

Anemia was a severe public health problem in the pastoral regions of Afar and Somali: 35% of women and 75% of children in Afar and 44% of women and 69% of children in Somali. Tigray and SNNPR had relatively much lower prevalence of anemia in women (11 and 12 percent prevalence, respectively). However, anemia prevalence among Ethiopian women decreased from 27% to 17% from 2005 to 2011, but this obscures important regional differences. The reduction in anemia is more likely due to malaria prevention and control and improved hygiene and sanitation²⁴.

DETERMINANTS OF ANEMIA IN PREGNANCY

Biological Risk Factors

Physiological changes in pregnancy

The hemoglobin concentration, hematocrit and red cell count fall during pregnancy because the expansion of the plasma volume is greater than that of the red cell mass. However, there is a rise in total circulating hemoglobin directly related to the increase in red cell mass. This in turn depends partly on the iron status of the individual. Plasma volume rises progressively throughout pregnancy with a tendency to plateau in the last 8 weeks. Women with multiple pregnancies have proportionately higher increment of plasma volume and in contrast women with poorly growing fetuses have a correspondingly poor plasma volume and red cell mass increases steadily between the end of first trimester and term. As with plasma volume the extent of the increase is related to the size of the foetus³¹.

Age

Although some studies have found that anemia is more common among adolescents, this appears to be a result of the

fact that adolescents are more often primigravidae (a woman who is pregnant for the first time) and not from young age per se. Two studies from Malawi confirm this finding. In a study carried out in Queen Elizabeth Central Hospital and Namitambo Health centre Malawi, univariate analysis showed an increased risk of anemia for women less than 20 years of age, but when corrected for gravidity and trimester at booking the increased risk with young age no longer existed³². Verhoeff et al in the Shire valley area showed that adolescent primigravidae had the lowest mean hemoglobin concentration and the highest prevalence of anemia (93.8%, n=495). Adolescent multigravidae, adult primigravidae and adult multigravidae had prevalence's of 87.7% (n=144), 90.7% (n=322) and 88% (n=2614) respectively. However, age was no longer associated with an increased risk of anemia when adjusted for gravidity³³.

One study conducted to investigate the prevalence of anemia and to find out the correlation between hemoglobin concentration and other variables like age, severity of anemia, trimesters in pregnancy, etc. in Nepalese pregnant women of Biratnagar, Morang District found that out of 364 subjects, 172 (47.25%) were diagnosed as anemic. The majority (68.60%) of these anemic pregnant women were mildly anemic whereas 29.06% were moderately and 2.32% were severely anemic (according to WHO definition). Prevalence of anemia was higher in these pregnant women at the second trimester (51.1%) and also at the 20-35 years age group (62.79%)³⁴.

One study conducted on the rate and risk factors for anemia among pregnant mothers in Jerreh Terengganu, Malaysia, found that age was found to be not a risk factor for anemia in their study which opposes the above studies. The mean age of respondents was 28.3 year-old. More than half of mothers were multigravidas. Of 47 respondents, 57.4% (95% CI: 43.0, 72.0) was anemic. The proportion of anemia was high for grand multigravidas mother (66.7%), those at third trimester of pregnancy (70.4%), did antenatal booking at first trimester (65.4%), poor haematitic compliance (76.5%), not taking any medication (60.5%), those with no co-morbid illnesses (60.0%), mothers with high education level (71.4%) and those with satisfactory monthly income (61.5%). The proportion of anemia was 58.3% and 57.1% for mothers with last child birth spacing of two years or less and more than two years accordingly. There was a significant association of haematitic compliance with the anemia (OR: 4.571; 95% CI: 1.068, 19.573)³⁵.

Another study conducted to determine the correlates of anemia among women of reproductive age in Ethiopia shows that, among (n=5963) women of reproductive age the prevalence of anemia was 27.4% (95% CI: 26.3-28.5%). Rural residence, poor educational and economic status, 30-39 years of age and high parity were key factors predisposing women to anemia. Again mean hemoglobin level significantly varied across age categories. The highest level of 12.9 g/dl was reported in the youngest (15-19 years) age group while the lowest level of 12.5 g/dl in 35-39 years age group. The overall pattern showed an approximately linear decline between the ages of 15-39 years (Figure 3). Compared to the youngest group, the risk of anemia is significantly higher in the age group 30-34 and 35-39 years with adjusted odds ratio (AOR) of 1.31 (95% CI: 1.07-1.60) and 1.56 (95% CI: 1.27-1.90), respectively³⁶.

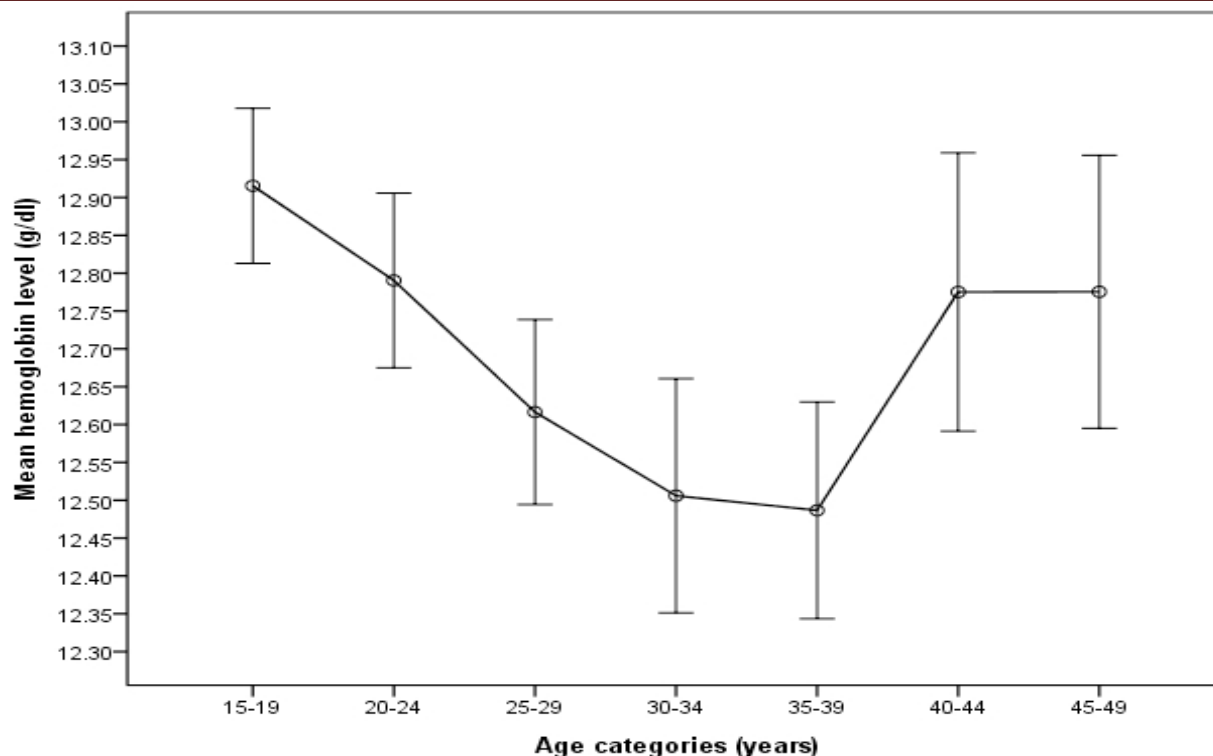


Figure 3: Mean blood hemoglobin level with 95% CI across different age categories, Ethiopia, 2005.

Nutritional Deficiencies

Iron deficiency

Iron is an essential component of hemoglobin, the oxygen-carrying pigment in the blood. Iron is normally obtained through the food diet and by recycling iron from old red blood cells and in the absence of the required iron blood concentrations, blood cannot carry oxygen effectively and hence normal functioning of every cell in the body will be affected. It is estimated that a median amount of 840-1210 mg of iron needs to be absorbed over the course of the pregnancy³⁷.

When the iron needs of pregnancy are not met, maternal hemoglobin falls below 11 g/dl. When the hemoglobin level is below 10 mg/dl (hematocrit under 33%), iron deficiency is suspected³⁸. Nutritional iron deficiency is the most common deficiency disorder in the world, affecting more than two billion people worldwide, with pregnant women at particular risk³⁹. Despite the lack of stringent criteria, problems with definitions and lack of substantial supportive data, in sub Saharan Africa anemia during pregnancy is most often believed to result from nutritional deficiencies, especially iron deficiency. WHO data show that iron deficiency anemia (IDA) in pregnancy is a significant problem throughout the world with a prevalence ranging from an average of 14% of pregnant women in industrialized countries to an average of 56% (range 35–75%) in developing countries⁴⁰.

In some instances, poor absorption of iron is aggravated by dietary contents. For example, diets rich in phytates and phenolic compounds prevent absorption of iron, thereby contributing to the anemic condition. Nutritional iron deficiency rarely occurs by itself; rather, it occurs in the presence of other nutritional deficiencies, although this fact is frequently overlooked. For example, deficiency of micronutrients such as folic acid, vitamins A, B12, riboflavin, and copper increase the risk of anemia because these micronutrients play important roles in hemopoiesis⁴¹. When

an iron deficient woman becomes pregnant, her need for iron will increase dramatically. Pregnancy is a setting where the normal physiological demands for iron display an extraordinary increase of such a magnitude, which has not recognized in other physiological situations⁴².

Folate deficiency

Folate plays a crucial role in the one-carbon metabolism for physiological nucleic acid synthesis and cell division, regulation of gene expression, amino acid metabolism and neurotransmitter synthesis. During pregnancy, increased folate intake is required for rapid cell proliferation and tissue growth of the uterus and the placenta, growth of the fetus and expansion of the maternal blood volume. Folate requirements are 5- to 10-fold higher in pregnant than in non-pregnant women, therefore pregnant women may be at risk for folate deficiency⁴³.

As a consequence of folate deficiency, homocysteine accumulates in the serum and is found to be associated with an increased risk in cardiovascular disease, late pregnancy complications such as pre-eclampsia and neural tube defects around the time of conception. The recommended folate intake for pregnant women is 400µg/day⁴⁴. Folate deficiency is a serious problem that affects women worldwide⁴⁵⁻⁴⁷. This deficiency is caused primarily by inadequate dietary intake⁴⁷. Typical folate intakes are suboptimal in the diets of many women of childbearing age, and folate intake is further limited by cooking losses and poor bioavailability estimated to be from 50% to 82%⁴⁸⁻⁵⁰.

Fortification of grains with folic acid has increased folate intake in several developed countries⁵¹, but these foods are generally not available in Ethiopia. Folate deficiency can also be a consequence of medical conditions that increase the need for folate or result in increased excretion of folate, including pregnancy, lactation, alcoholism, malabsorption, kidney

dialysis, liver disease, certain anemia's and medications that interfere with folate metabolism^{46-48,52}.

Folate deficiency is associated with several health risks. Over folate deficiency leads to megaloblastic anemia^{48,53}. Suboptimal preconception folate intake increases risk of clinical spontaneous abortion, preterm birth⁵², low birth weight and neural tube defects^{46,54}. Digestive disorders such as diarrhea, loss of appetite and weight loss can occur with folate deficiency, as can weakness, sore tongue, headaches, heart palpitations, irritability, forgetfulness and behavioral disorders⁵⁵.

In Ethiopia, protein and nutrient deficiencies are common and malnutrition is a grave concern⁵⁶⁻⁵⁹, but information on the prevalence of folate deficiency is limited to one study of pregnant women⁵⁷. Information on the prevalence and magnitude of folate deficiency is needed to determine whether folate deficiency is a public health problem in Ethiopia and to contribute to global data on folate deficiency. One cross-sectional study on folate deficiency in women of reproductive age in nine administrative regions of Ethiopia: an emerging public health problem, has found that, among 970 women aged 15 to 49 years from nine accessible regions of Ethiopia, forty-six per cent (46%) of women had severe folate deficiency ($\leq 4\text{ng/ml}$) and 21.2% had marginal folate deficiency ($> 4-6.6\text{ng/ml}$) with unequal prevalence across the country⁶⁰.

So, folate deficiency is widespread in Ethiopia and is related to diet. The high prevalence of folate deficiency emphasizes the need for sustainable folate intake through dietary diversification and appropriate public health interventions, such as supplementation during the perconceptional period and efforts to promote greater utilization of maternal health care services. Given that the plasma levels of folate are lower than are needed to support a healthy pregnancy, an investigation of the magnitude of neural tube defect and other pregnancy issues in the country is recommended and folate deficiency is widespread in Ethiopian women, emphasizing the need for sustainable folate intake through dietary diversification and appropriate public health measures⁶¹.

Vitamin B-12 deficiency

Anemia specifically caused by vitamin B12 deficiency occurs in 10– 28% of uncomplicated pregnancies⁶². Vitamin B12 can only be obtained from animal products [63]. More than 1000 μg of vitamin B12 is stored in fertile women eating a mixed diet⁶³. At term, foetal vitamin B12 stores should be 25–50 μg ⁶⁴. 20% of women show a physiological drop in vitamin B12 levels during pregnancy, with lowest levels reached at third trimester^{62,65}.

Maternal vitamin B12 determines foetal vitamin B12 levels⁶⁶. During pregnancy, vitamin B12 is transferred from mother to foetus by active transport across the placenta into foetal circulation which results in foetal serum level being double that of maternal serum levels^{64,67}.

Vitamin B12 deficiency can cause anencephaly (the absence of a brain, which causes a fetus to die a few hours after birth)^{68,69}. Schorah et al. found very low vitamin B12 levels in 3 anencephalic mothers compared with controls; this may be due to the fact that vitamin B12 is involved in the metabolism of neural tissue⁶⁹. Pathological changes that occur due to vitamin B12 deficiency are demyelination, axonal degeneration, and neuronal death⁶⁴.

For example, in Sidama Zone of Southern Ethiopia, maize and fermented enset products are the major staple foods contributing up to 90% of energy. Such low intakes of

animal products concomitant with infection and bacterial overgrowth may place pregnant women in Sidama at high risk of vitamin B-12 deficiency and possibly folate deficiency, especially in this malaria area, because some ant malarial drugs interfere with folate metabolism. Consumption of enset fermented by vitamin B-12 producing microorganisms may have increased vitamin B-12 levels in the diets and in plasma while at the same time enhancing non haem iron absorption¹.

Vitamin A

Symptoms of vitamin A deficiency include a variety of eye symptoms, such as night blindness, xerophthalmia (dry eyes, failure to produce tears), keratomalacia (drying and clouding of the cornea with ulceration), Bitot spots (keratin debris in the conjunctiva) and photophobia. Follicular hyperkeratosis (excessive development of keratin in hair follicles), which is also seen with general malnutrition, can be a manifestation of vitamin A deficiency. Ocular changes can be documented quantitatively using a dark adaptation test (e.g. the papillary threshold test - PTT) or using electro-retinography. Often change in night blindness is accessed via a simple before (the intervention) and after (the intervention or treatment) questionnaire. In babies born prematurely, symptoms of vitamin A deficiency include broncho-pulmonary dysplasia (a form of chronic lung disease). Night blindness is thought to be one of the first signs of vitamin A deficiency, followed by a diminished ability to fight infections especially respiratory and gastro enteric infections⁷⁰.

Vitamin A deficiency in pregnancy is known to result in night blindness, to increase the risk of maternal mortality and is associated with premature birth, intrauterine growth retardation, LBW and abruptio placentae. A study from Nepal showed that weekly vitamin A supplementation reduced maternal mortality by 40%. It was also found that the prevalence of iron-deficiency anemia in pregnancy was reduced from 76% in controls to 69% among those receiving vitamin A⁷¹.

A mother's vitamin A status during pregnancy can be an indicator of the vitamin A status of her child. One sign of Vitamin A deficiency (VAD) in women during pregnancy is night blindness. Six percent of women reported having trouble with their vision during the night but not during the day during their last pregnancy. Although this figure corrects for women with vision problems, in general, it may slightly underestimate the rate of night blindness. Night blindness is relatively higher in Amhara (12%) and Tigray (8%) than in other areas⁷².

Infections

Malaria

Malaria due to *Plasmodium falciparum* may cause severe anemia in pregnancy. It is estimated that in sub Saharan Africa 23 million pregnant women are exposed to malarial infection annually. Several studies have shown that protection against malaria contributes to the prevention of anemia in pregnancy thus highlighting the importance of chemoprophylaxis and other methods of malaria control. The adverse effects of malaria on maternal and fetal well being are thought to be for the most part due to the associated severe anemia. There is evidence that malaria can induce iron deficiency by several mechanisms: possibly through immobilizing iron in haemazoin complexes and loss of urinary iron, as well as reducing intestinal iron absorption during the acute illness period. However these effects

exerted by malaria on body iron status are still poorly understood, in part because biochemical and hematological indices of iron status are confounded by the malaria infection⁴⁰.

The other hypothesis is to look at the effect of altitude on the prevalence of malaria. In general, the situation in Ethiopia is that the *Dega zones* [cool and humid] (altitude above 2500 meters) with a mean annual temperature of 10-15 degree Celsius and much of the *Woinadega zones* [cool semi-arid] (altitude 1500-2500 meters) are malaria-free. Malaria usually occurs below an altitude of 2000 meters with short lived transmission following the rains. A linear decrease in the prevalence of malaria was also observed in another study conducted in Oromia, Amhara and SNNP regions with increase in altitude. According to UNICEF's malaria map, the regions with high anemia prevalence are subject to seasonal malaria with stable transmission of more than three months, leading to acquired immunity among people; such kind of transmission can gradually result in degraded hemoglobin levels. Though altitude can be used to describe the general distribution of malaria, other variables of importance are humidity, rainfall and temperature⁷³.

In Ethiopia, the Ministry of Health (MOH) stratifies the country into 3 levels with respect to malaria transmission: (1) non malarious (25% of the country); (2) highland (also referred to as "unstable malaria"; approximately two thirds of the country); and (3) endemic transmission with seasonal peaks (the remainder of the country). In addition, approximately 40% of malaria cases in the highland areas are caused by *P. vivax*. Current MOH policy is for pregnant women to receive chemoprophylaxis with weekly chloroquine and daily proguanil throughout pregnancy, but this policy has never been widely implemented⁷⁴. Although several studies have been conducted in different parts of the world to understand the association between parasitic infections and anemia among pregnant women, there is still not enough literature in Ethiopia.

Hookworm Infection

Hook worm infection is described to be one of the principal causes of iron deficiency anemia in developing countries especially in children. It is prevalent throughout the tropics and subtropics wherever there is faecal contamination of the environment and is acquired mainly by skin contact with contaminated soil or vegetation. Adult hook worms live in duodenum and jejunum of humans attached to the intestinal mucosa and suck blood. Once they leave the attached site this causes chronic blood loss from the mucosa. In people whose dietary intake of iron is low and whose blood iron stores are already depleted, hookworm infection can presumably give rise to iron deficiency anemia in just a few weeks, especially during pregnancy, when iron requirements are increased⁴⁰.

Soil-transmitted helminthes (STHs), such as hookworms (*Necator americanus* and *Ancylostoma duodenale*) and whipworms (*Trichuris trichiura*), contribute to iron deficiency anemia by ingesting blood and by damaging the intestinal mucosa during feeding. An analysis of the baseline (second trimester) data for an randomized controlled trials investigating the effectiveness of de-worming and iron supplementation in a population of more than 1000 pregnant women living in and around Iquitos in the Peruvian Amazon showed that women with moderate-to-heavy intensities of both hookworm and *Trichuris* infection were more than twice as likely to concurrently have anemia as those with no or

light infection. An analysis of the trial proper documented the effect of mebendazole and iron supplementation on anemia and on the presence and intensity of STH infections⁷⁵.

A clinical study conducted in Venezuela shows that intestinal parasitic infections, especially due to helminthes, increase anemia in pregnant women and the results of this are low pregnancy weight gain and intra uterine growth retardation, followed by low birth weight, with its associated greater risks of infection and higher perinatal mortality rates. In this clinical study pregnant women (n= 1038) from nine states were included and evaluated and the prevalence of intestinal parasitosis was evidenced in 73.9%: *A lumbricoides* 57.0%, *T trichiura* 36.0%, *G lamblia* 14.1%, *E hystolitica* 12.0%, *N americanus* 8.1%, *E vermicularis* 6.3%, *S stercoralis* 3.3%. Relative risk for anemia in those women with intestinal parasitosis was 2.56 ($P < 0.01$)⁷⁶.

One cross-sectional community based study conducted on pregnant women (n=388) living in three districts around Gilgel Gibe Dam area, southwestern Ethiopia showed that, those pregnant women who had a habit of walking bare foot had high anemia prevalence (57.8%). Walking bare foot might predispose to hookworm infection and consequently resulted in iron deficiency anemia especially in pregnant women. Hookworm infection rate was also associated with anemia in which those pregnant women infected with hookworm have times higher risk of developing anemia, as 68.4% of the pregnant women infected with hookworm were anemic. This finding is similar to the findings of other similar studies. There was a significant correlation between increasing hookworm parasite load, *A. lumbricoides* and *T. trichiura* and decreasing hematocrit values. This shows that as the helminth parasitic load increased the hematocrit level decreased; as a result the risk of developing anemia increase²⁸.

In general, those regions with high prevalence of anemia are lowlands and coastal regions where the soil is sandy. Sandy soils are known to allow greater hookworm mobility. The high temperature at low lands is also another environmental factor that supports hookworm life cycle. Due to these facts, residents of such low land places can exhibit high hookworm endemicity. In addition, agriculture is still the main source of living for this population especially in rural areas. Historically, hookworm has been a major occupational hazard for agricultural labourers due to the fact that they are highly in contact with soil, which is a requirement for the transmission of the parasite. Inadequate sanitation and the deposition of human faeces on soil propagate the lifecycle of hookworm. In fact, lack of access to toilet can also predispose people to other soil-transmitted helminthiasis and schistosomiasis which can also lower hemoglobin level⁷³.

A cross-sectional community-based study with analytic component was conducted among Ethiopian women (n=970) during June-July 2005 to assess the magnitude of anemia and deficiencies of iron and folic acid and to compare the factors responsible for anemia among anemic and non-anemic cases. The overall prevalence of anemia, iron deficiency, iron-deficiency anemia, deficiency of folic acid, and parasitic infestations was 30.4%, 50.1%, 18.1%, 31.3%, and 13.7% respectively. In this study, the most frequently-encountered intestinal helminthes were *Ascaris lumbricoids* (35.3%), followed by *Trichuris trichiura* (28.6%), *Entamoeba histolytica* (22.6%), *Schistosoma mansoni* (19.5%), and hookworm or *Ancylostoma duodenale* (16.5%) and graphically shown below as the author concluded⁷³.

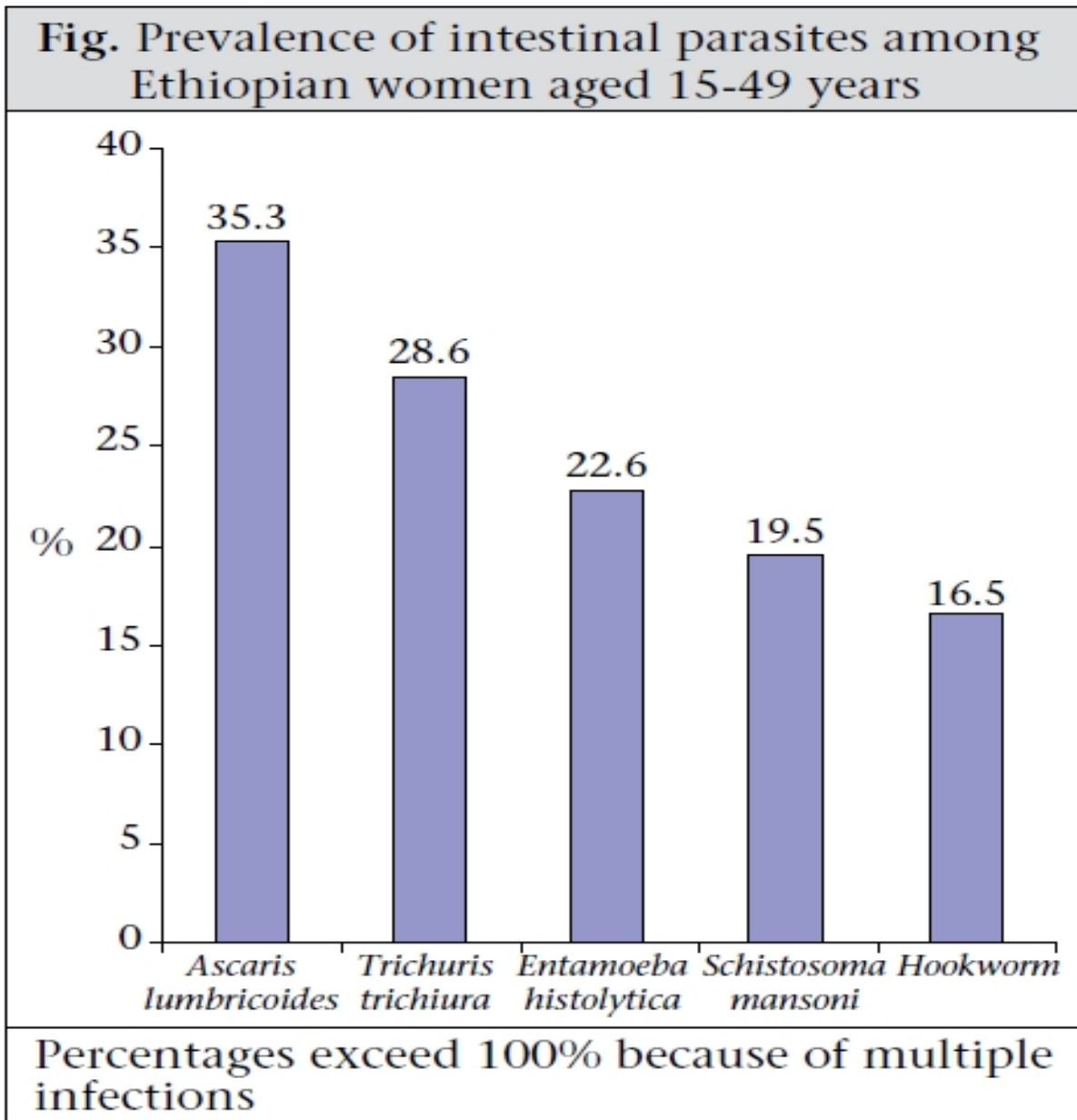


Figure 3: Prevalence of intestinal parasites among Ethiopian women aged 15- 49 years

Human Immune Deficiency Virus infection

HIV infection must now be included in the differential diagnosis of anemia in pregnancy. Where anemia is associated with leucopenia and thrombocytopenia, the antenatal health worker should be alerted to the possibility of AIDS. Transmission of HIV infection by blood transfusion is possible in developing countries, where there is a high prevalence of HIV positivity among donors and where the ability to screen for HIV is sub optimal. This further highlights the importance of the antenatal clinic in the prevention of anemia early in pregnancy, which may avoid the need for a blood transfusion later in the pregnancy⁴⁰.

Anemia is the most common hematological complication of the Human Immunodeficiency Virus (HIV) infection and may be consequent upon the effects of the virus itself or treatment with various drugs. The mechanisms of HIV induced anemia occur through three mechanisms of decreased red blood cell production, increased red cell destruction and ineffective production of red blood cells. The

etiology of HIV associated anemia is multifactorial and may include the infiltration of the bone marrow by tumor or infection, bone marrow suppression by the virus itself, the use of myelosuppressive drugs like Zidovudine or drugs that prevent the utilization of folate like cotrimoxazole. Other etiologies include decreased production of erythropoietin, red cell destruction as a result of auto antibodies to red blood cells, and nutritional deficiencies. Nutritional deficiencies could occur as a result of reduced intake due to difficult in swallowing as a result of oropharyngeal thrush, malabsorption or increased catabolism as a result of ill health and associated fever from various infections. Apart from iron and folate deficiency, other reported vitamin deficiencies in HIV infection include vitamin B12, vitamin B6 and vitamin A².

Anemia is the most frequent hematologic abnormality associated with HIV infection. It occurs in approximately 30% of patients with asymptomatic infection and in as many as 75% to 80% of those with AIDS. In pregnancy, HIV

infection is associated with lower levels of serum folate and serum ferritin. HIV infection can cause anemia (Figure 3) through the changes in cytokine production, altered erythropoietin (EPO) response to bone marrow, use of

antiretroviral drugs (especially zidovudine), and interaction with other coexisting chronic infections such as tuberculosis⁴¹.

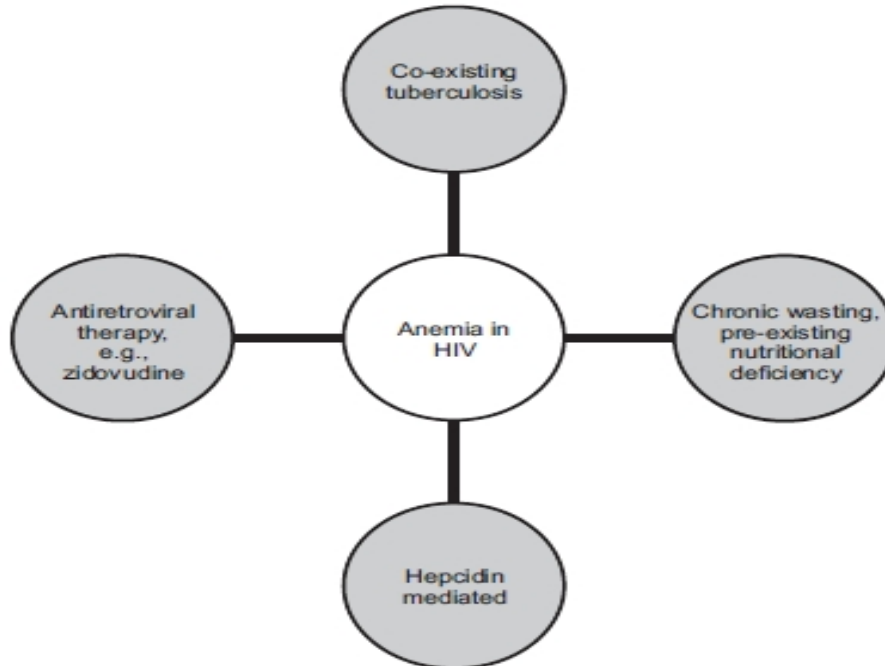


Figure 4: Causes of anemia in HIV

Behavioral determinants

A woman's own perceptions of pregnancy and her health status are major factors that will influence her health decision making. These health perceptions, not only reflect the cultural back ground but also a woman's role and status within the family and community⁴⁰.

Regional variations also exist in utilization of antenatal care services in Ethiopia. Women in Afar and Somali regions are less likely to seek antenatal health care services during pregnancy than the reference category, Oromo Region in this case. In some communities like the Afar, husbands are not willing to send their wives to be assisted by male health practitioners. The nomadic way of life and the strong traditional practice of using traditional birth attendants are identified as the responsible factors for low utilization of antenatal care in Afar and Somali regions. Conversely, women in Addis Ababa, Tigray, Gambella, Dire Dawa, SNNP and Benishangul Gumuz regions are more likely to seek antenatal care services than the reference region, though the magnitude varies. For example, the probability of seeking antenatal care for women in Addis Ababa, Tigray, Gambella and Dire Dawa is 3.98, 1.93, 1.77 and 1.55 times higher than women in Oromia Regional State, respectively. This may partly be attributed to the ease of access to health facilities in these regions as compared to Afar and Somali regions⁷⁷.

Socio-cultural and environmental determinants

One study was carried out to determine the frequency and duration of pronounced dietary cravings, aversions and pica during pregnancy among (n= 204) pregnant and lactating women attending two health facilities in Dar es Salaam City, Tanzania. The proportions of women with dietary cravings, aversions, and pica were 73.5%, 70.1% and 63.7% of all women respectively. More women (70.1%) experienced both

food cravings and aversions than either symptom alone. Foods craved most were meat (23.3%), mangoes (22.7%), yoghurt (20.0%) oranges (20.0%), plantain (15.3%) and soft drinks (13.3%). Foods avoided most were rice (36.4%), meat (36.4%) and fish (30.8%). Eggs, beans, tea and stiff porridge were also avoided. Reasons given for avoiding foods were unpleasant smell/taste (10.3%), to reduce nausea (11.8%), no particular reason (58.3%) and dislike by foetus (belief) (3.9%)⁷⁸.

In the cross sectional study conducted in south India showed that total of (n=339) adult pregnant women, most of the participants belonged to age group 25-32 year (24.5%) followed by old age group (>65 years) (16.5%). Of 339, 216 (63.7%) told that some vegetables/fruits should be avoided during pregnancy. Most of the illiterates (91.3%) told that papaya should not be eaten during pregnancy in comparison to 83.9% of literates. Most common reason for restriction of specified fruits/vegetables was abortion. Papaya is considered to be a fruit which is 'hot'. Conventionally 'hot' food items are avoided during pregnancy as it is thought that it will cause abortion. Similarly 'cold' foods are avoided during lactation as it might affect the quality and quantity of milk production. The main constituents of papaya latex are papain and chymopapain, which are potent uterine stimulants. A fully ripe papaya contains very little or a negligible quantity of the latex which will not provoke uterine contractions, so it can be eaten. On the other hand, the unripe or semi ripe papaya (which contains high concentration of the latex that produces marked uterine contractions) may have an adverse effect during pregnancy and should be avoided⁷⁹.

Another cross-sectional study of the nutritional significance of food aversions and cravings during pregnancy was conducted on 295 women in southern Ethiopia, Hadiya Zone

between February and May 1995. Slightly fewer than three-quarters (71%) of the women craved one or more foods, whereas about two-thirds (65%) avoided at least one food. Cereal foods, despite being staple foods in the area, were avoided by more women (41%) than any other foods. Livestock products, which were scarce at the time of the study, were craved by more women (55%) than any other foods. According to this study, the main foods that 81 (28%) of the women abstained from were milk and cheese (avoided by 44% each), linseed (16%), fatty meat (11%), and bananas (9%). All of the foods that the women mentioned as having been avoided (except *enset* bread, kale, and coffee, which none of the women abstained from) were also abstained from by 1% to 3% of the women. The reasons given for abstinence were fear that food would stick to the foetus, causing discoloration to the body, and fear that the baby would become too large to deliver easily. The majority of the women (90%) did not have reasons for their food aversions. A few believed that aversions were caused by a dislike of the food by the foetus⁸⁰.

IMPACT OF MATERNAL ANEMIA

Maternal Mortality and Morbidity

It is estimated that anemia may be responsible for as much as 20% of all maternal deaths in sub-Saharan Africa through three main mechanisms. Firstly, anemia makes women more susceptible to deaths from hemorrhage by lowering their hematological reserves for blood loss especially at birth. Severe anemia is associated with increased susceptibility to infection due to lowered resistance to disease, and Hb <4 g/dl is also associated with high risk of cardiac failure, particularly during delivery or soon after, making the woman likely to die if unable to reach good health facilities immediately⁸².

In Ethiopia, anemia is the most frequent morbidity among pregnant women with the prevalence ranging from 23–66.5%. There is an urban rural difference in the prevalence of anemia. As indicated by studies in Asendabo and Mettue, anemia among pregnant women was consistently higher in the rural women compared to the urban counterparts¹.

Infant mortality and morbidity

Every year more than 20 million infants are born with low birth weight worldwide. About 3.6 million infants die during the neonatal period. Two thirds of these deaths occur in southern Asia and sub-Saharan Africa. More than one third of child deaths are thought to be attributable to maternal and child under nutrition. Deficiencies in micronutrients such as folate, iron and zinc and vitamins A, B6, B12, C, E and riboflavin are highly prevalent and may occur concurrently among pregnant women⁸³.

One retrospective study carried out in the department of Gynecology and Obstetrics (Unit-I) of Liaquat University of Medical & Health Sciences Sindh-Pakistan from May 2011 to May 2012 showed that among (n=1225) pregnant women, 688 were anemic (Hb < 11g/dl) prevalence of anemia was 56.1%. Risk of preterm delivery was 56.25%. Ante partum hemorrhage was found in 44(6.4%) patients. Maternal death occurred in 6(0.9%). Low birth weight was found in 96(14.0%). Perinatal mortality was 16(2.3%) and intra-uterine death in 61(8.9%). So the authors conclude that, anemia in pregnancy is associated with adverse maternal and perinatal outcome⁸⁴.

MANAGEMENT OF ANEMIA IN PREGNANCY

Weekly Iron and Folic Acid Supplementation (WIFS)

WIFS is an approach that can be effective for ensuring adequate iron status of women, particularly before pregnancy and during the first trimester in communities where food-based strategies are not yet fully implemented or effective. Although the proven method for decreasing the risk for neural tube defects (NTDs) is through daily dosing with folic acid before pregnancy through the first trimester of pregnancy, WIFS provides an additional opportunity for ensuring adequate folate status before pregnancy and in the very early stages of pregnancy particularly for those who may become pregnant or do not know that they are already pregnant and are not covered by other programs. The weekly supplement should contain 60 mg iron in the form of ferrous sulphate (FeSO₄.7H₂O) and 2800µg folic acid, although evidence for the effective dose of folic acid for weekly supplementation is very limited⁸⁵.

Daily supplementation with iron-folate was associated with 73% reduction in anemia at term (RR = 0.27; 95% CI: 0.12 – 0.56; random model). There was no difference in rates of anemia at term with intermittent iron-folate vs. daily iron-folate supplementation (RR = 1.61; 95% CI: 0.82 – 3.14; random model). So, the authors conclude that iron supplementation has a significant benefit in reducing anemia and iron deficiency anemia at term. Iron in combination with folic acid also has a beneficial impact on anemia at term and should be routinely used in pregnant women at least in developing countries to reduce the incidence of anemia due to increased demands during pregnancy⁸⁶.

Another pragmatic randomized controlled trial which was done on comparison of routine prenatal iron prophylaxis and screening and treatment for anemia in Maputo, Mozambique showed that among pregnant women (n=4326) the women were randomly allocated to either routine iron (n=2184; 60 mg ferrous sulfate plus 400µg of folic acid daily throughout pregnancy) or selective iron (n=2142; screening and treatment for anemia and daily intake of 1 mg of folic acid). There was a suggestion of increased incidence of self-reported malaria during pregnancy (OR 1.37, 95% CI 0.98 to 1.92) in the Routine iron group. Birth data were available for 1109 (51%) in the Routine iron group and for 1149 (54%) in the Selective iron group. The birth outcomes were relatively similar in the two groups. From this pragmatic randomized controlled trial the authors concluded that routine iron prophylaxis during pregnancy did not suggest better maternal and child health (MCH) outcomes than screening and treatment for anemia in a setting of endemic malaria and HIV⁸⁷.

Another investigation was conducted in India to compare the efficacy, tolerability, and cost, of three oral iron preparations among the anemic pregnant women (n=60) of gestation (12-24 weeks). The patients were divided into 3 groups (n=20) and treated with combination of ferrous fumarate containing 100mg elemental iron along with folic acid 1.5mg. Vitamin B12 10mcg administered once a day, combination of ferrous bisglycinate containing 100mg elemental iron along with folic acid 1.5mg. Vitamin B12 10 mcg administered once a day and combination of carbonyl iron containing 100mg elemental iron along with folic acid 1.5mg. Vitamin B12 10 mcg was administered once a day respectively. Follow-up was done for 3 months. Hemoglobin gm%, mean corpuscular volume and reticulocyte count were assessed at 0,1,2,3 months and serum ferritin at 0 and 3 months. Nausea, vomiting, epigastric pain was significantly more with ferrous

fumarate but patient compliance was not affected due to them. Ferrous fumarate was the cheapest amongst all three treatments. So authors concluded that ferrous fumarate still could be considered best cost effective medication with tolerable side effects for treatment as well as prevention of iron deficiency anemia in pregnancy⁸⁸.

In Ethiopia, iron supplements were not widely consumed (<1% received the recommended 90 tablets in pregnancy), and at the community level were primarily perceived as anemia treatment rather than prevention. Community respondents were familiar with symptoms that correspond to severe anemia, but moderate anemia was not considered a priority problem. From the supply side, key barriers to iron supplementation included: poor awareness of government guidelines for universal iron supplementation during pregnancy; weak supply chain; poor use of antenatal care (ANC) and lack of monitoring and supervision of iron distribution, counseling and follow-up. In 2005 (the most recent national data available), coverage of iron supplements was very low: only 10 percent of mothers received any iron supplements during pregnancy, and less than one percent of mothers received the 180 tablets recommended by national policy. Consumption of dietary iron and vitamin-A rich was low, and iron-fortified foods were not widely available or consumed²⁴.

Blood Transfusion

Access to well-functioning blood transfusion services may be life-saving for patients presenting with acute severe anemia. In spite of the urgent and widespread need of blood in many African health care facilities, access to safe blood products remains largely insufficient, and important efforts are being made to organize sustainable, efficient and safe blood transfusion services. However, few studies have explored the use of and possibilities for blood transfusion services. A study conducted at Malawi showed that the mean Hb of transfused patients was 4.8 g/dl. Fifty-seven percent (59/104) of the transfusions were given to children diagnosed with malaria, and 17% (18/104) were given to pregnant women. During the study period, blood was in stock and available for transfusion within 1 hour of requisition. So from this study, the authors conclude that, in contrast to the advanced transfusion medicine in developed nations, their findings highlight the persistent and urgent need for life-saving blood transfusions in especially young children and pregnant women in Africa. The results indicated that blood transfusion services adapted to local conditions may be a realistic solution for providing safe blood products in developing countries. Serious challenges, such as HIV transmission and sustainable organization of low-risk blood donations should be addressed to assure access to safe blood products⁸⁹. There are no studies done in Ethiopia in relation to blood transfusion as an intervention to anemia in pregnant women.

Vitamin A supplementation

Vitamin A deficiency affects millions of women and children worldwide. Recent studies suggested that vitamin A and beta-carotene can enhance non-haemal iron absorption. Another issue is that frequencies of supplementation and dose levels may not be compatible. Supplements may result in excess levels causing harm; for example, high doses of vitamin A in pregnant women increase the risk of teratogenicity⁹⁰. In pregnancy, some extra vitamin A is required for growth and tissue maintenance in the fetus, for providing fetal reserves, and for maternal metabolism. There are potentially

adverse effects associated with Vitamin A supplementation during pregnancy. In the first 60 days post-conception, retinol is thought to be teratogenic. A relationship has been suggested between the incidence of birth defects and high vitamin A intakes during pregnancy, with an apparent threshold of near 10,000 international units (IU) per day. Increased maternal levels of preformed vitamin A (retinoic acid) have been shown to be associated with miscarriage and with malformations involving the central nervous and cardiac systems. A World Health Organization (WHO) expert group consultation concluded that daily doses of up to 10,000 IU (equivalent to 3000 mcg retinol) or 25,000 IU weekly after day 60 are probably safe, especially in areas where vitamin A deficiency is thought to be common⁷⁰.

Intermittent anti malaria therapy

Intermittent preventive therapy refers to the provision of two doses of an anti-malarial drug (sulphadoxine-pyrimethamine) to women during pregnancy, through antenatal care services. Treatment of malaria in pregnancy by this method has been shown to reduce the prevalence of both severe maternal anemia and low birth weight infants. However, although intermittent preventive therapy is part of the national health policy of many countries, coverage is often low as many women have limited access to antenatal care services or do not seek care until late in pregnancy. Insecticide-Treated Bed Net use is the key intervention for prevention of malaria infection and has demonstrated a positive effect on the prevalence of malaria and anemia in pregnant women.

Distribution of nets to vulnerable groups is a major focus of the global strategy of the Roll Back Malaria Partnership. As a result, provision of insecticide-treated nets to pregnant women is incorporated into routine antenatal services in many endemic countries. Environmental management to reduce the breeding grounds for mosquito larvae as well as larvicides can be part of a malaria prevention program where breeding sites are well defined⁸¹.

One randomized controlled trial of women attending antenatal clinic at the University of Port Harcourt Teaching Hospital, Nigeria from January 2010 to September 2010 was done to compare the effectiveness of proguanil versus sulphadoxine-pyrimethamine (SP) for malaria chemoprophylaxis in pregnancy.

Three hundred and fifty participants were recruited at booking, randomized into two groups using a table of random numbers and monitored till delivery. One group received daily proguanil while the other received SP for malaria prophylaxis. Blood samples were taken for their hematocrit and malaria parasites at booking and delivery. From this randomized controlled trial the results show that the prevalence of maternal malaria parasitaemia in this study was 29.9% at booking and 12.5% at delivery. The prevalence in women given SP and proguanil was 10.6% and 14.4% respectively. This was not statistically significant ($P=0.429$). There was no statistical difference in the incidence of preterm delivery ($P=0.262$), cord blood parasitaemia ($P=0.385$), low birth weight ($P=0.175$) and birth asphyxia ($P=0.367$) between the two study groups. So, the authors conclude that there was no significant difference between intermittent preventive treatment with sulphadoxine-pyrimethamine and the use of daily proguanil so larger studies with proguanil are warranted⁹².

Additionally, another cross sectional study was conducted to evaluate the effectiveness of Intermittent Preventive Treatment with SP among pregnant women attending the

antenatal clinic at Korle-Bu Teaching Hospital in Accra, Ghana. A total of 363 pregnant women (202 of IPTp users and 161 non-IPTp users) were recruited. A total of 15.3% of IPTp users had malaria compared with 44.7% of non-IPTp users ($P < 0.001$). A total of 58.4% of non-IPTp users were anemic compared with 22.8% of IPTp users ($P < 0.001$). When they controlled for other variables, the difference in the prevalence of malaria (odds ratio = 0.18, 95% confidence interval = 0.08–0.37) and anemia (odds ratio = 0.20, 95% confidence interval = 0.12–0.34) remained significant. Therefore, the recommended IPTp-SP regimen is useful in preventing malaria and anemia among pregnant women in Ghana. The growing resistance of parasites to SP requires an urgent evaluation of alternative drugs to SP⁹³.

Because of the generally low endemicity of malaria in Ethiopia, intermittent preventive treatment of pregnant women (IPTp) is not a part of the national strategy. In-stead, the focus of activities for malaria in pregnancy is on promoting universal Long-lasting insecticidal net [LLIN] coverage, giving special emphasis and priority to LLIN use among pregnant women, and prompt diagnosis and treatment of clinical cases when they occur.

Approaches used by the Federal Ministry of Health [FMOH] to target pregnant women are to:

- (i) Scale-up universal LLIN coverage and encourage households to have pregnant women (and children under five years of age) to use LLINs; and
- (ii) Ensure availability of prompt diagnosis and treatment of clinical cases in pregnant women at health facilities. The LLIN replacement scheme proposed in the National Strategic Plans for Malaria Prevention and Control 2011-2015 is the policy framework for continuous LLIN distribution primarily through the Health Extension Package. Two methods have been proposed to reach pregnant women:
 - (1) Providing one LLIN to every newly pregnant woman in selected kebeles over a one-year period, or
 - (2) Providing LLINs to households with children and pregnant women not currently being protected with LLINs.

Although the universal coverage strategy is to provide two LLINs per household, the HEW must make sure that pregnant mothers and children less than 5 years of age have preferential access to LLINs. Increasing ANC coverage is also one of the FMOH's priorities, and is supported by United States Agency for International Development [USAID]/Ethiopia Maternal and Neonatal Child Health [MNCH], family planning and reproductive health funding⁹⁴.

CONCLUSION

Anemia is a widespread global public health problem. Women are particularly vulnerable, and more than half of all pregnant women in developing countries suffer from anemia. Iron deficiency is the primary cause, but a variety of other nutritional deficiencies and infectious diseases contribute significantly to the global burden of anemia. The consequences of anemia are serious and include economic losses, maternal mortality and adverse birth outcomes. A variety of interventions for anemia prevention and control are available, addressing all the major causes, but experience with effective program implementation has been limited.

The current prevalence of anemia in women in developing countries is unacceptably high and a more intensive effort is

required to address it. Although there are many challenges to the management of anemia, a few examples and models of successful initiatives do exist. Effective anemia prevention and control requires analysis of the main causes of anemia in the target population followed by implementation of a package of relevant interventions, integrated within existing structures and services, including health care, agriculture and education, and the private sector (e.g., food processing). Failure of iron supplementation programs to improve hematological parameters has usually been blamed on noncompliance. It is time to reexamine the problem of anemia in pregnancy, to assess more carefully the local etiological factors that are responsible and then to design new strategies for prevention and treatment.

Generally fortification of foods with iron and folate, routine screening for anemia from adolescence, health education, and prompt treatment of infections and attendance of antenatal facilities by pregnant women can reduce the burden and in order to reduce maternal and perinatal morbidity and mortality, preventive strategies must be implemented and applied uniformly at all levels in primary, secondary and tertiary health-care centers.

REFERENCES

1. Tadege B. Determinants of anemia in pregnant women with emphasis on intestinal helminthic infection at bushulo health center southern Ethiopia. Addis Ababa University: Libraries Electronic, Thesis and Dissertations; 2009. AAU - Ethiopia.
2. Oliver E, Olufunto K. Management of Anemia in Pregnancy, Anemia, Dr. Donald Silverberg (Ed.) 2012; ISBN: 978-953-51-0138-3.
3. Kozuma S. Approaches to Anemia in Pregnancy. Journal of the Japan Medical Association 2009; 52(4): 214–218.
4. Haidar J, Rebeca P. Iron deficiency anemia is not a rare problem among women of reproductive ages in Ethiopia: A community-based cross-sectional study. BMC Blood Disorder 2009; 9:7doi:10.1186/1471-2326-9-7.
5. Worldwide prevalence of anemia, WHO Vitamin and Mineral Nutrition Information System, 1993-2005 [http://whqlibdoc.who.int/publications/2008/9789241596657_eng.pdf].
6. United Nations Children's Fund Micronutrient Initiative (UNICEF/ MI): Vitamin and Mineral Deficiency. A Global Progress Report. Ottawa 2004.
7. WHO: Major issues for nutrition strategies food and agriculture organization and WHO Theme paper no. 6. In FAO/WHO International conference on nutrition: WHO; 1992:12-23.
8. Cusick SE, Mei Z, Freedman DS, Looker AC, Ogden CL, Gunter E, Cogswell ME: Unexplained decline in the prevalence of anemia among US children and women between 1988-1994 and 1999-2002. Am J Clin Nutr 2008, 88:1611.
9. Gies S, Brabin BJ, Yassin MA, Cuevas LE: Comparison of screening methods for anemia in pregnant women in Awassa, Ethiopia. Tropical Medicine and International Health 2003, 8:301-309.
10. Viteri FE. Iron supplementation for the control of iron deficiency in population on risk. Nutr Rev 1997; 55:165-209.
11. Jamil KM, Rahman AS, Bardhan PK, Khan AI, Chowdhury F, Sarker SA, Khan AM, Ahmed T: Micronutrients and anemia. J Health Popul Nutr 2008; 26:340-355.
12. Baig-Ansari N, Badruddin SH, Karmaliani R, Harris H, Jehan I, Pasha O, Moss N, McClure EM, Goldenberg RL. Anemia prevalence and risk factors in pregnant women in an urban area of Pakistan. Food Nutr Bull 2008; 29:132-139.
13. Jemal H, Nekatibeb H, Urga K. Iron deficiency anemia in pregnant and lactating mothers in rural Ethiopia. East Afri Med J 1999; 76:618-622.
14. Adish AA, Esrey SA, Gyorkos TW, Johns T. Risk factors for iron deficiency anemia in preschool children in northern Ethiopia. Public Health Nutr 1999; 2:243-252.
15. Ethiopia Demographic and Health Survey: Preliminary Report. Addis Ababa; Central Statistical Agency, Addis Ababa, and ORC Macro Ethiopia Demographic and Health Survey 2005 Calverton, Maryland, USA 2006:156-157.
16. Gibson RS, Abebe Y, Stabler S, Allen RH, Westcott JE, Stoecker BJ, Krebs NF, Hambidge KM. Zinc, gravidity, infection, and iron, but not vitamin B-12 or folate status, predict hemoglobin during pregnancy in Southern Ethiopia. J Nutr 2008, 138:581-586.

17. Viteri FE. Iron supplementation for the control of iron deficiency in population on risk. *Nutr Rev* 1997; 55:165-209.
18. Jemal H, Nelson M, Abiud M, Gonfa A. Malnutrition and Iron deficiency in lactating women in Urban Slum Communities from Addis Ababa, Ethiopia. *East Afri Med J* 2003; 80:191-194.
19. Jemal H, Nelson M, Abiud M, Gonfa A. Daily versus weekly Iron supplementation and prevention of Iron deficiency anemia in lactating women. *East Afri Med J* 2003; 80(1):11-16.
20. Van den Broek NR. Anemia and micronutrient deficiencies. *British Medical Bulletin* 2003; 67: 149-160.
21. World Health Organization. Prevention and management of severe anemia in pregnancy. WHO 1993; WHO/FHE/MSM/93-5.
22. Gies S, Brabin BJ, Yassin MA and Cuevas LE. Comparison of screening methods for anaemia in pregnant women in Awassa. *Ethiopia Trop Med Int Health.* 2003; 8(4):301-309.
23. World Health Organization. Nutrition for Health and Development. A Global Agenda for Combatting Malnutrition.2000; Geneva: WHO.
24. Saldanha LS, Buback L, White JM, Mulgeta A, Mariam SG, Roba AC, Abebe H and Mason JB. Policies and program implementation experience to improve maternal nutrition in Ethiopia. *Food Nutri Bull* 2012; 33(2 Suppl):S27-50.
25. WHO/UNICEF/UNU. Iron deficiency anemia: assessment, prevention, and control. Geneva, World Health Organization, 2001. (WHO/NHD/01.3).
26. WHO and CDC. Worldwide prevalence of anemia 1993-2005; WHO Global database on anemia 2008.
27. Alem M, Enawgaw B, Gelaw A, Kena T, Seid M, Olkebe Y. Prevalence of anemia and associated risk factors among pregnant women attending antenatal care in Azezo Health Center Gondar town, Northwest Ethiopia. *J Interdiscipl Histopathol* 2013; x: x-x.
28. Getachew et al. Anaemia and associated risk factors among pregnant women in Gilgel Gibe dam area, Southwest Ethiopia. *Parasites & Vectors* 2012; 5:296.
29. Haidar J. Prevalence of anemia, deficiencies of iron, folic acid and their determinants in Ethiopian women. *J Health Popul Nutr* 2010; 28(4):359-368.
30. World Health Organization: Major issues for Nutrition Strategies of Food and Agriculture Organization and WHO, FAO/WHO international conference on nutrition. Geneva: World Health Organization, 1992:12-23. (Theme paper no.6).
31. World Health Organization: Nutrition for Health and Development. A Global Agenda for Combatting Malnutrition.2000; Geneva: WHO.
32. Baker SJ, De Maeyer EM. Nutritional anaemia: its understanding and control with special reference to the work of the World Health Organization. *American Journal of Clinical Nutrition* 1979; 32:368-417.
33. Brabin L, Verhoeff FH, Kazembe P, Brabin BJ, Chimsuku L, Broadhead R. Improving antenatal care for pregnant adolescents in Southern Malawi. *Acta Obstetrics and Gynaecology Scandinavia* 1998; 77: 402-409.
34. Sinha AK, Karki GM, Yadav S and Islam MN. Prevalence of anemia during pregnancy in the women of Eastern Nepal. *International Journal of Pharmaceutical & Biological Archives* 2012; 3(5):1051-1053.
35. Nik Rosmawati N, Nazr SM and Smail IM. The rate and risk factors for anemia among pregnant mothers in Jerreh Terengganu, Malaysia. *J Community Med Health Educ* 2012; 2:150. doi:10.4172/2161-0711.1000150.
36. Gebremedhin S, Enquesselie F. Correlates of anemia among women of reproductive age in Ethiopia: Evidence from Ethiopian DHS 2005; *Ethiop J Health Dev* 2011; 25(1):22-30.
37. Beard J.L. Effectiveness and strategies of iron supplementation during pregnancy. *American Journal of Clinical Nutrition* 2000; 71:1288s-1294s.
38. Xiong, X. et al. Anemia during pregnancy and birth outcome: A meta-analysis. *American Journal of Perinatology* 2000; 17(3): 137-146.
39. Alhossain A, Khallafallah and Mohamed M. Nutritional Anemia, Anemia, Dr. Donald Silverberg (Ed.) 2012, ISBN: 978-953-51-0138-3.
40. Munasinghe S and van den Broek N. "Anemia in pregnancy in Malawi - a review." *Malawi Medical Journal* 2006; 18(4):160-175.
41. Gangopadhyay R, Karoshi M and Keith L. Anemia and pregnancy: A link to maternal chronic diseases. *Int J Gynecol Obstet* 2011; 115 (Suppl 1):S11-S15.
42. Milman N. Prepartum anemia: prevention and treatment. *Ann Hematol* 2008; 87:949- 959.
43. Fekete et al. Effect of folate intake on health outcomes in pregnancy: a systematic review and meta-analysis on birth weight, placental weight and length of gestation. *Nutrition Journal* 2012; 11:75.
44. Lassi ZS, Salam RA, Haider BA and Bhutta ZA. Folic acid supplementation during pregnancy for maternal health and pregnancy outcomes. *Cochrane Database of Systematic Reviews* 2013; Issue 3. Art. No.: CD006896. DOI: 10.1002/14651858.CD006896.pub2.
45. McLean E, DeBenoist B, Allen LH. Review of the magnitude of folate and vitamin B12 deficiencies worldwide. *Food Nutr Bull* 2008; 29:S38-S51.
46. Antony A. In utero physiology: role of folic acid in nutrient delivery and fetal development. *Am J Clin Nutr* 2007; 85:S598-603.
47. Allen LH. Causes of vitamin B12 and folate deficiency. *Food Nutr Bull* 2008; 29:S20-34.
48. McNulty H. Folate requirements for health in different population groups. *Br J Biomed Sci* 1995; 52:110-9.
49. Institute of Medicine Food and Nutrition Board. Dietary reference intakes: dietary reference intakes for thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline. Washington, DC: The National Academies Press; 2000.
50. Winkels RM, Brouwer IA, Siebelink E, et al. Bioavailability of food folates is 80% of that of folic acid. *Am J Clin Nutr* 2007; 85:465-73.
51. Cusick SE, Mei Z, Freedman DS, et al. Unexplained decline in the prevalence of anemia among US children and women between 1988-1994 and 1999-2002. *Am J Clin Nutr* 2008; 88:1611-7.
52. McNulty H, Scott JM. Intake and status of folate and related B-vitamins: considerations and challenges in achieving optimal status. *Br J Nutr* 2008; 99:S48-54.
53. Siega-Riz AM, Savitz DA, Zeisel SH, et al. Second trimester folate status and preterm birth. *Am J Obstet Gynecol* 2004; 191:1851-7.
54. Pitkin RM. Folate and neural tube defects. *Am J Clin Nutr* 2007; 85:S285-8.
55. MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. *Lancet* 1991; 338(8760):131-7.
56. Jemal H, Hail MD, Demisse T, et al. Food, diet and nutrition. In: Berhane Y, Haile Mariam D, Kloos H, eds. The epidemiology and ecology of health and disease in Ethiopia. Addis Ababa: Shama Books; 2006.
57. Gibson R, Abebe Y, Stabler S, et al. Zinc, gravida, infection, and iron, but not vitamin B12 or folate status, predict hemoglobin during pregnancy in southern Ethiopia. *J Nutr* 2008; 138:581-6.
58. Haidar J, Pobocik RS. Iron deficiency anemia is not a rare problem among women of reproductive ages in Ethiopia: a community-based cross-sectional study. *BMC Blood Disorders* 2009; 9:7.
59. Haidar J, Nekatibeb H, Urga K. Iron deficiency anemia in pregnant and lactating mothers in rural Ethiopia. *East Afri Med J* 1999; 76:618-22.
60. Haidar J, Melaku U, Pobocik RS. Folate deficiency in women of reproductive age in nine administrative regions of Ethiopia: an emerging public health problem. *S Afr J Clin Nutr* 2010; 23(3):132-137.
61. Mekonnen Y, Mekonnen A. Factors influencing the use of maternal healthcare services in Ethiopia. *J Health Popul Nutr* 2003; 21:374-82.
62. Koebnick C, Heins UA, Dagnelie PC, et al. "Longitudinal concentrations of vitamin B12 and vitamin B12-binding proteins during uncomplicated pregnancy," *Clinical Chemistry* 2002; 48(6):928-933.
63. Milman N, Byg KE, Bergholt T, Eriksen L, Hvas AM. "Cobalamin status during normal pregnancy and postpartum: a longitudinal study comprising 406 Danish women," *European Journal of Haematology* 2006; 76 (6):521-525.
64. Korenke GC, Hunneman DH, Eber S, Hanefeld F. Severe encephalopathy with epilepsy in an infant caused by subclinical maternal pernicious anemia: case report and review of the literature. *European Journal of Pediatrics* 2004; 163(4-5):196-201.
65. Pardo J, Gindes L, Orvieto R. Cobalamin (vitamin B12) metabolism during pregnancy," *International Journal of Gynecology and Obstetrics* 2004; 84 (1): 77-78.
66. Relton CL, Pearce MS, Parker L. The influence of erythrocyte folate and serum vitamin B12 status on birth weight. *British Journal of Nutrition*, 2005; 93(5). 593- 599.
67. Ray JG, Blom HJ. Vitamin B12 insufficiency and the risk of fetal neural tube defects," *QJM—Monthly Journal of the Association of Physicians* 2003; 96(4), 289-295.
68. Molloy AM, Kirke PN, Brody LC, Scott JM, Mills JL, Effects of folate and vitamin B12 deficiencies during pregnancy on fetal, infant, and child development, *Food and Nutrition Bulletin* 2008; 29 (2): S101-S111.
69. Schorah CJ, Smithells RW, Scott J. Vitamin B12 and anencephaly, *The Lancet* 1980; 1 (8173): 880.
70. Van den Broek N, Dou L, Othman M, Neilson JP, Gates S, Gülmezoglu AM. Vitamin A supplementation during pregnancy for maternal and newborn outcomes. *Cochrane Database of Systematic Reviews* 2010; 11. Art. No.: CD008666. DOI: 10.1002/14651858.CD008666.pub2.
71. Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database of Systematic Reviews* 2006; 4. Art. No.: CD004905. DOI: 10.1002/14651858.CD004905.pub2.
72. Abuye C, Urgaa K and Kebede A. 3rd Annual conference of food and nutrition society of Ethiopia (FoNSE). Ethiopian Health and Nutrition Research Institute 2010, 45-47.

73. Teshome W and Bijlsma M. "The hidden hunger": Understanding the burden of anemia and its determinants among pregnant and non-pregnant women in Ethiopia. *African Journal of Food, Agriculture, Nutrition and Development* 2012; 12 (7):6913-29.
74. Newman RD, Hailemariam A, Jimma D et al. Burden of Malaria during Pregnancy in Areas of Stable and Unstable Transmission in Ethiopia during a Non-epidemic Year. *The Journal of Infectious Diseases* 2003; 187:1765–72.
75. Gyorkos TW et al. Trichuris and hookworm infections associated with anemia during pregnancy. *Tropical Medicine and International Health* 2011; 16 (4): 531–37.
76. Rodriguez-Morales AJ, et al. Intestinal Parasitic Infections among Pregnant Women in Venezuela. *Infectious Diseases in Obstetrics and Gynecology* 2006; 1–5.
77. Maternal health care seeking behavior in Ethiopia: Findings from Ethiopian Demographic and Health Survey (EDHS) 2005. Ethiopian society of population studies, Addis Ababa, 2008.
78. Nyaruhucha. C.N.M. Food cravings , aversions and pica among pregnant women in Dar es Salaam, Tanzania. *Tanzania Journal of Health Research* 2009; 11 (1): 29-34.
79. Patil R, Mittal A, DR V, Khan MI and Raghavia M. Taboos and misconceptions about food during pregnancy among rural population of Pondicherry. *Calicut Medical Journal* 2010; 8(2):1-5.
80. Tsegaye D. Food Aversions and Cravings during Pregnancy: Prevalence and Significance for Maternal Nutrition in Ethiopia. *Food Nutr Bull* 1998; 19(1):1-7.
81. MacDonald C, Mildon A, Neequaye M, Namarika R and Yiannakis M. Anemia – can its widespread prevalence among women in developing countries be impacted? A case study: effectiveness of a large-scale, integrated, multiple-intervention nutrition program on decreasing anemia in Ghanaian and Malawian women. In: Elit, L. and Chamberlain Froese, J. (eds) *Women's Health in the Majority World: Issues and Initiatives*. Nova Science Publishers Inc., New York 2007; 1–42.
82. Buseri F.I, Uko E.K, Jeremiah Z.A and Usanga E.A. Prevalence and Risk Factors of Anemia Among Pregnant women in Nigeria. *The Open Hematology Journal* 2008; 2:14-19.
83. Zerfu A. Micronutrients and pregnancy; effect of supplementation on pregnancy and pregnancy outcomes: a systematic review. *Nutrition Journal* 2013; 12:20.
84. Rizwan N, Uddin SF, Mumtaz F. Maternal anemia impact on maternal and perinatal outcome an observational study at University Hospital of Sindh-Pakistan. *International Journal of Medicine and Medical Sciences* 2013; 3(1):328-331.
85. WHO. Weekly iron–folic acid supplementation (WIFS) in women of reproductive age: its role in promoting optimal maternal and child health. Position statement. Geneva, World Health Organization, 2009.
86. Yakoob MY and Bhutta ZA. Effect of routine iron supplementation with or without folic acid on anemia during pregnancy. *BMC Public Health* 2011; 11(Suppl 3): S21.
87. Parkkali S, Abacassamo F, Nwaru BI, et al. Comparison of routine prenatal iron prophylaxis and screening and treatment for anaemia: pregnancy results and preliminary birth results from a pragmatic randomized controlled trial (PROFEG) in Maputo, Mozambique. *BMJ Open* 2013; 3: e001948. Doi: 10.1136/bmjopen-2012- 001948.
88. Patil S.S, Khanwelkar C.C, Patil S.K, Thorat V. M, Jadhav S.A and Sontakke A.V. Comparison of efficacy, tolerability, and cost of newer with conventional oral iron preparation. *Al Ameen J Med Sci* 2013; 6(1): 29-33.
89. H. F. Bugge et al. A study of blood transfusion services at a district hospital in Malawi. *The international journal of transfusion medicine*. *Vox Sanguinis* 2013; 104: 37–45.
90. Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database of Systematic Reviews* 2006; Issue 4. Art. No.: CD004905. DOI:10.1002/14651858. CD004905.pub2.
91. Jeremiah I, Kasso T, John CT .Proguanil versus Sulphadoxine-Pyrimethamine for Malaria Chemoprophylaxis in Pregnancy: A Randomised Controlled Trial. *J Clin Trials* 2012; 2:122. doi:10.4172/2167-0870.1000122.
92. Wilson NO, Ceesay FK, Obed SA et al. Intermittent Preventive Treatment with Sulfadoxine-Pyrimethamine against Malaria and Anemia in Pregnant Women. *Am. J. Trop. Med. Hyg* 2011; 85(1):12–21.
93. Briand V., Cottrell G., Massougbdji A. and Cot M. Intermittent preventive treatment for the prevention of malaria during pregnancy in high transmission areas. *Malaria Journal* 2007; 6:160.
94. USAIDS/CDC. PRESIDENT'S MALARIA INITIATIVE, Ethiopia Malaria Operational Plan FY 2013. http://pmi.gov/countries/mops/fy13/ethiopia_mop_fy13.pdf.

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