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Adults Hemoglobin Level in Atiafa Primary Health Care Center in Najran Area (5-7)/1433 H

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Abstract:

The aim of this study was to estimate hemoglobin Level among adults in Atiafa Primary Health Care Center in Najran Area, Saudi Arabia (5-7)/1433 H. A total of 90 adults were recruited of which, 48 were females and 42 were males. Male subjects were reclassified to cigarette smokers (n =18) and non-smokers (n = 24). Female subjects were reclassified to pregnant women (n =22) and non-pregnant women (n = 26). Anemia was assessed by hemoglobin level. The results showed that, hemoglobin level was significantly higher in males compared to females. Mean concentration of hemoglobin (15.064g/dL) for males was normal. Hemoglobin level was significantly higher in smokers compared to non-smokers, but both were normal, which suggested that anemia is not found among adults males sample. Mean hemoglobin level (12.10g/dL) of non-pregnant women was lower than cutoff value for determining anemia (low hemoglobin level). Based on hemoglobin value, 50.2% of female participants were anemic. Mean hemoglobin level of pregnant women was (10.98g/dL). A total of 24 adults non-smokers were reclassified to obese adults (n =10) and non-obese adults (n = 14). No significant different hemoglobin Level in obese adults as compared with non-obese adults.

Results of this study illustrated that anemia is highly prevalent among adults pregnant and non-pregnant women in Atiafa Primary Health Care Center in Najran Area, Saudi Arabia and suggests actions to eradicate anemia. These actions include increasing nutritional awareness and education for the purpose of changing inappropriate consumption patterns as well as fortification of certain foods in combination with nutritional program for pregnant women.

Chapter 1

Introduction

Definition of the problem:

Hemoglobin is Protein iron-containing respiratory pigment of vertebrate red blood cells that functions primarily in the transport of oxygen from the lungs to the tissues of the body, returning CO2 from the tissues to the lungs. Decrease level of hemoglobin leads to anemia. Anemia is present when there is a decrease in the level of hemoglobin in the blood below the reference level for the age and sex of the individual. The normal Hb (g/dL) level in male is (13.5–17.5) and in female (11.5–16).Anemia has massive complications on the vital organs if it's not managed. [1.2]

Statement and analysis of the problem:

Following menarche; adolescent females often do not consume sufficient iron to offset menstrual losses. As a result, a peak in the prevalence of iron deficiency frequently occurs among females during adolescence. So, the hemoglobin level in females are lower than males. Obese premenopausal women have significantly higher serum hepcidin levels compared to nonobese women with similar serum parameters of iron status. Obesity increases hepcidin levels and was associated with diminished response to oral iron therapy (hepcidin suppresses iron absorption, decreases hemoglobin level). [3.4]

Iron absorption is increased during pregnancy, when menstruations stop. Pregnant women still do not absorb sufficient additional iron. Cigarette smoking causes elevation of hemoglobin and hematocrit which is explained by elevation of carbon monoxide a major component of cigarette smoke which reduces oxygen tension in the body. This reduction increases production, maturity and release of erythrocytes from blood forming organs and thus elevates hemoglobin and hematocrit levels. [3,5]

The presence and nature of an anemia (low hemoglobin level) may be apparent from the clinical presentation. The cause of anemia may be blood loss, nutritional, hereditary disorder and increased demands such as growth and pregnancy. The hematocrit and hemoglobin level are used interchangeably in identifying the presence of an anemia. However, a routine measurement of the complete blood count (CBC) provides the most sensitive method for both detection and diagnosis. Thus, the clinical approach to an anemia involves both a bedside evaluation and the skilled use of the laboratory. [6]

Background information local and global:

About 40% of the world's population (i.e. more than 2 billion individuals) is thought to suffer from anaemia, i.e. low blood haemoglobin. Most of them have Iron Deficiency Anemia .In South East Asia, 779 million individuals or 57% of the total population in this region suffer from anaemia (WHO, 2001).In India (Sarin 1995) Number of deaths due to aneamia is 339 from 38565 .In Indonesia Number of deaths due to aneamia is 135 from 36062.In United Kingdom Number of deaths due to aneamia is 4195 from 36466. [7.8.9]

The prevalence of aneamia (reduced level of hemoglobin) among pregnant women, infants, and children under the age of 2 years in poor countries is over 50 %. Prevalence of anemia in preschool children aged 3 to 5 years, school-age children, and women of childbearing age is lower, but still significant. Reduced level of hemoglobin in infants and children is associated with retardation in growth and cognitive development and with lower resistance to infection. Nearly half of the pregnant women in the world are estimated to be anaemic. In non-industrialized countries, the aneamia is 2% - as compared with 23% in industrialized – countries. [3.10]

In Saudi Arabia most of the studies on nutritional status concentrate on preschool children who are under six years old. A total of 800 Saudi Students were enrolled in the study in Jeddah, Saudi Arabia 2000. There were 47.0% males and 53.0% females with an age ranging from 9 to 21 years. Anaemia was detected among 20.5% of students. Anaemia was significantly higher among older age groups (12–14 and 15–21 years) as compared to younger students (9–11 years).Studies that evaluated anemia among Saudi males are very limited. A recent study by Alhamdan (2004) evaluated anemia based on hemoglobin levels among adult and elderly males living in nursing home in Riyadh City. The study found 38% and 55% of adult and elderly subjects respectively, were anemic. [10.11]

Chapter 2

Objectives

General objective:

1/To screen adults in Atiafa Primary Health Care Center in Najran city (5-7)/1433 to estimate hemoglobin level.

Specific Objective:

2/To identify the relationship between gender and hemoglobin level.

3/To clarify the association between obesity and hemoglobin level.

4/To correlate the connection between pregnancy and hemoglobin level.

5/To evaluate the association between smoking and hemoglobin level.

Chapter 3

Literature review

General review

Hemoglobin has quaternary structure as it is made up of four polypeptide chains; two α chains and two β chains (α2β2), each with a heme prosthetic group. Despite little similarity in their primary sequences, the individual polypeptides of hemoglobin have a three-dimensional structure almost identical to the polypeptide chain of myoglobin.[12]

Role of Hemoglobin in Oxygen

Normally, about 97 per cent of the oxygen transported from the lungs to the tissues is carried in chemical combination with hemoglobin in the red blood cells. The remaining 3 per cent is transported in the dissolved state in the water of the plasma and blood cells. Thus, *under normal conditions*, oxygen is carried to the tissues almost entirely by hemoglobin. Reversible Combination of Oxygen with Hemoglobin. It was pointed out that the oxygen molecule combines loosely and reversibly with the heme portion of hemoglobin. When Po_2 is high, as in the pulmonary capillaries, oxygen binds with the hemoglobin, but when Po_2 is low, as in the tissue capillaries, oxygen is released from the hemoglobin. This is the basis for almost all oxygen transport from the lungs to the tissues.[13]

Maximum Amount of Oxygen That Can Combine with the Hemoglobin of the Blood. The blood of a normal person contains about 15 grams of hemoglobin in each 100 milliliters of blood, and each gram of hemoglobin can bind with a maximum of 1.34 milliliters of oxygen (1.39 milliliters when the hemoglobin is chemically pure, but impurities such as methemoglobin reduce this).Therefore, 15 times 1.34 equals 20.1, which means that, on average, the 15 grams of hemoglobin in 100 milliliters of blood can combine with a total of almost exactly 20 milliliters of oxygen if the hemoglobin is 100 per cent saturated. This is usually expressed as *20 volumes per cent.* The oxygen-hemoglobin dissociation curve for the normal person can also be expressed in terms of volume per cent of oxygen, instead of per cent saturation of hemoglobin. Amount of Oxygen Released from the Hemoglobin When Systemic Arterial Blood Flows Through the Tissues. The total quantity of oxygen *bound with hemoglobin* in normal systemic arterial blood, which is 97 per cent saturated,is about 19.4 milliliters per 100 milliliters of blood. On passing through the tissue capillaries, this amount is reduced, on average, to 14.4 milliliters (Po_2 of 40 mm Hg, 75 per cent saturated hemoglobin). Thus, *under normal conditions, about 5 milliliters of oxygen are transported from the lungs to the tissues by each 100 milliliters of blood flow.*[13]

Effect of Hemoglobin to "Buffer" the Tissue PO_2

Although hemoglobin is necessary for the transport of oxygen to the tissues, it performs another function essential to life. This is its function as a "tissue oxygen buffer" system.That is, the hemoglobin in the blood is mainly responsible for stabilizing the oxygen pressure in the tissues. This can be explained as follows. Role of Hemoglobin in Maintaining Nearly Constant PO_2 in the Tissues. Under basal conditions, the tissues require about 5 milliliters of oxygen from each 100 milliliters of blood passing through the tissue capillaries. Referring back to the oxygen-hemoglobin dissociation curve, one can see that for the normal 5 milliliters of oxygen to be released per 100 milliliters of blood flow, the Po_2 must fall to about 40 mm Hg. Therefore, the tissue Po_2 normally cannot rise above this 40 mm Hg level, because if it did, the amount of oxygen needed by the tissues would not be released from the hemoglobin. In this way, the hemoglobin normally sets an upper limit on the oxygen pressure in the tissues at about 40 mm Hg. Conversely, during heavy exercise, extra amounts of oxygen (as much as 20 times normal) must be delivered from the hemoglobin to the tissues. But this can be achieved with little further decrease in tissue Po_2 because of (1) the steep slope of the dissociation curve and (2) the increase in tissue blood flow caused by the decreased Po_2; that is, a very small fall in Po_2 causes large amounts of extra oxygen to be released from the hemoglobin. It can be seen, then, that the hemoglobin in the blood automatically delivers oxygen to the tissues at a pressure that is held rather tightly between about 15 and 40 mm Hg.[13]

Transport of Carbon Dioxide in Combination with Hemoglobin and Plasma Proteins - Carbamino-hemoglobin.

In addition to reacting with water, carbon dioxide reacts directly with amine radicals of the hemoglobin molecule to form the compound *carbaminohemoglobin* (CO_2Hgb). This combination of carbon dioxide and hemoglobin is a reversible reaction that occurs with a loose bond, so that the carbon dioxide is easily released into the alveoli, where the Pco_2 is lower than in the pulmonary capillaries. A small amount of carbon dioxide also reacts in the same way with the plasma proteins in the tissue capillaries. This is much less significant for the transport of carbon dioxide because the quantity of these proteins in the blood is only one fourth as great as the quantity of hemoglobin. The quantity of carbon dioxide that can be carried from the peripheral tissues to the lungs by carbamino combination with hemoglobin and plasma proteins is about 30 per cent of the total quantity transported that is, normally about 1.5 milliliters of carbon dioxide in each 100 milliliters of blood. However, because this reaction is much slower than the reaction of carbon dioxide with water inside the red blood

cells, it is doubtful that under normal conditions this carbamino mechanism transports more than 20 per cent of the total carbon dioxide.[13]

Oxygen-Binding Proteins - Hemoglobin: Oxygen Transport

Nearly all the oxygen carried by whole blood in animals is bound and transported by hemoglobin in erythrocytes (red blood cells). Normal human erythrocytes are small (6 to 9 m in diameter), biconcave disks. They are formed from precursor stem cells called hemocytoblasts. In the maturation process, the stem cell produces daughter cells that form large amounts of hemoglobin and then lose their intracellular organelles nucleus, mitochondria, and endoplasmic reticulum. Erythrocytes are thus incomplete, vestigial cells, unable to reproduce and, in humans, destined to survive for only about 120 days. Their main function is to carry hemoglobin, which is dissolved in the cytosol at a very high concentration (~34%by weight). In arterial blood passing from the lungs through the heart to the peripheral tissues, hemoglobin is about 96% saturated with oxygen. In the venous blood returning to the heart, hemoglobin is only about 64% saturated. Thus, each 100 mL of blood passing through a tissue releases about one-third of the oxygen it carries, or 6.5 mL of O_2 gas at atmospheric pressure and body temperature. Hemoglobin (*M*r 64,500; abbreviated Hb) is roughly spherical, with a diameter of nearly 5.5 nm. It is a tetrameric protein containing four heme prosthetic groups, one associated with each polypeptide chain. Adult hemoglobin contains two types of globin, two α chains (141 residues each) and two β chains (146 residues each). Although fewer than half of the amino acid residues in the polypeptide sequences of the α and β subunits are identical, the three-dimensional structures of the two types of subunits are very similar. Furthermore, their structures are very similar to that of myoglobin.[12]

Hemoglobin Undergoes a Structural Change on Binding Oxygen

X-ray analysis has revealed two major conformations of hemoglobin: the R state and the T state. Although oxygen binds to hemoglobin in either state, it has a significantly higher affinity for hemoglobin in the R state. Oxygen binding stabilizes the R state. When oxygen is absent experimentally, the T state is more stable and is thus the predominant conformation of deoxyhemoglobin. The binding of O2 to a hemoglobin subunit in the T state triggers a change in conformation to the R state. When the entire protein undergoes this transition, the structures of the individual subunits change little, but the subunit pairs slide past each other and rotate, narrowing the pocket between the **β** subunits. In this process, some of the ion pairs that stabilize the T state are broken and some new ones are formed.[12]

Hemoglobin Binds Oxygen Cooperatively

Hemoglobin must bind oxygen efficiently in the lungs, where the pO_2 is about 13.3 kPa, and release oxygen in the tissues, where the pO_2 is about 4 kPa.O_2 with high affinity would bind it efficiently in the lungs but would not release much of it in the tissues. If the protein bound oxygen with a sufficiently low affinity to release it in the tissues, it would not pick up much oxygen in the lungs. Hemoglobin solves the problem by undergoing a transition from a low-affinity state (the T state) to a high-affinity state (the R state) as more O_2 molecules are bound. As a result, hemoglobin has a hybrid S shaped, or sigmoid, binding curve for oxygen. A single-subunit protein with a single ligand binding site cannot produce a sigmoid binding curve even if binding elicits a conformational change because each molecule of ligand binds independently and cannot affect the binding of another molecule. In contrast, O_2 binding to individual subunits of hemoglobin can alter the affinity for O_2 in adjacent subunits. The first molecule of O_2 that interacts with deoxyhemoglobin binds weakly, because it binds to a subunit in the T state. Its binding, however, leads to conformational changes that are communicated to adjacent subunits, making it easier for additional molecules of O_2 to bind. In effect, the T n R transition occurs more readily in the second subunit once O_2 is bound to the first subunit. The last (fourth) O_2 molecule binds to a hem in a subunit that is already in the R state, and hence it binds with much higher affinity than the first molecule.[12]

Hemoglobin Also Transports H and CO_2

In addition to carrying nearly all the oxygen required by cells from the lungs to the tissues, hemoglobin carries two end products of cellular respiration H and CO_2 from the tissues to the lungs and the kidneys, where they are excreted. The CO_2, produced by oxidation of organic fuels in mitochondria, is hydrated to form bicarbonate:

$$CO_2 + H_2O = \quad H + HCO_3$$

This reaction is catalyzed by carbonic anhydrase, an enzyme particularly abundant in erythrocytes. Carbon dioxide is not very soluble in aqueous solution, and bubbles of CO_2 would form in the tissues and blood if it were not converted to bicarbonate. As you can see from the equation, the hydration of CO_2 results in an increase in the H concentration (a decrease in pH) in the tissues. The binding of oxygen by hemoglobin is profoundly influenced by pH and CO_2 concentration, so the interconversion of CO_2 and bicarbonate is of great importance to the regulation of oxygen binding and release in the blood. Hemoglobin transports about 40% of the total H and 15% to 20% of the CO_2 formed in the tissues to the lungs and the kidneys. (The remainder of the H is absorbed by the plasma's bicarbonate buffer; the remainder of the CO_2 is transported as dissolved HCO_3 and CO_2.) The binding of H and CO_2 is inversely

related to the binding of oxygen. At the relatively low pH and high CO_2 concentration of peripheral tissues, the affinity of hemoglobin for oxygen decreases as H and CO_2 are bound, and O_2 is released to the tissues. Conversely, in the capillaries of the lung, as CO_2 is excreted and the blood pH consequently rises, the affinity of hemoglobin for oxygen increases and the protein binds more O_2 for transport to the peripheral tissues. This effect of pH and CO_2 concentration on the binding and release of oxygen by hemoglobin is called the **Bohr effect,** after Christian Bohr, the Danish physiologist (and father of physicist Niels Bohr) who discovered it in 1904. The binding equilibrium for hemoglobin and one molecule of oxygen can be designated by the reaction

$$Hb+ O_2=HbO_2$$

but this is not a complete statement. To account for the effect of H concentration on this binding equilibrium, we rewrite the reaction as

$$HHb+ O_2=HbO_2+H$$

Where HHb_ denotes a protonated form of hemoglobin. This equation tells us that the O_2-saturation curve of hemoglobin is influenced by the H concentration. Both O_2 and H are bound by hemoglobin, but with inverse affinity. When the oxygen concentration is high, as in the lungs, hemoglobin binds O_2 and releases protons. When the oxygen concentration is low, as in the peripheral tissues, H is bound and O_2 is released. Oxygen and H are not bound at the same sites in hemoglobin. Oxygen binds to the iron atoms of the hemes, whereas H binds to any of several amino acid residues in the protein. A major contribution to the Bohr effect is made by His146 (His HC_3) of the _ subunits. When protonated, this residue forms one of the ion pairs—to Asp94 (Asp FG1)—that helps stabilize deoxyhemoglobin in the T state. The ion pair stabilizes the protonated form of His HC_3, giving this residue an abnormally high p*K*a in the T state. The p*K*a falls to its normal value of 6.0 in the R state because the ion pair cannot form, and this residue is largely unprotonated in oxyhemoglobin at pH 7.6, the blood pH in the lungs. As the concentration of H rises, protonation of His HC_3 promotes release of oxygen by favoring a transition to the T state. Protonation of the amino-terminal residues of the **β** subunits, certain other His residues, and perhaps other groups has a similar effect. Thus we see that the four polypeptide chains of hemoglobin communicate with each other about not only O_2 binding to their heme groups but also H binding to specific amino acid residues. And there is still more to the story. Hemoglobin also binds CO_2, again in a manner inversely related to the binding of oxygen. Carbon dioxide binds as a carbamate group to the amino group at the amino-terminal end of each globin chain, forming carbaminohemoglobin. When the concentration of carbon dioxide is high, as in peripheral tissues, some CO_2 binds to hemoglobin and the affinity for O_2 decreases, causing its release. Conversely, when hemoglobin reaches the lungs, the high oxygen concentration promotes binding of O_2 and release of CO_2. It is the capacity to communicate ligand binding information from one polypeptide subunit to the others that makes the hemoglobin molecule so beautifully adapted to integrating the transport of O_2, CO_2, and H by erythrocytes. When hemoglobin is isolated, it contains substantial amounts of bound BPG, which can be difficult to remove completely. In fact, the O_2-binding curves for hemoglobin that we have examined to this point were obtained in the presence of bound BPG. 2,3-Bisphosphoglycerate is known to greatly reduce the affinity of hemoglobin for oxygen—there is an inverse relationship between the binding of O_2 and the binding of BPG. We can therefore describe another binding process for hemoglobin. (12)

BPG binds at a site distant from the oxygen-binding site and regulates the O_2-binding affinity of hemoglobin in relation to the pO_2 in the lungs. BPG plays an important role in the physiological adaptation to the lower pO_2 available at high altitudes. For a healthy human strolling by the ocean, the binding of O_2 to hemoglobin is regulated such that the amount of O_2 delivered to the tissues is equivalent to nearly 40% of the maximum that could be carried by the blood. Imagine that this person is quickly transported to a mountainside at an altitude of 4,500 meters, where the pO_2 is considerably lower. The delivery of O_2 to the tissues is now reduced. However, after just a few hours at the higher altitude, the BPG concentration in the blood has begun to rise, leading to a decrease in the affinity of hemoglobin for oxygen. This adjustment in the BPG level has only a small effect on the binding of O_2 in the lungs but a considerable effect on the release of O_2 in the tissues. As a result, the delivery of oxygen to the tissues is restored to nearly 40% of that which can be transported by the blood. The situation is reversed when the person returns to sea level. The BPG concentration in erythrocytes also increases in people suffering from **hypoxia,** lowered oxygenation of peripheral tissues due to inadequate. Regulation of oxygen binding to hemoglobin by BPG has an important role in fetal development. Because a fetus must extract oxygen from its mother's blood, fetal hemoglobin must have greater affinity than the maternal hemoglobin for O_2. The fetus synthesizes *β* subunits rather than *α* subunits, forming *α2β2* hemoglobin. This tetramer has a much lower affinity for BPG than normal adult hemoglobin, and a correspondingly higher affinity for O_2.functioning of the lungs or circulatory system.(12)

Haemoglobin synthesis

Haemoglobin performs the main functions of red cells – carrying O_2 to the tissues and returning CO_2 from the tissues

to the lungs. Each normal adult Hb molecule (Hb A) has a molecular weight of 68 000 and consists of two α and two β globin polypeptide chains (α2β2) which have 141 and 146 amino acids, respectively. HbA comprises about 97% of the Hb in adults. Two other types, Hb A2 (α2δ2) and Hb F (α2γ2), are found in adults in small amounts (1.5–3.2% and < 1%, respectively). Haemoglobin synthesis occurs in the mitochondria of the developing red cell. The major rate-limiting step is the conversion of glycine and succinic acid to δ-aminolaevulinic acid (ALA) by ALA synthase. Vitamin B6 is a coenzyme for this reaction, which is inhibited by haem and stimulated by erythropoietin. Two molecules of δ-ALA condense to form a pyrrole ring (porphobilinogen). These rings are then grouped in fours to produce protoporphyrins. Finally, iron is inserted to form haem. Haem is then inserted into the globin chains to form Hb.(2)

Haemoglobin function

The biconcave shape of red cells provides a large surface area for the uptake and release of oxygen and carbon dioxide. Haemoglobin becomes saturated with oxygen in the pulmonary capillaries where the partial pressure of oxygen is high and Hb has a high affinity for oxygen. Oxygen is released in the tissues where the partial pressure of oxygen is low and Hb has a low affinity for oxygen. In adult haemoglobin (Hb A), a haem group is bound to each of the four globin chains; the haem group has a porphyrin ring with a ferrous atom which can reversibly bind one oxygen molecule. The haemoglobin molecule exists in two conformations, R and T. The T (taut) conformation of deoxyhaemoglobin is characterized by the globin units being held tightly together by electrostatic bonds. These bonds are broken when oxygen binds to haemoglobin, resulting in the R (relaxed) conformation in which the remaining oxygenbinding sites are more exposed and have a much higher affinity for oxygen than in the T conformation. The binding of one oxygen molecule to deoxyhaemoglobin increases the oxygen affinity of the remaining binding sites. This property is known as 'cooperativity' and is the reason for the sigmoid shape of the oxygen dissociation curve. Haemoglobin is, therefore, an example of an allosteric protein. The binding of oxygen can be influenced by secondary effectors hydrogen ions, carbon dioxide and red-cell 2,3-bisphosphoglycerate (2,3-BPG). Hydrogen ions and carbon dioxide added to blood cause a reduction in the oxygen-binding affinity of haemoglobin (the Bohr effect). Oxygenation of haemoglobin reduces its affinity for carbon dioxide (the Haldane effect). Red cell metabolism produces 2,3-BPG from glycolysis. 2,3-BPG accumulates because it is sequestered by binding to deoxyhaemoglobin. The binding of 2,3-BPG stabilizes the T conformation and reduces its affinity for oxygen. The P_{50} is the partial pressure of oxygen at which the haemoglobin is 50% saturated with oxygen. P_{50} increases with 2,3-BPG concentrations, which increase when oxygen availability is reduced in conditions such as hypoxia or anaemia. P_{50} also rises with increasing body temperature, which may be beneficial during prolonged exercise. Haemoglobin regulates oxygen transport as shown in the oxyhaemoglobin dissociation curve. When the primary limitation to oxygen transport is in the periphery, e.g. heavy exercise, anaemia, the P_{50} is increased to enhance oxygen unloading. When the primary limitation is in the lungs, e.g. lung disease, high altitude exposure, the P_{50} is reduced to enhance oxygen loading.(2)

Medical review

Haemoglobin disorder

Anaemia

Anaemia is present when there is a decrease in the level of haemoglobin in the blood below the reference level for the age and sex of the individual Male (13.5–17.5) Female(11.5–16).The presence and nature of an anemia may be apparent from the clinical presentation. Acute blood loss, when severe, can be expected to produce a hemorrhagic anemia; chronic blood loss will generally result in an iron deficiency anemia. More often, however, a routine measurement of the complete blood count (CBC) provides the most sensitive method for both detection and diagnosis. Thus, the clinical approach to an anemia involves both a bedside evaluation and the skilled use of the laboratory.(2.6)

Clinical presentation

The signs and symptoms of an anemia are a function of its severity, its rapidity of onset, and the age of the patient. Mild anemias produce little in the way of symptoms other than a loss in stamina and an increase in heart rate and dyspnea with exercise. This reflects the ability of the hemoglobin-oxygen dissociation curve to compensate for modest reductions in the hemoglobin level in the basal state. It also shows the loss of the capacity of the hemoglobin-oxygen dissociation curve to respond to situations of increased demand once it is used to compensate for the anemia. With more pronounced anemia, the patient's exercise capacity can be markedly reduced. Any exertion is accompanied by palpitations, dyspnea, a pounding headache, and rapid exhaustion. The rapidity of onset of the anemia is also important. Although the hemoglobin-oxygen dissociation curve can rapidly compensate for modest falls in the hemoglobin level, cardiovascular compensation for more severe anemia takes time. This situation is worsened if the anemia is the result of acute blood loss (a deficit in both red blood cells and plasma volume). The reduction in total blood volume jeopardizes the cardiovascular response. Patients with acute hemorrhagic anemia are at risk for signs and symptoms of both tissue hypoxia and acute vascular collapse. In contrast, patients with long-standing anemias are able to expand their total blood volume and compensate with an increase in cardiac stroke volume and changes in regional blood flow.(6)

Clinical evaluation

The cause of anemia may be suggested from the history and physical examination. Ongoing blood loss is an obvious and dramatic clue to the cause of the patient's anemia. The history can be equally revealing in diagnosing other types of anemia. A documented history of anemia that reaches back to childhood is highly suggestive of a hereditary disorder, especially a congenital hemolytic anemia. The sudden onset of pancytopenia in an otherwise healthy individual may be explained from the patient's history of occupational or environmental exposure to toxic chemicals or the introduction of a new medication just prior to development of the cytopenia. Race can also be an important clue, because many of the hemoglobinopathies and enzyme deficiency states follow ethnic lines.[6]

History

The patient should be questioned extensively regarding the timing of the onset of symptoms, transfusion history, past blood count measurements, nutritional habits, alcohol intake, and any associated symptoms of acute or chronic illness such as weight loss, fever, or night sweats. A few complaints are unique to specific types of anemia. For example, the adult iron-deficient patient may report craving ice, whereas children may be observed eating dirt or clay (picophagia). Complaints of a sore mouth and difficulty swallowing are expressed by patients with vitamin B_{12} and iron deficiency. The sickle cell anemia patient will have a lifelong history of episodic bone and joint pains.[6]

Laboratory Evaluation

Although the history and physical examination may point the way to the presence of anemia and suggest its cause, a thorough laboratory evaluation is essential to the definitive diagnosis and treatment of any anemia. The routine hematology laboratory offers several tests relevant to anemia diagnosis: the more routine tests such as the CBC and reticulocyte count as well as studies of iron supply that serve both as screening tests and a jumping-off point to diagnosis. A larger number of more specific tests come into play when one is confirming the diagnosis of specific anemic conditions.[6]

A. Complete Blood Count

The CBC includes determinations of the hemoglobin, hematocrit, red blood cell count, red blood cell volume; and hemoglobin content, platelet count, and white blood cell count. These measurements are provided by any of the common automated counters, including instruments manufactured by Abbott, Bayer, Beckman-Coulter, TOA, and Technicon.[6]

B. Hemoglobin/Hematocrit

The hematocrit and hemoglobin level are used interchangeably in identifying the presence of an anemia. Many counters directly measure the hemoglobin and then calculate the hematocrit from measurements of the red blood cell count and mean cell volume (MCV). Other counters measure the hematocrit from the red blood cell size-distribution curve. This can make the hemoglobin measurement somewhat more accurate, because artifacts introduced by cell agglutination can increase the MCV and falsely elevate the hematocrit. To diagnose an anemia, any patient value must be compared with a normal reference range.. At birth, the hemoglobin averages 17 g/dL with a hematocrit of 52%. These values then decrease during childhood only to recover during adolescence until a mean hemoglobin level of 16 g/dL (hematocrit of 47%) is reached in adult men and 13 g/dL (hematocrit of 40%) in menstruating women.These are mean values, however, and any normal population of men or women will vary around the mean in a gaussian distribution. Therefore, it is common practice to state 95% confidence limits (2 standard deviations [SD]) for the mean normal value. For the adult male hemoglobin level, this is 16 ±2g/dL, for the hematocrit, it is 47 ± 6%. For the adult female hemoglobin level, it is 13 ±2g/dL and for the hematocrit, it is 40± 6%. When a patient's hemoglobin or hematocrit falls within these limits, it is most likely normal. However, the actual probability that the patient's hemoglobin/ hematocrit is normal or abnormal will depend on the incidence of disease in the population. When the prevalence of anemia is high, the overlap of abnormal and normal populations will increase, thereby reducing both the sensitivity and specificity of the hemoglobin and hematocrit measurements. Of course, the lower the patient's hemoglobin value, the more likely it represents a true anemia. Normal values for the hemoglobin and hematocrit are also influenced by several environmental and physiologic factors. Populations living at higher altitudes have predictable increases in their hemoglobin levels of approximately 1 g/dL of hemoglobin for each 3-“4% decrease in arterial oxygen saturation. The same effect is produced by smoking because carbon monoxide decreases the hemoglobin-oxygen saturation. A patient who smokes more than one pack of cigarettes per day will show an increased hemoglobin level of between 0.5 and 1 g/dL. Slightly lower hemoglobin levels are seen in black populations, 0.5 g/dL below those of whites. During normal pregnancy, there is a steady decline in the hemoglobin level to 11-12 g/dL during the second and third trimesters. This decline is caused by an expansion of plasma volume and does not represent a true anemia. In fact, a pregnant woman's red blood cell mass is actually increased late in pregnancy. [6]

C. Mean Cell Volume

Automated counters produce a size-distribution curve for the red blood cell population, which is then used to calculate the mean MCV. The normal MCV is 90± 9 fL and generally

coincides with the peak of the Gaussian distribution of red blood cell size. The MCV accurately detects any general increase (macrocytosis) or decrease (microcytosis) in red blood cell volume. It is less sensitive to the presence of small populations of microcytes or macrocytes, because they have little impact on the mean. To detect small numbers of abnormal cells, the clinician should look at the calculated red cell distribution width and the shape of the size distribution curve, or, even better, inspect the stained blood smear. (6)

D. Mean Cell Hemoglobin

The automated counter provides calculated mean cell hemoglobin (ie, the hemoglobin level divided by the red blood cell count). The normal MCH is 32 ± 2pg. This is an excellent measure of the amount of hemoglobin in each individual red blood cell.(6)

E. Mean Corpuscular Hemoglobin Concentration

The counter also provides a calculated mean corpuscular hemoglobin concentration (MCHC). The normal value of the MCHC is 33± 3%. This is the least revealing value provided by the counter. Although it should provide a measurement of the relative concentration of intracellular hemoglobin, it is not very sensitive to disease states where hemoglobin production is defective. This is in part due to counter error but primarily reflects the fact that defects in hemoglobin production are accompanied by a simultaneous reduction in cell size. Thus, empty cells are also small cells. The principal value of the MCHC is to detect patients with hereditary spherocytosis who have very small, dense spherocytes in circulation. These spherocytes represent cells that have lost considerable intracellular fluid because of a membrane defect. When present in significant numbers, they will cause the MCHC to increase to levels in excess of 36%. (6)

F. Red Blood Cell Distribution Width

In addition to the MCV, MCH, and MCHC, automated counters provide an index of the distribution of red blood cell volumes, termed the red blood cell distribution width (RDW). Counters use two methods to calculate this value. The first is referred to as the RDW-CV. the RDW-CV is the ratio of the width of the red blood cell distribution curve at 1 SD divided by the MCV (normal RDW-CV = 13± 1 %). Since it is a ratio, changes in either the width of the curve or the MCV will influence the result.(6)

Cause of reduced hemoglobin level (anemia)

Anemia diagnosis can be organized as a three-branch algorithm based on routine laboratory test results. The first step is to categorize the erythropoietic abnormality as one of three functional defects: (1) a failure in red blood cell production, (2) an abnormality in cell maturation, or (3) an increase in red blood cell destruction. This first step relies on the CBC and reticulocyte index. Defects in production (hypoproliferative anemias) are characterized by a low reticulocyte production index coupled with little or no change in red blood cell morphology. Maturation disorders demonstrate a low reticulocyte production index together with either macrocytic or microcytic red blood cell morphology. In contrast, patients with increased red blood cell destruction owing to hemolysis show a compensatory increase in the reticulocyte index to levels greater than three times normal and red blood cell morphology that may or may not be distinctive for the disease process. This first step in classifying an anemia is important for both diagnosis and management. From the diagnostic viewpoint, each category encompasses a limited number of possibilities. This situation makes it possible to organize the rest of the laboratory evaluation around those tests that best discriminate among several diagnostic choices. Management of the patient will also vary according to the functional defect. For example, the need to provide a transfusion for a patient early in the course of the workup will depend on the expected ability of the patient to respond to a specific therapy. (6)

1-Hypoproliferative Anemias

A hypoproliferative anemia (ie, an anemia resulting from a failure in the erythroid marrow production response) can result from damage to the marrow structure or precursor stem cell pool, a lack of stimulation by erythropoietin, or iron deficiency. Patients with these conditions usually present with a normocytic, normochromic anemia of moderate severity. The reticulocyte production index is less than 2 and the marrow E/G ratio is less than 1:2. Measurements of red blood cell destruction such as the bilirubin and LDH are normal or decreased. In essence, this is the profile of a marrow that has not responded appropriately (increased red cell production) to the patient's anemia. Most anemias encountered in clinical practice are hypoproliferative. They are generally associated with a chronic illness, especially disorders with a significant inflammatory component. Iron deficiency is another prominent cause of hypoproliferative anemia. Therefore, a careful clinical evaluation is required to understand the cause of the anemia. (6)

2-Maturation Defects

Disruption of the erythroid precursor maturation sequence can result from deficiencies in vitamins such as folic acid and vitamin B_{12}, exposure to chemotherapeutic agents, or a preleukemic state. Since these are all defects in nuclear maturation, patients present with macrocytic anemias and megaloblastic bone marrow morphology. By contrast, defects in hemoglobinization, including severe iron deficiency and inherited defects in globin chain synthesis,

the thalassemias, produce a microcytic, hypochromic anemia and markedly ineffective erythropoiesis. (6)

3-Increased Red Blood Cell Destruction

Blood loss or hemolysis will stimulate a compensatory red blood cell production response. Thus, the increased cell destruction category of anemia is characterized by an increase in the reticulocyte production index to greater than three times normal and a similar increase in the E/G ratio to levels greater than 1:1. The impact of high levels of erythropoietin stimulation in the marrow is also apparent from the appearance of large numbers of polychromatic macrocytes (marrow reticulocytes) on the peripheral blood smear. Other changes in morphology may provide a specific clue as to the cause of a hemolytic anemia. (6)

4-Marrow-Damage Anemia

Disruption of the erythroid precursor pool or the structure of the marrow can produce a marrow-damage anemia. The severity of the anemia depends on the nature of the disorder. Relatively mild marrow-damage anemias are seen in association with drug toxicity and tumor infiltration. More severe anemias are typically seen in patients with acute leukemia and aplastic anemia. The prevalence of marrow-damage anemias in any population is a function of the incidence of various disease states and environmental challenges. Impairment of red blood cell production is anticipated in most patients receiving tumor chemotherapy. In contrast, aplastic anemia characterized by a marked reduction in all hematopoietic precursors is a relatively rare event. Higher rates of aplastic anemia in the developing world are usually a result of the level of exposure to toxic drugs and chemicals in the workplace and environment. Marrow-damage can result from direct invasion of the marrow structure by an infectious agent or immunosuppression of stem cell growth. Miliary tuberculosis is perhaps the best example of the first mechanism. Extensive involvement of the marrow as evidenced by widespread granuloma formation and marrow fibrosis can produce a marrow-damage anemia and in some cases a pancytopenia. Early on, the clinician's index of suspicion must be high to successfully make this diagnosis. The patient can present with little evidence of widespread tuberculosis and on hematologic evaluation may appear to have idiopathic myelofibrosis or a myelodysplastic syndrome. Therefore, a careful search for granulomas in the marrow biopsy specimen, using an acid-fast stain to help identify the organism, is essential. Aplastic anemia is seen following viral illnesses such as viral hepatitis, Epstein-Barr virus infection, HIV, and rubella. Parvovirus B_{19} infection can cause an acute, reversible pure red blood cell aplasia in patients with congenital hemolytic anemias (sickle cell anemia, hereditary spherocytosis, etc). In immunocompromised patients who fail to produce neutralizing antibody to parvovirus, a chronic form of red cell aplasia can develop. The most dramatic relationship of viral infection to severe pancytopenia is the fatal aplastic anemia seen during recovery from viral hepatitis. Generally, this occurs in young males who have had an uncomplicated episode of hepatitis, and is most common in low-income populations in Asian countries. Although this anemia was originally associated with non-A and non-B hepatitis, recent studies would appear to exclude hepatitis C as the putative agent. Thus, the responsible agent and the nature of the subsequent immune process that results in marrow stem cell suppression are still unknown. (6)

5-Malignancy & Marrow Damage

Metastatic malignancies such as prostate and breast carcinoma generally produce a relatively mild anemia without changes in other cell lines. The mechanism involved is a progressive interference with the support structure of the marrow. The tumor occupies the space needed for marrow precursors, stimulates collagen growth, and cuts off normal blood supply. The resultant disorganization is frequently detectable simply by inspecting the blood smear. The appearance of nucleated red blood cells in circulation in a patient with a mild, normocytic, normochromic anemia can be a tip-off to the presence of metastatic tumor within the marrow. (6)

6-Pure Red Blood Cell Aplasia

Isolated aplasia of erythroid progenitors (producing anemia without leukopenia or thrombocytopenia) can present as a self-limited aplastic crisis or as severe irreversible marrow damage anemia. As with pancytopenia, pure red blood cell aplasia can result from exposure to a number of drugs and infections. Short periods of pure red blood cell aplasia have been reported in patients with mycoplasma and parvovirus (HPV B_{19}) infections, mumps, and viral hepatitis. Patients with congenital hemolytic anemias, especially hereditary spherocytosis and sickle cell anemia, are especially sensitive to parvovirus infection. Patients with immunosuppression, especially those infected with HIV-1, may be unable to resolve an HPV B_{19} infection, resulting in severe, persistent red cell aplasia. In all of these situations, the patient presents with the sudden appearance of anemia without pancytopenia. Inspection of a marrow aspirate shows essentially normal cellularity and morphology except for the red cell progenitor component. Normal red cell precursors are virtually absent and may be replaced by giant pronormoblasts containing nuclear inclusions. (6)

7-Diamond-Blackfan Anemia

Diamond and Blackfan described a congenital form of pure red blood cell aplasia that appears early in childhood. By 6 months of age, 80% of children are anemic; by 9 months, 90% are affected. Mildly affected familial cases may not be diagnosed until later in childhood. The typical erythropoietic profile shows a somewhat macrocytic, normochromic

anemia, reticulocytopenia, and an absence of red blood cell progenitors in a marrow with normal white blood cells and platelet production. Serum levels of erythropoietin are increased. Many children have minor physical defects including strabismus and bony abnormalities of fingers and ribs. Disruption of the ribosomal protein gene, RPS19, localized to chromosome 19q13.2, has been implicated in a quarter or more of cases, with evidence suggesting two other loci in the remainder.The nature of the red blood cell defect in Diamond-Blackfan anemia is unclear. Studies suggest that erythroid progenitors are intrinsically abnormal, responding poorly to erythropoietin or SCF, and exhibiting accelerated programmed death. Although the presence of a humoral or cellular inhibitor has not been detected, 70% or more of patients with Diamond-Blackfan anemia will respond clinically to relatively low doses of prednisone. (6)

8-Anemias Associated with a Reduced Erythropoietin Response

Anemia is common in patients with acute and chronic inflammatory disease, renal insufficiency, and hypothyroidism. In each situation, there is an apparent failure in the erythropoietin stimulation of the marrow. Serum erythropoietin levels, although not decreased below basal levels, are not appropriately increased for the severity of the anemia. Marrow cellularity and reticulocyte response are typically hypoproliferative. The importance of this class of anemias cannot be overemphasized. The clinical incidence of hypoproliferative anemias associated with acute infection or chronic inflammatory disease (the anemia of chronic disease) is far greater than that of other types of anemia. In some cases, appearance of a typical hypoproliferative anemia is the first sign of underlying disease. The pattern of the anemia can also be of considerable value in the diagnosis of the etiology and severity of the disease process. It is important, therefore, that clinicians be skilled in evaluating the patient with a hypoproliferative anemia, even when the anemia is mild. (6)

9-Iron Deficiency Anemia

Iron deficiency is a leading cause of microcytic anemia in children and adults. When iron supply to erythroid marrow is deficient, red blood cell production is impaired and new cells released into circulation are poorly hemoglobinized. The severity of the anemia and the degree of microcytosis and hypochromia generally reflect the severity and chronicity of the iron-deficiency state. The prevalence of iron deficiency in a population depends on the interaction of several factors, including the adequacy of dietary iron supply and the incidence of disease states accompanied by malabsorption or chronic blood loss. In developing countries, inadequate nutrition is a major factor and iron-deficiency is the principal cause of nutritional anemia. In Europe and the United States, chronic blood loss is more frequently responsible for the iron deficiency. Full-blown iron-deficiency anemia is easy to diagnose. The SI is very low and the TIBC high, producing a percent saturation of less than 10%. The serum ferritin level is always less than 12 ìµg/L, the sTfR level is elevated (as is the serum TfR/serum ferritin ratio), and inspection of marrow aspirate particles reveals absent iron stores and sideroblasts. Patients with severe iron deficiency also present with a moderate to severe anemia and distinctive changes in red blood cell morphology. Once the hemoglobin falls to below 10 g/dL, erythropoietin stimulation of the marrow results in the production of cells that are morphologically abnormal. Initially, the cells are microcytic without abnormalities in cell shape or hemoglobin content. However, as the anemia worsens, new red blood cells become increasingly microcytic and hypochromic. While the hemoglobin level is in the range of 9-11 g/dL, the reduction in cell size is roughly equivalent to the loss of cell hemoglobin, so that cells tend to be uniformly microcytic with little or no hypochromia. There are also modest variations in cell size (anisocytosis) and cell shape (poikilocytosis). As the hemoglobin falls below 9 g/dL, cell morphology becomes increasingly bizarre, with the appearance of many misshapen cells (poikilocytes). This situation is a sign of increasing ineffective erythropoiesis in response to high levels of erythropoietin stimulation. Finally, the presence or absence of cigar- or pencil-shaped red blood cells and target cells can help in the differential diagnosis of iron deficiency from thalassemia. Cigar cells are only seen with iron-deficiency anemia, whereas target cells are associated with thalassemia. (6)

10-Thalassemia

In addition to iron deficiency, an inherited defect in globin chain synthesis is the other leading cause of microcytic anemia in children and adults. The frequency and severity of the several types of thalassemia depend on the racial background of the population. For certain subpopulations, the incidence of a microcytic, hypochromic anemia secondary to thalassemia can exceed that due to iron deficiency anemia. (6)

11- Sickle Cell Anemia

Sickle cell anemia, the homozygous form of hemoglobin S disease, presents early in life with a severe hemolytic anemia and vasoocclusive disease involving the marrow, spleen, kidney, and central nervous system (CNS). Involved children first complain of recurrent painful crises characterized as deep-seated bone and joint pain that may or may not be associated with other intercurrent illness. When frequent, these painful episodes are devastating, and over time, patients become disabled and dependent on pain medications.(6)

12- Macrocytic Anemias

Folic acid and vitamin B^{12} deficiency are primary causes of macrocytic anemia in adults. Both vitamins are essential for normal DNA synthesis, and high turnover tissues such as marrow are especially sensitive to any deficiency state. The marrow becomes megaloblastic; marrow precursors appear much larger than normal and are unable to complete cell division. This results in ineffective erythropoiesis, release of macrocytic red blood cells into circulation, and worsening anemia. The severity of the anemia and the degree of macrocytosis depends on severity and duration of the deficient state. Prevalence of folic acid deficiency depends on the frequency of diseases associated with a decreased dietary intake of folic acid, malabsorption, or an increased requirement. Alcoholism is a common cause of folic acid deficiency in Western societies because of the poor dietary habits of the alcoholic and alcohol's interference with folate metabolism. In developing countries, tropical and nontropical sprue are more common etiologies. Vitamin B_{12} deficiency can result from a dietary deficiency, an autoimmune process directed at intrinsic factor, or any one of a number of gastrointestinal disorders that lead to vitamin B_{12} malabsorption. (6)

13- The Dysplastic and Sideroblastic Anemias

The dysplastic and sideroblastic anemias are primary stem cell disorders, many of which eventually evolve to acute leukemia. Recognition and differential diagnosis of these disorders revolves around characteristic changes in film and marrow morphology. The dysplastic anemias present with varying combinations of anemia, leukopenia, and thrombocytopenia together with macrocytosis, distorted marrow precursor maturation, and ineffective erythropoiesis. Sideroblastic anemias are defined by the distinctive appearance of ringed sideroblasts on the Prussian blue stain of the marrow. Although the incidence of these disorders is low, only 1:100,000 population, they do represent a diagnostic and therapeutic challenge.(6)

14- Refractory Anemia (RA)

RA patients present with a mild to moderately severe anemia, variable macrocytosis, mild to moderate anisocytosis and poikilocytosis, and a hypoplastic, normal, or hyperplastic erythroid marrow. Many of the features of the other dysplastic and sideroblastic disorders are not present. Less than 5% of the marrow cells are blasts and there are less than 15% ringed sideroblasts. Cytogenetic studies generally do not reveal a specific chromosomal defect. Research studies of mutations of the ras oncogene have shown point mutations in less than 10% of RA patients. These data are in contrast to the higher incidence in RAEB and CMML. Since distinctive clinical and laboratory findings are less prominent in RA, it is important to exclude reversible marrow damage anemia or pancytopenia. Any history of exposure to radiation, drugs, or toxic chemicals is important. If the patient is young, has a significant exposure history, and demonstrates a somewhat hypoplastic marrow without morphologic or cytogenetic abnormalities, marrow damage is a good possibility. Of course, these same exposures can incite a preleukemic condition, presenting as RA or myelodysplasia. Similar to idiopathic aplastic anemia, there is now evidence that T-cell mediated suppression of marrow progenitors is an important component in the clinical picture in RA. However, the CD8 T-cell expansion is usually a secondary polyclonal response to one or more progenitor cell mutations, not a primary autoimmune disorder. (6)

15- Blood Loss Anemia

Acute blood loss has a direct impact on the integrity of the blood volume and oxygen supply to tissues. Sudden, severe hemorrhage can induce hypovolemic shock, cardiovascular failure, and death. When blood loss is more gradual, the hemoglobin level can fall to a point where oxygen delivery to vital organs is compromised. Chronic blood loss will deplete iron stores and produce an iron deficiency anemia. Therefore, diagnosis and management of a blood loss anemia must take into account the reason behind the loss, the rate and amount of blood loss, and the capacity of the patient to compensate for both volume losses and anemia.(6)

16- MEGALOBLASTIC ANEMIA

The common feature of all megaloblastic anemias is a defect in DNA synthesis that affects rapidly dividing cells in the bone marrow. All conditions that give rise to megaloblastic changes share in common a disparity in the rate of synthesis or availability of the four immediate precursors of DNA: the deoxyribonucleoside triphosphates (dNTPs): dA(adenine)TP and Dg (guanine)TP (purines), dT(thymine)TP and dC(cytosine)TP (pyrimidines).In deficiencies of either folate or cobalamin, there is failure to convert deoxyuridine monophosphate (dUMP) to deoxythymidine monophosphate (dTMP), the precursor of dTTP.This is because folate is needed as the coenzyme 5,10-methylene-THF polyglutamate for conversion of dUMP to dTMP; the availability of 5,10-methylene-THF is reduced in either cobalamin or folate deficiency.An alternative theory for megaloblastic anemia in cobalamin or folate deficiency is misincorporation of uracil into DNA because of a buildup of deoxyuridine triphosphate (dUTP) at the DNA replication fork as a consequence of the block in conversion of dUMP to dTMP.(14)

Many symptomless patients are detected through the finding of a raised mean corpuscular volume (MCV) on a routine blood count. The main clinical features in more severe cases are those of anemia. Anorexia is usually marked and there may be weight loss, diarrhea, or constipation. Glossitis, angular cheilosis, a mild fever in the more severely anemic patients, jaundice (unconjugated), and reversible melanin skin hyperpigmentation may also occur with deficiency of

either folate or cobalamin. Thrombocytopenia sometimes leads to bruising, and this may be aggravated by vitamin C deficiency or alcohol in malnourished patients. The anemia and low leukocyte count may predispose to infections, particularly of the respiratory or urinary tracts. Cobalamin deficiency has also been associated with impaired bactericidal function of phagocytes.(14)

Iron status and hemoglobin level

Iron deficiency is one of the leading risk factors for disability and death worldwide, affecting an estimated 2 billion people. Nutritional iron deficiency arises when physiological requirements cannot be met by iron absorption from diet. Dietary iron bioavailability is low in populations consuming monotonous plant-based diets. The high prevalence of iron deficiency in the developing world has substantial health and economic costs, including poor pregnancy outcome, impaired school performance, and decreased productivity. Recent studies have reported how the body regulates iron absorption and metabolism in response to changing iron status by upregulation or downregulation of key intestinal and hepatic proteins. Targeted iron supplementation, iron fortification of foods, or both, can control iron deficiency in populations. Although technical challenges limit the amount of bioavailable iron compounds that can be used in food fortification, studies show that iron fortification can be an effective strategy against nutritional iron deficiency. Specific laboratory measures of iron status should be used to assess the need for fortification and to monitor these interventions. Selective plant breeding and genetic engineering are promising new approaches to improve dietary iron nutritional quality. Human beings are unable to excrete iron actively, so its concentration in the body must be regulated at the site of iron absorption in the proximal small intestine. Diets contain both haem and non-haem (inorganic) iron; each form has specific transporters. A putative intestinal haem iron transporter (HCP1) has been identified, which is upregulated by hypoxia and iron deficiency, and might also transport folate.(15,16,17)

Estimates of occurrence of iron deficiency in industrialised countries are usually derived from nationally representative samples with specific indicators of iron status. By contrast, estimates from developing countries are often based only on haemoglobin measurements from restricted regions or target populations, and should be interpreted with caution. Prevalence estimates of iron deficiency anaemia (ie, iron deficiency and low haemoglobin) based on haemoglobin alone are overestimations because they fail to account for other causes of anaemia, such as nutritional deficiencies (eg, vitamin A deficiency), infectious disorders (particularly malaria, HIV disease, and tuberculosis), haemoglobinopathies, and ethnic differences in normal hemoglobin distributions. For example, in Côte d'Ivoire, iron deficiency was detected with specific indicators of iron status in about 50% of anaemic women and children.4 Even in industrialized countries, haemoglobin alone, which is used to detect iron deficiency anaemia, has poor sensitivity and specificity. Anaemia is regarded as a public health problem when the frequency of low haemoglobin values is more than 5% in the population. (18,19,20,21)

Nutritional iron deficiency arises when physiological requirements cannot be met by iron absorption from diet. Dietary iron bioavailability is low in populations consuming monotonous plant-based diets with little meat. In meat, 30–70% of iron is haem iron, of which 15–35% is absorbed. However, in plant-based diets in developing countries most dietary iron is non-haem iron, and its absorption is often less than 10%.The absorption of non-haem iron is increased by meat and ascorbic acid, but inhibited by phytates, polyphenols, and calcium. Because iron is present in many foods, and its intake is directly related to energy intake, the risk of deficiency is highest when iron requirements are greater than energy needs. situation happens in infants and young children, adolescents, and in menstruating and pregnant women. During infancy, rapid growth exhausts iron stores accumulated during gestation and often results in deficiency, if iron-fortified formula or weaning foods are not supplied. Excessive early consumption of cows' milk can also contribute to early-childhood iron deficiency. In a study of infants aged 6 months, frequency of iron deficiency anaemia was lowest in infants fed iron-fortified formula (about 1%) but occurred in 15% of breastfed infants, and 20% of infants fed cows' milk or non-fortified formula. In the USA, the introduction of iron-fortified weaning foods in the 1970s was associated with a reduction in the frequency of iron deficiency anaemia in infants and preschool children.36 In many developing countries, plant-based weaning foods are rarely fortified with iron, and the frequency of anaemia exceeds 50% in children younger than 4 years.6 In schoolage children, iron status typically improves as growth slows and diets become more varied.(22,23,24)

The frequency of iron deficiency begins to rise again, mainly in female individuals, during adolescence, when menstrual iron losses are superimposed with needs for rapid growth. Because a 1 mL loss of blood translates into a 0·5 mg loss of iron, heavy menstrual blood loss (>80 mL per month in about 10% of women) sharply increases the risk for iron deficiency. Other risk factors for iron deficiency in young women are high parity, use of an intrauterine device, and vegetarian diets. During pregnancy, iron requirements increase three-fold because of expansion of maternal red-cell mass and growth of the fetal–placental unit. The net iron requirement during pregnancy is about 1 g (equal to that contained in about 4 units of blood), most of which is

needed in the last trimesters. During lactation, because only about 0·25 mg of iron per day is excreted into breastmilk and most women are amenorrhoeic, iron requirement is low - only half of that of non-pregnant, non-lactating women.(25.26)

Increased blood loss from gastrointestinal parasites aggravates dietary deficiencies in many developing countries. Infections with *Trichuris trichiura* (whipworm) and *Necator americanus* (hookworm) cause intestinal blood loss and are important causes of iron deficiency anaemia. Revised estimates indicate that hookworms afflict more than 700 million people in tropical and subtropical regions. In endemic areas, hookworm infection is estimated to account for 35% of iron deficiency anaemia and 73% of its severe form, and deworming decreases the occurrence of anaemia. In a trial in Nepal, women who were given albendazole in the second trimester of pregnancy had a lower rate of severe anaemia during the third trimester, gave birth to infants of greater weight, and mortality of infants at 6 months decreased.48 Iron deficiency anaemia can also be caused by impaired iron absorption. Gastric acid is needed to maintain ferric iron forms in solution, and achlorhydria might be a substantial cause of iron deficiency, mainly in elderly people, in whom atrophic gastritis is common. Other common causes of lowered iron absorption and iron deficiency are mucosal atrophy in coeliac disease and, possibly, *Helicobacter pylori* infection, although a study of iron absorption showed no effect of *H pylori*.(27.28)

Industrialized countries

Although little direct evidence exists, the reduction in occurrence of iron deficiency in young children in industrialised countries has been attributed to iron fortification of infant formulas and weaning foods. Iron-fortified foods distributed through the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) have probably contributed to the fall of iron deficiency in underprivileged preschool children in the USA.104 At present, the low frequency of iron deficiency anaemia in adolescent and young women in the USA might be at least partly due to consumption of iron-fortified wheat flour, although other factors, including open-market fortification of food products, and use of vitamin and mineral supplements, have also had a role. More-specific evidence is provided by retrospective studies from Sweden that reported decrease of iron intake105 and increase of iron deficiency in young women106 since iron fortification of wheat flour was discontinued in 1994. By contrast, findings from Denmark, where iron fortification of wheat flour was discontinued in 1987, suggest no change in the frequency of iron deficiency in adults older than 40 years,107,108 but the data might have been confounded by the effects of increasing bodyweight, alcohol consumption, or both, contributing to increased values or serum ferritin.(29)

Developing countries

Universal iron fortification is generally recommended for countries where the risk of developing iron deficiency is high for all groups other than adult men and postmenopausal women. Up to now, no clear indication of efficacy of iron fortification in developing countries existed, because of several factors (panel 1). However, recent studies have shown convincingly that iron fortification can be effective. The iron compound and type of fortification should be chosen on the basis of the fortification vehicle, iron requirements of the target population, and iron bioavailability of the local diet (panel 2). Efficacy should be monitored with measurements of serum ferritin and, when possible, serum transferrin receptor, in addition to haemoglobin. Iron fortification efforts have been accelerated by the Global Alliance for Improved Nutrition (GAIN), an alliance of United Nation agencies, national governments, development agencies, and the private sector, funded mainly by the Bill & Melinda Gates Foundation. GAIN has awarded $38 million in grants to food fortification programmes in 14 countries, including iron fortification of soy sauce in China, fish sauce in Vietnam, and wheat and maize flour in South Africa. The foods most often used for mass fortification are the staple cereal flours. Iron is only poorly absorbed from high-extraction flours because of the presence of phytate and other inhibitory factors. Dried ferrous sulphate can be used in wheat flour that is consumed shortly after it is milled, but in most developing countries flour is stored for longer periods. Thus, elemental iron powders, which are less reactive, are widely used, despite their lower bioavailability. Findings from an efficacy trial in Thailand suggest that two forms of elemental iron, electrolytic iron and hydrogen-reduced iron, might be useful for fortification, but their bioavailability is only 50–79% that of ferrous sulphate. Two other forms of reduced iron, carbon-monoxide-reduced and atomized iron, are poorly absorbed and unlikely to be useful for food fortification. A trial in Sri Lanka failed to show a reduction in anaemia occurrence after 2 years of fortification of low-extraction wheat flour with either electrolytic or reduced iron, but fortification was probably too low.117 Wheat flour fortification with ferrous sulphate in Chile at 30 mg/kg has probably contributed to a strong decrease in iron deficiency.118 Fortification of maize flour in South Africa with ferrous fumarate has shown effectiveness in lowering anaemia, and improving iron status and motor development of infants in poor settings.119 Clear guide -lines on wheat flour fortification have recently been published.(29)

Studies in Saudi Arabia concentrate only on the population of young children and pregnant females or girls. Studies on

the whole school student population is lacking. The objectives of this study were to identify the nutritional habits and the prevalence of anaemia among school students in Jeddah, as well as to recognize the students' awareness of their anaemic nutritional status. Data were collected from a sample of Saudi school children in Jeddah City from 42 boys' and 42 girls' schools during the month of April 2000. Data collection was done by an in-person interview to collect socio-demographic factors, nutritional habits, weight and height. Haemoglobin was measured in a sample of 800 students selected at random from both genders and different age groups. Anaemia was defined according to the new WHO cut-off levels for haemoglobin as: blood haemoglobin <11.5 g/dl for the 5–11 years boys and girls;<12.0 g/dl for 12–14 years boys and girls; <12.0 g/dl for 15+ girls and <13.0 g/dl for 15+ years boys. Proportion and 95% confidence intervals (CI) were calculated and significance was considered when the 95% CI did not overlap. Anaemia was reported among 20.5% of school students. Anaemia was more prevalent among students of at least 12 years as compared to the younger age group. Also, anaemia was more marked among governmental school attendees and those born to low educated mothers. Menstruating girls were at around double the risk of being naemic than non-menstruating girls. Anaemia was associated with negative impact on school performance and was more marked among those who failed their exams as compared to students with excellent results. Skipping breakfast was reported by 14.9% of students and this habit did not differ by age, sex, body mass index or social class. Skipping breakfast was more marked among students with poor school performance as compared to those with very good or excellent results. Only 34.1% of anaemic school students were aware of being anaemic. Awareness was nearly equal in all age groups and social classes but girls were more aware of their anaemic status than boys. Iron deficiency anaemia appears to be prevalent among school students. At age 12 years and over, low social class and menstruating girls constitute the high-risk groups. Screening is recommended for high-risk groups and school health programs are crucial to improve students' nutritional habits, knowledge and awareness.[30]

Literature review based on objectives

Pregnancy outcome is influenced by many factors some of which include culture, environment, socioeconomic status and access to medical care. The hematological profile of pregnant women also has an impact on pregnancy and the outcome of the pregnancy. The most common hematological indices are the indicators of hemoglobin concentration. Low hemoglobin in the blood (anemia) is widely identified as a hematologic abnormality and it is associated with adverse pregnancy outcome. Anemia in women is variously defined with two most common being, either as a hemoglobin concentration less than 11.0 g/dL or less than the 5th percentile of the distribution, and is based on sex, age and stage of pregnancy (among pregnant women). In a cohort study conducted by Harrison on pregnant women in Southern Nigeria and those from South India in 1996, he found that mortality rate was proportional to the period of their pregnancy. Those at the late stage of pregnancy were vulnerable to complaints and consequently death might follow. Anemia contributes to low birth weight and miscarriages and it is also a primary cause of low immunity of both the mother and the child, which makes them vulnerable to several infections.[31]

The significance of low hemoglobin values during pregnancy for the health of the fetus has been a source of continuing controversy. Because around half of the world's women experience anemia during pregnancy, the impact of pregnancy anemia on fetal development is a question of great public health importance. Because of its high prevalence, if pregnancy anemia puts the fetus at even a modest risk of low birth weight, then a significant proportion of the low birth weight in the world could be prevented through anemia prevention. Preventing low birth weight will save child lives, because low birth weight is one of the strongest predictors of infant mortality. This question would be answered best by a randomized trial of iron supplementation. However, few trials have been conducted because it is unusual to find settings where the standard of antenatal care does not include iron supplementation to women who are known to have anemia. Those trials that have been conducted have been too small to generate definitive conclusions, and most have been conducted in populations where iron-deficiency anemia is rare. Several prospective studies have reported an association between pregnancy anemia and low birth weight (5-10), but a causal relation has not been established. These studies have suffered from several problems. First, in most populations, women who are anemic also have other characteristics that cause low birth weight. In the United States, for example, anemic women are more likely to be African American and poor. It is very difficult to control adequately for these differences between anemic and non-anemic women, because our measurement variables do not capture all that it means to be black and poor in the United States. Second, plasma volume expansion and lowered hemoglobin concentration are a physiologic response to pregnancy.[32]

Thus, women with mild "pregnancy anemia" may be a combination of those with iron deficiency (possibly associated with poor pregnancy outcome), and healthy women with a large plasma volume expansion (associated with good pregnancy outcome. Third, investigators of this question have measured hemoglobin at different times in pregnancy. In mid- pregnancy, hemoglobin concentrations drop as plasma volume expansion outpaces expansion of the red cell mass, while in late pregnancy, plasma volume

ceases to expand and hemoglobin concentrations rise if iron stores are adequate. These physiologic processes drive the hemoglobin concentration in different directions at different stages of pregnancy, and are also related to birth outcome. Thus, the shape of the relation of hemoglobin concentration to birth outcome will probably depend on when the hemoglobin is measured, although this has not been fully described. A spurious relation between anemia and preterm birth is created when hematocrit values at delivery are used, because of the physiologic rise in hematocrit in the late third trimester. Biologic interpretation of associations is especially problematic when investigators relate birth outcome to the lowest measured pregnancy hemoglobin value, which might occur at different times in pregnancy in different women and thus reflect different processes. Both plasma volume and red cell mass expand in pregnancy. Because the expansion in plasma volume is greater, the net result is that hemoglobin is diluted. In women with adequate iron nutrition, hemoglobin concentration starts to fall during the early part of the first trimester, reaches its lowest point near the end of the second trimester, and then gradually rises during the third trimester.1 Trimester-specific adjustments have been developed.(32)

Hemoglobin concentration increases in smokers because the inhaled carbon monoxide results in increased carboxyhemoglobin, which has no oxygen-carrying capacity. To compensate, hemoglobin levels increase. To take into account the resulting elevated hemoglobin concentration, the U.S. Centers for Disease Control and Prevention developed a smoking-specific hemoglobin adjustment to define anemia in smokers.6 Table 4 shows the values to add to normal hemoglobin cutoffs to define anemia in smokers. Alternatively, these values can be subtracted from observed hemoglobin values.(33)

In Saudi Arabia, Jeddah, a study was designed to determine relationship between iron deficiency anemia and smoking. Cigarette smoking causes elevation of hemoglobin and hematocrit which is explained by elevation of carbon monoxide a major component of cigarette smoke which reduces oxygen tension in the body. This reduction increases production, maturity and release of erythrocytes from blood forming organs and thus elevates hemoglobin and hematocrit levels while serum ferritin may be low (Van Liere and Stickney, 1963). In this study, 10.4% of the female students were tobacco smokers which include 6.3% ID and 4.1% IDA. However, the correlation between tobacco smoking, ID and IDA did not showed statically differences.(34)

Obesity is associated with low-serum iron concentrations. The inverse relationship between iron status and adiposity was first reported in 1962, when Wenzel et al unexpectedly found a significantly lower mean serum iron concentration in obese compared with non-obese adolescents. Most subsequent studies in pediatric and adult samples have shown similar results The etiology of the hypoferremia of obesity is uncertain. Among the proposed causes are deficient iron intake from an iron poor diet, and deficient iron stores owing to greater iron requirements in obese adults because of their larger blood volume. Recently, fat mass was described as a significant negative predictor of serum iron and this hypoferremia seemed not to be explained by differences in iron intake Adipose tissue is a very active endocrine organ secreting numerous hormones and cytokines associated with important systemic effects on different metabolic processes.(4)

Recently, hepcidin expression in adipose tissue has been described and shown to be increased in patients with severe obesity. Hepcidin is a small, cysteine-richncationic peptide produced by hepatocytes, secreted into plasma, and excreted in urine. Hepcidin expression is induced by iron stores and inflammation and is suppressed by hypoxia and anemia. Hepcidin is proposed to be a key regulator of iron metabolism and its discovery has changed our understanding of the pathophysiology of iron disorders. Adipose tissue of obese patients produced increased amount of proinflammatory cytokines contributing to the development of a low-grade systemic inflammation in these patients. At present, regulatory pathways that are generally thought to control liver hepcidin production include: (i) iron store-related regulation (ii) erythropoietic activity driven regulation, and (iii) inflammation related regulation. All are found to interact with liver cells to initiate the production of sufficient hepcidin for correct maintenance of iron homeostasis. The aim of this study was to assess the effect of obesity on hepcidin serum levels and its relation to treatment outcome of iron deficiency anemia in children.(4)

Obesity is associated with iron depletion and elevated levels of serum hepcidin. Further, their reduced iron status does not appear to be due to inflammation-induced iron sequestration within the liver, visceral, or subcutaneous adipose tissue. Our findings suggest obese women have a hepcidin-induced ID in which dietary iron is inefficiently absorbed by the body, similar to the recently described genetic condition iron-refractory iron deficiency anemia and corroborated by the decreased dietary iron absorption observed in obese, mildly iron deficient, women and children. Implications of these findings are significant and could impact iron supplementation and metabolism research in obese populations. Further studies with greater number of racially diverse participants and exploration of the tissue-specific interaction between hepcidin and ferroportin-1 at key iron acquisition and storage sites and quantification of tissue iron content in obese populations are warranted.(35)

Chapter 4

Method and Material

Study design:
This study is a facility based one that had made in Atiafa Primary Health Care Center. It is a descriptive, case study. Also, it is a quantitative research which includes quantitative and qualitative data.

Study population:
Study depended on taking adults (male and female) sample whose their age vary between 20-50 years old in Atiafa Primary Health Care Center, with the excluding of any group who takes medications or patients who have chronic diseases.

Study area:
Atiafa Primary Health Care Center is located in Atiafa district. It has a catchment area that was divided into 6 squares. The catchment area surrounded by Prince Salman street(Al Dobadh district) from west , king Saud street (Prince Mashal district) from east , Prince Salman street (Armed Forces) from north and king Abdulaziz street(Al kaldia district) from south. The number of population is 7264 (Saudi: 788- Non Saudi: 206) and the number of singles is 43 while the number of child less than one year is 137 and the number of child less than 5 years is 936,finally, the number of women in reproductive age is 1882. Most of people are public servant or officers and some of them workers. There are stores in front of it. There are government centers, schools and mosques. Families are usually small to moderate, this means it consists approximately from 4-7members.In most families they consist from parent and 2-5 children. Hygiene is provided in the area and there are no industrial factors there. The only source of pollution are cars and smokers. Another important thing is that there is no infection source as; sinks in the area.

Method of data collection:
Data Collection was from Atiafa Primary Health Care Center by structured interview which includes questionnaire and check list. Content analysis also was used from conditions that already diagnosed and available in laboratory and patients' files in registration system. Observation also was used in data collection.

***Sample selection*:**
A total of 90 adults (male and female) *between the age of 20-50 years old were selected* from Atiafa Primary Health Care Center in Najran city. *With the excluding of any groups who take medications or patients who have chronic diseases. Purposive, selective, Convenience were used to select the sample.*

Method of data analysis:
Statistical Package for Social Sciences program (SPSS) Version 9 was used in data analysis.

Chapter 5

Results

Data for hemoglobin concentration for male and female participants is shown in Table 1,5,6. These parameters were significantly higher in male group compared to female group. Acceptable value for hemoglobin for adult males are 13.5-18 g/dL; and for adult female are 12.5-16 g/dL[36]. Results of these measures for male participants were within these acceptable values (Table 5) whereas for female participants were lower than the acceptable values(Table 6). Also, hemoglobin value for male participants were within the normal range of hematological values for adult Saudis reported by Scott (1982). For smokers and non-smokers, hemoglobin values were also within the previous normal ranges (Table 5)(figure I,II) but the means of hemoglobin was significantly higher in smokers compared to non-smokers, (Table 2). For pregnant women, hemoglobin values were lower than the acceptable values (Table 4,6)(figure III,IV). No significant different hemoglobin level in obese adults as compared with non-obese adults (Table 3,7). The cutoff values for determining anemia for hemoglobin is <13.5 g/dL and <12.0 g/dL for adult male and female, respectively [36]. The percentage of participants with values below these cutoff values is presented in Table 1. However, anemia as determined by hemoglobin concentration and based on the previous cutoff values were found in nearly 50.1% of female participants. The previous findings were less notable among male participants.

Table 1 Mean of hemoglobin (± SD), hematocrit of males and females.

	Male(n=42)	Female(n=48)
Hemoglobin (g/dL)	15.078±1.375	12.±1.442
Hematocrit (%)	46.4	39.2
Percentage of anemia	2.3%	50.1%

Table 2 Mean of hemoglobin (± SD) and hematocrit concentration for male smokers and non-smokers.

	Smokers(n=18)	Non-smokers (n=24)
Hemoglobin (g/dL)	16.127±0.915	14.26±1.112
Hematocrit (%)	48.4	44.3

Table 3 Mean of hemoglobin (± SD) and hematocrit concentration for males (obese and non- obese people).

	Obese (n=10)	Non- obese (n=15)
Hemoglobin (g/dL)	14.08±0.862	14.44±1.239
Hematocrit (%)	44.4	45.1

Table 4 Mean of hemoglobin (± SD) and hematocrit concentration for pregnant and non-pregnant women.

	Pregnant(n=22)	Non-pregnant(n=26)
Hemoglobin (g/dL)	10.45±1.201	12.1±1.267
Hematocrit (%)	35.6	39.2

Table 5 Hemoglobin level in males (g/dL)

Class HB	**Frequency**	
	Smoking (g/dL)	**Non- Smoking(g/dL)**
11-12	0	1
12-13	0	0
13-14	0	9
14-15	3	5
15-16	4	9
16-17	6	0
17-18	5	0
Total	**18**	**24**

Table 6 Hemoglobin level in female (g/dL)		
Class HB	**Frequency**	
	Pregnant women	**Non-pregnant women**
7-8	1	0
8-9	1	0
9-10	5	4
10-11	6	10
11-12	6	4
12-13	2	4
13-14	1	4
14-15	0	0
Total	**22**	**26**

Table 7 Hemoglobin level in males for obese and non- obese people. (g/dL)		
Class HB	**Frequency**	
	Obese adults	**Non- obese adults**
11-12	0	1
12-13	0	0
13-14	5	4
14-15	2	2
15-16	3	7
Total	10	14

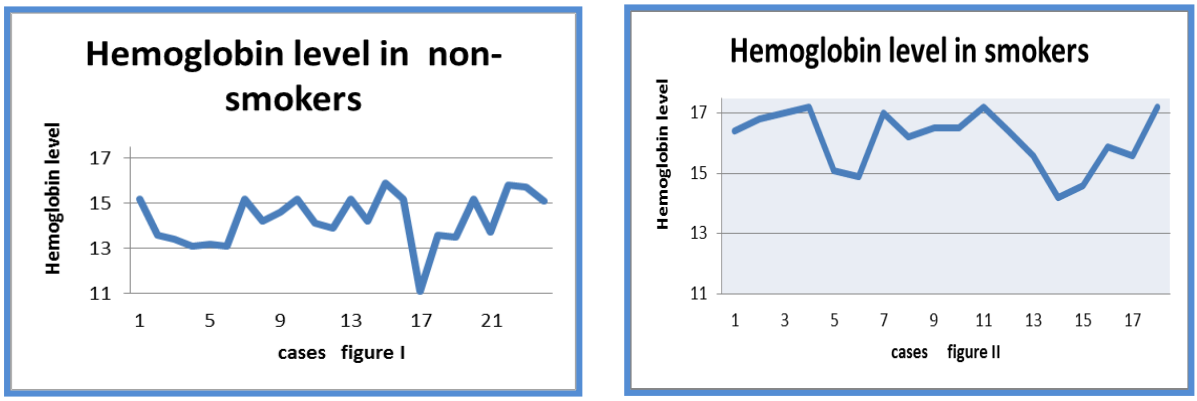
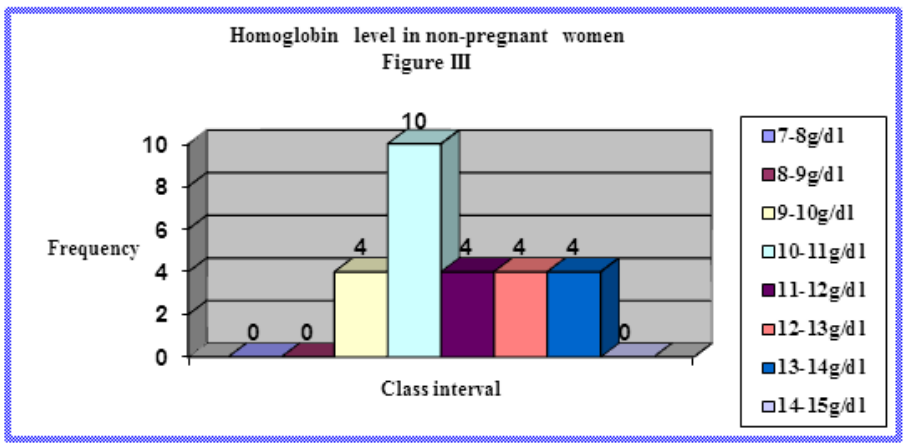
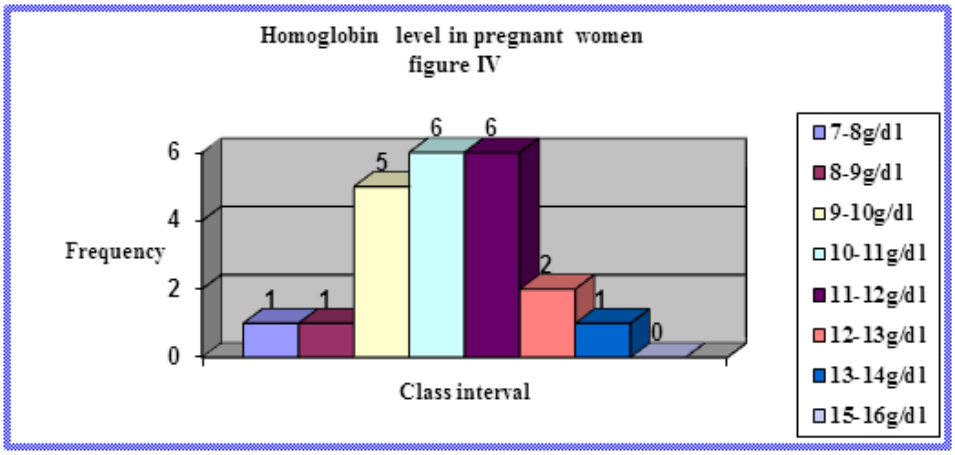


Figure (I.II) These curves show hemoglobin level in males (smoker, non-smoker).



(III) Histogram show hemoglobin level in non-pregnant women .The height of bar represent the frequency of each class interval.



(IV) Histogram show hemoglobin level in pregnant women .The height of bar represent the frequency of each class interval.

Chapter 6

Discussion

Anemia as determined by hemoglobin value was found in nearly 50.1% of female and 2.3% of male participants (Table 1). This is because hemoglobin value is an indicator of late stage of anemia[36]. For the male group, hematological parameters for adult males. Show anemia does not find in these groups. This is in agreement with several reports in other countries[37]. My results are not in agreement with results of some reports that found 38% of adult males living in Saudi Arabia, nursing home anemic based on their hemoglobin concentration values. Reason for this difference is the difference in sampling. This study recruited adult males by Purposive, selective, Convenience from Primary Health Care Center where as other studies recruited males from nursing homes. Subjects living in nursing homes are more likely to be undernourished compared to subjects living in ordinary homes. Among male participants and as expected, smokers compared to non-smokers had significantly higher mean hemoglobin value, which is in agreement with previous reports[38]. The elevation of hemoglobin by smoking is explained by elevation of carbon monoxide-a major component of cigarette smoke-which reduces oxygen tension in the body. This reduction increases production, maturity and release of erythrocytes from blood forming organs and thus elevates hemoglobin and hematocrit levels [39]. Cigarette smoking is prevalent among adult males as found in this study (42.85%) and other previous studies; 21.1% (Jarallah *et al*., 1999) and 34.4% (Siddiquie *et al*., 2001). Although this study found significant differences in hematological parameters between smokers and non-smokers, but they both were within normal ranges and not anemic. Among pregnant females group, this study found high prevalence of anemia as determined by hemoglobin level. The previous studies suggested that pregnancy is the major factor of anemia, especially Iron Deficiency Anemia(IDA).This is due to increase demand of nutritional elements (iron,B_{12},folic acid), inadequate nutrition ,and also high consumption of beverages that contain polyphenols-such as tea and coca-which could inhibit the absorption of non-heme iron. Fortification of some foods such as salts and juices in combination with additional intakes of iron from supplements and some changes in dietary consumption patterns can eradicated the anemia during pregnancy. This can be done by increasing the nutritional education and awareness among population as well as by governmental acts that makes fortification of some foods mandatory. In this study, hemoglobin level revealed that no significant difference in obese adults as compared with non-obese adults. This is not in agreement with several reports in other countries that found the obesity increased hepcidin levels and was associated with diminished iron absorption and leads to nutritional anemia. Reason for this difference is the difference in sampling. This study recruited mild obese people (BMI<35) whereas other studies recruited pathological obese people (BMI>40).

Chapter 7

Conclusion

The results of this study showed that anemia as measured by hemoglobin level was not found among adult males, both cigarette smokers and non-smokers, in a sample that has taken from Atiafa Primary Health Care Center in Najran Area, Saudi Arabia. In contrary, the anemia was prevalent among adult females, pregnant and non-pregnant women in a sample that has taken from Atiafa Primary Health Care Center in Najran Area, Saudi Arabia. These findings raise the need for action to eradicate anemia among females. Increasing public nutritional awareness and food fortification are examples of this action.

Recommendations

1. Estimating for hemoglobin level in high risk groups should be considered in routine examination annually in Primary Health Care Center by special staff to avoid a lot of complications.
2. Primary physician education (role play, group discussion, lectures) is needed in Primary Health Care Center by health staff to ensure a greater awareness of anemia and the testing needed to establish diagnosis as well as underlying causes.
3. Nutrition programs for pregnant women should be applied during antenatal care through giving appropriated, healthy food list that provide needed nutrition in Primary Health Care Center by special nutritionists to avoid a lot of complications.

Educational programs to improve public awareness of this problem and its causes. Nutrition education programs should be conducted in Primary Health Care Center especially for the women of child bearing age to advocate healthy dietary habits. Future research is needed to evaluate hemoglobin level in Najran city, Saudi Arabia.

Annexes

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Saudi Arabia kingdom

Najran University

College of Medicine

Name ……Age……..

Resident …….

Education level……

Occupation …….

Gender ☐ male ☐female

BMI= ☐ height= Weight=

☐ non obese ☐obese (moderate) ☐obese severe

Smoking ☐smoker ☐ non-smoker

Yes pregnancy ☐ on

First trimester	Second trimester	Third trimester

Hemoglobin level (g/dl)…….....…….

Hematocrit (%).....

Chronic diseases: …….

Medications: ……

This paper filled by ……