Chapter one
Introduction and Literature review

1. Introduction:-

1.1 Pregnancy:-

Pregnancy is the most important physiological state for human kind since as it assure continuation of the species, pregnancy produce major physical alteration in the mother , support the fetus as it develop the capability of independents, existence, and introduce a new organ in the form of the placenta that provides the link between the fetus and her mother (Hylten, 1985).

The mean duration of pregnancy is 38 weeks from the time of ovulation to birth. Pregnancy can be difficult time for the mother because profound adaptations occur in several body systems. Not only are there anatomical changes, but striking changes in her metabolism and physiology occur to support the pregnancy and prepare her body for delivery and lactation (Marieb and Hoehn, 2013).

1.1.1 Physiological changes during pregnancy:-

Maternal physiological changes in pregnancy are the normal adaptation that a woman undergoes during pregnancy to better accommodate the embryo or fetus. These changes such as; cardiovascular, hematologic, metabolic, renal and respiratory changes that became very important in the event of complications (Milman *et al.*, 2000).

1.1.1.1 Hematological changes during pregnancy:-

Total blood volume increases by 40% above non pregnant levels; plasma volume rises from 6 weeks gestation and stabilizes by 32-34 weeks, RBC mass increases early in the second trimester to 20-35% above non pregnant levels by term (Sarris *et al.*, 2009).

The disproportionate rise in plasma volume compared with the RBC mass result in haemodilution and decreased hemoglobin and hematocrit count. There is a physiological fall in Hb. HCT rises from the second to third trimester (Sarris *et al.*, 2009).

The plasma volume rises and the RBC mass and number of RBCs increases, the result is a fall in hematocrit, this decline in HCT is called (physiological anemia) or (dilutional anemia) of pregnancy. During pregnancy oxygen-carring capacity is higher than in the non-pregnant state (Riikonen *et al.*, 1994).

In Sudan it was found significant decrease in RBCs count, Hb, PCV, MCV, MCH and MCHC and significant increase in TWBCs, in pregnant women when compared with non-pregnant

The prevalence of anemia in different area of the Sudan was determined in New Halfa was 62.6% in 744 pregnant women(Adam *et al.*, 2005). In Wad Medani 52.5% in 200 pregnant women (Bushra *et al.*, 2010). And in Khartoum was found 33.8% in 100 pregnant women(Farah, 2012).

1.2 Literature review

1.2.1 Blood:-

Blood is vital mixture of cells and liquid pumped by the heart through arteries and veins. It reaches all of the cells in the body, bringing them oxygen and nutrient and taking away carbon dioxide and other waste products (Mehta and Hoffbrand, 2014).

1.2.1.1 Blood constituents:-

Blood is made up of many parts or components, such as red blood cell, white blood cell, platelets, plasma, clotting factors and small proteins. Blood account for 8% of the human body weight. The average adult has a blood volume of roughly 5 liters, composed of plasma and several kinds of cells, these formed element of the blood are erythrocytes (red blood cells, RBCS) haven't nucleus and filled by hemoglobin (composed of iron and protein called globins), leucocytes (white blood cells, WBCS) and thrombocytes (platelets). By volume the red blood cells constitute about 45% of whole blood, the plasma about 54.3%, and white cells about 0.7% (Mehta and Hoffbrand, 2014).

1.2.1.2 Blood disorders:-

Blood disorders can affect any one of the component of the blood; but the main affected on the cells of blood such as anemia and polycythemia (RBC disease); leukemia and inflammations (WBC disease); the platelets defect like (thrombocytopenia and thrombocytosis). Also affect the liquid portion of the blood (plasma) relative polycythemia due to loss of the plasma (Wintrobe *et al.*, 1942).

1.2.1.2.1 Anemia:-

Anemia is the state in which the hemoglobin concentration in the blood is below normal (i.e. 13.5g/dl in adult male and 11.5g/dl in adult female) (Woolf, 1998).

Anemia is functionally defined as an insufficient RBC mass to adequately deliver oxygen to peripheral tissue, for practical purposes, any of these concentration measurement are used to establish the presence of anemia. Most reference considered Hb concentration 14g/dl and 12g/dl as the lower limits or normal in adult men and women respectively. The mean normal values and the lower limits or normal range depend on the age and sex of the subjects (Wintrobe *et al.*, 1942).

1.2.1.2.2 Classification of anemia:-

1\ Kinetic:-

Red cells normally remain fairly constant in number suggesting that cell production is equal to cell destruction. Consequently, if cell numbers decline this must be due to either:

- A decrease in the production of red cells.
- An increase in the destruction, loss, “pooling or sequestration of red blood cells.

2\ Morphological:-

The size and hemoglobin content of the red cells are characteristic and useful diagnostic guide. Thus, if red cell numbers are decreased in relation to hemoglobin content and red cell mass, then the red cells will be larger than normal (macrocytic anemia). If hemoglobin and red cell mass are decreased in relation to the number of red cells, the red cells will

be smaller than normal and contain less hemoglobin (microcytic hypochromic anemia). If red cell size is unchanged, the anemia is termed (normocytic), and if the hemoglobin concentration of each cell is normal the additional term normochromic is applied (Woolf, 1998).

(I) Relative anemia:-

Is characterizes by a normal total red cell mass, such as a hematologic disorder but rather as disturbance in the regulation of the plasma volume (Thomas *et al.*, 1977).

(II) Absolute anemia:-

Absolute anemias are characterized by decreased red cell mass. The classification of the absolute anemia is difficult, since it raise take in to account kinetic, initially, all anemias should be divided in to anemia caused by decrease production and anemia caused by increased distraction of red cells. This differentiate is to a great extent based on the reticulocyte count subsequent diagnostic break down can be based on either morphologic or path-physiologic criteria (Thomas *et al.*, 1977).

1.2.1.2.3 Nutritional anemia:-

Anemia is one of the most common nutritional deficiency disorders in the world. Causes are due to deficiency of nutritional substances and it is need for erythropoiesis like the metals, protein, and vitamins (iron, folate vitB12, vitB6, vitC and copper) such as IDA, and megaloblastic anemia so important types (WHO, 1997).

Megaloblastic anemia resulting from nutritional causes is usually due to folate deficiency (Woolf, 1998).

1.2.2 Diagnostic method and investigation of anemia:-

A full blood count and film should be taken. Hb, HCT and RBCs are reduced.

1.2.3 Complete Blood Count (CBC):-

The complete blood count (CBC) is one of the most commonly blood tests, A complete blood count (CBC) gives important information about the kind and number of cells in the blood. A CBC helps the physician to check any symptom, such as weakness, fatigue or bruising, and also help to diagnose condition such as anemia, infection, and many other disorders, (CBC) used to measure overall health (Gruber, 1998).

A Complete Blood Count assesses all components of the blood (red blood cells, white blood cells and platelets). An abnormally high or low count could indicate the presence of various diseases (Gruber, 1998).

A complete blood count may be done as part of a regular physical examination. A blood count can give valuable information about the general state of the health (Gruber, 1998).

The complete blood count (CBC) includes:-

1.2.3.1 Hemoglobin (Hb):-

The hemoglobin molecule fills up the red blood cells. It carries oxygen, carbon dioxide and gives the red blood cell its red color. The hemoglobin test measures the amount of Hb in the blood a good test measured of the blood viability (Alberts and Bruce, 2005).

Hemoglobin is composed of globin and the iron containing heme compound protoporphyrin (Besa *et al.*, 1992).

1.2.3.2 Hematocrite (HCT) Packed Cell Volume (PCV):-

This test measures the amount of the space (volume) red blood cells take up in the blood. The value is given as percentage of red blood cells in volume of blood. Hematocrite and Hb values are two major tests that show if anemia or polycythemia is present (Alberts and Bruce, 2005).

1.2.3.3 Red blood Cell count (RBC):-

Red blood cells carry oxygen from the lung to the rest of the body. They also carry carbon dioxide back to the lung so it can be exhaled. If the RBC count is low (anemia), the body may not transport oxygen it needs. If the count is too high (polycythemia), there is a chance that the red blood cells will clump together and block tiny blood vessels (capillaries), this also make it hard for the red blood cells to carry oxygen (Alberts and Bruce, 2005).

1.2.3.4 Red Blood Cell Indices (absolute value):-

There are three red blood cell indices, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC).

1.2.3.5 White Blood Cell count (WBC, leucocytes):

White blood cells protect from the body. White blood cells are bigger than red blood cells but fewer in number. When a person has become infected the number of white blood cells rises very quickly (Alberts and Bruce, 2005).

1.2.3.5.1 Types of White Blood Cell (WBC differential):-

There major types of white blood cell are neutrophils, lymphocytes, monocytes, eosinophil, and basophiles, immature neutrophil called band

neutrophils are also part of this test. Each cell plays a different role in protecting the body. The number of each type of WBCS gives important information about the immune system. Too many or too few of the different types of WBCS can help in diagnosis of the infection, allergic or toxic reaction to medicine or chemical and many condition, such as leukemia (Alberts and Bruce, 2005).

1.2.3.6 Platelets (Thrombocyte) count:-

Platelets are the smallest type of the blood cells, they are important in blood clotting; when bleeding occur the platelets swell, clump together and form a sticky plug that help to stop the bleeding. If there are too few platelets uncontrolled bleeding may be a problem. If there are too many platelets there is a chance of blood clot forming in a blood vessel. Also platelets may be involved in hardening of the arteries (atherosclerosis) (Alberts and Bruce, 2005).

1.2.3.6.1 Mean Platelets Volume (MPV):-

Mean platelets volume measure the average amount of volume of plts. Mean platelets volume is used along with plts count to diagnose some types of diseases (Alberts and Bruce, 2005).

1.2.3.6.2 Platelets Distribution Width (PDW):-

Platelets distribution width can also be measure which show if the platelets are all the same or different sizes (Alberts and Bruce, 2005).

Table (1-1): Normal Ranges of Complete Blood Count (CBC)

(Alberts and Bruce, 2005):-

Parameter	Normal value	Parameter	Normal value
Hemoglobin (Hb):- g/dl		WBCs differential:- %	
Male	13-17	Neutrophils	50
Female	12-15	Lymphocytes	25-40
Infant	11-20	Monocytes	3-7
Newborn	14.5-24.5	Eosinophils	1-3
Hematocrite (HCT):- %		Basophiles	0-2
Male	39-50	RBCs indices:-	
Female	35-46	MCV	76-100fl
Infant	31-43	MCH	27-33pg
Newborn	30-44	MCHC	32-36 g/dl
RBCs COUNT:- $x10^{12}$/L		Platelets count:- $x10^{9}$/L	
Male	4.3-5.7	Adult	150-400
Female	3.5-5.1	Children	150-450
Infant	3.8-5.5	MPV:-	
Newborn	4.1-6.1	Adult	7.4-10.4 $x10^{9}$/L
RDW	11.5-14.5%	Children	7.4-10 $x10^{9}$/L
TWBC	3.5-9 $x10^{9}$/L	PDW	10-14%

1.3 Routine laboratory investigation during pregnancy:-

When a woman becomes pregnant, it is recommended that she receives a range of standard investigations. The “first antenatal screen” may be requested by the physician at the first appointment when pregnancy is confirmed, and the results later forwarded to the chosen Lead Maternity Career (LMC).

Tests in the first antenatal screen include:

- Complete blood count
- Blood group and antibody screen
- Rubella antibody status
- Syphilis serology
- Hepatitis B serology
- HIV (Sarris, *et al*, 2009).

1.4 Pregnancy and changes in pregnancy:-

Pregnancy is the most important physiological state for human kind since as it assure continuation of the species, pregnancy produce major physical alteration in the mother , support the fetus as it develop the capability of independent , existence ,and introduce a new organ in the form of the placenta that provides the link between the fetus and her mother (Hylten, 1985).

1.4.1 Anatomical changes:-

As pregnancy progresses, the female reproductive organs become increasingly vascular and engorged with blood, the enhanced vascularity increases vaginal sensitivity and sexual intensity. Prodded by rising levels of estrogen and progesterone, the breasts enlarge and engorge with blood, and their areola darken. The degree of uterine enlargement during pregnancy is remarkable, the uterus fill most of the pelvic cavity by 16 weeks. As pregnancy continues the uterus pushes higher into the abdominal cavity, exerting pressure on both abdominal and pelvic organs (Marieb and Hoehn, 2013).

1.4.2 Physiological changes during pregnancy:-

I. Hematological changes:-

Total blood volume increases by 40% above non pregnant levels; plasma volume rises from 6 weeks gestation and stabilizes by 32-34 weeks, RBC mass increases early in the second trimester to 20-35% above non pregnant levels by term (Sarris *et al.*, 2009).

The disproportionated rise in plasma volume compared with the RBC mass result in haemodilution and decreased hemoglobin and hematocrit

count. There is a physiological fall in Hb. An abnormal Hb <10.5 g/dl requires investigation, if iron stores are adequate; the HCT rises from the second to third trimester (Sarris *et al.*, 2009).

A. The plasma volume rises and the RBC mass and number of RBCs increases, the result is a fall in hematocrit, this decline in HCT is called (physiological anemia) or (dilutional anemia) of pregnancy. True anemia represents a fall in the oxygen transport capacity of blood relative to the normal physiological state. While during pregnancy oxygen-carring capacity is higher than in the non-pregnant state. (Riikonen *et al.*, 1994).

The plasma volume at term is about 1200 ml, which translation in to an increase of nearly 50%. The red cell mass increased by term ranges between 250 and 400 ml. HCT decline in second trimester, but rises slowly thereafter, the most equitable means of approaching the problem is to assing 11g/dl as the lower limit of normal Hb values during pregnancy.

Interestingly, high Hb values during pregnancy are not felicitous finding. Unexplained values above 13g/dl are associated with poor fetal outcome, including intrauterine growth retardation, low birth weight, and preterm birth. Not surprisingly, a rise in serum erythropoietin values appears to be a key factor in red cell mass expansion during pregnancy. Erythropoietin level rise to 50% above baseline by the second trimester. A more robust rise in serum erythropoietin level occurs in women who are iron deficient.

In normal pregnancy, the mean corpuscular volume (MCV) typically rises by approximately 4fl. A fall in red cell MCV is the earliest sign of iron deficient. Later the mean corpuscular hemoglobin (MCH) falls and finally anemia results (Milman *et al.*, 2000).

B. The WBCs count increase and may peak at over 20mg/ml in stress full condition. The neutrophil count begin to increase in the second month of pregnancy and plateaus in the second and third trimester, at which time the total WBC counts ranges from 90000-15000 cell/ micro L. there is no change in the absolute lymphocyte count (Riikonen *et al.*, 1994).

C. The platelets typically fall by approximately 10% in an uncomplicated pregnancy, in approximately 7% of women this fall is more sever and can result in thrombocytopenia (Plts count $<140\times10^9$/l). In over 75% of cases this is mild and of unknown cause, a condition referred to as incidental thrombocytopenia of pregnancy. Approximately 21% of cases are secondary to a hypertensive disorder will 4% are associated with immune thrombocytopenic purpura (ITP). No treatment is required and the infant is not affected. A pregnant woman will also become hypercoagulable, leading to increase risk for developing blood clots and embolisms, due to increase liver production of coagulation factors, mainly fibrinogen and factor VIII (Riikonen *et al.*, 1994).

D. Pregnancy alters the balance within the coagulation system to favour clotting which is assumed to be in preparation for controlling bleeding at the time of delivery. Concentration of clotting factors such as (VIII, IX, and X increase), as does fibrinogen, with levels increasing by up to 50%. Fibrinolytic activity is decreased, with a fall in concentration of endogenous fibrinolytic such as antithrombin and protein S.

The test of coagulation; activated partial thromboplastin time (APTT), prothrombin time (PT), and thrombin time (TT), remain normal.

This hypercoagulable state is exacerbated by the compressive effect of the gravid uterus on the iliac vessels, causing venous stasis in the lower limbs. This is more marked on the left as the left iliac vein is compressed by the iliac and the ovarian arteries. This predisposition for clotting results in the increased risk of venous thrombosis associated with pregnancy (Sarris, *et al*, 2009).

Table (1-2) Hematological Values in Pregnancy (Sarris *et al.*, 2009)**:-**

Blood counts	**Non Pregnancy**	**First trimester**	**Second trimester**	**Third trimester**
Hb (g/dL)	11.5-15	11.6-13.9	9.7-14.3	9.5-15
HCT%	40-45	31-41	30-39	28-40
RBC×10^{12}/L	3.5-4.5	3.4-4.6	2.8-4.5	2.7-4.4
MCV (fL)	80-100	80-100	85-105	80-100
MCH (pg)	27-32	30-32	30-33	29-32
MCHC (g/dL)	31-37	32.5-35.5	32.4-35.2	31.9-35.5
RDW (%)	<14.5	11.7-14.9	12.3-14.7	11.4-16.6
WBC×10^{9}/L	3.5-9.1	5.7-13.6	5.6-1614.8	5.6-17
Pleteltes×10^{9}/L	165-415	174-391	155-409	146-429

II. Hormonal changes and endocrine changes:-

Pregnant women experience adjustment in their endocrine system. Level of progesterone and estrogen rise continually throughout pregnancy, suppressing the hypothalamic axis and subsequently the menstrual cycle.

Estrogen is mainly produced by the placenta and is associated with the fetus well-being. Women also experience increased human chorionic gandotropin (β HCG) (Koller *et al.*, 1979).

Parathyroid hormone is increased which leads to increases of calcium uptake in the gut and reabsorption by the kidney. Adrenal hormones such as cortisol and aldosterone also increase. Human placental lactogen (hPL) is produced by the placenta and stimulate lipolysis and fatty acid metabolism by woman, conserving blood glucose for use by the fetus; it can also decrease maternal tissue sensitivity to insulin resulting in gestational diabetes (Koller *et al.*, 1979).

There is a relative maternal iodine deficiency, this caused by a 2-fold increase in renal loss (↑GFR+↓ reabsorption), and active transport of iodine to the fetus. Uptake of plasma iodide into the thyroid is increased by 3-fold. Increased thyroid-binding globin (TBG) hepatic synthesis leads to an increase in total thyroxin (T4) and tri-iodothyronine (T3). First trimester increased HCG lead to decreased TSH and increased T4. Second and third trimesters T4 decreases, third trimester TSH increases (Sarris *et al.*, 2009).

III. Cardiovascular changes:-

The women are the sole provider of nourishment for the embryo and later, the fetus and so her plasma and blood volume slowly increase by 40-50% over the corse of the pregnancy to accommodate the changes.

The increase is mainly due to an increase in plasma volume through increased aldosterone it results in an increase in heart rate (15 beat/ min more than usual), cardiac output increases by 50%, mostly during first trimester (Koller *et al.*, 1979). This helps propel the greater circulatory volume around the body.

The uterus presses on the pelvic blood vessels, which may impair venous return from the lower limbs, resulting in varicose veins and leg edema (Marieb and Hoehn, 2013).

IV. Renal changes:-

The kidneys produce more urine during pregnancy because of the mother's increased metabolic rate and the additional burden of disposing of fetal metabolic wastes. The glomerular filtration rate (GFR) commonly increases by 50%.then was decreased blood urea nitrogen (BUN) and creatinine and glucose urea (due to saturated tubular reabsorption) may be seen (Koller *et al.*, 1979).

Urinary stasis predisposes to UTI and pyelonephritis, mild glycosuria and/ or proteinuria can occur in normal pregnancy, serum albumin decreases, serum cholesterol increases, and total body water increases by 6-8l and plasma osmolality falls (Sarris *et al.*, 2009).

V. Gastrointestinal changes:-

During pregnancies woman can experience nausea and vomiting (morning sickness), which may be due to elevated β HCG and should resolve by 14-15 wks. Additionally, there is prolonged gastric empty time, decrease gastroesophgeal sphincter tone, which can lead to acid reflux, and decreased colonic motility, which lead to increase water absorption and constipation (Koller *et al.*, 1979).

VI. Respiratory system changes:-

Tidal volume increases markedly during pregnancy, while respiratory rate is relatively unchanged and residual volume decline. The increase in tidal volume is due to the mother's greater need for oxygen during pregnancy and the fact that progesterone enhances the sensitivity of the medullary respiratory center to carbon dioxide (Marieb and Hoehn, 2013).

All physiological changes are maximal late in the second trimester and then start to return to pregnancy level (Sarris *et al.*, 2009).

1.5 Anemia during pregnancy:-

More than half of the pregnant women in the world have hemoglobin levels indicative of anemia. Knowledge of the current situation of the condition in our environment is necessary. This knowledge will motivate antenatal caregivers toward early detection and prompt management of anemia in pregnancy (Cyril and Hyacinth, 2005).

The demand of the developing fetus placed the expectant mother at greater risk for nutritional anemias, especially deficiencies of iron and folate. Some chronic anemias present special hazards to the pregnant patient. Sickle cell disease, certain hemolytic anemia (Wintrobe *et al.*, 1942).

A. Physiological anemia or dilutional anemia of pregnancy:-

The plasma volume increases disproportionately to red cell mass. A reduction in the hematocrit and hemoglobin concentration usually stabilizes at 0.33L/L and 11g/dl respectively. Serve a useful purpose by enhancing placental perfusion, thereby facilitating oxygen and nutrient delivery to the fetus. An additional benefit is that fewer red cells are lost with the hemorrhage accompanying placental separation (Wintrobe *et al.*, 1942).

B. Nutritional anemia:-

When the hemoglobin concentration is less than 10.4g/dl a true reduction in red cell mass is likely present; however, because of variation in the magnitude of the hydremia, a fixed dividing line between the normal and abnormal is difficult to place in pregnancy. Red cells remain normochromic and normocytic unless deficiency of iron or folate supervenes (Wintrobe *et al.*, 1942).

Multiple factors lead to nutritional anemia in pregnancy. In developing countries life style, low socioeconomic condition, illiteracy and lack of knowledge of good dietary habits.

Anemia during pregnancy is associated with increased maternal morbidity and mortality, and contributes to 20% of the maternal mortality in Africa. Folate deficiency accounts for 95% of megaloblastic anemia in pregnancy. Iron deficiency anemia (IDA) is a major health problem during pregnancy (WHO, 1997).

1.6 Prevalence of anemia among pregnancy:-

Anemia affects almost two-thirds of pregnant women in developing countries and contributes to maternal morbidity and mortality and to low birth-weight. The predisposing factors include grandmultiparity, low socioeconomic status, and inadequate child spacing among others (Cyril and Hyacinth, 2005).

1.6.1 Prevalence of anemia among pregnancy in worldwide:-

Total of 190 pregnant women attended the antenatal clinic at Al-Hada Armed forces hospital Taif, Saudi Arabia. Prevalence of anemia was 26.8% which represent IDA 84% of all anemic patients. The prevalence of anemias were a high in third trimester 30.2% compare to 15% in first trimester and 14.8% in second trimester (Alzaharani, 2012).

The first large nutrition study in Ethiopia was conducted from June to July 2005 sample of 970 subjects, a 29.4% prevalence of anemia, 18% IDA prevalence. Signifying that the most probable causes of anemia is nutrition related and to some extent chronic illnesses (Haider, 2009).

The prospective, observational study of 1,369 pregnant women at 20 to 26 weeks of gestation to determined the prevalence and risk factors. Anemia is 90.5% had anemic, 75% had mild, 14.8% had moderate, and only 0.7% were severe anemic (Baig-Ansari *et al.*, 2008).

The retrospective study was done in 530 normal pregnant women in Enugu, southeastern Nigeria. To determine the prevalence of anemia in pregnant women, 40.4% were anemic, 90.7% had mild form, 9.3% had moderate, and there is no severe case. Anemia was significantly in third trimester (Cyril and Hyacinth, 2005).

1.6.2 Prevalence of anemia among pregnancy in Sudan:-

Study of 744 pregnant Sudanese women attended the antenatal clinic of New Halfa teaching hospital, eastern Sudan, 466(62.6%) had anemia, 52.4% had mild anemia, 8.1% had moderate anemia, and 2.2% had severe anemia. Anemia prevalence 73.2% was significantly high in grandmultigravidae (Adam *et al.*, 2005).

A cross-sectional study was done in Wad Medani hospital, central Sudan conducted to anemia, zinc and copper deficiencies among pregnant women. The result showed that; out of 200 pregnant women 104 (52.5%) had anemia and 3 (1.5%) had severe anemia. Iron deficiency was prevalent 25(12.5%). Gestational age was significantly inversely correlated with hemoglobin (Bushra *et al.,* 2010).

A cross-sectional descriptive and analytical study was done in Khartoum Teaching Hospital, Khartoum, Sudan. Conducted to investigate status of iron deficiency anemia among Sudanese pregnant women. Prevalence of anemia 33.8% the majority 85.2% were mildly anemic 11.1% were moderately and 3.7% were severe anemic (Farah, 2012).

1.7 previous studies:-

Variation in Hb level and some hematological indices during normal pregnancy research conducted to determine frequency of IDA in pregnant, 80 pregnant women in both Khartoum Teaching Hospital and Omdurman Maternity Hospital. 10% had Hb low level and 90% had normal Hb (Sana *et al.*, 2014)

Pregnancy physiological changes and laboratory values, normal and abnormal physiologic changes may occur during pregnancy and the laboratory values that indicate. It becomes significantly skewed from the values normally noted during pregnancy (Derricott and Cartwright, 2013).

Variation in some hematological indices during normal pregnancy research conducted was 200 pregnant women in Capital Hill Clinic Warri, Delta State, Nigeria. They found a significant decrease in Hb, PCV, and Plts count (Jacobs *et al.*, 2013).

A cross-sectional study covered 274 pregnant women who attended Lagos University Teaching antenatal care and hospital. They studied of hematological profile of normal pregnant women in Lagos, Nigeria. They found progressive decline in Hb concentration, PCV, RBCs count and platelets count, with increased in WBCs count (Aknibami *et al.*, 2013).

A case control study in which 100pregnant women, the study conducted at Omdurman Al Saudi Maternity Hospital in Sudan. A significant decrease was found in RBCs count, Hb, PCV, MCV, MCH and MCHC and significant increase in TWBCs, in pregnant women when compared with non-pregnant one (Elgari, 2013).

Physiological changes in hematological parameters during pregnancy, principally influenced by changes in the hormonal milieu. Many hematological changes also, occurring during these periods are physiological and are of inconsequential concern to the hematologist (Chandra *et al.*, 2012).

1.8 Rational:-

Pregnancy is a physiological status associated with many anatomical, physiological, hematological, and psychological changes. Anemia is a major hematological problem during pregnancy and had major effects; on the mother and later in the fetus. Early detection of these abnormalities will help to avoid many problems for both the mother and the fetus. Therefore, this study was designed to measure the changes of hematological parameters among pregnant women.

1.9 objectives:-

1.9.1 General objectives:-

Measurement of complete blood count on CBC status among Sudanese pregnant women in first, second and third trimester, in Algadaref town.

1.9.2 Special objectives:-

1. To study changes in hematological parameters; Hb, RBC, HCT, MCV, MCH, MCHC, RDW, TWBC, Plts count, MPV, and PDW during pregnancy.
2. To determine some demographic information such as; age, educational level, socioeconomic status, gravidity and maternal follow up during pregnancy.
3. To investigate the association between that demographic information on Hb level during pregnancy among the study population.
4. To determine severity of anemia among study population.

Chapter two

Material and methods

2.1 Study design:-

This is an analytical study.

2.2 Study population, study area and duration:-

One hundred and fifty pregnant women who attended Altaheli Maternity Hospital and some clinics in Algadaref town were enrolled in the study. Fifty women in each trimester. The study was conducted during the period from 17 June to 25 August in 2014.

2.2.1 Inclusion criteria:-

Sudanese pregnant women without any complication in pregnancy and with no history of medical condition were included in the study.

2.2.2 Exclusion criteria:-

Women with a complicated during pregnancy, or who were subjected to blood transfusion in last three months and with history of diseases that may affect the result such as; malaria, liver diseases, renal diseases, hypertension, diabetes mellitus, leshmaniasese, HBV, HCV and HIV..etc. were excluded from the study.

2.3 Data collection, analysis and presentation:-

Data was collected using instructed writing questionnaire by direct interviewing; regarding the; patient name, patient number, age, blood groups, previous blood transfusion, history of diseases, gestational age, residence, educational level, socioeconomic status, number of gravidity, maternal follow up, supportive supplements and tea intake, number of fetuses inside the uterus.

2.4 Sample collection:-

Using a sterile disposable syringe 2.5 ml of blood were collected and drained in EDTA container, mixed gently. The container was labeled clearly with the participant's number.

2.5 The investigation:-

CBC was done using **URIT 3010** automated hematological analyzer.

URIT has 20 parameters and 3 histograms. Such as TWBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, PLT, MPV, and PDW.

2.5.1 Principles of operation:-

- WBC/RBC/PLT; electrical impedance.
- Hb; Photoelectric colorimetric.
- Aspiration volume; 18µl.

Blood was highly diluted in a buffered electrolyte solution. The flow rate of this diluted sample was controlled by a mercury siphon or by displacement of a tightly fitting piston. This result is a measured volume of the sample passing through an aperture tube of specific dimensions. As blood cell was carried through the aperture, it displaces some of the conducting fluid and increases the electrical resistance. Which lasts as long as the red cell take to pass though the aperture, the height of the pulses produced indicates the volume of the cells passing through. The pulses can be displayed on anoscillo graph screen. The pulses are led to a threshold circuit provided with an amplitude discriminator for selecting the minimal pulse height, which will be counted. The height of the pulses is used to determine the volume of red cells (Lewis *et al.*, 2001).

2.5.2 Procedure:-

1- Put sample container on rotation device.

2- Opened the URIT hematological analyzer and adjusted the device.

3- Mixed the sample and put in the URIT.

2.6 Ethical consideration:-

The study was approved by the medical ethical committee of Medical Laboratories Science - SUST. A written consent was obtained from the participants after they had been informed with the objectives, benefit and expected outcome of the study. The participants were assured that the collected information will be kept confidential and will not be used for any other purpose than this study.

2.7 Data analysis and presentation:-

All the data were presented as means ± standard deviation and the main effect was the trimester. Comparison between the means was performed by One way ANOVA Test and Pearson Correlation Test was performed to assess the correlation between the Hb level with other variables. Statistical Package for Social Sciences (SPSS version 17) was used. All reported P values were considered significant at a level of $P \leq 0.05$.

Chapter Three

Results

3.1 Participants characteristics:-

Distribution of participants by the age:-

Distribution according to the age was found 30% from 15-24 years, 51.3% from 25-34 years and 18.7% from 35 and above seen in table 3-1.

The gravidity among study population:-

The participants were found 28% had primigravida and 72% had multigravida table 3-1.

Maternal follow up during pregnancy in the participants:-

In the study population showed that, 115 (76.7%) had maternal follow up but 35 (23.3%) had not received table 3-1.

The educational level in the study population:-

Distribution according to education showed that, 37% were illiterate, 31% had primary education, 19% had secondary education and 13% found to have high education figure 3-1.

The socioeconomic status among the participants:-

Distribution of the study group according to socioeconomic status showed that, 63.3% were of low socioeconomic status, 35.3% were of moderate status and 1.3% was of high status figure 3-2.

Table (3-1): Participant characteristic:-

Participant characters		Number	Percent
Age	**15-24**	45	30%
	25-34	77	51.3%
	>35	28	18.7%
Gravidity	**Primigravida**	42	28%
	Multigravida	108	72%
Maternal follow up	**Yes**	115	76.7%
	No	35	23.3%

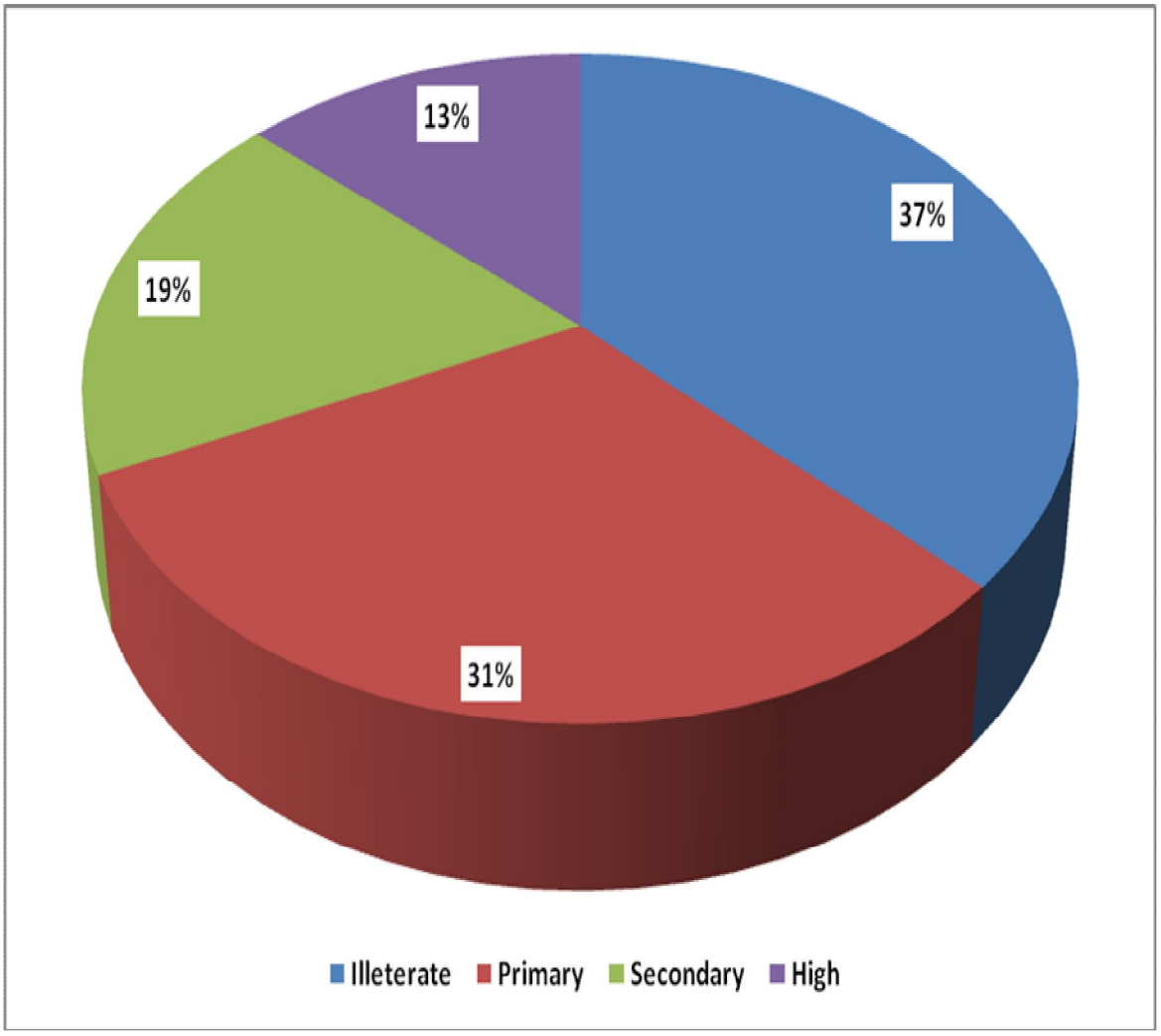

Figure (3-1) The education level in the study population.

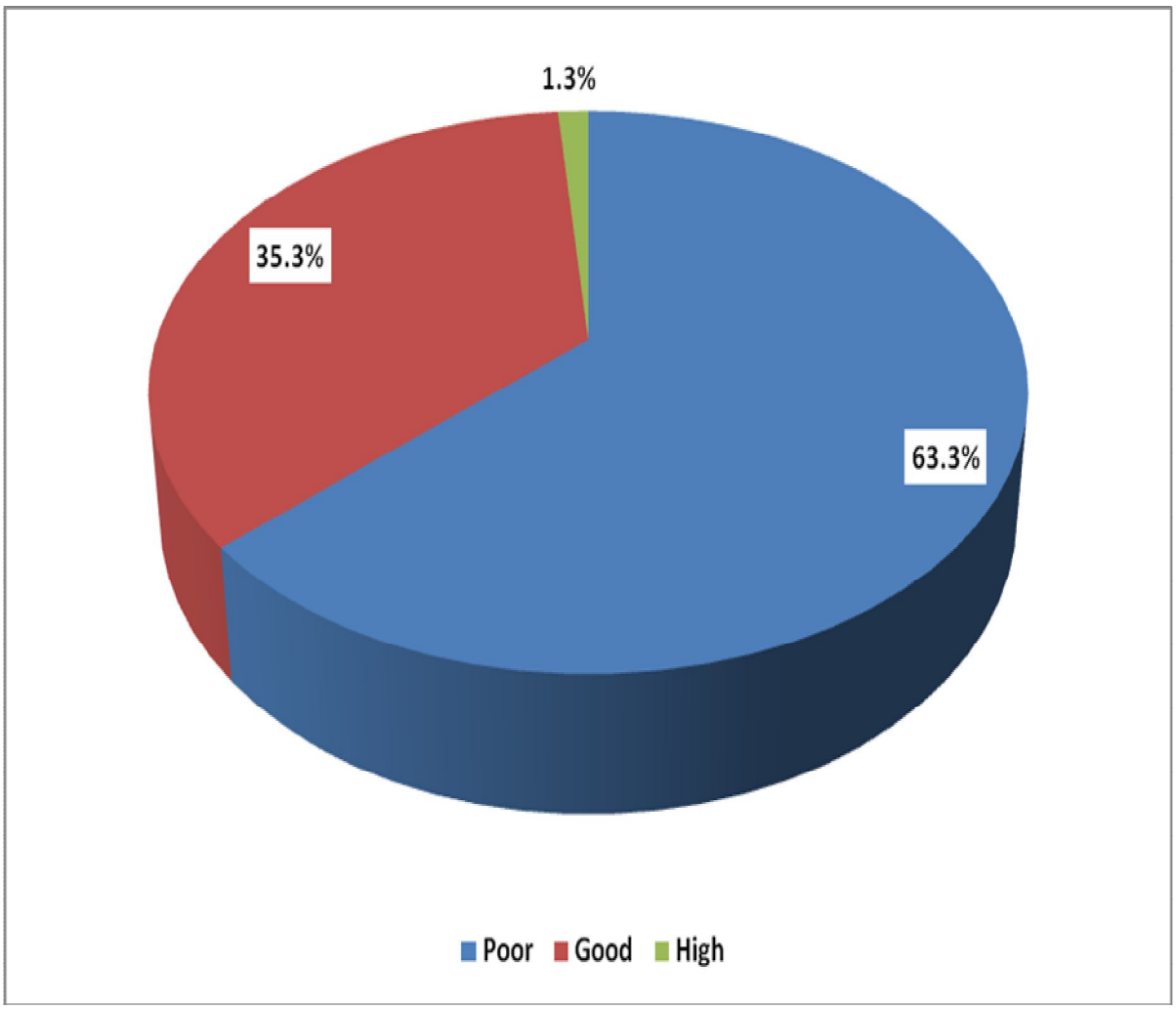

Figure (3-2) The socioeconomic status of the participants.

3.2 The effect of the gestational age on Hb, HCT, RBCs count and indices:-

The hemoglobin concentration was found in the first, second and third trimester respectively (11.37±1.3g/dl, 10.95±1.5g/dl and 10.64±1.9g/dl). Hematocrit values were not affected by the gestational age was found (30.74±2.9%, 30.14±2.9% and 29.94±4.8%) in the first, second and third trimester respectively.

RBCs counts were found (4.00±0.5×1012 cell/l, 3.76±0.4×1012 cell/l and 3.87±0.6×1012 cell/l) in the first, second and third trimester respectively.

Significant variations were found in the values of MCV (77.36±6.3 fl, 80.40±5.6 fl and 78.01±8.7 fl). As well as in the values of MCH (28.51±3.0pg, 29.09±3.1pg and 27.65±3.6pg) in the first, second and third trimester respectively.

MCHC of the pregnant ladies was found (36.95±2.7g/dl, 36.27±2.7g/dl and 35.32±2.8g/dl) in the first, second and third trimester respectively. In RDW (10.57± 1.2%, 10.69± 1.1% and 11.22± 1.5%) was significantly elevated in the first, second and third trimester respectively table 3-2.

Table (3-2): The effect of the gestational age on Hb, HCT, RBCs count and indices:-

Parameters	First trimester Mean± SD	Second trimester Mean± SD	Third trimester Mean± SD
HB (g/dL)	11.37 ± 1.3[a] (8.6 – 13.6)	10.95± 1.5[ab] (8.2 -14.7)	10.64± 1.9[b] (1.9 – 13.4)
HCT (%)	30.74 ± 2.9[a] (24.8 – 37.2)	30.14 ± 2.9[a] (25.2 – 37.9)	29.94 ± 4.8[a] (8.6 – 37.9)
RBCs×10^{12}(Cell/L)	4.00 ± 0.5[a] (3.05 – 5.46)	3.76 ± 0.4[b] (3.06 – 4.72)	3.87 ± 0.6[ab] (0.97 – 4.58)
MCV (FL)	77.36 ± 6.3[b] (56.8 – 87.3)	80.40 ± 5.6[a] (62.6 – 92.1)	78.01 ± 8.7[ab] (51.8 – 90.8)
MCH (PG)	28.51 ± 3.0[ab] (19 – 32.7)	29.09 ± 3.1[a] (20.7 – 36.4)	27.65 ± 3.6[b] (18.2 – 36.3)
MCHC (g/dL)	36.95 ± 2.7[a] (31.6 – 44.3)	36.27 ± 2.7[ab] (30.5 – 42.2)	35.32 ± 2.8[b] (22 – 41.2)
RDW (%)	10.57 ± 1.2[b] (8.7 – 15.5)	10.69 ± 1.1[b] (9.4 – 15.3)	11.22 ± 1.5[a] (9.1 – 15.8)

*Mean within the same row with different superscripts was significantly different at $P \leq 0.05$.

3.3 The effect of the gestational age on TWBCs **count, Platelets count and indices: -**

TWBCs was significantly increased in the first, second and third trimester (5.762± 1.7× 109 cell/l 6.958± 2.2×109 cell/l and 7.150± 2.9×109 cell/l) respectively.

Platelets count was significantly lower in the first, second and third trimester (285.200± 91.5×109 cell/l, 276.940± 78.0×109 cell/l and 243.400± 64.7×109 cell/l) respectively.

MPV was found did not vary with the trimester (9.67 ± 0.8 fl, 9.70 ± 1.0 fl and 9.88 ± 1.0 fl) in the first, second and third trimester respectively.

PDW was found did not vary with the trimester (11.6 ± 1.9 fl, 11.6 ± 2.4 fl and 12.4 ± 2.9 fl) in the first, second and third trimester respectively table 3-3.

Table (3-3): The effect of the gestational age on TWBCs **count, Platelets count and indices: -**

Parameters	**First trimester Mean± SD**	**Second trimester Mean± SD**	**Third trimester Mean± SD**
TWBCs×10^9Cell/L	5.762 ± 1.7[b] (2.8 – 11.1)	6.958 ± 2.2[a] (2.6 – 13.5)	7.150 ± 2.9[a] (3.2 – 15.4)
PLT ×10^9Cell/L	285.200 ± 91.5[a] (113 – 634)	276.940 ± 78.0[a] (138 – 466)	243.400 ± 64.7[b] (115 – 381)
MPV (fL)	9.67 ± 0.8[a] (8.1 – 12.5)	9.70 ± 1.0[a] (7.9 – 12.1)	9.88 ± 1.0[a] (8.1 – 12.3)
PDW (fL)	11.6 ± 1.9[a] (8.6 – 15.8)	11.6 ± 2.4[a] (7.5 – 19.8)	12.4 ± 2.9[a] (7.9 – 19.8)

*Mean within the same row with different superscripts was significantly different within the P value ≤ 0.05.

3.4 Distribution of the participants according to HB level and severity of anemia:-

Distribution of participants according to hemoglobin level showed that, 73(48.7%) had normal hemoglobin level (>11g/dL), 67(44.7%) had mild anemia (9 – 10.9 g/dL), 9(6%) had moderate anemia (7.1– 8.9g/dL) and only one patient (0.7%) was suffering from severe anemic (<7g/dL) figure 3-3.

3.5 Distribution of anemia according to gestational age:-

Mild anemia in the first, second and third trimester was found to be 11.3%, 15.3% and 18% respectively. With the same pattern, moderate anemia was represented by 0.7%, 2.7% and 2.7% respectively.

Severe anemia was detected in only one woman in the third trimester 0.7% figure 3-4.

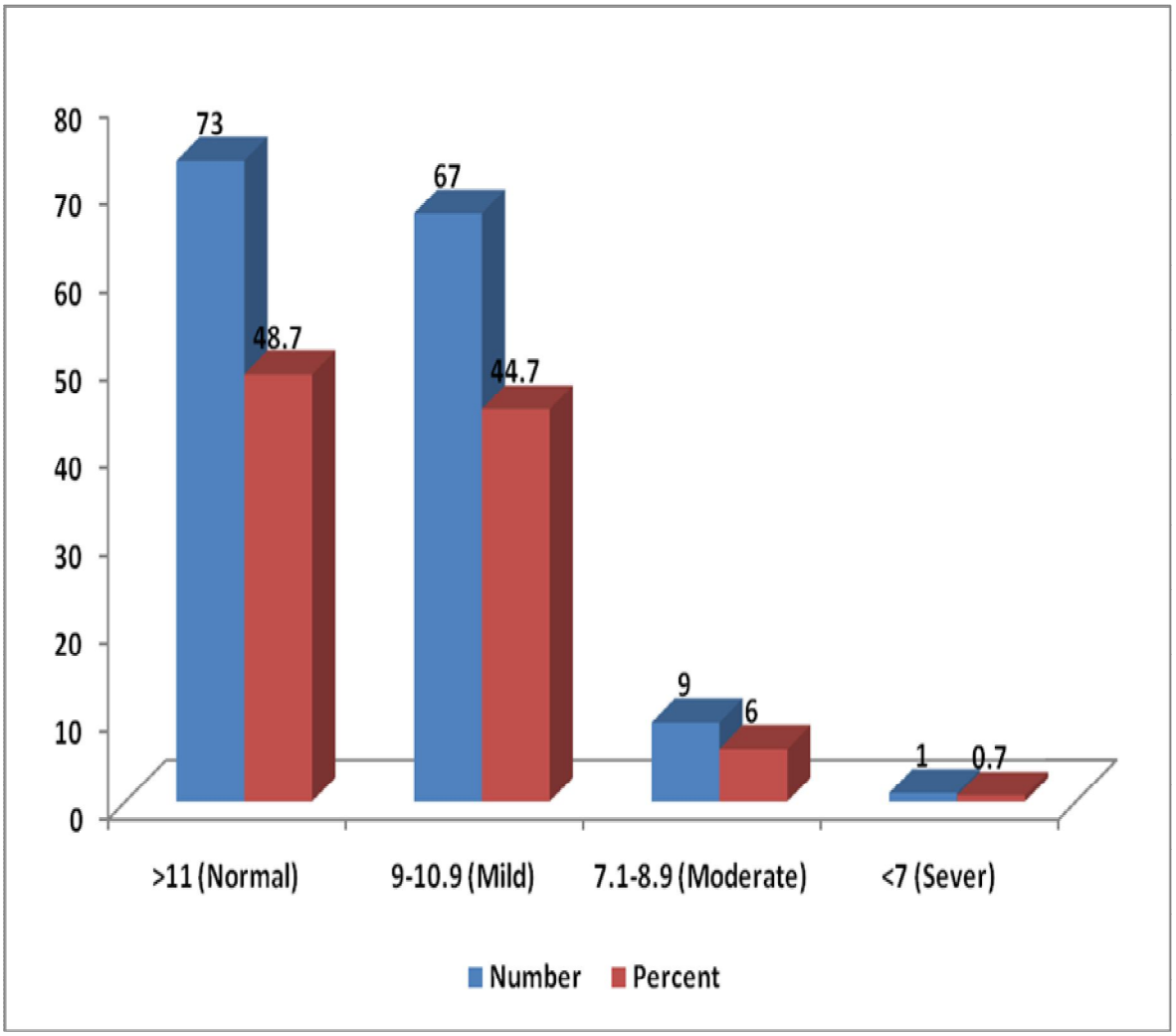

Figure (3-3) Distribution of the participants according to HB level and severity of anemia.

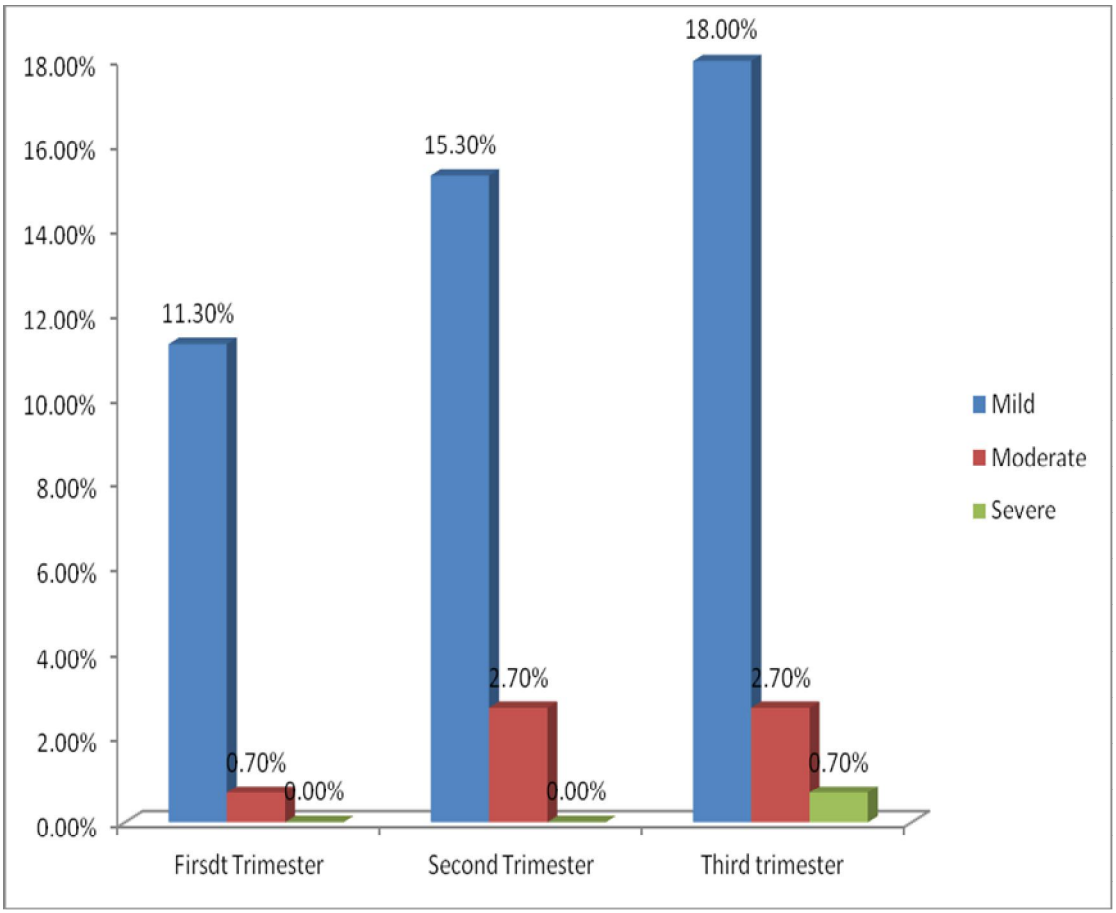

Figure (3-4) Distribution of anemia according to gestational age.

3.6 The correlation of hemoglobin level with educational level:-

The hemoglobin concentration did not correlate with either educational level or the socioeconomic status ($P \leq 0.05$).

It was found that 74 pregnant women had a normal HB level and they were distributed according to the educational level as follows 27(37%) illiterates, 20(27.4%)had primary education, 14(19.2%) had secondary education and 12(16.4%) had high education. Severe anemia was found in one pregnant woman who is illiterate. There were 9 women whom were found to have moderate anemia; 3(33.3%) of them were illiterate, and the same percentage was found to have primary education, one woman (11.1%) had secondary education and two women (22.2%) had high education table 3-4.

Table (3-4): The correlation of hemoglobin level with educational level:-

Character	Normal	Mild	Moderate	Severe	Total	Significant level
Illiterate	27 37%	25 37.3%	3 33.3%	1 100%	56 37.3%	NS
Primary	20 27.4%	23 34.3%	3 33.3%	0 0%	46 30.7%	NS
Secondary	14 19.2%	13 19.4%	1 11.1%	0 0%	28 18.7%	NS
High	12 16.4%	6 9%	2 22.2%	0 0%	20 13.3%	NS
Total	73 100%	67 100%	9 100%	1 100%	150 100%	NS

*NS: not significant in significant level at P value ≤ 0.05.

3.7 The correlation of hemoglobin level with socioeconomic status:-

Women with normal hemoglobin were distributed: 38(52.1%) of poor status, 33(45.2%) good status, 2(2.7%) of high socioeconomic status. Women with moderate anemia were distributed to 5(55.6%) of poor status and 4(44.4%) of good status. There was one woman with severe anemia whom was found to be of poor socioeconomic status table 3-5.

Table (3-5): The correlation of hemoglobin level with socioeconomic status:-

Socioeconomic status	Normal	Mild	Moderate	Severe	Total	Significant level
Poor	38 52.1%	51 76.1%	5 55.6%	1 100%	95 63.3%	NS
Good	33 45.2%	16 23.9%	4 44.4%	0 0%	53 35.3%	NS
High	2 2.7%	0 0%	0 0%	0 0%	2 1.3%	NS
Total	73 100%	67 100%	9 100%	1 100%	150 100%	NS

*NS: not significant in significant level at P value ≤ 0.05.

Chapter four

Discussion, conclusion and recommendations

4.1 Discussion:-

During pregnancy, the body undergoes normal physiologic changes. These changes affect mother laboratory results. In the absence of illness, the body can generally compensate for these changes.

Some of these changes are well-known, such as the reduction in hematocrit and hemoglobin levels, which is termed physiological or delutional anemia of pregnancy (Derricott and Cartwright, 2013).

In this study a progressive decline in Hb concentration was found from the first to the third trimester, but a drop from the first to the second trimester; this is on line with the findings of (Akinbami *et al.*, 2013)

The progressive decline in Hb concentration from the first to the third trimester may be due to an increased demand for iron and nutrients as pregnancy progresses. More iron is required to meet the expansion of maternal Hb mass and the needs for fetal growth (Marrieb and Hoehn, 2013). Another physiological cause is that, progesterone and estrogen release a renin. Renin causes sodium retention which will be followed by an increase in the plasma volume at a higher rate than the increase in the cells mass causing a fall in the hemoglobin level and leading to physiological anemia (Akinbami *et al.*, 2013).

In spite of the of this decline in haemoglobin concentration most of the

women maintained a good haemoglobin concentration throughout pregnancy as the mean values of haemoglobin did not fall below the cut-off point (10g/dl) for anaemia ; this finding is supported by the findings of (Akinbami *et al.,* 2013).

In this study the HCT values were insignificantly decreased with the progress of the trimesters, but without any significant difference between the trimesters. The general changes in the CBC current findings agrees with (Milman *et al.,* 2000) who reported that the plasma volume at term increases nearly by 50% and HCT declines in the second trimester, but rises slowly thereafter. They claimed the most equitable means of approaching the problem is to assess 11g/dl as the lower limit of normal Hb values during pregnancy. Akinbami *et al.*, (2013) stated that despite the physiological hemodilution associated with pregnancy, which also contributes to the drop in HCT in the first and second trimester, in late pregnancy, plasma volume increases at a slower rate, inducing a slight rise in hematocrit that may account for the slight rise in HCT in the third trimester.

This study revealed a significant decrease in RBCs count between the first and second trimester, and an insignificant increase in the third trimester when compared with the other two trimesters. This might be due to increased nutritional demands for the fetus growth process which is managed by an increased stimulation of erythropoietin; or it may be due

to mother took a supplementation in the third trimester especially (Marrieb and Hoehn, 2013).

Akinbami *et al.*, (2013) and Elgari, (2013) found controversial results to those of the current work with regard to all the RBCs indices. This variation may be attributed to variation in supportive supplementation during pregnancy and or nutritional habits (Jacobs *et al.*, 2013).

In this study it was found an increase in the TWBCs count with a significant variation between the first trimester when compared with the second and third trimesters, which accords with the results of Jacobs *et al.*, (2013).This increase may be due to WBCs being responsible for the body defense during pregnancy (Jacobs *et al.*, 2013).

A gradual decrease in PLT count was observed in the study this is in agreement with Akinbami *et al.*, (2013). This gradual reduction in PLT count as pregnancy advance may be due to hemodilution secondary to expansion of the plasma volume. The PLT count in normal pregnancy may decrease by approximately 10%, with most of this decrease occurring during the third trimester, although the absolute PLT count tends to remain within the normal reference range in most pregnant women (Akinbami *et al.*, 2013).

In this study the majority of anemia was found at the mild stage and the most occurrence of anemia in the third trimester.

Farah, (2012) conducted a study in Khartoum and reported that, the majority of anemia was in the mild stage 85.2%, whereas moderate anemia was 11.1% and 3.7% was severe cases, and in Pakistan predomination of mild anemia was reported by Baig-Ansari *et al.*, (2010) and also, Bushra *et al.*, (2010) showed that, gestational age is inversely correlated with hemoglobin. These results are compatible with the results of the current study. Higher occurrence of anemia in the third trimester might be due to increased nutritional demand for the fetus in the third trimester, as well as mild anemia might be restricted in the mild stage by supplements that were taken (Marrieb and Hoehn, 2013).

In the current study there no association was found between anemia and multi-gravidity, which contradicting the work of Adam *et al.*, (2005) who reported a significant association between anemia and multi-gravidity in New Halfa Town.

In the current study there no association was found between anemia and age that agreed with the (Bushra *et al.*, 2010).

4.2 **Conclusion**

The study concluded that,

1- hematological parameters (Hb, HCT, RBCs, MCV, MCH, MCHC, PLT, MPV and PDW)showed changes during pregnancy period mostly decrease with progress in trimester stages and there increase in (TWBcs and RDW). they showed statistical significant association when assessed according to gestational age, except HCT.

2- Anemia with different degree of severity was found among slightly higher than fifty of the studied women (51.3%), among whom mild anemia was the most common.

3- The demographic information (age, gravidity, maternal follow up (ANC) booking, education and socioeconomic level) weren't associated with anemia situation.

4.3 **Recommendations**

This study recommends the following:-

- Anemic pregnant women need further investigation in order to identify the etiology whenever possible, despite commencing the usual treatment with iron and folate.
- Antenatal care and efforts should be geared toward the early detection and treatment of anemia before delivery.
- Hematological references values for the pregnant women should be provided in Sudan to facilitate research.
- Nutritional sessions should be provided for the community through multimedia, schools, health visitors and other health providers.

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Appendix (1)

جامعة السودان للعلوم والتكنولوجيا

كلية الدراسات العليا

قسم امراض الدم والمناعة الدموية

الموافقة المستنيرة للمراة الحامل

الرقم :----------

الأسم :----------

سيتم اخذ عينة دم من الوريد بحجم 2.5 مل بواسطة حقنة الطعن المعقمة المعروفة وذلك بعد تعقيم منطقة سحب العينة بواسطة مطهر؛جميع الادوات المستخدمة لأخذ العينة معقمة ومتبع فيها كل وسائل السلأمة المعملية وليس هناك اثار جانبية لهذا السحب او ربما يحصل الم خفيف اثناء سحب العينة او تورم بسيط فى منطقة اخذ العينة وسوف يزول سريعا.

الغرض من اخذ العينة اجراء بحث علمي وسوف نقوم بعمل تحليل صورة كاملة للدم يتم تسليم المريض نسخة من النتائج ويتم الأحتفاظ بالنسخ الأخرى في سرية تامة .

اوافق انا المذكورة اعلأه على اخذ عينة الدم المطلوبة لاجرا الفحص للدراسة .

الأمضاء ----------

التاريخ -----/----/2014م

Appendix (2)

جامعة السودان للعلوم والتكنولوجيا

كلية الدراسات العليا

قسم امراض الدم والمناعة الدموية

Questionnaire for research

Name ----------

Number --------

Age----------

Blood group ---

Transfusion during three month ago Yes ( ) No( )

Education level: No ( ) primary ( ) secondary ( ) high ( )

Socioeconomic status: poor ( ) good ( ) high ( )

Gravidity: primigravide( ) multigravide( ) numbers of gravid-----

Duration pregnancy:First trimester( )second trimester( )third trimester( )

History of disease: Malaria( ) liver disease( ) hypertension( )

DM( ) renal disease ( ) leshmaniasese ( ) Others ----------

Maternal follow up: No ( ) Yes ( )

Number of fetus in side uterus by U/S: One ( ) Twins ( )

Hematological investigation result:-

Hb	**HCT**	**RBCs**	**MCV**	**MCH**	**RDW**	**MCHC**	**TWBCs**	**Plts**	**MPV**	**PDW**
g/dl	**%**	**Cell/L**	**FL**	**Pg**	**%**	**g/dL**	**Cell/L**	**Cell/L**	**FL**	**%**