Sudan University of Science and Technology
College of Graduate Studies

Complete Blood Count of Sudanese females with Breast Cancer attending Radiation and Isotope center in Khartoum state

تعداد الدم الكامل لمريضات سرطان الثدي السودانيات في المركز القومي للعلاج بالأشعة والطب النووي بولاية الخرطوم

A Thesis is submitted in partial Fulfillment of the Degree of MS.C in Medical Laboratory Science (Hematology and Immune Hematology)

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2014

بِسْمِ اللّهِ الرِّحْمَنِ الرِّحِيمِ

قال الله تعالى

اللَّهُ نُورُ السَّمَوَاتِ وَالْأَرْضِ مَثَلُ نُورِهِ كَمِشْكَاةٍ فِيهَا مِصْبَاحٌ الْمِصْبَاحُ فِي زُجَاجَةٍ
الزُّجَاجَةُ كَأَنَّهَا كَوْكَبٌ دُرِّيٌّ يُوقَدُ مِنْ شَجَرَةٍ مُبَارَكَةٍ زَيْتُونَةٍ لَا شَرْقِيَّةٍ وَلَا غَرْبِيَّةٍ
يَكَادُ زَيْتُهَا يُضِيءُ وَلَوْ لَمْ تَمْسَسْهُ نَارٌ نُورٌ عَلَى نُورٍ يَهْدِي اللَّهُ لِنُورِهِ مَنْ يَشَاءُ
وَيَضْرِبُ اللَّهُ الْأَمْثَالَ لِلنَّاسِ وَاللَّهُ بِكُلِّ شَيْءٍ عَلِيمٌ

صدق الله العظيم
سورة النور الآية ٣٥

Dedication

To my dear parents d me to this study , To my only lovely sister and To my brothers.

To my teachers and all whom I love and respect I dedicate this work

Acknowledgment

All thanks to Allah who give me health to carry out this work and reach this level

Special and great thanks to Dr. Sana Eltahir for her supervision, guidance and continuous encouragement through this study.

My thanks extended to all the members of hematology department in radiation and isotope center for the help given to me with this study

My sincere thanks to my small family they encourage me until reach this level.

Abstract

Breast cancer comprises 10.4% of all cancer incidence making it the second most type of non skin cancer and the fifth most common cause of cancer death. Breast cancer is about 100 times more common in women than in men, but survival are equal in both. it constitutes 13-35% of all female cancer. The aim of this study is to determined the Complete Blood Count in Sudanese females with breast cancer under treatment with (Chemotherapy, Radiation or mastectomy) .

This is a hospital based case control study conducted to measure complete blood count in females with breast cancer, 100 blood sample were collected from females with breast cancer compared to 20 healthy females

The sample was collected in EDTA anti coagulated and tested to measure Complete blood count using automated cell counter (sysmax KX 21) to find out ; the hemoglobin concentration (Hb), Red blood cells count (RBCs) , Packed cell volume (PCV) ,RBCs indices , White blood cells (WBCs) count and Platelet count. blood film were prepared to evaluate cell morphology.

The result of this study showed that there was decrease in mean of Hb (7.66) , PCV (31.98), MCV (83.03), MCHC (27.03) and PLTs (295.88)

while there were normal value in the mean of WBCs count. also, the result showed 65% of patients were anemic 27% was Microcytic Hypochromic and 35% was Normocytic Normochromic. the result showed that the mean value of Hb and PLTs in patients receiving chemotherapy was significantly reduced with P-value (0.00) while the WBCs was not affected . The result showed a significant reduction in Hb , PCV , MCV and PLTs in females with breast cancer according to breast feeding.

The study concluded that the chemotherapy has a significant effect on Hb and PLTs in patients with breast cancer while WBCs was not affected .
Also, there is no significant difference in Hb, WBCs and PLTs according to mastectomy of breast.

المستخلص

يمثل سرطان الثدي ١٠.٤ ٪ من جميع حالات السرطان مما يجعله ثاني أكثر الانواع شيوعا والسبب الخامس الأكثر شيوعا للوفاة . سرطان الثدي هو حوالي المئة مرة أكثر شيوعا في النساء أكثر من الرجال ، فهو يشكل ١٣-٣٥ ٪ من مجموع حالات السرطان للإناث ولكن فرص البقاء على قيد الحياة متساويه في كليهما.

الهدف من هذه الدراسة هو تحديد تعداد الدم الكامل في الإناث السودانيات المصابات بسرطان الثدي تحت العلاج الكيميائي أوالاشعاعي أو استئصال الثدي

هذه دراسة وصفية بأثر رجعي اجريت لقياس تعداد الدم الكامل في الإناث المصابات بسرطان الثدي من خلال جمع مئه عينة من الإناث المصابات بسرطان الثدي لمقارنتها مع عشرون عينه جمعت من إناث صحيحات

جمعت عينات الدم في حاويات تحتوي علي مانع التجلط بطريقة عشوائية من مرضى سرطان الثدي واختبرت لمعرفة الهيموجلوبين (خضاب الدم) و عدد الخلايا البيضاء وكريات الدم الحمراء وحجمها ومعدل تركيز الخضاب في كل منها وفي حجم معين من كريات الدم الحمراء المضغوطة بعد ذلك تم الكشف على مسحات الدم الرقيقة المصبوغة لمعرفة الشكل العام للخلايا، وتميز وعد خلايا الدم البيضاء لمعرفة التغيرات المصاحبة للسرطان

اظهرت نتائج هذه الدراسه ان هناك انخفاضا في معدل الهيموجلوبين (خضاب الدم)، حجم كريات الدم الحمراء ومعدل تركيز الخضاب ومعدل تركيز الخضاب في حجم معين من كريات الدم الحمراء وعدد الصفائح الدموية بينما كان عدد كريات الدم البيضاء ضمن المعدل الطبيعي عند المرضى

كما اظهرت الدراسه ان ٦٥ % من المريضات مصابات بفقر الدم

ايضا: اظهرت الدراسه ان معدل الهيموجلوبين (خضاب الدم) و الصفائح الدمويه انخفضت بشكل ملحوظ لدى المريضات اللواتي يتعالجن بالعلاج الكيميائي في حين لم تتاثر كريات الدم البيضاء و اظهرت الدراسه انخفاضاً بشكل كبير في معدل الهيموجلوبين ومعدل تركيز الخضاب في كريات الدم الحمراء و معدل تركيز الخضاب في حجم معين من كريات الدم الحمراء المضغوطه والصفائح الدمويه نتيجة للرضاعه الطبيعيه.

وخلصت الدراسة إلى أن العلاج الكيميائي له تأثير كبير على الهيموغلوبين و والصفائح الدمويه المرضى الذين يعانون من سرطان الثدي في حين لم تتأثر الكريات البيضاء.

أيضا ، ليس هناك اختلافاً كبيراً في الهيموجلوبين وكريات الدم البيضاء والصفائح الدموية وفقا لاستئصال الثدي

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List of abbreviations:

ALA : Amino levulinic acid

AGM : Aorta gonads mesonphro region

CBC: Complete blood Count

EDTA: ethylene diamine tetra acetic acid

ESAs: Erythropoiesis stimulating agents

FNA: Fine needle aspiration

FN: Febrile neutropenia

Hb: Hemoglobin

Hct: Hematocrit

MCV: Mean Cell volume

MCH: Mean Cell Hemoglobin

MCHC: Mean Cell Hemoglobin Concentration

PCV: Packed Cell volume

RBCs: Red Blood Cells

SLN; Sentinel lymph node

SPSS: Statistical Packages Social Science

WBCs: White Blood Cell

CHAPTER ONE

1. Introduction and Literature Review

1.1 Introduction:

The Complete Blood Count (CBC) are an essential and basic hematological tests and are one of the most frequent order laboratory procedure in hematological disorder. It consist of a series of tests that determine number , variety, percentage, concentration and quality of the blood cell .The findings in the complete blood count give valuable diagnostic information about the hematological and other body system, prognosis ,response to treatment and recovery (Dacie and lewis, 1991; Dacie and lewis 1977)

Complete Blood Count includes: hemoglobin (Hb) level, packed cell volume (PCV) value, red blood cells (RBCs) count, white blood cells (WBCs) count, platelets count in addition to red cell indices, morphological examination and differential leucocytes count.(Dacie and lewis; 1977)

Cancers are a group of disease that cause cells in the body to change and grow out of control. Most types of cancer cells eventually form a lump or mass called a tumor and are named after the part of the body where the tumor originates.(Jemal, *et al* ; 2006).

Breast cancer it is type from cancer it begins in breast tissue, which is made up of glands for milk production called lobules, and the ducts that connect lobules to the nipple. In many developed countries it is second most frequent cause of cancer – related mortality. It is a significant public health problem in virtually all industrialized societies and the most common cancer among American women after skin cancer, affected more than 200.000 women each year and making up most a third of all cancer diagnoses in women. Yet breast cancer continues to affect women of all ethnic groups, all ages, and all walks of life. Breast cancer mortality is high in the Sudan and most patients are detected of later stage of the disease due to lack of awareness and absence of screening programs.(Dacie and lewis ; 1991)

1.2 Literature Review:

1.2.1. Physiology of blood :

Blood is a highly specialized form of connective tissue composed of several cellular elements and a fluid element. The cellular elements of blood determine its categorization as red or white blood cells, or as platelets. The fluid element is known as blood plasma. This plasma is composed of water, proteins, hormones, vitamins, amino acids, lipids, carbohydrates and inorganic salts, next to water, which comprises 90% of its composition. Blood is circulated around the body through blood vessels by the pumping action of the heart this continual flow maintains a constant environment for body cell .(Ross and Wilson ; 2007)

1.2.2. Haematopoiesis :

The processes by which blood cell formed is called haematopoiesis in first few weeks of gestation the yolk sac is main site of haematopoiesis. The definitive haematopoiesis drives from a population of stem cells first observed on the dorsal aorta termed the aorta gonads mesonphro region(AGM). These common precursors of endothelial and haematopoietic cells are believed to sead the liver and spleen and bone marrow and from 6 weeks until 6 – 7 months of fetal life the liver and spleen are the major haematopoietic organs and continue to produce blood cells until about 2 weeks after birth. The bone marrow is most important site from 6 to 7 month of fetal life.During the normal childhood and adult life marrow is the only source of new blood cells .In infancy all the bone marrow is haematopoietic but during adult life haematopoietic marrow is confide to the central skeleton and proximal end of the femurs site of haematopoiesis.(Hoffbrand, *et al;* 2006).

1.2.2.1 Erythrocytes (red blood cell):

The red blood cells (the most numerous of cellular component) are produce by proliferation of precursor erythroblast in the bone marrow. The entire process which red cells are produce in bone marrow is called erythropoiesis.

The mature circulating erythrocyte is a biconcave disc measure about 7-8 micrometer in diameter with thickness about 1.5 – 2.5 μm. It has a surface to volume ratio that enables optimal gaseous exchange to occur . The cell main function is oxygen delivery throughout the body.(Dacie and lewis ;1991)

The biconcave form of red cell and membrane which made of specialized deformable protein fibers, enable the cell to pass through capillaries of small diameter. It's shape also provides a large surface area for the exchange of

respiratory gases. Red destruction usually after a mean life span of 120 days when the cells are removed extra vascular by the macrophage of the reticuloendothetial system. .(Dacie and lewis **;** 1991)

1.2.2.2 Leukocyte (white blood cell):

Are cells of the immune system involved in defending the body against both infectious disease and foreign materials it derived from a multipotent cell in the bone marrow known as hematopoietic stem cell. They live for about three to four days in the average human body.(Wintrob, *et al:* 1981)

They classified as granulocytes or Agranulocytes:

1.2.2.2.1. Granulocytes (polymorphonuclear leukocytes): characterized by the presence of differently staining granules in their cytoplasm when viewed under light microscopy. These granules (usually lysozymes) are membrane-bound enzymes that act primarily in the digestion of endocytosed particles. There are three types of granulocytes: neutrophils, basophils, and eosinophils .(Wintrob, *et al;* 1991)

Neutrophile: This cell has a characteristic dense nucleus consisting between 2 – 5 lobes and pale cytoplasm containing many fine pink –blue (azurophilic) or gray blue granules.The life span of neutrophile in the blood is 10 hours. These cell counts for more than half the circulating leucocytes. They are main defense cells of the body against pyogenic bacterial infections.

Eosinophil: Eosinophils are little larger than neutrophils, they have two nuclear lobs or segments and the cytoplasm is full of granules that assume a characteristic pink-orange color . They inter the inflammatory exudates and

have special role in allergic responses in defense against parasite and in removal of fibrin formed during inflammation. (Wintrob, *et al* 1981; Hoffbrand , *et al* 2006)

Basophiles**:** Basophils are rarest (less 1%) of circulation leukocyte. Their nuclear segments tend to fold up on each other resulting in a compact irregular dense nucleus , large variable size dark blue or purple granules of the cytoplasm often obscure the nucleus ,they rich in histamine, serotonin and heparin substance so it responsible for allergic and antigen response by releasing this chemical causing vasodilatation. (Wintrob, *et al* 1981; Hoffbrand , *et al* 2006)

1.2.2.2.2. A granulocytes (mononuclear leukocytes): characterized by the absence of granules in their cytoplasm. Although the name implies a lack of granules these cells do contain non-specific azurophilic granules, which are lysosomes. The cells include lymphocytes, monocytes, andmacrophages.

Monocytes: They are largest of the circulation leukocytes in diameter, they have gray cytoplasm the nucleus is large and curved often in shape of horse shoe. They are activiely phagocytic but have specialized function as well. On migration in to the tissue they become transformed in to actively phagocytic macrophage as which are found in many organs particularly in spleen, liver, pulmonary alveoli and peritoneum. They have surface receptors for immunoglobin both lgE and IgM. This enhances their phagocytic potential and facilitates their ability to phagocytes erythrocytes coated with antibodies, this applies particularly to those macrophages lying in splenic and hepatic sinusoids and intimate contact with circulating cells.

Their activity is also enhanced by activation of complement and play an important role on the cellular immune response. (Wintrob, *et al;* 1991)

Lymphocytes**:** Lymphocytes are the immunologically competent cells which add specificity to the attack. It's small cell measuring about 6 -10mm in diameter. The nucleus is round or oval it stain dark by usual romanowesky stain the chromatin appearing dense. The narrow rim of cytoplasm is moderately basophilic and contains not more the few vascular and azurophilic granules. (Ross and Wilson ; 2007)

The immune response depends on two type of lymphocyte B and T lymphocyte. Function of B lymphocyte production of antibodies from plasma cell, block pathogen invasion, activate the complement system, and enhance pathogen destruction. T- lymphocytes are cell of cell mediated immune response. (Ross and Wilson ;2007)

1.2.2.3. Thrombocytes (platelet):

It's small, disk shaped clear cell fragments 2–3 μm in diameter, which are derived from fragmentation of precursor megakaryocytes. The average lifespan of a platelet is normally just 5 to 9 days. Platelets are a natural source of growth factors. They circulate in the blood of mammals and are involved in hemostasis , leading to the formation of blood clots. (Ross and Wilson ; 2007)

1.2.3. Hemoglobin :

It‘s a colored (red color) respiratory pigment found in the red cell. The main function of red cells is to carry O_2 to the tissue and return carbon dioxide

(CO_2) from tissue to the lung. In order to a chive this gaseous exchange they contain the specialized protein haemoglobin. The normal adult blood contain Hb A and also small quantities of two other Hb; HbF and HbA_2.(Hanzetti G ; 1966)

1.2.3.1. Hemoglobin synthesis and function :

The hemoglobin begins to be produced during the proerythroblast stage of the RBC cycle. The synthesis takes place in the mitochondria and ribosome by a series of biochemical reactions. In the mitochondria, the synthesis of the heme portion of hemoglobin takes place. Here, heme synthesis begins with the condensation of glycine and succinyl-CoA to form δ-aminolevulinic acid (ALA). ALA then leaves the mitochondria and form porphobilinogen through a series of reaction forms coproporphyrinogen. This molecule then returns to the mitochondria and produce protoporphyrin.(OshiroI, et al; 1982)

Proto-porphyrin is then combined with iron to form heme. Heme then exits the mitochondria and combines with the globin molecule which is synthesized in the ribosome. .(Hanzetti, 1966; OshiroI, et al 1982)

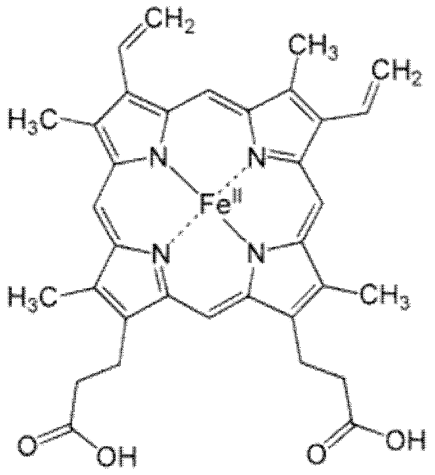


Figure (1.2): Hemoglobin structure.(Hanzetti, 1966; OshiroI, et al 1982)

The red cell in systemic arterial blood carries O_2 from the lung to the tissues and return in venous blood with CO_2 to the lung. As the haemoglobin molecule loads and unloads O_2 the individual globin chains in Hb molecule move on each other. The α_1, β_1 and α_2, β_2 contacts stabilize the molecule. The β chains slid on the α_1, β_2 and α_2, β_1 contact during oxygenation and deoxygenating. When O_2 is unloaded the β chains are pulled a part, permitting entry of metabolite 2,3 diphosphoglycerate (2,3 DPG) resulting in a lower affinity of molecule for O_2 (Lewis, *et al*; 2005).

Hb is measured to detect anemia, polycythemia and their severities and also to monitor an anemic patient response to treatment. (Lewis, *et al*; 2005).

1.2.4. Anemia :

Anemia is present when hemoglobin level in blood is below than the lower limit of the normal range for the age and sex of individual . Hemoglobin value of less than 13.5 gm/dl in a man or less than 12.0

gm/dl in a woman. Normal values for children vary with age.(Hoffbrand, *et al* 2002)

Anemia is a decrease in number of red blood cells (RBCs) or quantity of hemoglobin less than the normal in the blood. Also it defined as decreased oxygen-binding ability of each hemoglobin molecule due to deformity or lack in numerical development as in some other types of hemoglobin deficiency. It is a common problem for cancer patients and often result from the therapies used to suppress or control the tumors . Anemia is associated with weakness, or fatigue, general malaise, fast heart, beat Shortness of breath , trouble breathing when doing things like walking, climbing stairs, or even talking, dizziness, chest pain ,swelling in the hands and/or feet and pale skin. These symptoms are often complicated by coexisting diseases. There are many compromises that are necessary when one has a symptomatic anemia, this can affect the tolerability of therapy. Anemia is also associated with a poorer prognosis and increased mortality.(Hoffbrand, *et al* 2002 ; Frank, *et al* 1989)

1.2.4.1. Classification of anemia:

Anemia is classified based on the size of red blood cells; this is done on microscopic examination of a peripheral blood smear with red blood indices . The size is reflected in the mean corpuscular volume (MCV). If the cells are smaller than normal (under 80 fl), the anemia is said to be microcytic hypochromic such as (Iron deficiency anemia , Thalassemia, Anemia of chronic disease and lead poising) (Lewis, *et al* 1977)

; if the MCV are normal size (80–110 fl) it is normocytic normochromic such as hemolytic anemia, anemia of chronic disease (some cases), after acut blood loss, renal disease, bone marrow failure post chemo therapy and if they are larger than normal (over 100 fl), the anemia is classified as macrocytic normochromic anemia such as megaloblastic anemia ,liver disease and a plastic anemia (Lewis, *et al* 1977)

Also , anemia can be classified based on underling pathological processes , the cause of anemia in particular patient:

- Decreased red cell production or inadequate RBCs production , which include : .Nutritional anemia, bone marrow atrophy and bone marrow infiltration
- Blood loss : bleeding such as hemorrhages or abnormal menstrual bleeding
- Hemolysis :Break down or destruction of red cells .
- Chronic illness secondary to refractory anemia : inflammatory gastro intestinal , Malignancies , cancer , arthritis ,kidney or liver acute or chronic infection (Dacie, *et al;* 1977)

1.2.4.Laboratory Diagnosis :

1.2.4.1.Complete blood count (CBC) :

Complete blood count (CBC) test is one of the most common order blood tests. It's a calculation of cellular (formed element) of blood. These calculation are generally determined by special machines that analyze the different components of blood in less than minute.(Auther, *et al* 2001; Jones, *et al* ;1996)

1.2.4.1.1. A major portion of complete blood count is :

1) Measure the number of red blood cell.
2) Measure the number of white blood cell.
3) Platelets count.
4) The total amount of hemoglobin in the blood.
5) The size of red blood cells , mean corpuscular volume (MCV).
6) The CBC also provides specific information about the size and hemoglobin content of individual red blood cells. This determined from the additional following measurement: Mean corpuscular hemoglobin (MCH) .Mean corpuscular hemoglobin concentration (MCHC).(Jones, *et al;* 1996)

1.2.4.1.2. Red blood cell (RBC) count:.

If the RBC count is low (anemia), the body may not be getting the oxygen it needs. If the count is too high (a condition called polycythemia), there is a chance that the red blood cells will clump together and block tiny blood vessels (capillaries).It count in million in per cubic milliliter (mil/mm^3). (Dacie, *et al* ; 1977)

1.2.4.1.3. White blood cell count:

White blood cells protect the body against infection. If an infection develops, white blood cells attack and destroy the bacteria, virus, or other organism causing it. White blood cells are bigger than red blood cells but fewer in number it's measured in thousands per cubic milliliter (c/mm^3) of blood . (Dacie, *et al* ; 1977)

1.2.4.1.4. Platelet (PLT) count:

Platelets (PLT) are the smallest type of blood cell. They are important in blood clotting. When bleeding occurs, the platelets swell, clump together, and form a sticky plug that helps stop the bleeding. It measured in thousands per Cubic milliliter (c/mm^3) of blood. (Dacie, *et al* ; 1977)

1.2.4.1.5. Hemoglobin Estimation :

Hemoglobin concentration (Hb) of a solution may be estimated by measuring its color, its power of combining with oxygen or carbon monoxide, or by its iron content.(Lafterety, *et al* ; 2000)

1.2.4.1.6 Hematocrit (HCT):

Measures the percentage of the volume of whole blood that is made up of red blood cells. This measurement depends on the number of red blood cells and the size of red blood cells .The principle of PCV based on complete packed of red cell during centrifugation to obtain red cell column , then the ratio expressed as percentage against the whole blood . (Dacie, *et al;* 1977) HCT methods carried out on blood contained in capillary tubes 75mm in length and having internal diameter of about 1mm. Plain tube used for anti coagulated blood sample, the tubes coated inside with 1intrnational unit of heparin for capillary blood. The centrifuge used for the capillary tube provides centrifugal force of c 12000g, and 5 min. Centrifugation results in a constant PCV. The PCV value is read by using reading device (Lewis, *et al* ;2001)

1.2.4.1.7. Red Cell Indices:

The red cell indices include the mean corpuscular volume (MCV), mean corpuscular hemoglobin(MCH) and mean cell hemoglobin concentration MCHC. The indices used to classifying anemia and distinguish between iron deficiency and thalasseamia (Lafterety JD *etal* 1988; Jones NC *etal* ;1996)

MCV:Is the average volume of the RBCs and size measured in femtoliters (FL) .Low MCV value found in microcytic anemia raised MCV value found in macrocytic aneamia, marked reticulocytosis and chronic alcoholism and new born infant (Lafterety, *et al;* 1988)

MCH is the average weight of Hb in RBCs expressed in pictogram (pg) .Low MCH value found in microcytic hypo chromic anemia raised MCH value are found in macrocytic anemia also raised in new born.

MCHC: It's the concentration of Hb in each individual erythrocyte expressed by g/l .Low MCHC values are found in iron deficiency anemia and thalassemia trait. Increase MCHC can occur marked spherocytosis (rarely).((Lafterety, *et al* ; 1988)

1.2.4.8. Examination of peripheral blood Picture (PBP) :

In this test, a drop of blood is spread (smeared) on a slide and stained with a special dye. The slide is looked at under a microscope. The number, size, and shape of red blood cells, white blood cells, and platelets are recorded. Blood cells with different shapes or sizes can help diagnose many blood diseases, such as leukemia, malaria, or sickle cell disease.(Vector, et al; 1999)

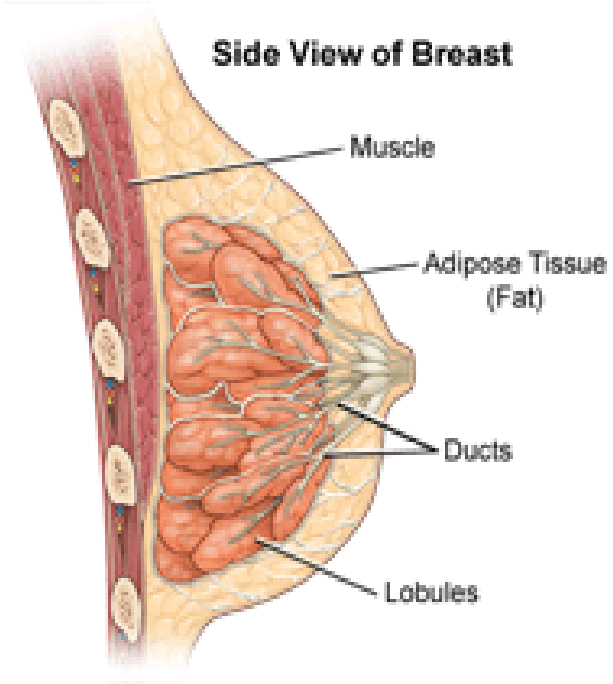
1.2.5. Cancer :

Is a broad group of diseases involving cells divide and grow uncontrollably forming malignant tumors and invading nearby parts of the body. The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream. Not all tumors are cancerous; benign tumors do not invade neighboring tissues and do not spread throughout the body. There are over 200 different known cancers that affect humans.(National Cancer Institute, 2013)

1.2.5.1. Structure of the breast:

Each breast has 15 to 20 sections, called lobes, that are arranged like the petals of a daisy. Each lobe has many smaller lobules, which end in dozens of tiny bulbs that can produce milk. The lobes, lobules, and bulbs are all linked by thin tubes called ducts. These ducts lead to the nipple in the center of a dark area of skin called the areola.(National Cancer Institute,2012; Ramsay, *et al; 2005*)

The breast is an organ which whose structure reflects its special function: the production of milk for lactation. The epithelial component of the tissue consists of lobules, where milk is made, which connect to ducts that lead out to the nipple The breast tissue is encircled by a thin layer of connective tissue called fascia. The deep layer of this fascia sits immediately on top of the pectoralis muscle, and the superficial layer sits just under the skin. The skin covering the breast is similar to skin elsewhere on the torso and has similar sweat glands, hair follicles, and other characteristic features.



Figu**re (1.3) Structure of breast**: *(*Ramsay*, et al;* 2005)

1.2.5.2. Breast cancer:

Breast cancer is a type of cancer that begins in breast tissue, which is made up of glands for milk production called lobules, and the ducts that connect lobules to the nipple. In many developed countries it is the second most frequent cause of cancer – related mortality. It is a significant public health problem in virtually all industrialized societies it is the most common cancer among american women after skin cancer, affected more than 200.000 women each year and making up most a third of all cancer diagnosed in women. Yet breast cancer continues to affect women of all ethnic groups, all

ages, and all walks of life. Breast cancer mortality is high in Sudan and most patients are detected of later stage of the disease due to lack of awareness and absence of screening programs. (Sariego ; 2010)

1.2.5.3. Pathophysiology of breast cancer :

Breast cancer, like other cancers, occurs because of an interaction between an environmental factor and a genetically susceptible host. Normal cells divide as many times as need and stop. They attach to other cells and stay in place in tissues. Cells become cancerous when they lose their ability to stop dividing, to attach to other cells, to stay where they belong, and to die at the proper time. Normal cells is programmed to die (apoptosis) when they are no longer need. Until then, they are protected from cell death by several protein clusters and pathways. One of the protective pathways is the PI3K/AKT pathway , another is the RAS/MEK/ERK pathway. Sometimes the genes along these protective pathways are mutated in a way that turns them permanently "on", rendering the cell incapable of death when it is no longer needed. This is one of the steps that causes cancer in combination with other mutations. These mutations are either inherited or acquired after birth. Presumably, they allow further mutations, which allow uncontrolled division, lack of attachment, and metastasis to distant organs.

Mutations that can lead to breast cancer have been experimentally linked to estrogen exposure. Also ,Failure of immune surveillance, which function is removal of malignant cells throughout one's life and abnormal growth factor signaling in the interaction between stromal cells and epithelial cells all can facilitate malignant cell growth. (Adrian Lee, *et al* ;2009)

1.2.5.4. Incidence of breast cancer in Sudan:

The broad ethnic and climatic diversity of Sudan makes it in many ways a microcosm of Africa. Sudan is experiencing a bur going cancer epidemic, that carries many challenges that are characteristic of developing countries. This include a high incidence of advanced difficult to treat at presentation, and high cancer burden that is related to infectious disease. (Radation and Isotop center Khartoum ; 2009)

Table(1.1): Incidence of breast cancer according to age group: .(Radation and Isotop center Khartoum , 2009)

Age/year	Frequency	Percent
11-20 years	30	0.6
21-30 years	394	8.1
31-40 years	1270	26
41-50 years	1343	27.5
51-60 years	961	19.6

61-70 years	639	13.1
70 years+	244	5
Total	4892	100

Incidence of breast cancer show high percentage 26% at 31-40 years old and 27.5% at the 41-50 years old, this are the productive age.(Radation and Isotop center Khartoum , 2009)

Table (1.2): Frequency of breast cancer in sudan according to tribes: Radation and Isotop center Khartoum ,2009)

Tribe	Frequency	Percent
Galy'a	949	19.4
Shaigy'a	448	9.2
Dongla	378	7.7
Hassany'a	213	4.4
Mahas	159	3.3
Nuba	151	3.1

Bederia	135	2.8
Kawahla	130	2.7
Gwama'a	87	1.8
Halfawe	82	1.7
Other tribes	2160	46.6
Total	4892	100

Distribution of breast cancer showed highest percent between galy'a followed by shaigy'a,dongola,hassany'a,mahas,respectively. This is indicates that northern of Sudan is the more epidemic area with breast cancer.(Radation and Isotop center Khartoum ,2009)

1.2.5.5. Classification of breast cancer:

Breast cancer can be classified by different schema Each of these schemes classify the cancers based on different criteria and serve a different purpose they include *:* Classification based on pathology, Classification according to grade, classification according to receptor status and classification according to presence or absence of genes (American Society of Clinical Oncology,*2012)*

1.2.5.6. Sign and symptoms of breast cancer:

Most commonly the first sign is a lump in the breast the woman usually finds the lump .Sometimes the lump is seen on a screening mammogram

before it can be felt .It present all the time and does not get smaller or go away with the menstrual cycle .It may feel like it is attached to the skin or chest wall and cannot be moved. also it feel hard, irregular in shape and very different from the rest of the breast tissue usually it's not painful pain is more often a symptom of a non-cancerous (benign) condition. Changes in breast shape or size ,skin changes: The skin of the breast may become dimpled or puckered, redness, swelling and increased warmth, itching of the breast or nipple changes(discharge from the nipples) also the patients can presented with bone pain, nausea, loss of appetite, weight loss and jaundice . (American Cancer Society, 2009; Breast Cancer and the Environment , 2012)

1.2.5.7. Risk factor of breast cancer:

A breast cancer risk factor is something that increases a person's chance of developing breast cancer. Knowledge about risk factors can change the way of understand the risk of breast cancer and the actions taken to reduce the risk. Some risk factors can be changed: they can be modifiable. This risk factor include :

Gender**:** The cancer is 100 times more common among women than men.

Aging**:** the risk of developing breast cancer increases with age.

Genetic risk factors About 5% to 10% of breast cancer cases are thought to be hereditary, meaning that they result directly from gene defects (mutations) inherited from a parent . (Breast Cancer and the Environment , 2012)

Family history of breast cancer Breast cancer risk is higher among women whose close blood relatives have this disease (mother, sister, or daughter) it doubles a woman's risk**. (**Breast Cancer and the Environment , 2012)

1.2.5.8. Anemia in patient with breast cancer :

Anemia are common in patient with breast cancer .It's prevalence depending on the extent of disease , type and duration of anticancer therapy , in which anemia can be mild Hb < 12g/dl , or severe Hb > 8g/dl . Also patient with breast cancer can suffer from anemia which directly related to cancer , such as cytokines or anemia due to bone marrow infiltration by lymphoma or cancer .(M. Dicato ; 2010)

1.2.5.9. Diagnosis of breast cancer:

Most types of breast cancer are easy to diagnose by microscopic analysis of a sample or biopsy of the affected area of the breast. However, there are rarer types of breast cancer that require specialized lab exams. The two most commonly used screening methods are: physical examination of the breasts by a healthcare provider and mammography .Can offer an approximate

likelihood that a lump is cancer, and may also detect some other lesions, such as a simple cyst. When these examinations are inconclusive, a healthcare provider can remove a sample of the fluid in the lump fine needle aspiration and (FNA) for microscopic analysis to help establish the diagnosis . Together , physical examination , mammography, and FNA can be used to diagnose breast cancer with a good degree of accuracy. **(**Ting Bao, *et al* ; 2011)

1.2.5.10. Treatment of breast cancer :

The treatment of breast cancer depends on various factors, including the stage of the cancer. Aggressive treatments are employed in accordance with the poorer the patient's prognosis and the higher the risk of recurrence of the cancer following treatment. *(*Ting Bao, *et al* ; 2011*)*

Breast cancer is usually treated with surgery, which may be followed by chemotherapy or radiation therapy, or both, hormone receptor-positive cancers are often treated with hormone-blocking therapy over courses of several years. Monoclonal antibodies, or other immune-modulating treatments, may be administered in certain cases of metastatic and other advanced stages of breast cancer. (Ting Bao, *et al* ; 2011)

1.2.5.10.1. Surgery:

Depending on the staging and type of the tumor surgical removal of physical tumor along with some of the surrounding tissue is necessary. One or more lymph nodes may be biopsied during the surgery , the lymph node sampling is performed by a sentinel lymph node biopsy (SLN) is the first node that drains the tumor, and subsequent SLN mapping can save 65-70% of patients

with breast cancer from having a complete lymph node dissection for what could turn out to be a negative nodal basin. (Massarut *, et al* ; 2006)

standard surgeries include: mastectomy: Removal of the whole breast, quadrantectomy: Removal of one quarter of the breast and lumpectomy: Removal of a small part of the breast. (Herceptin trastuzumab , 2000)

1.2.5.10.2.Radiation Therapy:

Radiation is an adjuvant treatment for most women who have undergone lumpectomy and for some women who have mastectomy to eliminates the microscopic cancer cells that may remain near the area where the tumor was surgically removed . Radiation therapy involves using high-energy X-rays or gamma rays that target a tumor or post surgery tumor site. This radiation is very effective in killing cancer cells that may remain after surgery or recur where the tumor was removed. It can be delivered by either external beam radiotherapy or internal radiotherapy (brachytherapy) (Massarut, *et al* ; 2006)

radiation affects normal cells and cancer cells alike, causing some damage to the normal tissue around where the tumor was. Healthy tissue can repair itself, while cancer cells do not repair themselves as well as normal cells. For this reason, radiation treatments are given over an extended period, enabling the healthy tissue to heal . (Massarut, *et al* ; 2006 ; Mastectomy vs. Lumpectomy, 2013)

1.2.5.10.3. Chemotherapy :

Chemotherapy is predominantly used for cases of breast cancer in stages 2–4, and is particularly beneficial in estrogen receptor-negative (ER-) disease. The chemotherapy medications are administered in combinations, usually for periods of 3–6 months.Most chemotherapy medications work by destroying fast-growing and/or fast-replicating cancer cells, either by causing DNA damage upon replication or by other mechanisms. However, the medications also damage fast-growing normal cells, which may cause serious side effects. (Massarut, *et al* ; 2006)

1.2.6. The effect of chemotherapy- radiotherapy and surgery on complete blood count :

Drug treatment (chemotherapy) is the most likely to cause anemia .One of the main features of cancer cells is that they multiply more rapidly than normal cells, and this exposes a weakness of cancer cells, which is exploited by anti-cancer treatment. (Massarut, *et al* ;2006)

The genetic information within every cell is held within the chromosomes of the nucleus – this is where the cell's DNA is stored .To reproduce, a cell basically splits in two, and in this process the chromosomes must copy themselves and then divide into two, providing each new cell with a complete set of chromosomes. Cancer drugs are designed to block the copying of the cell's chromosomes, which therefore prevents the cell from multiplying. (Elting, *et al* ; 2001)

Unfortunately it is extremely difficult to produce a cancer drug that will only block the multiplication of cancer cells and leave normal cells alone. Cell duplication is a normal process it is part of the body's continual repair and

renewal of old and damaged cells and so an inevitable consequence of cancer treatment is that normal cells are damaged too.

Bone marrow is a very active tissue, and cancer treatment can sometimes be very hard on normal bone marrow, causing anemia. As the bone marrow manufactures all of the blood cells, including the white cells are needed to fight infections, a person receiving cancer treatment can also be more prone to infections if their white cell count drops. (Elting, *et al* ; 2001)

1.2.6.1.Thrombocytopenia:

Thrombocytopenia is a common side effect of chemotherapy, responsible of increasing risk of bleeding and delay of treatment in cancer patients. It is currently unknown how chemotherapeutic agents affect platelet production and whether the platelet precursors megakaryocytes represent a direct target of cytotoxic drugs. But there is a study that investigated the effects of chemotherapeutic agents on primary megakaryocytes by using a culture system that recapitulates in vitro human megakaryopoiesis and found that cytotoxic drugs predominantly destroyed megakaryocytic progenitors at early stages of differentiation. Immature megakaryocytes could be protected from chemotherapeutic agents by the cytokine stem cell factor (SCF), which binds the c-kit receptor expressed on hematopoietic stem and progenitor cells. In chemotherapy-treated megakaryocytes, scf activated akt (protein kinas B), neutralized the mitochondrial apoptotic machinery, and inhibited caspase activity. Interfering with akt activation abrogated the antiapoptotic effects of scf, whereas exogenous expression of constitutively active akt inhibited drug-induced apoptosis of primary megakaryocytes, indicating the

akt pathway as primarily responsible for scf-mediated protection of megakaryocyte progenitors. (Kaushansky ;1996)

1.2.6.2 Neutropenia:

Cytotoxic chemotherapy suppresses the hematopoietic system, impairing host protective mechanisms and limiting the doses of chemotherapy that can be tolerated. Neutropenia, the most serious hematologic toxicity, is associated with the risk of life-threatening infections The degree and duration of the neutropenia determine the risk of infection. Neutrophils are the first line of defense against infection as the first cellular component of the inflammatory response and a key component of innate immunity. Neutropenia blunts the inflammatory response to nascent infections, allowing bacterial multiplication and invasion. Because neutropenia reduces the signs and symptoms of infection, patients with neutropenia often may present with fever as the only sign of infection. In this setting, patients with fever and neutropenia, or febrile neutropenia (FN), must be treated aggressively, typically with intravenous antibiotics and hospitalization, because of the risk of death from rapidly spreading infection. (Kaushansky ;1996)

1.2.8. Treatment of chemotherapy-induced anemia:

The treatment of chemotherapy-induced anemia depends on the grade and on the symptoms of anemia. two options are at the disposal of the clinician for the treatment of anemia in cancer patients: transfusion of packed red blood cells and the use of erythropoiesis-stimulating agents (ESAs). The goal of the treatment is to relieve the symptoms of anemia such as fatigue and dyspnea. (Zeuner, *et al* ;2003)

1.2.8.1. Transfusion:

Transfusion of packed red blood cells offers a rapid increase in hemoglobin and hematocrit levels and is hence the ideal option in patients requiring rapid correction of anemia. Most people tolerate a blood transfusion easily – it can often be done as an outpatient procedure – and the obvious advantage is that an immediate improvement in someone's condition can be obtained. There is a small but present risk of transmission including transfusion-related reactions, congestive heart failure, bacterial contamination, viral infections and iron overload . Therefore the availability of a treatment that can reduce or eliminate the need for transfusion has always been much sought after.
Such a treatment exists in the form of erythropoietin. *(*Zeuner, *et al* ***;***2003***)***

1.2.8.2. Erythropoiesis-stimulating agents (ESAs) :

Erythropoietin is a hormone, produced naturally within the body that acts upon the bone marrow to stimulate the 'stem' cells of the marrow to divide and produce more red cells. The majority of erythropoietin is produced by specialized cells within the kidneys. These cells are sensitive to the amount

of oxygen circulating in the blood and when the oxygen level drops (as occurs in anemia) then the cells produce extra erythropoietin, which in turn results in more red cells being produced.

Treatment with ESAS has been shown to reduce transfusion rates in cancer patients. *(*Zeuner, *et al ;*2003*)*

1.3. Rationale

Breast cancer is one of the most common types of cancer worldwide and frequency occurrence. Approximately 30% of breast cancer patient treated from the disease will develop a local recurrence and/or distant metastasis.

A patient with relapsed breast cancer can live with the disease for many years, therefore, it is important to maintain a good quality of life allowing patients to enjoy an active life .

Treatment of breast cancer may cause side effects, in order to minimize these effects, researchers in field should have to know these effects which is can help in improving the outcome .

Anemia are common in patient with breast cancer .It's prevalence depending on the extent of disease , type and duration of anticancer therapy , in which anemia can be mild Hb < 12g/dl , or severe Hb > 8g/dl . Also patient with breast cancer can suffer from anemia which directly related to cancer , such as cytokines or anemia due to bone marrow infiltration by lymphoma or cancer

1.4. Objective

4.1. General Objective:

To study the effect of treatment with chemotherapy on Sudanese females patients with breast cancer attending Radiation and Isotopes Center (RIC).

1.3.2 Specific Objective:

1. To measure Hemoglobin, packed cell volume, red blood cell count , red blood cell indices, total white blood cells and platelets count(Hb, PCV, MCV,MCH, MCHC,RBCs, WBCs and PLTs) in female with breast cancer at different stages of cancer.
2. To determine the different types of anemia at different stages of breast cancer.
3. To determine the hematological parameter in breast cancer patients according to breast feeding .
4. To measure the hematological parameter according to chemotherapy treatment .

CAPTER TWO

2. Material and Method

2.1. Study design:

This is a hospital based case control study conducted in Khartoum State to measure Complete blood count in females with breast cancer attending Radiation and Isotopes Center –Khartoum during the period from September to December 2013 .

2.1.1. Study population :

Apparently adult female's patients with breast cancer were randomly selected. The sample size was 120. One hundred of them were patients and 20 were control.

2.1.2. Inclusion criteria :

All females patients with breast cancer treated with chemotherapy and surgery attending Radiation and Isotopes Center –Khartoum.

2.1.3. Exclusion criteria :

All females free from breast cancer and female with breast cancer before treatment .

2.1.4 Data collection :

Data was collected using designed questionnaires including: name, age, tribe, history of disease, type of treatment and other data .

2.1.5. Sample collection :

From all participants 2.5ml of venous blood samples were collected using sterile disposable plastic syringe by applying a non traumatic vein puncture

technique. The samples were collected in a commercial container (EDTA) as anticoagulant and blood was mixed gently by inverting the container several times and tested within 6 hours .

2.1.6 Material Required:

- Syringe and Container with EDTA anticoagulant.
- Alcohol (70% disinfectant).
- Cotton.
- Slides for blood film (forested end slide).
- Spreader or cover glass.
- Capillary tubes.
- Leishman's stain.

2.1.7. Ethical consideration :

A written informed consent was obtained from all patients and control group including in this study, all of them agreed to participate .

2.1.8. Data processing :

All data was written in master sheet and analyzed by medical statistical package for social sciences (SPSS) .Data was presented in a form of tables and figures .

2.2. Methods :

2.2.1. Complete blood count :

Complete blood count was determinate by the sysmex (**KX 21**) to determine the following hematological parameters:

1. Hb g/dl.
2. PCV%.

3. RBCs count x 10^{12}/l.
4. PLTs count x 10^{9}/l.
5. WBCs count x 10^{12}/l
6. Red cell indices :

i. Mean corpuscular volume [MCV /fl].
ii. Mean corpuscular hemoglobin [MCH /pg].
iii. Mean corpuscular hemoglobin concentration [MCHCg/dl].

2.2.2. Principle :

There are two transducer chambers one used to count WBCS and HB together and the other used to count RBCS and platelets.

A portion of blood is separated from the aspirated whole blood and mixed with the diluents in a pre-set ratio , a defined amount of this dilution is sent to the detection chamber and passed through a small opening known as the aperture. There are also electrodes on each side of the aperture – and direct current passes through these electrodes. The direct current resistance between the electrodes changes as the blood suspension pass through the aperture. This resistance causes an electrical pulse change proportional to the size of the blood cell. These electrical data are converted into graphical displays of volume distribution curves, or histograms.

2.2.3 Procedure:

1. The instrument was checked up for the sufficient of the solutions (cell pack, stromatolyser), also checked electric power supply machine has full battery and earthed connected then the power key was Pressed on .

2. The sample was mixed well and entered to probe, then the start switch was pressed, when the LCD screen was displayed analyzing the sample was removed. 30 sec and the result was printed out .

2.2.4 Quality Control:

Quality control is of great importance for obtaining highly reliable data over a long period of time as is the consistent monitoring of the instrument for preventing troubles for detection of problem .before starting sample analyzed control blood (ELGHTCHCK-ZWP) using control.

2.3. Peripheral blood picture :

2.3.1. Materials :

1. Slides.
2. Spreader.
3. RAL stain.
4. Pipettes.

2.3.2. Preparation of Blood Film:

2.3.2.1. Procedure:

1. A drop of well mixed anticoagulant venous blood sample was placed on a glass slide. 1-2 cm away from one end.
2. A spreader with smooth edged was placed infront of the blood drop and with a backward movement the edge of the spreader touches drop of blood.

3. After the spreading of blood drop along the edge of the spreader, the spreader was moved forward at one angle of 45cºand with a suitable speed.
4. The thin film was then stained by wright-giemsa stain .

2.3.2.2. Principle of Wright Giemsa stain :

Giemsa's stain is a member of the Romanowski group of stains, which are defined as being the black precipitate formed from the addition of aqueous solutions of methylene blue and eosin, dissolved in methanol and glycerol to form stock solution . The stain is consist of 1): A cationic dye: mixture of Azure A, Azure B, Methylene Violet and Methylene Blue that gives the nuclear blue color. 2) An anionic dye: Most commonly eosin Y is used to stain cytoplasm with pink color .

2.3.2.3. Procedure :

The slid was floated with stain for 3 minutes, double volume of phosphate buffer PH 6.8 was then added, the mixture is allowed to stand on the film for 7 minutes, washing was then applied using the buffer and the back of the film was cleaned and allowed to dry.

The differential leucocytes count was performed by usingx10,x40 and x100 oil immersion lens and it was done in the ideal area of examination by examine subsequent

CHPTER THREE

3. Results

A known diagnostic females patients with breast cancer were collected from Isotope and Radiation Center of Khartoum total numbers of 120 samples ranged from 26 to 66 years were entered into the study, 100 were patients and 20 were as control group during period from September to December 2013.

3.1. Demographic Data :

The study showed the distribution of patients age which is ranged from 26 to 66 as seen in table (3.1).

Table (3.2) showed the distribution and frequency of study population according to tribe galia (30%), shigia (12%), halaween (4%), mahas (4%), bederia (3%), kwahla (3%) and others.

The marital status of study population showed that (77%) were married and (33%) were single females as seen in table (3.3)

3.2. Laboratory Data :

The study showed the mean of Hb g/dl ,PCV %, MCV fl, MCH pg, MCHC g/dl, RBCs , WBCs $x10^{12/l}$ and PLTs $x10^{9}/l$ for test group were : (7.6 ±5.67) , (31.9 ±5.45), (83.0 ± 5.40), (27.0 ± 2.40), (31.0 ±3.05), (4.3 $x10^{6}$ ± 1.01), (6.1$x10^{6}$ ± 2.80) and (295.8$x10^{6}$ ± 101.14) respectively compared to control group (12.8 ± .656),(38.0 ± 1.79), ((86.5 ± 3.48), (28.5 ± 1.23), (4.5$x10^{6}$ ±.366), (8.0$x10^{6}$ ± 2.70) and (340.9$x10^{6}$ ± 63.63) respectively. Table (3.4)

Table (3.5), showed the distribution of different types of anemia in the study population 65% of patient were anemic with Hb concentration <7.6g/dl, 38% of them were normocytic normochromic cells and 27% were microcytic hypochromic cells.

The study have described significant difference in mean of Hbg/dl ,PCV%, MCHpg and PLTs (7.25 ± 1.75) , (31.26 ± 3.95), (27.60 ± 5.78), (315,15 ± 118.39) respectively, according to breast feeding as indicated in table (3.6).

The result showed the mean level of Hb, WBCs and PLTs for patients receiving chemotherapy (7.29 ± 5.80) , (6.33 ± 3.05) and (290 ± 103.98) respectively . Table (3.7)

The result find the Patients treated with mastectomy had Hb with mean (7.6 ± 5.73) which is reduced compared to control group, while WBCs($7,99x10^6$ ± 2.69) and PLTs($300,62x10^6$ ± 98.41) count showed normal value compared to control group .Table (3.8)

Table (3.1): Distribution of the study population according to (Age):

Age/years	Frequency	Percent (%)
26-35y	34	28.3
36-45y	39	32.5
46-55y	36	30.0
56-65y	6	5.0
66+y	5	4.2
Total	**120**	**100.0**

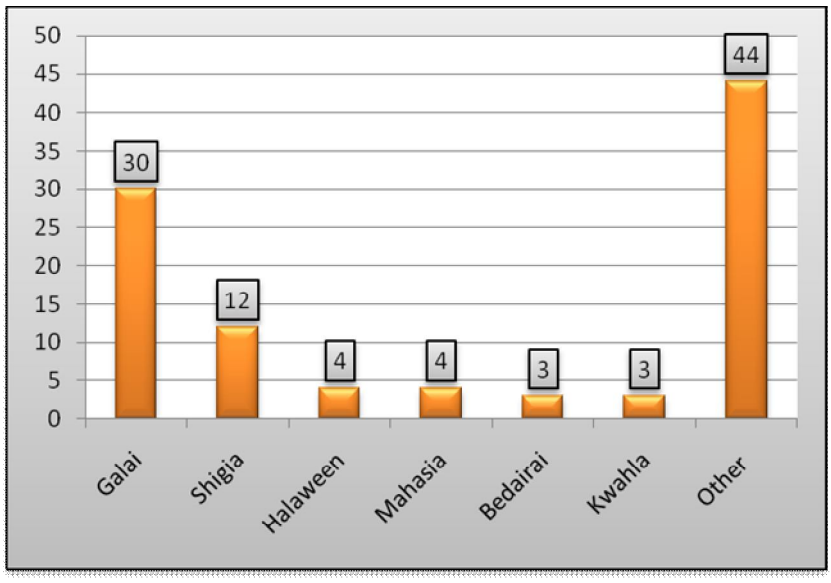


Figure (3.2): Distribution of the study population according to (Tribes)

Table (3.3) Distribution of study group according to marital status :

Marital state	Frequency	Percent (%)
Married	77	77%
Single	33	33%
Total	100	100%

Table (3.4):Mean of hematological parameters in study population:

Group Statistics

		N	Mean	Std. Deviation	Sig.(2-tailled)
Hb g/dl	Case	100	7.66	5.67	0.000
	Control	20	12.82	.656	0.000
Pcv %	Case	100	31.98	5.45	0.000
	Control	20	38.05	1.79	0.000
Mcv fl	Case	100	83.03	5.40	0.008
	Control	20	86.50	3.48	0.001
Mch pg	Case	100	27.03	2.40	0.007
	Control	20	28.55	1.23	0.000
Mchc g/dl	Case	100	31.05	3.06	0.003
	Control	20	33.30	.864	0.001
Rbcs	Case	100	4.30	1.01	0.228
	Control	20	4.58	.366	0.035
Wbcs	Case	100	6.12	2.80	0.009
	Control	20	8.00	2.70	0.011
Plts	Case	100	295.88	101.14	0.000
	Control	20	340.90	63.63	0.001

Table (3.5): Distribution of the study sample according to type of anemia:

Peripheral blood picture	Frequency	Percent (%)
Microcytic Hypochromic	27	26.7
Normocytic Normochromic	38	37.5
Normal	35	35.8
Total	**100**	**100.0**

Table (3.6):Hematological parameter in females with breast cancer according to breast feeding :

Hematological parameters		No	Mean	Std. Deviation	P. value
RBCs	Breast feeding	77	4.52	1.66	.049
	No breast feeding	33	9.00	12.72	.388
WBCs	Breast feeding	77	6.37	2.51	.067
	No Breast feeding	33	8.41	3.06	.138
Hb	Breast feeding	77	7.25	1.75	.152
	No Breast feeding	33	12.24	.63	.016
PCV	Breast feeding	77	31.26	3.95	.042
	No Breast feeding	33	38.58	2.75	.021
MCV	Breast feeding	77	83.47	5.78	.132
	No Breast feeding	33	88.04	4.26	.086
MCH	Breast feeding	77	27.60	2.35	.843
	No Breast feeding	33	28.41	2.07	.833
MCHC	Breast feeding	77	32.70	1.67	.038
	No Breast feeding	33	31.27	1.14	.018
Platelets	Breast feeding	77	315.15	118.39	.044
	No Breast feeding	33	445.57	126.20	.201

Table(3.7):Mean of Hb ,WBCs and PLTs in patients treated with chemotherapy:

Chemotherapy		N	Mean	Std. Deviation	Sig.(2-tailed)
Hb	Case	83	7.29	5.80	0.000
	control	20	12.82	.656	0.000
Wbcs	Case	83	6.33	3.05	0.008
	control	20	8.00	2.70	0.011
Plts	Case	83	290.68	103.98	0.000
	control	20	340.90	63.63	0.000

Table (3.8): Mean of Hb , WBCs and PLTs in patients after mastectomy

	Syrgary	N	Mean	Std. Deviation
Hb	Yes	75	10.60	5.74
	Control	20	12.83	5.58
Wbcs	Yes	75	7.99	2.79
	Control	20	8.50	3.21
Plts	Yes	75	300.62	98.42
	Control	20	340.64	110.96

Table (3.9): Frequency of the study population according to staging of the disease :

stage	Frequency	Percent (%)
II	39	39
III	26	26
IV	25	25
I	6	6
0	3	3
V	1	1
Total	**100**	**100.0**

Table (3.10): Mean of Hb , WBCs and PLTs according to stage of disease:

		N	Mean	Std. Deviation
Hb	0	3	7.83	6.78
	I	6	9.63	4.88
	II	39	7.21	5.35
	III	26	6.89	6.15
	IV	25	7.41	5.87
	V	1	.00	.00
	Total		7.66	5.67
Wbcs	0	3	5.00	2.34
	I	6	5.05	2.63
	II	39	6.06	2.94
	III	26	5.47	2.03
	IV	39	6.06	3.40
	V	1	2.60	.00
	Total	100	6.12	2.80
Plts	0	3	355.00	152.07
	I	6	321.16	125.54
	II	39	292.17	95.29
	III	26	290.50	98.11
	IV	25	296.72	108.40
	V	1	230.00	.00
	Total	100	295.880	101.14

CHAPTER FOUR

4. Discussion, conclusion and Recommendation

4.1 Discussion :

Breast cancer is a common and worldwide type of cancer it is the most common cause of death among females . (Sariego J ., 2010).

This study was conducted to measure complete blood count in females with breast cancer attending Radiation and Isotope center in Khartoum state.

Complete blood count is an essential and basic hematological test and is one of the most frequent order laboratory procedure in hematological disorders.

The treatment of breast cancer can lower the blood count so the CBC is a routine blood test done regularly during the treatment and the result of this test show how the vital organs functioning and how the treatment is effective . (Saini *etal* ., 2011)

The result showed that the mean of Hb , PCV, MCV and MCHC were decreased compared to control group. This means there is highly significant differences between the two groups. This result was similar to the result obtained by Jeffery etal (2002) , who detect the relationship between the reduction in the hemoglobin level and the quality of life during chemotherapy . This reduction may be related to the action of the anticancer treatment or from the cancer itself which cause bone marrow suppression .

In this study, the mean value of WBCs were in the limit of standard reference value and there was no significant difference between the mean of

this parameter in patients and control group . These result disagreed with Adesons etal., (2003), who stated that the patients receiving chemotherapy is under high risk of developing neutropenia.

This result showed that the mean of platelet count signficantly decreased compared to control group , in which there was a highly significant correlation between the two groups with P value (0.000) . This results agreed with Cella, etal., (2004), who stated that there is a direct effect of anti cancer treatment on the three line of blood cells,(RBCs ,WBCs and PLTs).

The present study showed that there was 65% of patient were anemic with Hb concentration <7.6g/dl, 38% of them were normocytic normochromic cells and 27% were microcytic hypochromic cells.

This study showed a significant reduction in mean of Hb , PCV ,MCV and PLTs in breast cancer with breast feeding compared to control group .

Also, the study showed that the mean value of Hb and PLTs in patient receiving chemotherapy was significantly decreased compared to control group this reduction may be related to the chemotherapy, while: the WBCs does not affected by chemotherapy .This result agreed with Ann Zeuner, Michele Signore etal (2007) who stated that thrombocytopenia is a common effect of chemotherapy agents on primary megakaryocytes cusing distructin

In this study, the mean of Hb was highly decreased in breast cancer patient in grade 111, followed by those in grade 11 and 1V, this means that the mean of Hb was affected by grading of disease . The mean of WBCs and PLTs also indicated that there was correlation between WBCs ,PLTs and the grading of the disease . This result disagreed with Bloom and Richardson

etal,. (2004) who stated decrease in Hb in grade 11 most followed by grade 111.

4.2. Conclusion

This study concluded :

1. The mean of Hb , PCV ,MCV , MCH, RBCs and PLTs count were significantly decreased in breast cancer patients.
2. WBCs were in the limit of control group.
3. The most common type of anemia in females with breast cancer is normocytic normochromic followed by microcytic hypochromic .
4. The mean of Hb , PCV , MCV, MCH , WBCs and PLTs count were significantly reduced in breast cancer patient that have breast feeded there children .
5. Hb, PLTs count showed a significant correlation with the chemotherapy .
6. WBCs and PLTs are not affected by mastectomy while Hb was mildly reduced .

4.3. Recommendations :

This study recommended the following :

1. Breast cancer patient under treatment should be monitored regularly , in order to minimize or delay development of anemia and thrombocytopenia .
2. Patients with breast cancer should receive epoboitein and folic acid to minimize the effect of treatment on bone marrow .
3. More parameters such as serum haptoglobins to detect hemolysis and iron profile in serum should be measured to be more specific about the cause of reduction in Hb and red cell indices in patients with breast cancer.
4. More researches should be done in this filed with larger sample size to expanded the awareness with this disease.

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Appendix

بسم الله الرحمن الرحيم

جامعة السودان للعلوم والتكنولوجيا

كلية الدراسات العليا

.....

استبيان لدراسة تأثير سرطان الثدي على مكونات الدم وطرق علاجه عند النساء

الاسم .....

القبيلة.....

العمر :.....

الحاله الاجتماعيه.....

نوع العلاج.....

الجرعة:.....

التشخيص:

مرحلة المرض:.....

نوع الأنيمياء.....

نتائج مكونات الدم.....

- WBCS: ……..…….. µl
- RBCS: …….. µl
- HGP: ……. Pg
- HCT: …… %
- MCV: ……..….. Fl
- MCH: …….…….. Pg
- MCHC: ……..…… g/dl
- PLTs: ……..…… µl

PBP:

……..…….

……..

Comment:

……..……..

International normal range of hematological parameter :

Red Blood Cell Count	
Men	$5.0 \pm 0.5 \times 10^{12}$/L
Women	$4.3 \pm 0.5 \times 10^{12}$/L
Haemoglobin	
Men	13.5-18 g/dL
Women	11.5-16 g/dL
Packed Cell Volume (PCV) Or Haematocrit (Hct)	
Men	0.45 ± 0.05(L/L)
Women	0.41 ± 0.05 (L/L)
Mean cell Volume (MCV)	92 ± 9Fl
Mean cell Haemoglobin (MCH)	29.5 ± 2.5pg
Mean cell Haemoglobin Concentration (MCHC)	33 ±1.5 g/dl
Platelet Count	$280 \pm 130 \times 10^{9}$/L
White Blood Cell Count	$4 - 10 \times 10^{9}$/L
Differential Count	
Neutrophils	$2.0 - 7.0 \times 10^{9}$/L (40 – 80%)
Lymphocytes	$1.0 - 3.0 \times 10^{9}$/L(20 – 40%)
Monocytes	$0.2 - 1.0 \times 10^{9}$/L (2-10%)
Esinophils	$0.02 - 0.5 \times 10^{9}$/L (1-6%)
Basophils	$0.02 - 0.1 \times 10^{9}$/L (<2-2%)