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Evaluation of Complete Blood Count in Sudanese Patients with Hyperthyroidism and Hypothyroidism

تقييم قياس الدم الكامل للمرضى السودانين المصابين بزيادة ونقصان هرمونات الغدة الدرقية

A dissertation submitted in partial fulfillment for the requirements of M.Sc. degree in medical laboratory science

(Hematology and Immunohematology)

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الآيـــة

قال تعالى :

إِنَّا عَرَضْنَا الْأَمَانَةَ عَلَى السَّمَاوَاتِ وَالْأَرْضِ وَالْجِبَالِ فَأَبَيْنَ أَنْ يَحْمِلْنَهَا وَأَشْفَقْنَ مِنْهَا وَحَمَلَهَا الْإِنسَانُ إِنَّهُ كَانَ ظَلُومًا جَهُولًا)

صدق الله العظيم

{سورة الأحزاب الاية 72}

Dedication

To my mother who candle the light for me.....

To the sole of my father .....

To my sisters .....

To my brothers.....

To my teachers.....

To my colleagues.....

Acknowledgement

I thank God first and foremost to give health and strength until I reached this stage, also I would like to thank my supervisor **Dr. Elshazali Widaa Ali** who helped me in preparation and accomplishing of this study. My special thank to staff of Antalya Medical Center Laboratory whom provided me with samples.

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Abbreviation

Abbreviation	Full text
BFU-E	Blood Forming Unit –Erythroid
CFU-E	Colony Forming Unit –Erythroid
CBC	Complete Blood Count
DPG	Di phospho Glyceride
dl	Deciliter
EDTA	Ethylene Diamine Tetra Acetic Acid
FL	Femtoliter
G	Gram
Hb	Hemoglobin
HCT	Hematocrit
Hi	Meth hemoglobin
IgE	Immunoglobulin Epsilon
KD	Kilodalton
L	Liter
ML	Mililiter
MCV	Mean Corpuscular Volume
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
MIU	Micro International Unit
nmol	Nanomol
O2	Oxygen
PCV	Packed Cell Volume
Pg	Pigogram
PLT	Platelt
P.value	Probability value
R	Pearson correlation
RBC	Red Blood Cell
T3	Tri- iodothyronine
T4	Thyroxin
TSH	Thyroid Stimulating Hormone
TRH	Thyrotrophin Releasing Hormone
TSI	Thyroid Stimulating Immunoglobulin
TWBCs	Total White Blood Cells

Abstract

This is a case control study carried out in Khartoum state in Antalya Medical Center during the period from August 2015 to April 2016. One hundred patients were enrolled, 50 with hyperthyroidism and 50 with hypothyroidism; in addition, 50 healthy volunteers were included as a control group. Forty six of patients with hyperthyroidism and 40 of patients with hypothyroidism were females, while 4 of patients with hyperthyroidism and 10 of those with hypothyroidism were males. Thirty of control group were females, while 20 of control group were males. Mean of patients age between (34±12) year , while mean of control age between (35±17) year.

Three ml of venous blood was withdrawn from each participant, then placed in blood tube containing EDTA which act as anticoagulant.

Complete blood count was performed using an automated cell counter (Sysmex KX-21N). The results were analyzed by statistical package of social science (SPSS). The result showed a significant decrease in hemoglobin level, hematocrit, mean corpuscular volume and mean cell hemoglobin in patient with hyperthyroidism compared to control group (P. *value* <0.05). Hemoglobin level, hematocrit,mean corpuscular volume and mean cell hemoglobin and mean cell hemoglobin concentration showed significant decrease in hypothyroid patient when compared with control group (P. *value*< 0.05).

No significant difference was found in mean total leukocyte counts when compared in the study groups (P. *value* >0.05). Neutrophilia have been observed in hypothyroidism patients (P. *value* <.*05*).

Platelet count showed no significant difference in hyperthyroidism and hypothyroidism groups when compared with control group *(*P. *value* >0.05). There was no statistically significant correlation between red cell parameters, total leukocyte counts, and platelet count of hyper -and hypothyroidism patients

and age (P. *value* >0.05). Also no statistically significant correlation was found red cell parameters, total leukocyte counts, and platelet count of hyper- and hypothyroidism patients and T4 (P. *value* >.05).

There was statistically significant correlation between MCH of hyperthyroidism patients and T3 (P. *value <.05*), while other red cell parameter, total leukocyte count differential count, and platelet count showed no statistically significant correlation with T3 (P. *value* >.05).

There was statistically significant correlation between MCV, MCH, and MCHC of hyperthyroidism patients and TSH. Hb, HCT and MCH of hypothyroid patient showed significant correlation with TSH (P. *value <.05*) while total leukocyte count, differential count and platelet count showed no statistically significant correlation with TSH (P. *value* >.05).

In conclusion, hyperthyroidism and hypothyroidism have negative effective on Hb , Hct and MCH, while it has no effect on total WBCs count or platelet count.

ملخص الأطروحة

هذه دراسة حالة ومجموعة ضابطة أجريت في ولاية الخرطوم في مركز أنطاليا الطبي خلال الفترة من شهر أغسطس2015م حتى أبريل2016م .ثم أختيار مائة مريض،50 مصابين بزيادة هرمونات الغدة الدرقية و50 مصابين بإخفاض هرمونات الغدة الدرقية بالاضافة الى 50 شخص سليم كمجموعة ضابطة. 46من المرضى المصابين بزيادة هرمونات الغدة الدرقية و40 من المرضى المصابين بنقصان هرمونات الغدة الدرقية كانو إناث، بينما 4 من المرضى المصابين بزيادة هرمونات الغدة الدرقية و10 من المرضى المرضى المصابين بنقصان هرمونات الغدة الدرقية كانو زكور. 30من المجموعة الضابطة كانو إناث بينما 20 من المجموعة الضابطة كانو زكور. متوسط اعمار المرضى مابين (34±12) سنة ، بينما متوسط اعمار المجموعة الضابطة ما بين (35±17) سنة.

تم أخذ 3مل من الدم الوريدي من كل مشارك ووضعت في انبوب دم يحتوي على EDTAالمضاد للتجلط وذلك لحساب الدم الكامل بأستخدام عداد الخلايا الآلي وتم تحليل النتائج بواسطة برنامج الحزم الأحصائية للعلوم الاجتماعية.

أظهرت الدراسة أن هنالك أنخفاض ذو دلالة أحصائية في متوسط تركيز خضاب الدم الكلي (الهيموغلوبين) ومتوسط حجم الدم المكدس ومتوسط حجم الخلية ومتوسط خضاب الخلية لدى مرضى ارتفاع هرمونات الغدة الدرقية بالمقارنة بالمجموعة الضابطة (القيمة المعنوية اصغر من 0.05).

أظهرت الدراسة أن هنالك أنخفاض ذو دلالة أحصائية في متوسط تركيز خضاب الدم الكلي ومتوسط حجم الخلية ومتوسط حجم الدم المكدس ومتوسط خضاب الخلية ومتوسط تركيز خضاب الخلايا لدى مرضى أنخفاض هرمونات الغدة الدرقية بالمقارنة بالمجموعة الضابطة (القيمة المعنوية اصغر من 0.05).

أظهرت الدراسة أن هنالك أنخفاض ذو دلالة غير أحصائية في متوسط عدد الصفائح الد لدى مرضي زيادة وأنخفاض هرمونات الغدة الدرقية بالمقارنة بالمجموعة الضابطة (القيمة المعنوية اكبر من 0.05

أظهرت الدراسة أن هنالك أنخفاض ذو دلالة غير أحصائية في متوسط عدد كريات الدم البيضاء لدى مرضي زيادة وأنخفاض هرمونات الغدة الدرقية بالمقارنة بالمجموعة الضابطة (القيمة المعنوية اكبر من 0.05

أظهرت الدرسة أن هنالك أرتفاع في متوسط الخلايا المتعادلة لدي مرضى أنخفاض هرمونات الغدة الدرقية (القيمة المعنوية اصغر من 0.05).

أظهرت الدرسه أنه لايوجد أرتباط ذو دلالة أحصائية مابين معدلات قياس خليه الدم الحمراء،والعدد الكلي لكريات الدم البيضاء،والصفائح الدموية لدى مرضى زيادة وأنخفاض هرمونات الغدة الدرقية والعمر.

أظهرت الدرسه أنه لايوجد أرتباط ذو دلالة أحصائية مابين معدلات قياس خليه الدم الحمراء،والعدد الكلي لكريات الدم البيضاء،والصفائح الدموية لدى مرضى زيادة وأنخفاض هرمونات الغدة الدرقية وهرمون.T4 الثايروكسين

أظهرت الدراسة أن هنالك أرتباط ذو دلالة أحصائية مابين متوسط خضاب الخلية وهرمون ال T3 لدى مرضى زيادة هرمونات الغدة الدرقية (القيمة المعنوية اصغر من 0.05)،بينما لا يوجد اي أرتباط ذو دلالةأحصائية بين معدلالت قياس خلية الدم الاخرى والعدد الكلي لكريات الدم البيضاء،والصفائح الدموية لدى مرضى زيادة وأنخفاض هرمونات الغدة الدرقية مع هرمون ال T3 (القيمة المعنوية اكبر من0.05).

أظهرت الدراسة أن هنالك أرتباط ذو دلالة أحصائية مابين متوسط حجم الخلية ومتوسط خضاب الخلية ومتوسط تركيز خضاب الخلايا مع الهرمون المحفز للغدة الدرقية (TSH) لدي مرضي زيادة هرمونات الغدة الدرقية.كما ان هنالك أرتباط ذو دلالة أحصائية مابين متوسط تركيز خضاب الدم الكلي ومتوسط حجم الدم المكدس ومتوسط خضاب الخلية مع الهرمون المحفز للغدة الدرقية (TSH) لدى مرضى أنخفاض هرمونات الغدة الدرقية(القيمة المعنوية اصغر من 0.05).

وفي الخاتمة، أضطرابات الغدة الدرقية لها تأثير سلبي على تركيز خضاب الدم الكلي، حجم الدم المكدس وخضاب الخلية بينما لا يوجد اي تأثير على كريات الدم البيضاء والصفائح الدموية.

Chapter One
Introduction and Literature Review

Chapter One

Introduction and Literature Review

1.1 Introduction

The thyroid gland is the largest and important endocrine gland in the body, it is located in the anterior side of the neck it has two lobes and thin follicular cells with type of epithelial tissue origin. Hormonal output from the thyroid is mediated by thyroid stimulating hormone (TSH or thyrotropin) secreted by anterior pituitary. The secretion of thyrotropin itself is mediated by thyrotropin-releasing hormone, secreted by hypothalamus. Thyroid gland synthesizes and secrets two major hormones: thyroxin [T4] and tri-iodothyronine [T3]; these hormones are necessary for maturation and production of RBC. Thyroid hormones play a role in Hb production in adult and maturation of Hb in fetus, this hormone enhance erythropoiesis through proliferation of immature erythroid progenitor and increase secretion of erythropoietin. The common disorder of thyroid is hyperthyroidism, hypothyroidism and thyroid nodules which are benign neoplasm but can change to cancer (Dorgalaleh *et al*; 2013).

Hypothyroidism is the deficiency of thyroid hormone production, it may occur as a congenital abnormality or congenital deficiency of any enzyme concerned with hormone synthesis. When the deficiency is congenital it is referred to as cretinism, the affected child is a mentally retarded (Sukkar *et al;* 1998).

Hyperthyroidism is characterized by high level of thyroid hormones; it can occur at early age or later in life. Patients with hypothyroidism are usually complains of loss of weight, weakness and tiredness after slight exertion, there is affine tremor which can seen in the hand, patient commonly complain of palpitations and the eye may be protruding (Sukkar *et al;*1998).

Thyroid hormone have important effect on erythropoiesis through hyper proliferation of immature erythroid progenitors and increase secretion of erythropoietin by inducing erythropoietin gene expretion. The thyroid hormone also augment repletion of hypoxia indusable facter1 and then motivate growth of erythroid colonies. These hormones also intensify erythrocyte 2,3 DPG compactness which enhance the delivery of oxygen to tissue. With regard to lymphocyte, T3 is a precursor substance for normal B cell formation in bone marrow through its mediation of pro-B cell proliferation (Dorgalaleh *et al*; 2013).

The metabolic abnormalities associated with hypothyroidism include; anemia, hyperlipidemia and reversible increase in creatinine (Mitra *et al*; 2010).

Hyperthyroidism can cause certain forms of anemia on the one hand or hyper proliferation of immature erythroid progenitors on the other hand. Regarding leucocytes and thrompocyte, slightly depressed leukocyte count, neutropenia and thrombocytopenia have been observed in hypothyroidism patients. Furthermore, elevated normal or, slightly depressed total leukocyte counts have been found in hyperthyroid patient, with only arelative decrease in the number of neutrophils and arelative increase in the number of eosinophils and mononuclear cells (Kawa *et al*;2010).

1.2 Literature review

1.2.1 Blood

Blood is classified as a connective tissue with an excessive and complex liquid intracellular material (the plasma) in which the blood cells or formed elements are suspended. The proportion of the plasma to cells can be determined by spinning sample of blood in a centrifuge tube which PCV: percentage volume of whole blood occupied by packed red cells (haematocrit or packed cell volume) (Sukkar *et al;* 1998).

1.2.1.1 Blood Functions

1. Blood is the main transportation vehicle of the body it carries oxygen and nutrients to tissue and waste products of metabolism, carbon dioxide and urea, to lung and kidney. Most of the hormones are carried from endocrine gland to target organs.
2. Blood circulation helps to distribute heat around the body from metabolically active and warmer organs (e.g.liver and gut), to peripheral organs, therepy, helping to maintain an even body temperature.
3. Buffers in the blood - like haemoglobin, plasma proteins, bicarbonate and other- help to keep the hydrogen concentration of extracellular fluid constant at pH of 7.4.
4. Blood plays a vital protective function against infection by virtue its leucocytes and antibodies in the plasma.
5. Furthermore, injury to blood vessels is followed by blood clotting which stops further loss of this vital fluid (Sukkar *et al*; 1998).

1.2.1.2 Blood components

Blood components divided into:-

1. Formed elements (blood cells): of which there are three types: red cells (erythrocytes), white cells (leucocyte), and platelets (thrombocytes).

2- Plasma:

Plasma consist of organic and in organic substance dissolved in water. plasma protein constitute most of plasma solutes, by weight there are three types: albumin, globulin and fibrinogen. Cells normally do not take up plasma proteins used amino acid to make their own proteins. Thus plasma protein must be viewed differently formed most the other organic constituents of plasma, use as the medium for transport to form cells. In contrast most plasma protein performs their function in the plasma itself or in the interstitial fluids (Widmaier *et al*;2006).

1.2.1.3 Blood formation (haematopoiesis)

All of the blood cells are a progeny of single type of cell named haemopoietic stem cell .The processes involved in production of all the various cells of blood from the haematopoietic stem cells are collectively called haemopoiesis.

These processes of haemopoiesis include self renewal stem cell, commitment of most progeny of stem cells to differentiate ultimately into particular cell type, proliferation of progenitor cell and their differentiation along a pathawy leading to a particular kind of mature blood cell (Lee *et al*; 1999).

1.2.1.3.1 Sites of haematopoiesis

Formation of blood cells occurs at different anatomical sites during the course of development from embryonic to adult life. Production of blood cells commences in the yolk sac of the embryo, but then shifts to the liver and to lesser extent to the spleen so that this organs become the dominant sites of production between the second and seventh month of gestation. The liver and spleen are then suppressed by the bone marrows which serve as only important

site of blood cell production after birth. An exception is lymphocyte production, which occurs in other organ, in addition to bone marrow in adult life (Firkin *et al*; 1989).

Haemopoietic tissue fills all of the cavities within the bone of the newborn, but with increase age, becomes localized in the cavities of the upper shafts of the femur and the humerus, pelvis, spine, skull and bones of thorax. The total volume of haemopoitic tissue in adults is 1-2 liters. This tissue is referred to red marrow because of its macroscopic appearance; the remaining bone marrow in the more peripheral regions of the skeleton contain predominantly fat, and is termed yellow marrow, also occupies a volume of 1-2 liters and serve as a reserve space in to which haemopoietic tissue can expand in response to an increased demand for blood cell production. Only in pathological situations does significant haemopoietic activity occur in the liver, spleen and other sites during adult life, when it is referred to as extramedullary haemopoiesis (Firkin *et al*; 1989).

1.2.1.4 Erythropoiesis

Process by which red blood cells are formed; it is stimulated by decreased O_2 in circulation, which is detected by the kidneys, which then secrete the hormone erythropoietin. This hormone stimulates proliferation and increased differentiation of red cell precursor which activate erythropoiesis in the haemopoietic tissue, ultimately producing red blood cells (Sukkar *et al*; 1998).

1.2.1.4.1 Stages of erythropoiesis

1.2.1.4.1.1 Red cell progenitors

BFU-E

a population of bone marrow–residing progenitor cells derived from CFU-S cells, responsible for the formation of erythrocytes; they require low

concentrations of erythropoietin to undergo a “burst” of mitotic activity to form a very large number of CFU-E(Themal *et al* ;2004)**.**

CFU-E

CFU-e is a stage of erythroid development between the BFU-e stage and the pro-erythroblast stage. CFU-e colony assay is designed to detect how many colony-forming-units of erythroid lineage there are in a hematopoietic tissue (bone marrow, spleen, or fetal liver), which may be reflective of the organism’s demand for oxygen delivery to the tissues or a hematopoietic disorder(Themal *et al* ;2004).

1.2.1.4.1.2 Red cell precursors

1. Proerythroblast

Least mature cell in erythropoiesis, it characterized by their size about 20µm and having very dense nuclear structure with narrow layer of cytoplasm, homogeneous in appearance, with a lighter zone at the center; they stain deep blue after Romanwosky staining(Themal *et al* ;2004).

2. Basophilic erythroblast

Display similar characteristic to proerythroblast but having smaller nuclei and chromatin is more coarsely structured(Themal *et al* ;2004).

3. Polychromatic erythroblast

The immature cell in which the cytoplasm displays a grayish blue hue, it is still able to divide(Themal *et al* ;2004).

4. Orthochromatic erythroblast

The cell in which the cytoplasm taking on a pink hue, which contain a lot of hemoglobin and are no longer able to divide, the nuclei gradually condense in to

small black spheres without structural definition that eventually are expelled from the cells(Themal *et al* ;2004).

5. Reticulocyte

Anucleated young erythrocyte contain ribosome's that precipitate into reticular structures after special staining (supravital stain) (Themal *et al* ;2004).

6. Mature red blood cell

Mature erythrocytes are unique among the cells of human tissues in that they normally lack nuclei and cytoplasmic structures such as lysosomes, and mitochondria. They exist in large blood vessels as biconcave discs, but their shape changes to a parachute-like conformation in the capillaries, which have a diameter less than that of erythrocytes in the bioconcave disc form. The membranes of red cells are elastic and thus rapidly resume the bioconcave disc form after the red cells re-enter large vessels. Loss of flexibility or elasticity lead to membrane damage and shape change which is accompanied by diminished lifespan of the red cell in many different forms of anemia (Firkin *et al*; 1989).

The main function of red blood cell is to carry oxygen to the tissue and to return carbon dioxide from the tissue to the lungs (Hoffbrand and Moss; 2011).

1.2.1.5 Haemoglobin

Hemoglobin is aconjugate protin of molecular weight 64000KD, consisting of Polypeptide chains to each of which a haem group is attached. Each globin chain bears a haem group whose central iron atom is the site at which oxygen attaches to haemoglobin. The type of hemoglobin chain synthesized by erythroid precursors undergoes progressive change with time after conception, and the nature of globin chains dictates the oxygen-binding properties of the haem (Firkin *et a*l; 1989).

1.2.1.5.1 Haemoglobin function

- The red cells in systemic arterial blood carry oxygen from the lungs to the tissue and return in venous blood with carbon dioxide to lungs. As the hemoglobin molecule loads and unloads oxygen the individual globin chains in the hemoglobin molecules move on each other, when oxygen is unload the beta chains are pulled apart, permitting entry of the metabolite 2, 3- diphosphoglycerate resulting in alow affinity of the molecules for oxygen (Hoffbrand Moss; 2011).
- Haemoglobin being a protin which act as one of the buffer in the blood.
- Haemoglobin can also combin with gases other than oxygen and carbon dioxide for Example: Hb has greater affinity to carbone monoxide than to oxygen (Sukkar *et al*;1998).

1.2.1.5.2 Normal haemoglobin types

1.2.1.5.2.1 Adult haemoglobins

Haemoglobin A

Comprises about 97 percent of the hemoglobin of adult red cells. It consist of two alpha (α) and two beta (β) chains with the structural formula. The alph chain contains 141 amino acids, and the β chain, 146. Small amount of Hb-A are detected in the fetus as early as the eighth week of life , Hb-A almost completely replaces Hb-F, and the adult pattern is fully established by six months(Firkin *et al*, 1989).

Hemoglobin A_2

Minor hemoglobin in the adult red cell. It has the structural formula of α2δ2 , the delta chain containing 146 amino acids .The alpha chain is identical to that of Hb-A. Hb-A_2 is present in very small amounts at birth and reaches the adult level of 1.2-3.2 percent during the first year of life. Elevation of Hb-A_2 is a

feature of some types of thalassaemia and occasionally occurs in megaloblastic anaemia and unstable haemoglobin disease. Hb-A_2 may be reduced in iron deficiency (Firkin *et al*, 1989).

1.2.1.5.2.2 Fetal hemoglobin (Hb-F)

Hb-F is the major respiratory pigment from early intra-uterine life up to term. It has the structural formula α2γ2, each gamma chain consisting of 146 amino acids. Hb-F accounts for 70-90 percent of total haemoglobin. It hen falls rapidly to 25 percent at 1 month, and 5 percent at 6 months. Hb-F is elevated in some haemoglobinopathies and thalassaemia syndromes (Firkin *et al*, 1989).

1.2.1.5.2.3 Embryonic hemoglobin's

Hb-Gower 1 and Gower 2

Both are confined to the embryonic stage of development. They contain epsilon (ε) and zeta (ζ) chains, Hb Gower 1 being ζ2ε2 and Hb Gower 2, α2ε2(Firkin *et al*, 1989).

1.2.1.5.2.4 Hb Protland

Found in trace amounts throughout intra-uterine life and in neonate. It has the structural formulaζ2γ2 (Firkin *et al*, 1989).

1.2.1.6 Leucopoiesis

It is the process of formation of white blood cells. The white blood cells may be divided into two broad groups: the phagocytes and immunocytes. Granulocytes which include three types of cell: neutrophils, eosinophils, and basophils-together with monocytes comprise the phagocytes. Only mature phagocyte and lymphocyte are found in normal peripheral blood. The lymphocyte, their precursor cells and plasma cells make up the immunocyte population (Hoffbrand and Moss;2011).

The function of phagocytes and immunocytes in protecting the body against infection is closely connected with two soluble protein systems of the body: immunoglobulin and complement (Hoffbrand and Moss;2011).

1.2.1.6.1 Granulopoiesis

The process by which granulocytes are formed.

1.2.1.6.1.1 Granulopoietic stages

1. Myeloblast

A cell of variable size that has a large nucleus with fine chromatin and usually two to five nucleoli; the cytoplasm is basophilic; granules are present.

The normal bone marrow contains up to 5% of myloblasts. Mylobasts give rise by cell division to promyelocyte.

2. Promyelocyte

They are slightly larger cells and have developed primary granules in the cytoplasm. These cells then divide and differentiate to Myelocytes.

3. Myelocyte

Myelocytes have specific or secondary granules. The nuclear chromatin now more condensed and nucleoli are not visible. Separate mylocytes of the neutrophil, eosinophil and basophil series can be identified. The mylocytes give rise by cell division and differentiation to metamyelocytes.

4. Metamyelocyte

Non-divided cell, have an indented or horse-shape nucleus; their cytoplasm filled with primary and secondary granules.

5. Band form

Between the metamyelocytes and fully marure neutrophil are termed 'band' or stab form. This cell may occur in normal peripheral blood, they do not contain the clear, fine filamentous connections between nuclear lobes that is seen in mature neutrophil (Hoffbrand and Moss; 2011).

6. Neutrophil

This cell has a characteristic dense nucleus consisting of between two and five lobes, and a pale cytoplasm with an irregular outline containing fine pink-blue granules or grey- blue granules. The granules are divided into primary, which appear at the promylocyte stage, and secondary (specific) which appear at the myelocyte stage and predominant in the mature neutrophil. Both types of granules are lysosomal in origin. The life span of neutrophils in the blood is only 6-10 hours (Hoffbrand and Moss;2011).

7- Eosinophil

These cells are similar to neutrophils, except that the cytoplasmic granules are coarser and deeply red staining and there are rarely more than three nuclear lobes. Eosinophil mylocytes can be recognized but earlier stages are indistinguishable from neutrophil precursors. The blood transit time for eosinophils is longer than for neutrophils. They enter inflammatory exudates and have a special role in allergic responses, defence against parasites and removal of fibrin formed during inflammation (Hoffbrand and Moss;2011).

8- Basophil

They have many dark cytoplasmic granules which overlie the nucleus and contain heparin and histamine. In the tissue they become mast cell. They have immunoglobulin (IgE) attachment sites and their degranulation is associated with histamine release (Hoffbrand and Moss;2011).

1.2.1.6.2 Monopoiesis

Monopoiesis is the process by which monocytes are formed

1 -Monoblast

The least mature of the morphological recognizable members of the monocyte macrophage series, and are very similar in appearance to myeloblast. They located predominantly in the bone marrow, which is the major site of monocyte production.

2 -Promonocyte

It is similar in size to the promyelocyte but has a more irregularly shaped, nucleus contains nucleoli; the cytoplasm contain granules often arranged in a localized region and the granules are larger and more basophilic than in mature monocyte (Firkin *et al*;1989).

3- Mature monocyte

These are usually larger than the other peripheral blood leucocytes and possess a large central oval or indented nucleus with clumped chromatin. The abundant cytoplasm stains blue and contains many fine vacuoles, giving a ground-glass appearance, cytoplasmic granules are also often present. The monocyte precursor in the marrow (monoblasts and promonocytes) are difficult to distinguish from myeloblasts and monoctes (Hoffbrand and Moss; 2011).

1.2.1.6.3 Lymphocytes

Lymphocyte pass through a series of developmental changes in the course of evolving into various lymphocyte subpopulations, mature lymphocytes are engaged in extensive recirculation through the extra vascular and vascular compartment. This is important in facilitating the recognition of foreign antigens by lymphocytes. Cell-mediated and antibody-mediated immune responses

involve complex sequence events in which lymphocyte subsets interact with other subset of lymphocyte (Firkin *et al*;1989).

1.2.1.6.3.1 Lymphopoiesis

Lymphopoiesis is the process by which lymphocytes are formed.

1 -Lymphoblast

Lymphoblasts are slightly smaller than myeloblasts which they resemble, except that the ratio of the diameter of the nucleus to that of cell tends to be grater and the number of nucleoli per nucleus tends to be fewer than in the myloblast, and it is actively divided cell (Firkin *et al*;1989).

2- Prolymphocyte

Differ from blast by subtle changes sush as slightly more clumped chromatin ,alesseing of nucler prominence and changes in sickness of nuclear chromatin

(Bernadette ; 1995)

3- Large lymphocyte

Large lymphocyte between 12-16 µm in diameter, and is round in outline. The nucleus is round or slightly intended and it is chromatin is more clumped than in the lymphoblast, the cytoplasm is more abundant than in the lymphoblast and is usually pale blue, some granules may present in cytoplasm (Firkin *et al*;1989).

4- Small lymphocyte

Small lymphocytes are between 9-12 µm in diameter and are thus smaller than segmented granulocytes. The cytoplasm usually forms only a thin medium to deeply basophilic rim encircling around or marginally indented nucleus which contain deeply staining heavily clumped chromatin (Firkin et al; 1989).

1.2.1.6.4 Thrombopoiesis

Platelets are formed in the bone marrow by megakaryocytes, and are subsequently released into the vascular compartment where they play an essential role in haemostasis.

1.2.1.6.4.1 Megakaryocytic series

1-Megakaryoblast

The most immature stage platelet development,which resembles the myeloblast in its basic feature. These cells amount to less than eight percent of the total megakaryocyte population.

2-Promegakaryocyte

The next stage in the sequence of maturation,and larger than its precursor because it has undergone endoreduplication which is nuclear replication without division of the cell. Promegakaryocyte make up about 25 percent of megakaryocytes, and have deeply basophilic cytoplasm containing some basophilic granules,the nucleus may be lobulated,and the chromatin is more deeply basophilic than in the megakaryoblast.

3-Mature megakaryoblast:

Range from 30-90μm in diameter and contain 4 to 16 nuclear lobes with coarsely clumped chromatin.The expanse of cytoplasm stains light blue and contains many small red-purple granules.Platelets appear to be formed by protrusion into the bone marrow sinusoids of pseudopods of megakaryocyte

cytoplasm,which detach into the bloodstream and fragment to yield small discoid platelets.

4-Mature platelet

Platelets are the small,anucleated,terminal,stage of development of the megakaryocytic series. They are discoid and have adiameter of 1-4µm. The cytoplasm stains blue and contains small red-purple granules which are centrally located in platelets in blood films.(Firkin *et al*;1989).

1.2.2 Complete blood count

Complete blood count also known as full blood count or blood panel give information about the cells in a patient blood such as cell count for each cell type and the concentration of haemoglobin (Verso;2013).

1.2.2.1 Haemoglobin estimation

The haemoglobin concentration of a solution may be estimated by several methods: by measurement of its colour, by its power of combining with oxygen or carbon monoxide or by its iron content. The clinical methods to be described are all colour or lightintensitymatching techniques, which measure at the same time with different degrees of efficiency any proportion of inert pigments, methaemoglobin(Hi) or sulphaemoglobin ,that may be present. The Hb of blood can be determined accurately by spectrophotometry. The blood is diluted with cyanide ferricyanide reagent and the absorbance is measured at 540nm and Hb is calculated with special formula(Dacie and Lewis;1996).

1.2.2.2 Haematocrit

The haematocrit or packed cell volume (PCV) refers to the proportion of the volume of red cells relative to the total volume of the blood. High-speed

centerfugation in the microhaematocrit procedure used to sediment the red cells yields highly reproducible results. The values do not correspond strictly to those obtained by electronic automated devices which derive a result by multiplying the red cell count by the mean red cell volume. The (Firkin *et al*;1989).

1.2.2.3 Red cell count

The red blood cell count (RBC) is itself used in diagnostic haematology, but it also of importance because it permits the mean cell volume (MCV) and mean cell haemoglobin (MCH) to be calculated. However, a manual red cell count in which cell are counted visually is so time consuming and has such poor precision that both it and the red cell indices derived from it are of limited use in routine practice. The reference method for the RBC is an automated rather than a manual count (Dacie and Lewis;1996).

1.2.2.4 Red cell indices

1.2.2.4.1 Mean corpuscular volume

The mean volume of cells was formerly determined by dividing the total volume of red cells(derived from the PCV) by the number of red cells in that particular sample of blood. Automated electronic-particle counting devices have revolutionized the estimation of the MCV. Most devices measure the electrical impedance caused by red cell as it passes through the counting mechanism, and the extent of the impedance provide an accurate indication of the volume of each cell. The MCV derived by this means therefore provides a reliable index of the average size of red cells,which is a guide of conciderable importance to the nature of the disorder underlying an abnormality in the hemoglobin level. A subnormal MCV is indicative of microcytosis, and an elevated MCV indicative of macrocytosis.(Firkin *et al*;1989).

1.2.2.4.2 Mean corpuscular hemoglobin

The main amount of haemoglobin per red cell (MCH) is also rapidly and reliably estimated by automated electronic counting devices by dividing the total amount of haemoglobin by the number of red cells in a sample of blood. A subnormal MCH occurs in microcytosis, but is even lower when microcytosis occurs in conjuction with a subnormal concentration of haemoglobin in the red cell, as in thalassaemia minor or iron deficiency.(Firkin *et al*; 1989).

1.2.2.4.3 Mean corpuscular haemoglobin concenteration

The mean haemoglobin concenteration with in the red cell (MCHC) reflects an entirely different parameter than the MCH. It is derived by dividing the concenteration of haemoglobin in g/dl by the volume of red cell in ml/dl. A subnormal MCH is usually indicative of an abnormality where interference with the synthesis of haemoglobin is greater than that of other constituents of red cells, as in thalassaemia or iron deficiency. Elevated value reflect dehyderation of the erythrocytes, and one of the relatively few important clinical causes of this phenomenon is spherocytosis (Firkin *et al*;1989).

1.2.3 Thyroid gland

The thyroid is the largest single endocrine gland, it weights 20-25g but it varies with age ,sex and physiological condition, such as pregnancy and lactation.

The gland lies in the anterior triangle of the neck,closely applaied to the trachea. The thyroid gland is formed of two lateral lobes, it is only endocrine gland that does not store its hormone within the cell but in follicular cavities surrounded by the cell. The main histological feature of thyroid follicle is a spherical structure formed of single layer of epithelial cells surrounded cavity filled with a colloid material.The type of epithelial cells forming the follicles varies according to the activity of the gland(Sukkar *et al;*1998).

1.2.4 Thyroid hormones

Thyroid gland produce thyroxine(T4), tri-iodothyronine(T3) and calcitonin (sukkar *etal*;1998). Iodine is necessary for the production of T3 andT4. Adeficiency of iodine lead to decreased production of T3, T4 and enlarges the thyroid tissue and will cause disease known as thyroid goiter. The major form of thyroid hormone is (T4) ,which has alonger half-life than (T3) (Irizary and Lisandro;2014).The function of thyroid gland is controlled by the hypothalamopituitary axis. The hypothalamus produces a thyrotrophin-releasing hormone(TRH), under influence of TRH the adenohypophysis produces thyroid stimulating hormone(TSH) which influences thyroid function in different way (Sukkar *et al*;1998).

1.2.5 Hyperthyroidism

Hyperthyroidism is characterized by high blood levels of thyroid HormonesT3andT4; can occur at early age or it may occur later in life (sukkar *et al*; 1998). This condition is commonly caused by development of Graves' disease; which an autoimmune disease in which anomalous antibodies stimulate the thyroid to secrete excessive quantities of thyroid hormone(Siegenther, 2007). The increased thyroid hormone secretion is due to abnormal immunoglobulins (IgGs) known as thyroid stimulating immunoglobulins (TSI). They seem to be act by stimulating TSH receptors in the follicular cells. Due to the increase T3 and T4 output, TSH secretion is inhibited and its circulating level in thytrotoxicosis is usually low (Sukkar *et al*; 1998).

1.2.5.1Sign and symptoms

- The patient usually complains of loss of weight in spite of good appetite.
- Weakness and tireness after slight exertion.

- Nervosness.
- There is afine tremor in hand.
- Palpitation.
- The eye may be protruding.
- Wet,warm skin.
- Menstrual disturbances.
- Thyroid enlargement (Sukkar *et al;*1998).

1.2.6 Hypothyroidism

Hypothyroidism is the deficiency of thyroid hormone production. May occur as a congenital absence of the thyroid or congenital deficiency of any of the enzymes concerned with hormone synthesis. Hypothyroidism can occur at adolescence or later in life (Sukkar *et al*;1998).

Hypothyroidism is caused either:-by inadequate function of the gland itself (primary hypothyroidism due to: Iodine deficiency, previous thyroidectomy, previous radioiodine treatment), or by not enough stimulation by thyroid stimulating hormone (centeral hypothyroidism, due to: lesion, compressing pituitary [pituitary adenoma, meningioma, glioma], surgery or radiation to the pituitary (Persani;2012).

The metabolic abnormalities associated with hypothyroidism include; anemia, hyperlipidemia and reversible increase in creatinine (Mitra *et al*; 2010).

Hyperthyroidism can cause certain forms of anemia on the one hand or hyper proliferation of immature erythroid progenitors on the other hand. Regarding leucocytes and thrompocyte, slightly depressed leukocyte count, neutropenia and thrombocytopenia have been observed in hypothyroidism patients. Furthermore, elevated normal or, slightly depressed total leukocyte counts have been found in hyperthyroid patient, with only arelative decrease in the number

of neutrophils and arelative increase in the number of eosinophils and mononuclear cells (Kawa *et al*;2010).

1.2.7 Previous studies

A study by Dorgalaleh *et al* attempted to evaluate the effect of hypo- and hyperthyroidism on blood cell count and RBC indices revealed statistically significant difference between two groups of patients in RBC count, MCH, MCHC, Hb and HCT(P-value<0.05), but the difference was not significant for TWBC and PLT counts and MCV (P-value>0.05) (Dorgalaleh *et al*; 2013).

A retrospective study was conducted in western Kenya between January 2008 and December 2011 to determine the thyroid hormone and haematological indices level in thyroid disorder patients. RBC, platelet count and Hb level were analyzed and the result showed that, the WBC, RBC, Hb and platelet count in immunological thyroid disease were not statistically significant. Concluded that, the presence of anemia due to low RBC in thyroid disease is not statistically associated with thyroid hormone (Iddah *et al*; 2013).

Another study about clinical relevance of thyroid dysfunction in human haematopoiesis: biochemical and molecular studies conducted in 2010, revaled that hypo- and hyperthyroidism modify thyroid receptor gene expression in haematopoietic progenitor cell in vivo. Thyroid hormone deficiency resulted in decrease in total blood count and clonogenic of BFU-E. In contrast, hyperthyroid patients presented increased clonogenic growth and BFU-E number. Hb level were analyzed and TWBC,RBC,HCT,MCV,MCH and MCHC were measured and the result showed that Hb and RBC are increased in hyperthyroid patients and decreased in hypothyroid patients, HCT and MCV showed significant increase in both groups.MCH and MCHC show significant decrease in hypo- and hyperthyroid patients (Kawa *et al*; 2010).

Astudy about immunological and haematological chganges in patients with hyperthyroidism or hypothyroidism was conducted in Iran, it concluded that mean MCV was significant lower in hyperthyroid patients and the mean count

of RBC and RBC related indices such as Hb and HCT were significantly lower in hypothyroid patients (Jafarzadeh *et al*; 2010)

1.3 Rationale

Thyroid hormone have important role in metabolism and proliferation of blood cells. Thyroid dysfunction induce different effect on blood cells, metabolic abnormality associated with hypothyroidism include anemia also Hyperthyroidism can cause certain forms of anemia on the one hand or hyper proliferation of immature erythroid progenitors on the other hand some studies about these effects were conducted to determine the CBC of patients with hypothyroidism and hyperthyroidism but showed conflict results, identification of CBC abnormalities of patients with hypothyroidism and hyperthyroidism will improve management protocol and avoid complications.

1.4 Objectives

1.4.1 General objective

To evaluate complete blood count in Sudanese patients with hyperthyroidism and hypothyroidism.

1.4.2 Specific objectives

- To determine HB, HCT, RBC count, RBC indices, total and differential WBC count, and PLT count in patients with hyperthyroidism and hypothyroidism using haematology analyzer.
- To correlate CBC results with patients' age.
- To correlate the haematological parameters with thyroid hormones.

Chapter Two
Materials and Methods

Chapter Two

Materials and Methods

2.1 Study design

This study is a case control study conducted to measure some haematological parameter in Sudanese patients with thyroid disorders.

2.2 Study population and sample size

One hundred Sudanese patients with thyroid disorders (50 with hyperthyroidism and 50 with hypothyroidism) and 50 healthy volunteer as a control group were enrolled in this study.

2.3 Study area and duration

The study was conducted in Antalya Medical center in the period from August 2015 to April 2016.

2.4 Inclusion criteria

Sudanese patients with hypothyroidism or hyperthyroidism.

2.5 Exclusion criteria

Patients with conditions known to affect the CBC such as pregnancy,infection, bleeding disorder and with any medical condition were excluded from the study.

2.6 Equipments and disposables

A. Vacutainer holder with disposable needles.
B. EDTA vacutainer tube (3ml).
C. 70% alcohol "ethanol".
D. Cotton.
E. Automated haematological analyzer (sysmex KX-21N).

2.7 Reagents

Commercial reagents were provided by Sysmex KX-21N manufacturer; consist of:

A. Diluent.
B. Cell pack (stromatolyzer).
C. Cell clearance (detergent).

2.8 Methods

2.8.1 Sample collection

Three milliliter (ml) of venous blood was collected from each participant, under aseptic conditions, after cleaning the area around the vein with 70% alcohol, then pour into EDTA blood container and mixed well before processing.

2.8.2 Complete blood count and thyroid hormones

CBC was performed using automated haematology analyzer (Sysmex KX-21N, JAPAN). Results of thyroid hormones were obtained from patients medical files.

2.9 Ethical considerations

This study was approved by the faculty of medical laboratory sciences and informed consent was obtained from each participant before sample collection.

2.10 Data collection and analysis

Data was collected by designed questionnaire, and analyzed by SPSS program (version 20). Frequency and percent of qualitative variables were calculated. Quantitative variables were presented as mean ± SD.Means of haematological parameters in patients with hyper- or hypothyroidism were compared with those

of control group using independent T-test. Pearson correlation was used to correlate haematological parameters with thyroid hormones.

Chapter Three
Results

Chapter Three

Results

A total of 100 Sudanese patients with thyroid disorders were enrolled in this study, 50(50%) with hypothyroidism and 50(50%) with hyperthyroidism. In addition, 50 healthy volunteers were included as a control group.

Forty six (92%) of patients with hyperthyroidism and 40 (80%) of patients with hypothyroidism were females, while 4(8%) of patients with hyperthyroidism and 10(20%) of those with hypothyroidism were males. 20(40%) of the control subjects were males and 30(60%) were females (Table 3-1).

Table (3-1): Distribution of study subjects according to gender.

Gender	**Hyperthyroidism**		**Hypothyroidism**		**Control**	
	Frequency	%	Frequency	%	Frequency	%
Female	46	92%	40	80%	30	60%
Male	4	8%	10	20%	20	40%
Total	50	100%	50	100%	50	100%

As shown in table (3-2) and (3-3) Hb, HCT and MCH of both hyperthyroidism and hypothyroidism patients showed significant decrease when compared to those of control group, MCV of hyperthyroid patients showed significant decrease when compared to those of control group, MCHC of hypothyroid patients showed significant decrease when compared to those of control group.

Table (3-2): Comparison of red cell parameters in patients with hyperthyroidism and control group

Parameters	**Group**				*P.value*
	Hyperthyroidism		**Control**		
	Mean	**±SD**	**Mean**	**±SD**	
Hb (g/dl)	12.7	1.2	13.7	1.4	0.00
Hct (%)	37.2	3.6	39.6	3.5	0.00
RBC ($\times 10^{12}$/L)	4.5	0.4	4.6	0.5	0.15
MCV (fl)	81.7	5.0	85.0	3.9	0.00
MCH (Pg)	28.1	2.5	29.5	2.2	0.00
MCHC (g/dl)	34.3	1.6	34.8	1.3	0.09

Table (3-3): Comparison of red cell parameters in patients with hyporthyroidism and control group

Parameters	**Group**				*P.value*
	Hypothyroidism		**Control**		
	Mean	**±SD**	**Mean**	**±SD**	
Hb (g/dl)	12.5	1.7	13.7	1.4	0.00
Hct (%)	37.6	4.3	39.6	3.5	0.01
RBC ($\times 10^{12}$/l)	4.5	0.5	4.6	0.5	0.34
MCV (fl)	82.9	7.3	85.0	3.9	0.07
MCH (Pg)	27.6	3.3	29.5	2.2	0.00
MCHC (g/dl)	33.2	1.5	34.8	1.3	0.00

No statistically significant difference was found in each of total WBCs count and Platelet count in patients with either hypo- or hyper- thyroidism compared to control group. Neutrophil count showed significant increase in hypothyroidism patients group (Tables 3-4 and 3-5)

Table (3-4): Comparison of total WBCs count, and PLT count in hyperthyroid patient and control group.

Parameters	**Group**				*P.value*
	Hyperthyroidism		**Control**		
	Mean	**±SD**	**Mean**	**±SD**	
TWBCs(×10^3/ML)	5.8	1.7	6.3	1.8	0.12
Neutrophils (%)	52.2	10.7	48.3	11.3	0.08
Lymphocyte (%)	37.5	9.3	40.5	10.6	0.13
Mix (%)	10.2	3.4	10.7	3.9	0.55
PLT (×10^3/ML)	304.0	86.9	319.7	70.6	0.326

Table (3- 5): Comparison of total WBCs count, and PLT count in hypothyroid patients and control group.

Parameters	Group				*P.value*
	Hypothyroidism		Control		
	Mean	±SD	Mean	±SD	
TWBCs($\times 10^3$/ML)	6.6	1.9	6.3	1.8	0.42
Neutrophil(%)	53.3	10.4	48.3	11.3	0.02
Lymphocyte(%)	37.2	8.9	40.5	10.6	0.09
Mix (%)	9.7	3.0	10.7	3.9	0.20
PLT($\times 10^3$/ML)	310.7	89.4	319.7	70.6	0.49

There was no statistically significant correlation between red cell parameters and age in patients with either hypothyroidism or hyperthyroidism (Table 3-6).

Table (3-6): Correlation of red cell parameter of hyper and hypothyroid patients with age.

Parameter	Hyperthyroidism		Hypothyroidism	
	Pearson correlation (r)	*P.value*	Pearson correlation (r)	*P.value*
Hb(g/dl)	0.10	0.47	-0.06	0.63
Hct(%)	0.12	0.38	-0.08	0.55
RBC($\times 10^{12}$/l)	0.10	0.48	-0.09	0.49
MCV(fl)	0.06	0.66	-0.00	0.95
MCH(Pg)	-0.01	0.94	0.00	0.98
MCHC(g/dl)	-0.07	0.59	0.02	0.87

Also there was no statistically significant correlation between each of Total WBCs count, and PLT count and age in patients with both hyper- and hypothyroidism (Table3-7).

Table (3-7): Correlation of total WBCs count, and PLT count of hyper- and hypothyroidism patients with age.

Parameter	**Hyperthyroidism**		**Hypothyroidism**	
	Pearson correlation (r)	***P.value***	**Pearson correlation (r)**	***p.value***
TWBCs(×10^3/ML)	0.07	0.61	-0.02	0.89
Neutrophil(%)	0.06	0.66	0.27	0.06
Lymphocyte(%)	-0.05	0.72	-0.27	0.09
Mix(%)	-0.05	0.72	-0.18	0.20
PLT(×10^3/ML)	-0.06	0.66	0.03	0.80

There was statistically significant positive correlation between MCV, MCH, and MCHC of hyperthyroid patients and TSH. Hb, HCT and MCH of hypothyroid patient showed significant negative correlation with TSH (Table 3-8).

Table (3-8): Correlation of red cell parameter of hyper- and hypothyroid patients with TSH.

Parameter	Hyperthyroidism		Hypothyroidism	
	Pearson correlation (r)	*P.value*	Pearson correlation (r)	*P.value*
Hb(g/dl)	0.22	0.12	-0.30	0.03
Hct(%)	0.07	0.61	-0.28	0.04
RBC(×10^{12}/l)	-0.20	0.16	-0.05	0.70
MCV(fl)	0.43	0.00	-0.26	0.06
MCH(Pg)	0.47	0.00	-0.27	0.05
MCHC(g/dl)	0.33	0.01	-0.23	0.10

There was no statistically significant correlation between Total WBCs, and PLT of hyper and hypothyroidism patients and TSH Table (3-9).

Table (3-9): Correlation of Total WBCs, and PLT count of hyper- and hypothyroidism patients with TSH.

Parameter	**Hyperthyroidism**		**Hypothyroidism**	
	Pearson correlation (r)	***P.value***	**Pearson correlation (r)**	***p.value***
TWBCs($\times 10^3$/ML)	-0.22	0.11	0.01	0.93
Neutrophil(%)	0.01	0.91	-0.26	0.06
Lymphocyte(%)	0.03	0.82	0.32	0.06
Mix(%)	-0.13	0.33	-0.14	0.32
PLT($\times 10^3$/ML)	0.01	0.91	0.07	0.58

There was no statistically significant correlation between red cell parameter of hypo- and hyperthyroid patients and T4 (Table3-10).

Table (3-10): Correlation of red cell parameter of hyper - and hypothyroidism patients with T4.

Parameter	**Hyperthyroidism**		**Hypothyroidism**	
	Pearson correlation (r)	***P.value***	**Pearson correlation (r)**	***P.value***
Hb(g/dl)	-0.10	0.47	0.21	0.40
Hct(%)	-0.03	0.79	0.06	0.64
RBC($\times 10^{12}$/l)	0.14	0.31	-0.15	0.29
MCV(fl)	-0.25	0.07	0.26	0.06
MCH(Pg)	-0.24	0.08	-0.26	0.06
MCHC(g/dl)	-0.12	0.38	0.20	0.15

There was no statistically significant correlation between total WBCs, and PLT count of hyper- and hypothyroidism patients and T4 (Table3-11).

Table (3-11): Correlation of total WBCs, and PLT count of hyper and hypothyroidism patients with T4.

Parameter	**Hyperthyroidism**		**Hypothyroidism**	
	Pearson correlation (r)	***P.value***	**Pearson correlation (r)**	***p.value***
TWBCs($\times 10^3$/ML)	0.22	0.11	-0.23	0.10
Neutrophil(%)	-0.22	0.12	-0.01	0.92
Lymphocyte(%)	0.18	0.19	-0.02	0.85
Mix(%)	0.16	0.24	0.22	0.12
PLT($\times 10^3$/ML)	-0.13	0.17	-0.02	0.85

There was statistically significant negative correlation between MCH of hyperthyroid patients and T3, while other red cell parameter showed no statistically significant correlation with T3 (Table3-12).

Table (3-12): Correlation of red cell parameters of hyper - and hypothyroidism patients with T3.

Parameter	Hyperthyroidism		Hypothyroidism	
	Pearson correlation (r)	*P.value*	Pearson correlation (r)	*P.value*
Hb(g/dl)	-0.15	0.27	-0.06	0.66
Hct(%)	-0.03	0.80	-0.06	0.67
RBC($\times 10^{12}$/l)	0.10	0.46	-0.14	0.32
MCV(fl)	-0.24	0.08	0.07	0.59
MCH(Pg)	-0.30	0.03	0.04	0.78
MCHC(g/dl)	-0.25	0.07	-0.02	0.89

There was no statistically significant correlation between total WBCs, and PLT count of hyper- and hypothyroidism patients and T3 (Table3-13).

Table (3-13): Correlation of total WBC, and PLT count of hyper - and hypothyroidism patients with T3.

Parameter	**Hyperthyroidism**		**Hypothyroidism**	
	Pearson correlation (r)	***P.value***	**Pearson correlation (r)**	***p.value***
TWBCs(×10^3/ML)	0.17	0.21	-0.20	0.15
Neutrophil(%)	-0.12	0.39	0.02	0.85
Lymphocyte(%)	0.10	0.48	-0.11	0.44
Mix(%)	0.10	0.48	0.37	0.07
PLT(×10^3/ML)	-0.13	0.17	-0.02	0.85

Chapter Four

Discussion, Conclusion and Recommendations

Chapter four

Discussion, conclusion and recommendations

4.1 Discussion

This study was carried out in Khartoum, Sudan, during the period from August 2015 to April 2016 to evaluate haematological parameters in patients with thyroid disorders.

The results of the study reavaled that, Hb level, HCT, MCH of both study groups (hypo –and hyper thyroidism patients) and MCHC of hypothyroidism group were significantly decreased when compared with control group; RBC count showed no statistically significant difference in both hyperthyroid and hypothyroid groups. This finding is in agreement with that of the study done by Dorgalaleh *et al;* (2013) who reported statistically significant difference between two group of patients in RBC,MCH,MCHC,Hb and HCT but the difference was not statistically significant for WBC and PLT counts (Dorgalaleh *et al;*2013). This finding is in disagreement with that of the study done by Kawa *et al;* (2010) who found statistically significant increased in Hct, RBC count and decreased in MCH and MCHC in both groups. Variation in these results can be related to the facts that reported by Horton *et al*.,1976,who report that, hypothyroidism can cause certain forms of anaemia on the one hand or hyperproliferation of immature erythroid progenitors on the other hand (Horton *et al*;1976). This is further supported by Perlman *et al*., 1983, who reported that, anemia is not frequently observed in patients with hyperthyroidism, whereas erythrocytosis is fairly common. It has been founded that all haematological parameter return to normal when an euthyroid state is achieved (Perlman and Sternthal;1983).Patients with thyroid disorder on this study on treatment .

MCV was significantly decreased in hyperthyroid patients when compared with control group. This finding agrees with that of the study done by jafarzadeh *et al*;2010 who also found that, mean red cell volume MCV is significantly decreasd in the hyperthyroid patients in comparison with euthyroid group. The underlying mechanism for this alteration is un known. One possible mechanism may be premature aging of erythrocyte in circulation of hyperthyroid patients (Arumanayagam *et al*;1994).

The result of the present study showed that, no statistically significant difference in total leukocyte count or platelet count in both groups when compared with control group. This is similar to study done by Dorgalaleh *etal*; (2013) in Iran who found that total WBCs count in both patient groups compared control group did not showed any significant difference (Dorgalaleh *et al*;2013).

Neutrophil showed significant increased in hypothyroid patient when compared control group this is result disagree with the result reported by Kawa (2010) who found that aslightly depressed total leucocyte count, neutropenia and thrombothytopenia have been observed in hypothyroidism patients (Lima *et al*;2006).

There was no statistically significant correlation between age and each of red cell parameter, total leukocyte count, differential count and platelet count of hyper and hypothyroidism patients.

There was statistically significant positive correlation between MCV, MCH, MCHC of hyperthyroid patient and TSH. Hb, HCT and MCH of hypothyroid patient showed significant negative correlation with TSH, while total leukocyte count, differential count and platelet count show no statistically significant correlation with TSH.

There was no statistically significant correlation between red cell parameters and leukocyte parameters of hyper- and hypothyroidism patients with T4.

There was statistically significant negative correlation between MCH of hyperthyroid patient and T3, while other red cell parameter, total leukocyte count, differential count and platelet count showed no statistically significant correlation with T3.

4.2 Conclusions

- Thyroid disorders have negative effect on Hb , Hct and MCH, while it has no effect on total WBCs count or platelet count.
- Patients with hypothyroidism have increased neutrophil counts.
- There was a positive correlation between MCV,MCH and MCHC of hyperthyroid patient and TSH.
- There was a negative correlation between Hb,HCT ,and MCH of hypothyroid patients and TSH.
- There was a negative correlation between MCH of hyperthyroid patients and T3.

4.3 Recommendations

- Patients with hypothyroidism and hyperthyroidism should be evaluated for probable hematological changes by performing CBC.
- Further studies should be done with large sample size and take in consideration iron profile.

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Appendix

Sudan University of Science and Technology

College of Graduate Studies

Questionnaire

Evaluation of Complete Blood Count in Sudanese patients with Hyperthyroidism and Hypothyroidism

date:……

Serial number: …….....

Age:…….....

Sex: Male ( ) Female ( )

Test:

Tsh:……..……MIU\ml

T3:…….nmol\L

T4:……nmol\L

CBC:

Hb…… TWBCs……

Hct…….. Neutrophil……

MCV…… Lymphocyte……

MCH…….. Monocyte……

MCHC…….. Eosinophil……

Platelet…… Basophil…….