قال تعالى:

{وابِتَغِ فَمَا آتاكَ الله الدَّارَ الآخرةَ ولا تنسَ نصِيبكَ من الدُّنِيَا وأَحْسِنَ كَما أَحْسَنَ الله إلَيْكَ ولاتَبِغِ الفَسَادَ في الأَرضِ إنَّ الله لا يُحِبُّ المُفسِدينَ (77)}

صدق الله العظيم

(سورة القصص الآية 77)
Dedication

To the candle which burns to light my life..

My Mother

To the one who live to achieve all my dreams..

My Father

To those who believe in me..

My brothers and my sisters

To those who have made it possible

My Teachers

To those who encourage me and are always around me..

My Friends
Acknowledgement

Thanks first and last for Allah who enabled me to conduct this study by his grace and provided me with strength and patience to complete my project.

For all those who have supported me, and helped me in this research, I send my thanks and deepest gratitude.

Special and deepest regard for my supervisor Pro. Shadia Abdalatti for her help and close supervision.

My thanks are also extended to the staff of National Health Insurance Fund for their kind assistance.

My gratitude is also extended to the staff of Hematology Department of their help throughout the study.
Abstract

Hypertension is a major risk factor for coronary heart disease and ischemic as well as hemorrhagic stroke. The elevation of platelets and red blood cell count and indices values in hypertensive patients associated with hypertensive target organ damage and arterial disease. Evaluation of platelets and red blood cells count and indices could be useful in prediction and differentiation of coronary and thrombotic events.

This a case control study carried out in the National Health Insurance Fund in Al Gazeera State during the period March to June 2014, the study aimed to measure platelet count and platelet indices and red blood cell indices. In this study 100 individuals were included, 70 used as cases (hypertensive patients) and 30 individual as control healthy group their age ranges from 20 to 80 years. EDTA anticoagulated venous blood samples were collected from known diagnostic hypertensive patients and control group.

The samples were analyzed using automated hematological analyzer to measure platelet count and platelet indices (Mean Platelet Volume, Platelet Distribution Width and Platelet Large Cell Ratio) and red blood cell indices (mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC).

Hypertensive participants significantly higher (P≤ 0.05) values than the control individuals for MPV (11.17 ±1.4 fL compared to 9.146±0.78fL), P-LCR (27.94±4.90% compared to 16.00 ±1.85%) and platelets count (235.60±61.28 X10/L compared to 210.23 ±46.33 X 10/L) respectively. No significant variation was observed in PDW. RBCs indices were significantly affected by hypertension higher (P≤ 0.05) values than of the control group individuals for RBC count (4.62 ±0.54 X10^{12}/L compared to 4.32 ±0.56 X10^{12}/L), HCT (36.23±4.18% compared to 32.91±5.92 %) MCV (84.13±4.56fl compared to 81.95 ± 5.22fl), MCH (27.66 ±2.11 pg compared to 26.30 ±2.56 pg), No
significant variation was observed in MCHC. Platelet and red blood cell indices are significantly affected by hypertension. Their clinical utility and association with disease activity in patients with hypertension should be further investigated.
المستخلص

ارتفاع ضغط الدم هو عامل خطر رئيسي لأمراض القلب التاجية والدماغية وكذلك السكتة الدماغية النزفية، ارتفاع الصفائح الدموية، وخلايا الدم الحمراء والمؤشرات القيم في مرضاي

ارتفاع ضغط الدم يرتبط مع ارتفاع ضغط الدم الضرر الجهاز المستهدف و أمراض الشرايين. تقييم الصفائح الدموية وخلايا الدم الحمراء العد ومؤشرات يمكن أن تكون مفيدة في التنبؤ والتفرقة بين الأحداث التاجية و الجلطات.

الفترة خلال الجزيرة ولاية في الوطنى التأمين الصحي صندوق في الدراسة أجريت هذه الدموية الصفائح عدد قياس إلى الدراسة وهدفت عام 2014، مارس 2014 وجزيران من شملت 100 الدراسة. هذه مؤشرات العصراء الدم وخلايا الدم الحمراء الصفائح ومؤشرات تتراوح من الاحصاء و 30 مجموعة الدم ضغط مرضاي ارتفاع شخص، 70 من الحالات أعمارها 20-80 عاما.

مرضى مشخصين من الوريدي في حاويات تحتوي على إملاح البواتسيوم الثلاثي الدم جمع عينات تم ومجموعه اصعاء. الدم ضغط ارتفاع بمرض الدموية الصفائح عدد الأليل ليحلل الدم لقياس بواصع الهياج العينات المرضاي والأصعاء تحليل تم وقد وعدد كريات الدم الحمراء ومؤشراتكما. أظهرت هذه الدراسة ان هناك فرق تشخيصي في تعداد ومؤشرات الصفائح الدموية وتداعي ومؤشرات كريات الدم الحمراء بين مجموعه المرضاي الغير مستقرن ومجموعه الاصعاء (القيمة الإحتمالية 0.05).

مرضى ضغط الدم المسجلين ذات دلاله إحصائى على بكثير (القيمة الإحتمالية 0.05) من غير المصابين، ضغط الدم لمتوسط حجم الصفائح الدموية (11.7±1.4 مقارنه 9.14±0.78 في ميلر)، ولتعداد الصفائح الدموية (19.2±1.4 مقارنه 24.7±3.3) مئتي لتر، ونسبة الصفائح الدموية الكليه كبيره (21.7±0.16 مقارنه 16.00±16.00)، وعرض توزيع الصفائح الدموية لم يحدث اي فرق إحصائى.

تعداد كريات الدم الحمراء ومؤشراتها احدث فرق إحصائى ذو دلاله إحصائى لدى مرضاي ضغط الدم (القيمة الإحتمالية 0.05)، التعداد كريات الدم الحمراء (0.62±0.54 مقارنه 0.43±0.56×10^12/لتر) الهيماتوكرت (2.71±1.91 مقارنه 5.92±4.18 بيكو جرام)، وتوزيع حجم كريه الدم
(81.95 ± 5.22 مقارنة 84.13 ± 4.56 فيمتو ليتر)، متوسط هيموغلوبين الكريه الحمراء (66 ± 2.11 مقارنة 30 ± 2.56 بيكو جرام)، ومتوسط تركيز الهيموغلوبين في الكريه الحمراء لم يحدث أي فرق إحصائي.

مؤشرات الصفائح الدموية ومؤشرات كريات الدم الحمراء تتأثر بشكل كبير من ارتفاع ضغط الدم وينبغي مواصلة التحقق والمزيد من التأكد من فوائد مؤشرات صفائح الدم والكريات الحمراء مع نشاط المرض في المرضى الذين يعانون من ضغط الدم.
List of Abbreviations

BP : Blood Pressure
CBC : Complete Blood Count
DASH : Dietary Approaches to Stop Hypertension
DBP : Diastolic Blood Pressure
DNA : Deoxyribonucleic Acid
EDTA : Ethylene Diamine Tetra Acetic acid
EPO : Erythropoietin
Fl : FemtoLiter
HIT : Heparin Induce Thrombocytopenia
HTN : Hypertension
LVH : Left Ventricular Hypertrophy
MCH : Mean Corpuscular Hemoglobin
MCHC : Mean Corpuscular Hemoglobin Concentration
MCV : Mean Corpuscular Volume
MPV : Mean Platelet Volume
N.S : Not significant
PCT : Platelet-Crit
PDGF : Platelet Derived Growth Factor
PDW : Platelet Distribution Width
P-LCR : Platelet Large Cell Ratio
PLT : Platelet
PRP : Platelet Rich Plasma
RBC : Red Blood Cell
RDW : Red Cell Distribution Width
SBP : Systolic Blood Pressure
SD : Stander Deviation
TTP : Thrombotic Thrombocytopenic Purpura
UD : Upper Discriminator
WCHT : White coat hypertension
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Chapter One

1-Introduction and Literature Review

1.1 Introduction:

Platelets are small, irregularly shaped clear cell fragments which do not have nucleus. They circulate in the blood of mammals and are involved in hemostasis, leading to the formation of blood clots. Platelet indices include [mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR)], and platelet count are indicators of platelet function and activity. High blood pressure is associated with thrombotic events, especially cardiovascular. Platelet activation is involved in the pathogenesis of the thrombotic complications of hypertension (Boos et al, 2007). Platelet function and activity have been reported to be influenced significantly by high blood pressure these changes may have a role in the genesis of hypertension vascular disease. Platelets were significantly higher in the hypertensive group compared to normotensive, The elevation of platelet count and platelet indices values with increasing severity of hypertensive disease may contribute to the pathogenesis of thrombosis-related complications in hypertension (Al-Muhana et al., 2006).

RBC indices are mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and hematocrit (HCT). The development of hypertension is also accompanied by changes in properties of blood, which can affect the blood flow. There was a significant relationship between the haematocrit and high blood pressure (Wannamethee and Shaper, 1994).

Hypertension is associated with increase red blood cell aggregation which can lead to capillary slow flow; these findings might be relevant to the ethiopathogenesis of this disease (Kesler et al., 2006).
1.2 Literature review:

1.2.1 Hemostasis:
Hemostasis is a process which causes bleeding to stop, meaning to keep blood within a damaged blood vessel (the opposite of hemostasis is hemorrhage). It is the first stage of wound healing. This involves blood changing from a liquid to a gel. Intact blood vessels are central to moderating blood's tendency to clot. The endothelial cells of intact vessels prevent blood clotting with a heparin-like molecule and thrombomodulin and prevent platelet aggregation with nitric oxide and prostacyclin. When endothelial injury occurs, the endothelial cells stop secretion of coagulation and aggregation inhibitors and instead secrete von Willebrand factor which initiate the maintenance of hemostasis after injury. Hemostasis has three major steps: vasoconstriction, temporary blockage of a break by a platelet plug and blood coagulation, or formation of a fibrin clot. These processes seal the hole until tissues are repaired (Marieb et al, 2010)

1.2.2 Platelets:
Platelets or thrombocytes are small, irregularly shaped clear cell fragments that do not have a nucleus (Campbell, 2008). They are derived from fragmentation of precursor megakaryocytes in the bone marrow. The average life span of platelets is normally just 5 to 9 days. Platelets are natural source of growth factor. They circulate in the blood of mammals and are involved in hemostasis, leading to the formation of blood clot. If the number of platelets is too low, excessive bleeding can occur. However, if the number of platelets is too high, blood clot can be formed (thrombosis), which may obstruct the blood vessels and result in such events as stroke, myocardial infarction, pulmonary embolism,
or the blockage of blood vessels to other parts of the body, such as the extremities of the arms or legs. An abnormality or a disease of the platelets is called thrombocytopenia (Maton et al., 1993), which could be due to either a low number of platelets (thrombocytopenia), decrease in function of platelets (thrombasthenia), or an increase in the number of platelets (thrombocytosis). There are disorders that reduce the number of platelets, such as heparin-induced thrombocytopenia (HIT) thrombotic thrombocytopenic purpura (TTP) that typically cause thrombosis, or clots, instead of bleeding. Platelets release a multitude of growth factors have including platelet-derived growth factor (PDGF), a potent chemotactic agent, and TGF beta, which stimulate the deposition of extracellular matrix. Both of these growth factors have been shown to play a significant role in the repair and regeneration of the connective tissue. (Sanchiz et al., 2007 and O’Connell et al., 2008). Other healing associated growth factors produced by platelets include basic fibroblast growth factor, insulin-like growth factor 1, platelet-derived epidermal growth factor, and vascular endothelial growth factor. Local application of these factors in increased concentrations, through platelet-rich plasma (PRP), has been used as an adjunct to wound healing for several decades (Celotti et al., 2006). The function of platelets is the maintenance of hemostasis. This is achieved primarily by the formation of thrombi, when arterial wall damage triggers a cascade of events starting with platelets adhesion to the damaged vessels area, which then leads to platelets activation, aggregation and finally thrombus formation. Arterial wall de-endothelialisation or injury to atheromaous plaque (Greer et al., 2003).

1.2.2.1 Platelets Formation:

Platelets are produced during blood cell formation (thrombopoiesis), thrombopoiesis refers to the process of thrombocyte generation. Thrombocytes
are ligations of the cytoplasm from megakaryocytes. A single megakaryocyte can give rise to thousands of thrombocytes. (Schulman et al., 1960).

Thrombopoietin stimulates megakaryopoiesis, the process of megakaryocyte maturation and differentiation. Thrombopoietin, upon release, binds to its receptor, c-mpl, found on megakaryocyte progenitor cells. Following binding, intracellular signalling leads to megakaryocyte growth, maturation, membrane stability, platelet granule formation and the demarcation of the cytoplasm into regions destined to fragment into mature platelets. These "proplatelet processes" further fragment into platelets. This last step of proplatelet process and platelet formation, in vitro, has been shown to be independent of thrombopoietin (Schulman et al., 1960).

1.2.2.2 Platelet structure:

Structurally the platelet can be divided into four zones, from peripheral to innermost: Peripheral zone, Sol-gel zone, Organelle zone and Membranous zone. The peripheral zone is rich in glycoproteins required for platelet adhesion, activation, and aggregation. For example, GPIb/IX/X; GPVI; GPIIb/IIIa. The sol-gel zone is rich in microtubules and microfilaments, allowing the platelets to maintain their discoid shape. The organelle zone is rich in platelet granules. Alpha granules contain clotting mediators such as factor V, factor VIII, fibrinogen, fibronectin, platelet-derived growth factor, and chemotactic agents. Delta granules or dense bodies contain ADP, calcium, serotonin, which are platelet-activating mediators. The membranous zone contains megakaryocytic smooth endoplasmic reticulum-derived membranes organised into a dense tubular system, responsible for thromboxane A2 synthesis. The dense tubular system is connected to the surface platelet membrane to aid thromboxane A2 release (Michelson 2013).
1.2.2.3 Platelet functions:

The main function of platelets is to contribute to hemostasis: the process of stopping bleeding at the site of interrupted endothelium. They gather at the site and unless the interruption is physically too large, they plug the hole. First, platelets attach to substances outside the interrupted endothelium: adhesion. Second, they change shape, turn on receptors and secrete chemical messengers: activation. Third, they connect to each other through receptor bridges: aggregation (Yip et al., 2005). Formation of this platelet plug (primary hemostasis) is associated with activation of the coagulation cascade with resultant fibrin deposition and linking (secondary hemostasis). These processes may overlap: the spectrum is from a predominantly platelet plug, or "white clot" to a predominantly fibrin clot, or "red clot" or the more typical mixture. The final result is the clot. Some would add the subsequent clot retraction and platelet inhibition as fourth and fifth steps to the completion of the process and still others a sixth step wound repair (Berridge et al., 2012).

1.2.3 Platelet indices:

Circulating platelets are very different in size, metabolism, and functional activity, the largest are more reactive and produce a greater quantity of thrombogenic factors (Thompson et al., 1994 and Martin et al., 1996). Automated counters provide platelet counts and generate the MPV and a measure of their size variability (PDW). The great dispersion of platelet volumes (log-normal distribution) depend on the process of platelet production, by cytoplasm fragmentation of megacaryocyte and pro platelet formation. Platelet volume seems to be correlated with megacaryocyte ploidy, even though the exact mechanism is not completely known. The increase of MPV in conditions with increased platelet turnover is probably mediated by several cytokines (interleukin 6 and 11 and thrombopoietin) that affect megacaryocyte
ploidy and result in the production of larger and more reactive platelets (Corash et al., 1987 and Hoffman et al., 1995). Whether platelets recently released from bone marrow are larger and tend to shrink as they age remains controversial. In healthy subjects, there is a nonlinear inverse correlation between MPV and platelets concentration: MPV tends to decrease in subjects with higher platelet count (Bessman. A et al., 1996) this relationship is such that the platelet mass is relatively constant within a large interval of platelet counts. The MPV reference intervals should, therefore, be expressed as a function of platelet concentration. This wide dispersion of normal values limits the usefulness of MPV as a screening test to clinical conditions characterized by extreme values such as some hereditary thrombocytopenia (Wiskott- Aldrich syndrome, in which there are decreased values, and Bernard –Soulier syndrome, in which values are increased). In the deferential diagnosis of acquired thrombocytopenia, distinguish forms with increased MPV (of peripheral origin with increased platelet function and normal megakaryocytes function: immunologic thrombocytopenic purpura and disseminated intravascular coagulation) from those with normal or decrease MPV (In which there is defect in platelets production: acute leukemia, bone marrow aplasia, and chemotherapy or radiation therapy) (Macchi et al, 2002).

The MPV is useful also for monitoring recovery in thrombocytopenia because of an early increase with respect to the platelet concentration (Balduini et al., 1999), even though not all analyzer can provide this parameter in cases of severely low platelet count. Because an increase of the MPV is a known marker of platelet activation, several investigation have been performed to verify if this increase is associated with a risk of thrombotic disease (Endler et al., 2002 and Buttarello et al., 2007). The results have been controversial. An increase in the MPV is considered an independent risk factor for myocardial infarction in patients with coronary disease (Endeler et al, 2002), and for death or recurrent vascular events after an acute myocardial infarction (Martin et al, 1996). Other
studies have shown an increased of MPV in patients with acute ischemic stroke, but the association between elevated values and stroke outcome is a matter for debate (Greisenegger et al., 2004). Abnormally low MPV values correlated primarily with thrombocytopenia when it is due to impaired production as in a plastic anemia (Buttarello et al., 2007).

In healthy populations, there is a direct relationship between MPV and PDW; this relationship is maintained in idiopathic thrombocytopenic purpura and chronic myeloid leukemia, in which both are increased. This does not occur in a plastic anemia or megaloblastic anemia or during chemotherapy, in which the MPV decreases with an increasing PDW. The PDW can also be useful in differentiating reactive thrombocytosis from the essential type, especially when it is combined mathematically with the MPV and platelet count to obtain discriminate function (Osselaer et al., 1997).

The recommended anticoagulant for a CBC determination including platelet indices is Di or Tri potassium of ethylene Diamine Tetra Acetate (This is recommended by international council for standardization., 1993). When blood comes in contact with EDTA, platelet rapidly change shape from disk with diameters of 2 to 4 to spheroids covered with filamentous extensions. The platelet spherical transformation is initially isovolumetric, but within 1 or 2 hours, the volume progressively changes to reach equilibrium condition, even if not definitive. As a consequence, the MPV increases from 7.9% within 30 minutes to 13.4% over 24 hours (Bowles, et al., 2005) if measured by the impedance method or decreases by nearly 10% when measured by the optical method, probably owing to the dilution of the cytoplasm content with a decrease of the refractive index. Various attempts to mathematically correct for this phenomenon have failed owing to the unpredictable behaviour of individual samples in terms of intensity and time to equilibrium (Bowles, et al., 2005).

With the use of EDTA, the MPV is, therefore, not a very reliable index (Lippi et al., 1990). The same considerations hold true for PDW, which in certain
counters can be influenced by platelet concentration—the analysis of platelet size distribution becomes problematic in thrombocytopenic samples. The lack of standardization and the dependency of results on pre analytic variables and on the measurement method used require different reference intervals (van den Bossche et al., 2002), and allows for poor comparison of clinical studies carried out in non-standard conditions. As a result, despite the many articles published regarding the possible clinical usefulness of platelet indices, in daily practice, they must still be considered little more than experimental. (Van den Bossche et al., 2002).

1.2.3.1 PDW (Platelet distribution width):
PDW is the distribution width on 20% frequency level with the peak taken as 100%. The unit applied is fl (femto-liter = 10^{-15}), the PDW has been receiving attention due to its usefulness for distinguishing between reactive thrombocytosis and thrombocytosis associated with myeloproliferative disorder. Determination of the PDW reference range is fundamental, and the association of this parameter with the platelet number and mean platelet volume may be used for the diagnosis and differentiation of several pathologies. (Mariela et al., 2009).

1.2.3.2 MPV (mean platelet volume):
Mean platelet volume is a machine-calculated measurement of the average size of platelets found in blood and is typically included in blood tests as part of the CBC. Since the average platelet size is larger when the body is producing increased numbers of platelets, the MPV test results can be used to make inferences about platelet production in bone marrow or platelet destruction problems, High MPV thus appears correlated with myeloproliferative disease or thalassemia; and low MPV, with cytotoxic drugs or marrow hypoplasia. Addition of MPV to the platelet count allows subtler disorders to be detected
(when the platelet count is normal), and allows distinction of the cause of thrombocytopenia. (Bessman and Gilmer ., 1996).

1.2.3.3 P-LCR (Platelets-large cell ratio):

P-LCR was significantly decreased in patients with thrombocytosis than in normal while it was increased in thrombocytopenia. In patients with high counts, P-LCR was significantly decreased in reactive thrombocytosis than neoplastic thrombocytosis. P-LCR was increased in destructive thrombocytopenia than those with hypoproliferative thrombocytopenia though it was not statistically significant. P-LCR was inversely related to platelet count and directly related to PDW and MPV. Platelet large cell ratio if properly utilised can be a good aid in the differential diagnosis of conditions associated with abnormal platelet counts (Babu and Basu et al., 2004).

1.2.4 Normal value of platelet indices:

Reference intervals (normal population reference range) where developed for KX-21N using normal individuals the range for each parameter –PDW, MPV, Were determined and displayed in table (1.1)

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<tr>
<td>Male</td>
<td>8.1-12.4</td>
<td>9.8-18</td>
<td>10.7-45</td>
</tr>
<tr>
<td>Female</td>
<td>8.5-12.4</td>
<td>9.4-18.1</td>
<td>14.3-44</td>
</tr>
</tbody>
</table>

(Sysmex corporation, 1999).

1.2.5 Red Blood Cells:

Red blood cells, or erythrocytes, are the most common type of blood cells and the vertebrate organism’s, it is derived from heamatopoietic stem cells in bone marrow, following a series of maturation steps directed largely by the hormone erythropoietin (EPO), red cells enucleate and enter the circulatory system. In circulation these small flexible biconcave cells containing haemoglobin
transport O2 from the lungs to the periphery and CO2 back from the periphery to the lungs. They lack a cell nucleus and most organelles to accommodate maximum space for haemoglobin (Lee et al, 1999). 2.4 million new erythrocytes are produced per second. The cells developed in the bone marrow and circulate for about 100-120 days in the body before their components are recycled by macrophage. Each circulation takes about 20 seconds. Approximately a quarter of the cells in the human body are red blood cells (Lee et al, 1999).

Erythrocytes remain in hyperglycemic environment throughout their life span and thus are subjected to series of compositional changes, which in turn affect their flow properties through alteration of deformation at individual level and aggregation at collective level. (Singh and Shin, 2009).

1.2.5.1 Red Blood Cell formation:

Formation of red blood cells terms erythropoiesis, is the process which produces red blood cells (erythrocytes). It is stimulated by decreased O2 in circulation, which is detected by the kidneys, which then secrete the hormone erythropoietin (Sherwood et al, 2005). This hormone stimulates proliferation and differentiation of red cell precursors, which activates increased erythropoiesis in the hemopoietic tissues, ultimately producing red blood cells (Sherwood et al, 2005). In postnatal birds and mammals (including humans), this usually occurs within the red bone marrow. In the early fetus, erythropoiesis takes place in the mesodermal cells of the yolk sac. By the third or fourth month, erythropoiesis moves to the liver (Palis et al., 1998).

After seven months, erythropoiesis occurs in the bone marrow. Increased level of physical activity can cause an increase in erythropoiesis. However, in humans with certain diseases and in some animals, erythropoiesis also occurs outside the bone marrow, within the spleen or liver. This is termed extramedullary erythropoiesis (Le et al, 2010).
The bone marrow of essentially all the bones produces red blood cells until a person is around five years old. The tibia and femur cease to be important sites of hematopoiesis by about age 25; the vertebrae, sternum, pelvis and ribs, and cranial bones continue to produce red blood cells throughout life (Le et al, 2010).

1.2.5.2 Red Blood Cell structure:

A typical human erythrocyte has a disk diameter of approximately 6.2–8.2 µm and a thickness at the thickest point of 2–2.5 µm and a minimum thickness in the centre of 0.8–1 µm, being much smaller than most other human cells. These cells have an average volume of about 90 fL with a surface of about 136 µm², and can swell up to a sphere shape containing 150 fL, without membrane distension (Mary Louise Turgeon 2004).

As red blood cells contain no nucleus, protein biosynthesis is currently assumed to be absent in these cells, although a recent study indicates the presence of all the necessary biomachinery in the cells to do so (Kenneth and Bridges 2007).

The blood's red color is due to the spectral properties of the hemic iron ions in hemoglobin. Each human red blood cell contains approximately 270 million of these hemoglobin biomolecules, each carrying four heme groups; hemoglobin comprises about a third of the total cell volume. This protein is responsible for the transport of more than 98% of the oxygen (the remaining oxygen is carried dissolved in the blood plasma). The red blood cells of an average adult human male store collectively about 2.5 grams of iron, representing about 65% of the total iron contained in the body (Kenneth and Bridges 2007)

1.2.5.3 Red Blood Cell function:

The haemoglobin absorbs oxygen in the lungs, travels through blood vessels and brings oxygen to all other cells via the heart. Since the blood cells go through
both the lungs. The most important function of red blood cells is the transport of oxygen. (to collect oxygen), through the heart (to be pumped around the rest of the body to give all cells oxygen) and back to the heart to be re-pumped to the lungs (to again collect oxygen), it is said that the blood in your body travels in a double circuit, going through your heart twice before it completes one full circulation of the body. A fact which makes mammalian red blood cells different to all other cells is that, when they are mature, red blood cells do not have a nucleus. All other vertebrates have red cells with nuclei (Kabanova S. et al., 2009).

Mammalian RBCs are unique among vertebrates as they are non-nucleated cells in their mature form. These cells have nuclei during development, but push them out as they mature. This gives more space for haemoglobin. Mammalian RBCs also lose all other cellular organelles such as their mitochondria, Golgi apparatus and endoplasmic reticulum. As a result of not having mitochondria, the cells use none of the oxygen they carry. Instead they produce the energy carrier ATP. Because of the lack of nuclei and organelles, mature red blood cells do not contain DNA and cannot synthesize any RNA. They cannot divide, and have limited repair capabilities. This also makes sure no virus can target mammalian red blood cells (Zimmer and Carl, 2007).

1.2.6 Red blood Cell indices:

Red blood cell indices are measurements that describe the size and oxygen-carrying protein (hemoglobin) content of red blood cells. The indices are used to help in the differential diagnosis of anemia. They are also called red cell absolute values or erythrocyte indices. The indices include these measurements: mean corpuscular volume (MCV); mean corpuscular hemoglobin (MCH); mean corpuscular hemoglobin concentration (MCHC); and red cell distribution width (RDW). (Pagana et al. 1998).
There is significant literature documenting relations of blood pressure with the erythrocyte measures of RBC, hematocrit, and hemoglobin in clinical and epidemiological studies but not with MCV. Clinical studies have indicated a class of patient with positively correlated erythrocyte measures (e.g., RBC, hematocrit, and hemoglobin) and blood pressure. This condition, variously called “stress polycythemia,” “relative polycythemia,” “spurious polycythemia,” and “pseudopolycythemia,” has been used to describe a clinical condition in which a raised hematocrit is associated with a normal total-body red cell mass, with normal or slightly reduced total-body plasma volume, and with hypertension, obesity, “stress,” and heavy cigarette smoking (I sbister JP, 1987).

Population-based studies extending to the mid-1960s uniformly demonstrate positive relations of blood pressure with the erythrocyte measures of RBC, hematocrit, and hemoglobin. Almost every one of these studies demonstrate positive correlation coefficients with DBP, but weaker positive relations involving SBP were noted only in some subsets of subjects (McDonough et al 1965).

1.2.6.1 Mean corpuscular volume (MCV):

MCV is the index most often used. It measures the average volume of a red blood cell by dividing the hematocrit by the RBC. The MCV categorizes red blood cells by size. Cells of normal size are called normocytic, smaller cells are microcytic, and larger cells are macrocytic. These size categories are used to classify anemias. Normocytic anemias have normal-sized cells and a normal MCV; microcytic anemias have small cells and a decreased MCV; and macrocytic anemias have large cells and an increased MCV. Under a microscope, stained red blood cells with a high MCV appear larger than cells with a normal or low MCV. The MCV is measured in femtoliters, using automated methods this value is derived by dividing the summation of the red cell volumes by the erythrocyte count (Lee et al. 1999)
MCV is calculated by the following formula:

\[
MCV = \frac{\text{Hematocrit} \times 10}{\text{RBC} \times 10^{12}/L}
\]  

(Lee et al. 1999).

1.2.6.2 Mean corpuscular hemoglobin concentration (MCHC):

The MCHC measures the average concentration of hemoglobin in a red blood cell. This index is calculated by dividing the hemoglobin by the hematocrit. The MCHC categorizes red blood cells according to their concentration of hemoglobin. Cells with a normal concentration of hemoglobin are called normochromic; cells with a lower than normal concentration are called hypochromic. Because there is a physical limit to the amount of hemoglobin that can fit in a cell, there is no hyperchromic category. (Pagana et al. 1998)

Just as MCV relates to the size of the cells, MCHC relates to the color of the cells. Hemoglobin contains iron, which gives blood its characteristic red color. When examined under a microscope, normal red blood cells that contain a normal amount of hemoglobin stain pinkish red with a paler area in the center. These normochromic cells have a normal MCHC. Cells with too little hemoglobin are lighter in color with a larger pale area in the center. These hypochromic cells have a low MCHC. Anemias are categorized as hypochromic or normochromic according to the MCHC index (Lee et al. 1999).

MCHC is calculated by the following formula:

\[
\text{MCHC} = \frac{\text{Hb (g/dL)} \times 100}{\text{Hematocrit} \%}
\]  

(Lee et al. 1999).

1.2.6.3 Mean corpuscular hemoglobin (MCH):

The average weight of hemoglobin in a red blood cell is measured by the MCH. The formula for this index is the sum of the hemoglobin multiplied by 10 and
divided by the RBC. MCH values usually rise or fall as the MCV is increased or decreased (Lee et al. 1999).

MCH is calculated by the following formula:

\[
\text{MCH} = \frac{\text{Hb (g/dL) } \times 10}{\text{RBC } (x \times 10^{12}/\text{L})}
\]

(Lee et al., 1999).

1.2.6.4 Red cell distribution width (RDW):

The RDW measures the variation in size of the red blood cells. Usually red blood cells are a standard size. Certain disorders e.g: anemia, iron and vit B₁₂ deficiency, cause a significant variation in cell size (Pagana et al. 1998).

1.2.6.5 Normal value of red blood cell indices:

Normal results for red blood cell indices are as follows:
- MCV 82-98 fl (femtoliters)
- MCHC 31-37 g/dl
- MCH 26-34 pg (picograms)
- RDW 11.5-14.5 %. (Lewis, et al. 2001).

1.2.7 Hypertension:

Hypertension (HTN) or high blood pressure is a cardiac chronic medical condition in which the systemic arterial blood pressure is elevated. It is the opposite of hypotension. Hypertension is classified as either primary (essential) hypertension or secondary hypertension; about 90-95% of cases are categorized as primary hypertension, which means high blood pressure with no obvious medical cause. The remaining 5-10% of cases (secondary hypertension) are caused by other conditions that affect the kidneys, arteries, heart or endocrine system. (Carretero and Oparil, 2000).
1.2.7.1 Frequency of hypertension:
In the year 2000 it was estimated that nearly one billion people or ~26% of the adult population had hypertension worldwide. It was common in both developed (333 million) and undeveloped (639 million) countries. However rates vary markedly in different regions with rates as low as 3.4 % (men) and 6.8% (women) in rural India and as high as 68.9% (men) and 72.5% (women) in Poland (Kearney, et al. 2004). In 1995 it was estimated that 43 million people in the United States had hypertension or were taking antihypertensive medication, almost 24% of the adult population. (Burt, et al. 1995). The prevalence of hypertension in the United States is increasing and reached 29% in 2004. (Ostchega, et al. 2007) it is more common in blacks and Native Americans and less in white and Mexican Americans, rates increase with age, and is greater in the south eastern United States. Hypertension is more prevalent in men (though menopause tend to decrease this deference) and those of low socioeconomic status. (Carretero and Oparil, 2000).

1.2.7.2 Historical perspective:
The basis for measuring blood pressure was established by Stephen Hales in 1733. Initial description of hypertension as a disease came among others from Thomas young in 1808 and specially Richard Bright in 1836 (Esunge, 1991).
Studies in the 1920s demonstrated the public health impact of untreated high blood pressure; treatment options were limited at the time. Before pharmacological treatment for hypertension became possible, three treatment modalities were used, all with numerous side effects strict sodium restriction, sympathectomy (surgical ablation of parts of the sympathetic nervous system), and pyrogen therapy (injection of substance that caused fever, indirectly reducing blood pressure). (Dustan et al 1996).
The first chemical for hypertension, sodium thiocyanate, was used in 1900 but had many side effects and was unpopular. (Sunge, 1991)
Several other agents were developed after the Second World War, the most popular and reasonably effective of which were tetramethyleammoniumchloride and its derivative hexamethonium, hydrolazine and reserpine (Sunge, 1991). A major breakthrough was archived with the discovery of the first well tolerate orally available agents, the first was chlorothiazide (Sunge, 1991).

1.2.7.3 Classification of hypertension:
1.2.7.3.1 Classification of hypertension according to diastolic blood pressure and systolic blood pressure values:

Blood pressure is usually classified based on systolic and diastolic blood pressures. A systolic or the diastolic blood pressure measurement higher than the accepted normal values for the age of the individual is classified as prehypertension or hypertension (Klaus, 1987). Hypertension has several sub-classification including, hypertension stage I, hypertension stage II, and isolated systolic hypertension. Isolated systolic hypertension refers to elevated systolic pressure with normal diastolic pressure and is common in the elderly. Individuals older than 50 years are classified as having hypertension if their blood pressure is consistently at least 140 mmHg systolic or 90 mmHg diastolic. Patients with blood pressure higher than 130/80 mmHg with concomitant presence of diabetes mellitus or kidney disease require further treatment. Hypertension is an excessively high elevation in blood pressure during exercise is between 200 and 230 mm Hg. (Klaus, 1987) Exercise hypertension may indicate that an individual is at risk for developing hypertension at rest.
Table (1.2) classification of hypertension (Klaus, 1987):

<table>
<thead>
<tr>
<th>Classification</th>
<th>Systolic pressure</th>
<th>Diastolic pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mm Hg</td>
<td>kPa</td>
</tr>
<tr>
<td>Normal</td>
<td>90-119</td>
<td>12.0-15.9</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120-139</td>
<td>16.0-18.5</td>
</tr>
<tr>
<td>Stage 1</td>
<td>140-159</td>
<td>18.7-21.2</td>
</tr>
<tr>
<td>Stage 2</td>
<td>≥ 160</td>
<td>≥ 21.3</td>
</tr>
<tr>
<td>Isolated systolic hypertension</td>
<td>≥ 140</td>
<td>≥ 18.7</td>
</tr>
</tbody>
</table>

1.2.7.3.2 Classification of hypertension according to cause:

1.2.7.3.2.1 Essential hypertension:

Essential hypertension is the most prevalent hypertension type, although no direct cause has been identified, there are many factors such as sedentary lifestyle, smoking, stress, visceral obesity, potassium deficiency (hypokalemia), (kyrou, et al. 2006) obesity (more than 85% of cases occur in those with a body mass index greater than 25), salt (sodium) sensitivity, (Lackland DT and Egan BM 2007) Alcohol intake and vitamin D deficiency that increase the risk of developing hypertension. (Lee, et al. 2008). Risk also increase with aging, some inherited genetic mutation, and having a family history of hypertension. (Luma and Spiotta, 2006) An elevated level of rennin, a hormone secreted by the kidney, is another risk factor, as is sympathetic nervous system over activity. (Rahmouni, et al, 2005). Insulin resistance, which is a component of syndrome X (or the metabolic syndrome) is also though to contribute to hypertension. Recent studies have implicated low birth weight as a risk factor for adult essential hypertension (Uchiyama, 2008).

1.2.7.3.2.2 Secondary hypertension:

Secondary hypertension by definition results from an identifiable cause. This type is important to recognize since it is treated differently to essential hypertension, by treating the underlying cause of the elevated blood pressure.
Hypertension results in the compromise or imbalance of the path physiological mechanisms, such as the hormone-regulating endocrine system, that regulate blood plasma volume and heart function. Many conditions cause hypertension, some are common and well recognized secondary causes such as Cushing`s syndrome, which is a condition where the adrenal glands overproduce the hormone cortisol. (Dodt C et al, 2009) In addition, hypertension is caused by other conditions that cause hormone changes such as hyperthyroidism, hypothyroidism, and certain tumors of the adrenal medulla (e.g., pheochromocytoma). Other common causes of secondary hypertension include kidney disease, obesity metabolic disorder, pre-eclampsia during pregnancy, the congenital defect known as coarctation of the aorta, and certain prescription and illegal drugs (Dodt C et al, 2009).

1.2.7.4 Signs and symptoms of hypertension:
In essential hypertension mild to moderate essential hypertension is usually asymptomatic (Pitts and Adams 1998). In secondary hypertension some additional signs and symptoms suggest that the hypertension is caused by disorders in hormone regulation. Hypertension combined with obesity distributed on the trunk of the body, accumulated fat on the back of the neck, wide purple marks on the trunks on the abdomen (abdominal striae), or the recent onset of diabetes suggests that an individual has a hormone disorder known as Cushing`s syndrome. Hypertension caused by other hormone disorders such as hyperthyroidism, hypothyroidism, or growth hormone excess will be accompanied by additional symptoms specific to these disorders. For example, hyperthyroidism can cause weight loss, tremors, and heart rate abnormalities, reddening of the palms, and increased sweating (Lee, et al. 2010). Signs and symptoms associated with growth hormone excess include coarsening of facial features, protrusion of the lower jaw, enlargement of the tongue, (Khandwala and Hasnain, 2009) excessive hair growth, darkening of the
skin colour, and excessive sweating. (James et al, 2005) other hormone disorders like hyperaldosteronism may cause less specific symptoms such as numbness, excessive urination, excessive sweating, electrolyte imbalances and dehydration, and elevated blood alkalinity (Chrousos et al, 2009).

In pregnancy hypertension in pregnant woman is one symptom of pre-eclampsia. Pre-eclampsia can progress to a life threatening condition called eclampsia, which is the development of protein in the urine, generalized swelling, and sever seizures. Other symptoms indicating that brain function is becoming impaired may precede these seizures such as nausea, vomiting, headache, and vision loss (Gibson and Paul 2009).

1.2.7.5 **Pathogenesis of hypertension:**

Most of the mechanisms associated with secondary hypertension are generally fully understood. However, those associated with essential (primary) hypertension are far less understood. What is known is that cardiac output is raised early in the disease course, with total peripheral resistance (TPR) normal; over time cardiac output drops to normal levels but TRP is increased. Three theories have been proposed to explain this:

1. Inability of the kidney to excrete sodium, resulting in natriuretic factors such as arterial natriuretic factor being secreted to promote salt excretion with the side effect of raising total peripheral resistance.

2. An overactive Renin-antagonism system leads to vasoconstriction and retention of sodium and water. The increase in blood volume plus vasoconstriction leads to hypertension. (Pimenta and Oparil, 2009)

3. An overactive sympathetic nervous system, leading to increased stress responses. (Takahashi, 2008)

It is also known that hypertension is highly heritable and polygenic (caused by more than one gene) and a few candidate genes have been postulated in the etiology of this condition. (Sagnella and Swift, 2006)
1.2.7.6 Effect of hypertension on platelets and red blood cells:
Hypertensive patients displayed significantly lower erythrocyte fluidity. Similarly, significantly elevated values for haematocrit, plasma and whole blood viscosity, as well as aggregation tendency were observed compared to controls. Although differing in these respects from controls, there were no obvious relationships between these rheological variables and either systolic or diastolic blood pressure. The significantly lower erythrocyte fluidity and other changes in haemorheological variables of red blood cells found in hypertensive patients may be explained by an enlarged metabolic pool of free calcium ions in these red blood cells. It is suggested that the molecular mechanisms underlying the evolution of essential hypertension are multifactorial rather than being based on a single molecular derangement (Sandhagen et al, 1990).

Gestational hypertension is characterized by a contracted plasma volume with hemoconcentration and hyperviscosity. Additional rheological parameters are an elevated red blood cell aggregation and impaired erythrocyte deformability (Heilmann, 1994).

MPV elevated in patients with HTN. It can be independently associated with systolic BP and diabetes mellitus. These findings imply that platelet activation contribute to the pathogenesis of thrombotic complications in hypertensive crises (Karabacak et al, 2014).

The relation between blood pressure and red cell measures is probably mediated by whole blood viscosity. Hematocrit is a determinant of whole blood viscosity. Viscosity affects peripheral resistance to blood flow, and peripheral resistance affects DBP. At high RBC levels, MCV may be “downregulated.” This may lower whole blood viscosity and partially reduce DBP without compromising flow (Dan Sharp et al, 1996).

Essential hypertension is associated with increased risk of arterial thrombotic disease. Among other factors, enhanced platelet activity contributes significantly to this phenomenon. An increased level of circulating monocyte–
platelet aggregates (MPAs) represents one of the most robust markers of platelet activation; furthermore, these aggregates are also believed to contribute to the pathophysiology of atherothrombotic disease. Putative mechanisms that contribute to platelet activation in essential hypertension include endothelial dysfunction, neurohumoral (sympathetic and renin–angiotensin systems) overactivity, decreased platelet nitric oxide (NO) biosynthesis, and platelet degranulation secondary to increased shear (Eugenia G. et al, 2010).

RDW is higher in prehypertensive and hypertensive patients compared with healthy controls independently of age, inflammatory status and anemia. Higher RDW values are strongly correlated with higher systolic and diastolic blood pressures (Tanindi et al, 2012).

1.2.8 Previous studies:
A lot of studies have been conducted on patients with high blood pressure to see the effect of hypertension on blood platelets and red blood cells, (Mustafa Karabacak et al, 2013) reported that MPV elevated in patients with hypertension than in normal individuals. (Boos CJ et al, 2007) found a decrease in PDW in hypertensive patients compared to normotensive individuals. (Christopher et al, 2007) reported that a significant relationship between the MPV and the PDW, systolic blood pressure and platelet count, There is a stepwise increase in platelet activation indices, despite similar platelet counts, with increasing severity of hypertensive disease. This may contribute to the pathogenesis of thrombosis-related complications in hypertension. (Al-Muhana et al, 2006) observed that there were no significant differences between hypertensive group and normotensive group in the levels of RBC, MCV, HCT, MCH and MCHC. (Massimo et al, 1992) reported that Hematocrit was positively and significantly correlated with systolic and diastolic blood pressure.
1.3 Rationale:
Worldwide, hypertension is estimated to cause 7.5 million deaths; World Health Organization (2014) reported that about 12.8% of the total of all death. Hypertension is a major risk factor for coronary heart disease and ischemic as well as hemorrhagic stroke. Complications of raised blood pressure include heart failure, peripheral vascular disease, renal impairment, retinal hemorrhage and visual impairment. Treating systolic blood pressure and diastolic blood pressure until they are less than 140/90 mmHg is associated with a reduction in cardiovascular complications.
According to the latest WHO data published in April 2011 Hypertension deaths in Sudan reached 12,281 or 3.33% of total deaths. The age adjusted death rate is 67.67 per 100,000 of population.
The elevation of platelets and red blood cell count and indices values in hypertensive patients associated with hypertensive target organ damage and arterial disease. Evaluation of platelets and red blood cells count and indices could be useful in prediction and differentiation of coronary and thrombotic events.
1.4 Objectives:

1.4.1 General objectives:
Estimation of platelets count and platelets volume indices and red blood cell count and red blood cell indices among hypertensive patients in Aljazeera state.

1.4.2 Specific objectives:
1. To measure platelet count and platelet indices and the red blood count and their indices in the hypertensive group and compare it with control group.
2. To detect the association of platelet count and platelet indices and red blood cell count and red blood cell indices between hypertensive patients and normotensive healthy group.
3. To test the correlation between platelet indices and red blood cell indices with the hypertension.
Chapter Two

2.0 Material and methods

2.1 study design:
This is a case control study, enrolled between March 2014 and June 2014 to measure the platelets indices and red blood cells indices among hypertensive patients attending Alshaheed Alzubier Health Center in Algazeera State.

2.2 Study population:
70 hypertensive patients and 30 normotensive individuals as control group.

2.2.1 Inclusion Criteria:
Hypertensive patients without medical complication (already diagnosed as hypertensive), study group criteria are in appendix 1.

2.2.2 Exclusion Criteria:
Diabetic patients, pregnant womans, patients who have blood transfusion in the last year, smokers and who with other diseases which alter the study parameter.

2.3 Data collection:
A Questioner was designed to obtain some information about the participants. The questioner form is in appendix 3.

2.4 Sample collection:
Blood was collected in EDETA (Ethylene-diamine-tetra-acetic acid) and mixed well before analyzed; the samples were examined as quickly as possible.

2.5 Platelets and red blood cell indices measurement:
Platelets and red blood cells indices were measured by Sysmex KX-21N HematologyAnalyzer. (Kobe 651-0073-, Jaban)

2.5.1 Principle of the instrument (sysmex KX-21N):
Measurement of blood cells (RBCs, WBCs, Platelets, and Hb) concentration obtained by aspiration of small volume of well mixed K2 EDTA blood by sample probe and mixed with isotonic diluents in nebulizer. Diluted mixture
aspiration delivered to RBC aperture bath for providing information about RBC and platelet based on cell sizes, particle of 2 to 20 counted platelets, above 36 fl as red cells. Some portion of aspirated mixture induced into WBC bath in which haemolytic reagent (Stromatolyzer) was added automatically to measure Hb concentration in a build calorimeter, based on cyanomethemoglobin (HiCN). Blood cells counted and size information generated in triplicate pulses according to electronic conductivity, and translated into digital numbers using in build calculator programmed and designed for count that RBC, WBC count hence three values were directly measured (RBC, WBC, Hb), and displayed on (LCD). Other values of red cell indices platelet count, leukocyte differential and absolute count calculated from given information and automated constructed histogram, the result printed out according to a setting mode.

2.5.2 Supplies and equipment:

- 12 x 75 Plastic test tubes and rack
- Cotton
- EDTA containers.
- Syringes.
- Plastic rack.
- Sample mixer.

2.5.3 Procedure of analysis:

The reagent needed was checked for expiry date before use. The power switch was turned and background check was automatically performed and the vend (vend for analysis) was appear sample number inputted by pressing simple number, then number of sample was entered. Then entered was pressed. Sample was mixed sufficiently. The tube was sited to the sample probe, and in that condition the start switch was pressed. When the LCD screen display analyzing
the tube was removed. After that the executor automatic analysis and the result was print out.

2.6 Blood pressure:

2.6.1 Principle:
Arterial pressure was measured by the doctor for the participants via a Sphygmomanometer (mercury device) When the monitor finishes taking the blood pressure, the cuff deflates and the results show on the display. The top number is the systolic blood pressure and the bottom number is the diastolic blood pressure.

2.7 Ethical consideration:
- The study was approved by the Medical Ethical Committee of National Health Insurance Fund.
- Written consent was obtained from all participants after had been informed in details with the objectives, benefit and expected outcomes of the study.
- The information collected from the patients was confidential and will not be used for any purpose other than this study.

2.8 Data analysis:
All the data were presented as means ± standard deviation. Comparison between the means was performed by student's t test as described by Gomez and Gomez (1984) using Statistical Package for Social Sciences (SPSS version 14.0)
CHAPTER THREE

Result

(3.1) Effect of hypertension on platelets count and platelet indices:
Table (3.1) shows a significant variation in means of platelets indices between hypertensive patients and control group (P≤ 0.05) of platelets count, MPV and P-LCR the mean of this indices increased in hypertensive compared to the normal control group. There is no significant variation of PDW due to hypertension (P≥0.05).

(3.2) Effect of hypertension on erythrocytes count and red cell indices:
Table (3.2) shows significant variation in red blood cell indices between hypertensive patients and the control group (P≤0.05) of RBC count, HTC, MCV and MCH. And there is no significant variation on MCHC (P≥0.05) between the two groups.
Table (3.1) Effect of hypertension on platelets count and indices:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean± Std deviation</th>
<th>P.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count($X10^9$/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>235.60±61.28</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>210.23±46.33</td>
<td>*</td>
</tr>
<tr>
<td>MPV (fl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>11.17±1.43</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>9.14±0.78</td>
<td>*</td>
</tr>
<tr>
<td>PDW (fl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>11.14±1.39</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>11.65±1.80</td>
<td>N.S</td>
</tr>
<tr>
<td>P-LCR (fl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>27.94±4.90</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>16.00±1.85</td>
<td>*</td>
</tr>
</tbody>
</table>

* Significant at $P \leq 0.05$

N.S.: not significant
No of case 70
No of control 30
Mean of SBP = 150 mmHg
Mean of DBP = 95 mmHg
Table (3.2) Effect of hypertension on Red blood cell count and red blood cell indices:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean± Std. Deviation</th>
<th>P.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBCs count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>4.62±0.54</td>
<td>*</td>
</tr>
<tr>
<td>Control</td>
<td>4.32±0.56</td>
<td></td>
</tr>
<tr>
<td>HCT%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>36.23±4.18</td>
<td>*</td>
</tr>
<tr>
<td>Control</td>
<td>32.91±5.92</td>
<td></td>
</tr>
<tr>
<td>MCV(fl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>84.13±4.56</td>
<td>*</td>
</tr>
<tr>
<td>Control</td>
<td>81.95±5.22</td>
<td></td>
</tr>
<tr>
<td>MCH(pg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>27.66±2.11</td>
<td>*</td>
</tr>
<tr>
<td>control</td>
<td>26.30±2.56</td>
<td></td>
</tr>
<tr>
<td>MCHC(g/dl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>31.63±1.40</td>
<td>N.S.</td>
</tr>
<tr>
<td>control</td>
<td>32.04±1.38</td>
<td></td>
</tr>
</tbody>
</table>

* Significant at P≤ 0.05
N.S.: not significant
No of cases 70
No of control 30
Mean of SBP = 150 mmHg
Mean of DBP = 95 mmHg
(3.3) Correlations analysis of blood pressure and Platelet indices in the hypertensive patients:

Table (3.3) shows that there was a high significant correlation between SBP and Platelet count and MPV (P.values <0.01), while there is a significant negative correlation between SBP and PDW (P.value < 0.05). No significant correlation between SBP and P-LCR was found (P.value > 0.05).

No significant correlation was found between DBP and Platelet count, MPV, PDW, and P-LCR in the hypertensive patients (P-values >0.05).

(3.4) Correlations analysis of blood pressure and red blood cell indices in hypertensive patients:

Table (3.4) shows that there is no significant correlation between SBP and RBC count, MCV, MCH, and MCHC ( P.values >0.05), while there is a high significant negative correlation between SBP and HCT (P-value <0.01).

There is no significant correlation between DBP and RBC count, MCV, MCH, or MCHC (P.values>0.05), while there is a significant positive correlation between DBP and HCT (P-value <0.05).
Table (3.3) Correlations analysis of blood pressure and Platelet count and platelet indices in the hypertensive patients:

<table>
<thead>
<tr>
<th></th>
<th>Diastolic</th>
<th>Systolic</th>
<th>Platelet count</th>
<th>MPV</th>
<th>PDW</th>
<th>P-LCR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systolic</strong></td>
<td>Pearson Correlation</td>
<td>1</td>
<td>0.372**</td>
<td>0.424**</td>
<td>-0.262*</td>
<td>0.177</td>
</tr>
<tr>
<td><strong>Diastolic</strong></td>
<td>Pearson Correlation</td>
<td>1</td>
<td>-0.044</td>
<td>-0.056</td>
<td>0.178</td>
<td>-0.146</td>
</tr>
<tr>
<td><strong>Platelet count</strong></td>
<td>Pearson Correlation</td>
<td>-0.044</td>
<td>0.372**</td>
<td>1</td>
<td>0.317**</td>
<td>0.091</td>
</tr>
<tr>
<td><strong>MPV</strong></td>
<td>Pearson Correlation</td>
<td>-0.056</td>
<td>0.424**</td>
<td>0.317**</td>
<td>1</td>
<td>0.069</td>
</tr>
<tr>
<td><strong>PDW</strong></td>
<td>Pearson Correlation</td>
<td>0.178</td>
<td>-0.262*</td>
<td>0.091</td>
<td>0.069</td>
<td>1</td>
</tr>
<tr>
<td><strong>P-LCR</strong></td>
<td>Pearson Correlation</td>
<td>-0.146</td>
<td>0.177</td>
<td>0.183</td>
<td>0.377**</td>
<td>0.220</td>
</tr>
</tbody>
</table>

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Sample number is 70

Mean of SBP = 150 mmHg

Mean of DBP = 95 mmHg
Table (3.4) Correlations analysis of BP and red blood cell count and red blood cell indices in hypertensive patients:

<table>
<thead>
<tr>
<th></th>
<th>Diastolic</th>
<th>Systolic</th>
<th>RBC count</th>
<th>HCT</th>
<th>MCV</th>
<th>MCH</th>
<th>MCHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>Pearson Correlation</td>
<td>1</td>
<td>0.126</td>
<td>-0.332**</td>
<td>-0.041</td>
<td>0.052</td>
<td>-0.176</td>
</tr>
<tr>
<td>Diastolic</td>
<td>Pearson Correlation</td>
<td>1</td>
<td>0.152</td>
<td>0.285*</td>
<td>-0.041</td>
<td>-0.117</td>
<td>0.123</td>
</tr>
<tr>
<td>RBC count</td>
<td>Pearson Correlation</td>
<td>0.152</td>
<td>0.126</td>
<td>1</td>
<td>0.334**</td>
<td>0.025</td>
<td>-0.200</td>
</tr>
<tr>
<td>HCT</td>
<td>Pearson Correlation</td>
<td>0.285*</td>
<td>-0.332**</td>
<td>0.334**</td>
<td>1</td>
<td>0.308**</td>
<td>0.048</td>
</tr>
<tr>
<td>MCV</td>
<td>Pearson Correlation</td>
<td>-0.041</td>
<td>-0.041</td>
<td>.025</td>
<td>0.308**</td>
<td>1</td>
<td>0.490**</td>
</tr>
<tr>
<td>MCH</td>
<td>Pearson Correlation</td>
<td>-0.117</td>
<td>0.052</td>
<td>-0.200</td>
<td>0.048</td>
<td>0.490**</td>
<td>1</td>
</tr>
<tr>
<td>MCHC</td>
<td>Pearson Correlation</td>
<td>0.123</td>
<td>-0.176</td>
<td>0.131</td>
<td>0.378**</td>
<td>0.384**</td>
<td>0.462**</td>
</tr>
</tbody>
</table>

**. Correlation is significant at the 0.01 level (2-tailed).

Sample number is 70
Mean of SBP = 150 mmHg
Mean of DBP =95 mmHg
Chapter Four

4. Discussion, conclusion and recommendations

4.1 Discussion:

The main aim of this study is to measure the changes in platelets count and its indices and red blood count and its indices in hypertensive patients. Higher values of platelet count were found in hypertensive patients than the control group (235.60±61.28 X10/L compared to 210.23±46.33 X 10/L) this finding is disagree with that of (Christopher. Boos et al., 2007) who observed there is similarities in the platelet count between the hypertensive and control groups ( P.value ≥0.05).

In this study statistically significant differences were observed between the two groups, MPV values of hypertensive patients were higher than the healthy control group(11.17±1.4fL compared to 9.146±0.78fL), these finding is online with that of (Karabacak et al., 2014), and (Mustafa Karabacak et al., 2013) who reported that MPV elevated in patients with hypertension than in normal individuals(P.value ≤0.05). Lower values for PDW were found in hypertensive group than the control, these findings are online with that of (Boos et al., 2007) who found a decrease in PDW across the study group (P = 0.001).

There is a high significant correlation between SBP and Platelet count and MPV under 1% level of significance (p-values <0.01), this accords with the finding of (Christopher. et al., 2007) who reported that a significant relationship between the MPV and the PDW, systolic blood pressure and platelet count, There is a stepwise increase in platelet activation indices, despite similar platelet counts, with increasing severity of hypertensive disease. This may contribute to the pathogenesis of thrombosis-related complications in hypertension.

In this study the mean of RBC count (4.62±0.54 X10^{12}/L compared to 4.32±0.56 X10^{12}/L), HTC (36.23±4.18% compared to 32.91±5.92 %), MCV (84.13±4.56fl compared to 81.95±5.22fl) and MCH(27.66±2.11pg compared
to 26.30±2.56 pg) of the hypertensive subjects were higher than that of the normotensive group, this result is conversing with that of (Al-Muhana et al., 2006) who observed that there were no significant differences between these two groups in the levels of RBC, MCV, HCT, MCH and MCHC (p>0.05). The no variation value finding with regard to MCHC is online with the current study.

There is a high significant negative correlation between SBP and HCT (Dan S. Sharp et al., 1996) which is online with the present study. In the present study there is significant positive correlation between Diastolic blood pressure and HCT this accords with that of (Massimo et al., 1992) who reported that Hematocrit was positively and significantly correlated with systolic and diastolic blood pressure.
4.2 Conclusion:
The study demonstrated that hypertension had adverse effects on platelets and red blood cells indices; elevated the value of this indices in hypertensive patients may be useful in guiding the physician toward more exhaustive diagnostic procedure to detect and follow up the complication of HTN as Target Organ Damage (TOD) and toward a better control of blood pressure in addition to other risk factor to prevent cardiovascular morbidity and atherosclerotic events in these patients.
4.3 Recommendations:

1. Platelets indices can be used as a simple and cost-effective tool to monitor the progression and control of HTN.

2. The increased MPV could be the cause of the end result of vascular complications so it should be further studied.

3. The elevation of MCV and HCT in hypertensive patients increase the viscosity of the blood which is risk factor of cardiovascular morbidity and atherosclerotic events so it should be monitored.
References


Michelson (2013), Platelets, p. 117-118


World Health Organization Department of Health Statistics and Informatics in the information, Evidence and research cluster, Global Health Observatory (GHO) data. Raised blood pressure 2011-2014


Appendix 1:
Characteristics of Hypertensive participants:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number</th>
<th>Percent %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>44</td>
<td>62%</td>
</tr>
<tr>
<td>Female</td>
<td>26</td>
<td>38%</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-40</td>
<td>15</td>
<td>22%</td>
</tr>
<tr>
<td>41-60</td>
<td>26</td>
<td>37%</td>
</tr>
<tr>
<td>&gt;60</td>
<td>29</td>
<td>41%</td>
</tr>
<tr>
<td><strong>Weight (Kg)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>60-69</td>
<td>21</td>
<td>30%</td>
</tr>
<tr>
<td>70-79</td>
<td>35</td>
<td>50%</td>
</tr>
<tr>
<td>&gt;80</td>
<td>13</td>
<td>19%</td>
</tr>
<tr>
<td><strong>Family history of hypertension</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>45</td>
<td>64%</td>
</tr>
<tr>
<td>No</td>
<td>25</td>
<td>36%</td>
</tr>
<tr>
<td><strong>Salt intake</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>27</td>
<td>39%</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>11%</td>
</tr>
<tr>
<td><strong>HTN duration (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-12</td>
<td>58</td>
<td>82%</td>
</tr>
<tr>
<td>13-18</td>
<td>10</td>
<td>15%</td>
</tr>
<tr>
<td>&gt;18</td>
<td>2</td>
<td>3%</td>
</tr>
<tr>
<td><strong>Type of drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amilo</td>
<td>27</td>
<td>40%</td>
</tr>
<tr>
<td>Limopril</td>
<td>Up to taste</td>
<td>40%</td>
</tr>
<tr>
<td>Lasocar h</td>
<td>Little salt</td>
<td>20%</td>
</tr>
<tr>
<td><strong>Aspirin intake</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No salt</td>
<td>47%</td>
</tr>
<tr>
<td>No</td>
<td>38</td>
<td>53%</td>
</tr>
<tr>
<td><strong>Diuretic intake</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>25</td>
<td>36%</td>
</tr>
<tr>
<td>No</td>
<td>45</td>
<td>64%</td>
</tr>
</tbody>
</table>
Appendix 2:
Sysmex KX-21N Automated Hematology analyzer

Sysmex KX-21 N instrument overview
Appendix 3:

Questioner form

1-sex:
- Male
- Female

2-Age group:
- Less than 20
- 21-40
- 41-60
- More than 60

3-Duration: .................................................................

4-Family history: ...........................................................

5-Type of drugs: ............................................................

6-Dose of drugs: ...........................................................

7-Diuretics: .................................................................

8-Aspirin intake: ...........................................................

9-Last blood pressure: ..................................................

10-Salt intake:
- Up to taste
- Little salt
- No salt

11-Weight: ..............................................................

12-Excluded cases:
- Pregnancy
- Smoking
- Cancer
- Diabetes
- Near blood transfusion