بسم الله الرحمن الرحيم

Republic of Sudan

Ministry of Higher Education and scientific Research

University of Shendi

Faculty of Graduate Studies and Scientific Research

Determination of Complete blood Count and D.dimer among Female with Preeclampsia in Shendi Town.

A thesis Submitted for partial fulfillment of the Msc Degree in Medical Laboratory Sciences in (Haematology)

By

Salwa Mohammed Osman

BSc. (Shendi University)

Supervisor

Dr: Omkalthoum Osman Hamad

Assistant professor – Shendi University
PHD. in Haematolgy

August-2018

الآية

بسم الله الرحمن الرحيم

قال تعالي

﴿فَتَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ وَلَا تَعْجَلْ بِالْقُرْآنِ مِن قَبْلِ أَن يُقْضَى إِلَيْكَ وَحْيُهُ وَقُل رَّبِّ زِدْنِي عِلْماً﴾

صدق الله العظيم

سـورة طه – الآيــة (١١٤)

الإهـــــداء

إلى من زرع في نفسي حب الخير والفضيلة إلى القنديل الذي أهتدي به في ليل الحياة المظلم

إلى القيم التي أستدل بها دربي إلى من حصد الأشواك عن دربي ومهدي لي طريق العلم

إلى من تعب من أجل راحتي وإرضائي أسال الله عز وجل أن يمد في عمرك ويديم عليك الصحة

أبي الغالي (محمد عثمان عبد اللّه)

إلى من غمرتني بالحنان لتبعد عني قسوة الأيام إلى من منحتني قلبها وعمرها إلى الواحة التي

أستظل بها من هجير الحياة إلى مصدر فخري واعتزازي إلى من تضئ الدنيا بوجودها

إلى منبع الحب والعطف إلى من برضاها نصل أعلى الجنان

أمي الحبيبة (بتول سعيد عبد اللّه)

في فمي نغماً أردده مدى الدهر،،، وفي روحي مناجاة ورمزاً للوفاء الأبدي

إلى ذلك النيل الذي اجتاح كل السدود لكي يصيب بداخلي إلى رمز الوفاء

والتضحية الذي علمني معنى الثبات في أصعب المواقف ومعنى الصبر على الشدائد

إلى روح عمتي الطاهرة...

إلي من يشاركوني أحزاني وأفراحي وأضاءوا حياتي بابتسامتهم الغالية ونهلت وسوف أنهل من محبتهم إلي ما لا نهاية وادعوا رب الكون أن يحفظهم لي من كل الأشرار ويمد في أعمارهم

أخي وأخواتي

إلي من تحلى بالإخاء وتميز بالوفاء والعطاء إلي ينبوع الصدق الصافي معه سعدت، إلي من كان ملاذي وملجئ .. إلي من تذوقت معه أجمل اللحظات..

إلى محمد منصور

الشكر والعرفان

سيبقى في حنايا النفس لأهل الفضل عرفانا جميلا..

فأكتب أحرفا بمداد النور وأبقى أنشر الشكر الجزيلا..

الشكر أولا للخالق الذي أضاء الكون بنوره البهي له وحده أسجد خاشعة شاكرة لنعمته وفضله في إتمام هذا الجهد.. فما كان لم يكن إلا بفضله.. وما صار لم يصر إلا ببركته وتقديره..

والشكر لسراج الأمة المنير.. وشفيعها النذير البشير.. محمد صلى الله عليه وسلم بكل فخر واعتزاز..

والشكر لمن قدموا لنا الكثير باذلين بذلك جهودا كثيرة في بناء جيل الغد لتبعث الأمة من جديد.. أسمى آيات الشكر والتقدير لمن حملوا أقدس رسالة في الحياة.. ومهدوا لنا طريق العلم والمعرفة..

أساتذتي الأجلاء ولاسيما

الدكتورة الفاضلة الجليلة

الدكتورة: أم كلثوم عثمان حمد

التي قدمت لي كل عون وإرشاد وبذل وعطاء واستقطاع من وقتها الغالي ولم تبخل علي بشيء لإتمام هذا البحث.. ومن لا يشكر الناس لا يشكر الله فما عندي من قول لن يكن كافيا ليكافيها جعله الله في ميزان حسناتها..

والشكر لكل من قدم لي المساعدة والعون لإتمام هذا البحث.

List of abbreviations

DIC	Disseminated intravascular coagulation
EDTA	Ethylene Diamine Tetra Acetic acid
FDP	Fibrin degradation product
Hb	Haemoglobin
HICN	Haemoglobin Cyanide
HIV	Human Immunodeficiency Virus
HLA	Human leucocyte antigen
HPA	Human platelet antigen
ITP	Idiopathic thrombocytopenic purpura
IgE	Immunoglobulin E
IL-5	Interleukin-5
ICSH	International Committee Standardization Of Haematology
MCV	Main cell volume
MCH	Mean cell haemoglobin
MCHC	Mean cell haemoglobin concentration
MCV	Mean Cell Volume
MCSF	Monocyte colony stimulating factor
PCV	Packed Cell Volume
PV	Polycythaemia Vera
RBCs	Red Blood Cells
SCF	Stem cell factor
SLE	Systemic lupus erythemtosus
WBCs	White Blood Cells

Abstract

The study was conducted in Shendi town during the period from April to July 2018 that aimed to determine Complete blood count and D-dimer in women with preeclampsia and compared with control.

A total of 50 venous blood samples were collected into EDTA anticoagulant containers, then mixed well and transfered to the laboratory, following standard procedures to prevent contamination, and the Complete blood count was counted using automated haematology analyzer, and the D-dimer estimated using ichroma.

The gather data was analyzed using statistical package of social science.

The results showed that there was significant variation between hematological parameter values of women with preeclampsia and control in , Neutrophil, lymphocyte MPV, Hb and PCV (pv <0.05) while

there was no significant variation in RBCs, MCV, MCH, MCHC, Platelet count and D-dimer pv (0.055, 0.290,0.106, 0.119, 0.628, 0.111) respectively.

The study conclude that the preeclampsia affect in haemoglobin and haematocrit and also lead to neutrophilia and lymphocytopenia and no effect in D-dimer.

الخلاصــة

أجريت هذه الدراسة بمدينة شندي في الفترة ما بين شهر ابريل ٢٠١٨م إلـــى شـــهر يوليـــو ٢٠١٨م وهدفت لقياس تعداد الدم الكامل والدى دايمر بين الحوامل بتسمم الحمـــل والحوامـــل الطبيعية.

تم جمع عدد٥٠عينة دم وريدي في مضادات تجلط (أدتا)، وتم حفظها فـــي ظـــروف مثاليـــة لحمايتها من التلوث ومن ثم تم تعداد الدم الكامل عن طريق جهاز تعداد الدم الكامـــل.وتعـــداد دى دايمر بواسطة جهاز ايكروماو ٣٠ عينة كنترول.

تم تحليل البيانات باستخدام برنامج الحزم الإحصائية للعلوم الاجتماعية أوضـــحت النتـــائج أن هناك فرق ذو دلالة إحصائية بين متوسط تعداد خلايا الدم البيضاء وحجم الـــصفائح الدمويـــة والهموقلوبين والحجم الحشوي للدم ونسبة الخلايا العدلة والخلايا اللمفاوية بين الحوامل بتـــسمم الحمل والحوامل الطبيعيين.

أظهرت نتائج التحليل الإحصائي عدم وجود فرق ذو دلالة إحصائية في تعداد الصفائح الدموية وتعداد خلايا الدم البيضاء وتعداد كريات الدم الحمراء ومتوسط حجم الخلية الحمراء ومتوســـط الهيموقلوبين في الخلية الحمراء ومتوسط تركيز الهموقلوبين في الخلية الحمراء و D-dimer.

خلصت الدراسه الى وجود تاثير تسمم الحمل على الهيموقلوبين ومتوسط حجم الخليه الحمراء وايضا يودى الى زيادة الخلايا العدله ونفصان في الخلايا الليمفاويه ولا يوجـــد تـــاثير علـــى D.dimer

List of contents

List of tables

List of figures

Chapter One

Introduction

Rationale

Objectives

1-1: Introduction

Preeclampsia is a disorder of pregnancy characterized by the onset of high blood pressure and signs is proteinuria. After 20 weeks of gestation. Disorder that can affect all of organs in pregnancy.

Awoman with preeclampsia whose condition is worsening will develop other signs and symptoms known as severe features These include a low number of platelets in the blood.

Abnormal kidney or liver function, pain over the upper abdomen ,changes in vision ,fluid in the lungs ,or a sever headache. Avery high blood pressure reading also is considered a sever feature. Preeclampsia can be heterogeneous, diagnosing preeclampsia may not be straight forward .

preeclampsia without sever feature may be asymptomatic. Many cases detected through routine prenatal screening.

A family history in a first degree relative increased the risk of preeclampsia four to eight fold illustrating the strong genetic influence.

a women has double the risk of preeclampsia if pregnant by partner who had previously fathered an affected pregnancy.

All women who present with new onset hypertension should have the following tests complete blood count ,extrinsic coagulation factor, liver enzyme, peripheral smear, 24hour urine for protien and D-dimer.

Complete blood count is the one of the most ferr queenly and most time –onored laboratory tests in hematology evaluation consist of components and offers the clinician variety related to the health of bone marrow .represented by the number and types of cells in the peripheral circulation. [1]

D-dimer is a fibrin degradation product or FDP, asmal protein fragment present in the blood after blood clot is degraded by fibrinolysis.

D-dimer concentration by blood test to help diagnose thrombosis.

Haematological change thate appear in preeclampsia pregnancy include plateiet dysfunction and thrombocytopenia related to release of thromboxan A2 induce platelet aggregation and endothelial damage.

Alteration in the hemoglobin and erythrocytic parameters most frequently hemoconcentration manifested with increased hematocrit due to increased endothelial permeability.

Preeclampsia is a risk factor for thrombosis.

Preeclampsia being highly thrombotic and procoagulant state.

D.dimer was used as a marker for degradation of fibrin.

Some scientists suggested thate increase hematocrit in blood of women with preeclampsia. thrombocytopenia. leucocytosis and high level D-dimer in sever preeclamps.

1-2: Rationale

Preeclampsia is condition observed during pregnancy and threatens the life of both mother and fetus. Preeclampsia and its complication it considered one of the commonest obstetrical complication in Sudan and constitutes a major source of morbidity and mortality worldwide overall 10%--15% of maternal deaths are directly associated with preeclampsia and eclampsia, Preeclampsia can reduced intravascular volume which lead to renal failure also Preeclampsia is associated with the deposition of fibrin and increased fibrin degradation products in microvascular which result in dysfunction of some of the maternal organs.

in addition to haematological abnormalities include reduced platelet production and its life span .

some previous study reported that preeclampsia in third trimester of pregnancy is associated with elevated level of D.dimer .So we want to determine this hematological changes in women with preeclampsia in shendi town .

1-3: Objectives

1-3-1: General objective

Determination complete blood count and D.dimer in women with preeclampsia .

1-3-2: Specific objectives

1. To estimate Hb, PCV, RBCs count and RBCs indices in women with preeclampsia.
2. To Calculate white blood cells and differential count in women with preeclampsia.
3. To measure Platelet count and MPV in women with preeclampsia.
4. To estimate D-dimer in women with preeclampsia.
5. To compare the obtained result between women with preeclampsia and control .

Chapter Tow

Literature review

2. Literature review

2.1. Haemopiesis

Haemopoiesis is the mechanism by which blood cell are synthesis [4] haemopoietic cells first appear in the yolk sac of the 2 – week embryo [2].

By 8 week blood making has become established in the liver of the embryo, and by 12 – 16 weeks the liver has become the major site of blood cell formation. It remains an active haemopoietic site until a few weeks before birth. The spleen is also is also active during this period, particularly in the production of lymphoid cells and the fetal thymus is transient site for some lymphocytes [3].

The highly cellular bone marrow becomes an active blood making site from about 20 weeks of gestation and gradually increases its activity until it becomes major site of production about 10 weeks. Later at birth, active blood making red marrow occupies the entire capacity of the bones and continue to do so for the first 2 – 3 years after birth [3]

The red marrow is then very gradually replaced by in active, fatty, yellow, lymphoid, marrow. The later begin to develop in the long bone and continue until, 20 – 22 years [3].

Red marrow is present only in the upper ends of the femurs and humorous and the flat bones of the sternum, ribs cranium, pelvic and vertebrae, however because of the growth in body size that has occurred during this period, the total amount of the active bone marrow is nearly identical in the child and the adult.

In old age, red marrow sites are slowly replaced with yellow in active marrow [3].

About two – third of its mass function in white cells production and one third in red cell production, however, as we have already seen there are approximately 700 times as many red cells as white cells in peripheral blood – this apparent anomaly reflect the shorter life span and hence greater turnover of the white blood cells in comparison with the red blood cells.

2.1.1. Erythropiesis:

Erythropoiesis is mechanism by which red blood cell are synthesis.[3]

Mature red blood cells develop from haemocytoblast, this development make about 7 days and involves 3 – 4 mitotic cell division, so that each stem cell gives rise to 8 or 16 cells [3].

The various cell types in erythrocyte development characterized by:

- The gradual appearance of hemoglobin and disappearance of RNA in the cell.
- The progressive degeneration of the cells nucleus which is eventually extruded from the cells.
- The gradual loss of cytoplasm organelles for example: Mitochondria.
- Gradual reduction in cell size [3].

Young red cell is called reticulocyte because of a net work of ribonucleic acid (Reticulum) present it's cytoplasm as the red cell mature the reticulum[32].

Between two and six percentage a new born babies circulating red cells are reticulocytes. But this reduces to less than 2.5 % in the healthy adult. However the reticulocytes count increase considerably in condition of acute haemotysis of red cells. Reticulocytes normally take about 4 days to mature in to an erythrocyte [3].

In health erythropoiesis is regulated so that the number of circulating erythrocyte is maintained within a narrow range. Normally a little less than 1% of the body's total red blood cells are produced per day and these replace and equivalent number that reached the end of their life span. However that still represents a hug 200×10^9 cell.

Erythropoiesis is stimulated by hypoxia, however, oxygen lack does not act directly on the haemopoietic tissue but instead of stimulates the production of hormones, erythropoietin. The hormone stimulates haemopoietic tissue to produce red blood cells [3].

Erythropoietin is glycoprotein; it is inactivated by the liver and excreted in the urine. It is now established that erythropoietin is formed with in the kidney by

the action of renal erythropoietic factor. Erythrogenin on plasma protein, erythropoietingenin [3].

Erythrogenin is present in the juxta glomerular cells of the kidneys and is released in to the blood in response to hypoxia in the renal arterial blood supply[3].

Various other factors can affect the rate of erythropoiesis by influencing erythropoietin production[3].

Thyroid hormones, thyroid–stimulating hormones, adrenal cortical steroids, adrenocorticotrophic hormones all promote erythropoietin formation and so enhance red blood cells formation (erythropoiesis). In thyroid deficiency and anterior pituitary deficiency, an anemia may occur due to reduced erythropoiesis[3].

The following table shows the dietary requirements for sufficient red blood cell production [3]

Table (2-1):

Dietary Elements	Role in RBCs production
Protein	Require to make RBCs protein and also for globin part of haemoglobin.
Vitamin B_6	Not clear what the role of is, but deficiency has occasionally been associated with an anemia.
Vitamin B_{12} and folic acid	Needed for DNA synthesis and are essential in the process of red cell metabolism.
Vitamin C	Require for folate metabolism and also facilitates the absorption of iron extremely low level of vitamin C are made before any problem occur. An anemia caused by lack of vitamin C (scurvy) is now extremely rare.
Iron	Required for the haem part of haemoglobin.
Copper and Cobalt	There is rare evidence that these two trace mineral are essential for the production of RBCs in other animals. But not in human.

2.1.2. Haemoglobin

Haemoglobin is iron-containing protein attached red blood cell that transport oxygen from the lungs to the rest of the body. Haemoglobin bonds with oxygen in the lung exchanges it for carbon dioxide at cellular level, and then transport the carbon dioxide back to the lung to be exhaled [4].

Each red blood cell contains approximately 640 million haemoglobin molecules. Each molecules of normal adult haemoglobin consist of four poly peptide chains two alpha (a_2) and two beta (β_2) each with it is own haem group. The molecular weight of haemoglobin 68.000 [4].

Haem synthesis occurs largely in the mitochondria by a series biochemical reactions commencing with the condensation of glycin and succinyle co-enzyme A under the action of the key rate-limiting enzyme δ-amino laevulinic acid synthase. Byridoxal phosphate (vitamin B_6) is a co-enzyme for this reaction which is stimulated by erythropoietin which gives δ-amino laevulinic acid inside mitochondria which gives prophobilinogen outside the mitochondria to give uroporphyrinogen which give coproporphyrinogen to protoporphyrin which combine with iron to form the hem part [5].

Gloin synthesis occurs largely in ribosome which contain from poly peptide chain [5].

Globin synthesis from amino acids such as glycin, lysine, leucin, glutamic acid, arginin, asparatic and … etc.

Each molecule of haem combines with globin chain made on poly ribosomes. A tetramer of four globin chains each with it is own haem group in a ' pocket ' then formed to make up haemoglobin molecule [5].

Whether haemoglobin binds with oxygen or carbon dioxide depend on the relative concentration of each around the red blood cell. When it reaches the oxygen-rich lung, it releases the less abundant carbon-dioxide to bind with oxygen, when it goes back out into the body where cells are producing carbon dioxide, it release the oxygen and bind with carbon dioxide this is called the Boher effect [4].

When carbon monoxide is present, it competes with oxygen at the haem binding sites. And since haemoglobin is 200 times more likely bind with carbon monoxide, forming very bright red form of haemoglobin as low as 0.02% in the air can cause nausea and headache, 0.1% causes un consciousness and death (compare that with normal 20% oxygen saturation of the air) heavy smoker, who expose themselves regularly to carbon monoxide, may have as many as 20% of their hemoglobin's oxygen sites blocked by carbon monoxide [(4)].

Haemoglobin abnormalities result in very serious hereditary disease, such as sickle cell anemia and thalassemia [(4)].

Haemoglobin is made up of four subunits with a haem (iron-containing) group in each for oxygen binding. There are slightly different haemoglobin in adult when compared to children fetuses [(4)].

High 2–3 diphosphoglycerate levels are found people who live in high altitudes, this chemical allows larger amount of oxygen to be delivered to the tissue, preventing altitudes sickness [(4)].

Like all proteins the ' blue print' for haemoglobin exists in DNA (the material that makes up genes). Normally, on in divided has four genes that two genes code for the alpha chain. Two other genes code for the beta chain (two additional genes code for gamma chain in fetus) [(6)].

The alpha chain and the beta chain are made in precisely equal amount, despite the differing. Number of genes. The protein chain join in developing red blood cells, and remain together for the life of the red blood cell[(5)].

There are hundreds of haemoglobin variants that involve genes both from the alpha and beta gene clusters. The list below touches on some of the more common and important haemoglobin variants.

2.1.2.1. Types of haemoglobin

Normal types: Embryo haemoglobin which found in the first weeks of gestation

- $Gower_1$ which contain of two epsilon(a_2) and two zeta (δ_2) chain *
- $Gower_2$ which contain of two epsilon (a_2) and two alpha (a_2) chain

- Part land which contain of two epsilon (a_2) and two gamma ($\square_2$) chain

Haemoglobin F (Fetal haemoglobin) : This type is major respiratory pigment in intrauterine life which found in fetuses and new born babies, it compose from two alpha (a_2) chain and two gamma ($\square_2$) chain, and its replaced by haemoglobin A, shortly after birth, only small amount of haemoglobin F are made after birth(5).

Some disease, such as sickle cell anemia, a plastic and leukemia have abnormal types of haemoglobin and higher amount of haemoglobin F (5).

Haemoglobin A" adult haemoglobin": This is the most common types of haemoglobin found normally in adult. Some disease, such as sever from thalassemia, may cause haemoglobin F level to be high(7).

Haemoglobin A <sub>2 : This is normal type of haemoglobin contain of two alpha ($\square_2$) and two *gamma ($\square_2$) chain (6).

Haemoglobin A_2 is found in small amount in adult about 2%.

Abnormal types of haemoglobins : Haemoglobin S: Is the most common of abnormal haemoglobin and the basic of sickle cell trait and sickle cell disease, differ from normal adult haemoglobin only by single amino acid substitution, valine replacing glutamic acid 6th position of the beta chain globin(5).

Haemoglobin C: Is abnormal haemoglobin with substitution of lysine for glutamic acid at 6th position of the beta globin (9).

Haemoglobin E: Is abnormal haemoglobin, It formed when glutamic acid is replaced by lysine at 26th position of beta chain of globin.

Punjab haemoglobin D: Is abnormal haemoglobin with substitution of glutamine residue for glutamic acid at 121th position of the Beta globin chain (9)

Haemoglobin Arab: Is abnormal haemoglobin with substitution of lysine residue for glutamic acid at 121th position of the Beta chain (9)

Haemoglobin H: Is abnormal haemoglobin containing from four beta (β_4) chains and this haemoglobin is unsuitable for life (9).

Haemoglobin Bart: Is abnormal haemoglobin containing from four alpha ($\square_4$) chains and this* haemoglobin is unsuitable for life (9)

2.1.2.2. Haemoglobin derivatives

Oxygenhaemoglobin: Is a normal forms of haemoglobin that a attaches to oxygen by ferrous iron ($Fe^{+2} – o^{-2}$)

Carbo-amino haemoglobin: Is a normal form of haemoglobin that attaches to the carbon dioxide.

Carboxyhaemoglobin: Is a normal forms of haemoglobin that a attacks to the carbon monoxide instead of oxygen or carbon dioxide. High amount of this type of abnormal haemoglobin prevent the normal movement of oxygen by blood.

Sulfohaemoglobin: Is an abnormal form of haemoglobin that cannot carry oxygen. It may result from certain medicines such as phenaccetin or sulfonamides.

Met haemoglobin: When the iron that is part of haemoglobin is changed to ferric state so that doesn't carry oxygen.

2.1.3 Packed cell volume

The haematocrit is considered an integral part of a person's complete haemogram or complete Blood count along with the haemoglobin concentration, white blood cell count, and platelet count[11].

The haematocrit or packed cell volume are on the measures of The proportion of blood volume that is occupied by red blood cells. It's normally. normally 45±7 (38-52%) for males and 42±5 (37-47%) for females [11].

Elevated PCV: In case danger fever, where the full blood counts done, Daily, high haematocrit is danger of an increased risk of dengue shock syndrome[10]

Polycythaemia Vera is associated with elevated haematocrit. [10]

Smoking, COPD, and other pulmonary condition associated with hypoxia may elicit an increased production of red blood cells , this increase is mediated by the increased level of erythropoietin by the kidney in response to hypoxia[10].

There have been cases where the blood for testing was in advertently drawn from the same arm with the intravenous running in a transfusion of packed red cells. In this sample the haemoglobin measurement will be high because it is measuring the fluted being transfused (that is mostly red blood cells) rather than

the diluted serum, in this case, the haematocrit measurement will be artificially very high[11].

Lowered PCV: Lowered haematocrit can imply significant haemorrhage. MCV, RDW can be quiet help full in evaluating- lower – than – normal haematocrit, because can help the clinician determine whether blood loss is chronic or acute. The MCV is the size of red blood cell and RDW is relative measure of the variation in size of the red cell population. A low haematocrit with a low m c v with high RDW suggest a chronic iron deficient erythropoiesis, but normal RDW suggest blood loss that is more acute such as haemorrhage [11]. Conversely, if blood for haematology testing a drawn from proximal to that of an intravenous infusing line fluid into patient, the blood sample will be diluted by those fluid and the haematocrit will be or artificially low [11].

2.1.3.1 Estimation of PCV

The packed cell volume can be determined by centrifuging heparinized blood in a capillary tube (also known as a micro haematocrit tube). Is typically centrifuged at10.000 RPM for five minute, This Separates the blood into layers (packed cell, Buffy coat -WBC_s + platelet, plasma). And the tube read by haematocrit reader [11].

And estimated haematocrit as a percentage may be derived by multiplying haemoglobin concentration in g/dl three times and dropping the units [10].

2.1.4 Red blood cells

- Total red blood cells is the number of red cells is given as an absolute number per litre.
- Haemoglobin - The amount of hemoglobin in the blood, expressed in grams per decilitre. (Low hemoglobin is called anaemia.)
- Hematocrit or packed cell volume (PCV) - This is the fraction of whole blood volume that consists of red blood cells [9].

2.1.4.1 RED CELL INDICES

Red cell indices most frequently used in the investigation of anaemia are:

* Mean cell haemoglobin concentration (MCHC.

*Mean cell volume (MCV).

* Mean cell haemoglobin (MCH) [9].

MCHC : The MCHC gives the concentration of haemoglobinin g/l in 1 litre of packed red cells. It is calculated from the haemoglobin (Hb) and PCV.

A guideline reference range for MCHC in health is 315–360 g/l (31.5–36.0 g/dl.

* Low MCHC values are found in iron deficiency anaemia and other conditions in which the red cells are microcytic and hypochromic (MCHC may be normal in thalassaemia trait).

*An increased MCHC can occur in marked spherocytosis but this is a rare condition. Arise MCHC is more often due to a calculation error or an incorrect haemoglobin or PCV [9].

MCV: The mean red cell volume (MCV) provides information on red cell size. It is measured in femtolitres (fl) and is determined from the PCV and electronically obtained RBC count ,A guideline reference range is 80–98 fl.[9]

- **Low MCV values**: are found in microcytic anaemias particularly iron deficiency anaemia, anaemia of chronic disease and thalassaemia. The MCV is low in infancy (about 70 fl at 1 year of age) [9].
- **Raised MCV values**: are found in macrocytic anaemias, marked reticulocytosis.

MCH: The MCH gives the amount of haemoglobin in picograms (pg) in an average red cell. It is calculated from the haemoglobin and electronically obtained RBC count[9].

A guideline reference range for MCH in health is27–32 pg [9].

Low MCH values: are found in microcytic hypochromic anaemias and also when red cells are microcytic and normochromic, In thalassaemia minor the MCH is low even when anaemia is mild (MCHC is often normal) [9].

Raised MCH values: are found in macrocytic normochromic anaemias. MCH is also raised in neoborns.[9]

2.1.5 Leucopoiesis

Is a form of hematopoiesis in which white blood cells are formed in bone marrow.

2-1-5-1Granulopoiesis

The blood granulocytes and monocytes are formed in the bone marrow from a common precursor cell.

In the granulopoietic series progenitor cells, myeloblasts, promyelocytes and myelocytes form a proliferative or mitotic pool of cells while the metamyelocytes, band and segmented granulocytes make up a post-mitotic maturation compartmen. The bone marrow normally contains more myeloid.

2.1.5.2 Control of granulopoiesis

The production of neutrophil leucocytes involves the action of a variety growth factors including granulocyte colony-stimulating factor(G-CSF), granulocyte–macrophage-colony-stimulating factor (GM-CSF), IL-3, and macrophage colony-stimulating factor (M-CSF).

Eosinophils are derived from myeloid progenitors in response to T-cell derived cytokines and growth factors including IL-3, GM-CSF and IL-5.

IL-5 is plays an important role in regulation of terminal differentiation and post-mitotic activation of eosinophils.

Cytokines elaborated by T cells, macrophages, regulate the production of basophils and mast cells. The major growth and differentiation factor for basophils is IL-3, whereas the growth and development of mast cells requires the presence of stem cell factor (SCF).

Cytokines and growth factors, such as monocyte colony stimulating factor (M-CSF), GM-CSF and IL-3, allow the commitment along monocytic pathways.

2.1.5.3Classification of WBCs

May be divided into two broad groups: the phagocytes and Theimmunocytes. Granulocytes, which include neutrophils, eosinophils and basophils-together with monocytes comprise the phagocytes.

(Neutrophil (polymorph)):

Size (13 μm in diameter), characteristic dense nucleus consisting of between two and five lobes, and a pale cytoplasm with an irregular outline containing many fine pink-blue or grey-blue granules. The granules are divided into primary, which appear at the promyelocyte stage, contains (myeloperoxidase, acid phosphatase and other acid hydrolases) and secondary (specific) which appear at the myelocyte stage and predominate in the mature neutrophiL, contains (collagenase, lactoferrin and lysozyme). The lifespan of neutrophils in the blood is only6-10h. [6]

Neutrophil precursors: These do not normally appear in normal peripheral blood but are present in the marrow. The earliest recognize:

1-Myeloblast: large nucleus, fine chromatin, 2-5 nucleoli, basophilic cytoplasm, no granules.

2- Promyelocyte: large cell, have primary granules in cytoplasm.

3-Myelocyte: specific or secondary granules, chromatin condensed, nucleoli not visible.

4- Metamyelocyte: non dividing cell, indented or horse shoe shaped nucleus, have primary and secondary granules.

5- Band (stab or juvenile): between meta and mature.

6- Mature neutrophil: contain Barr body, 10-12μm, dence nucleus consist of-5 lobes, pale cytoplasm contain fine pink-blue or grey –blue granules.

Eosinophils: These cells are similar to neutrophils, except that the cytoplasmic granules are coarser and more deeply red staining and there are rarely more than three nuclear lobe,Eosinophilmyelocytes can be recognized but earlier stages are indistinguishable from neutrophil precursors.

Basophils: Occasionally seen in normal peripheral blood. They have many dark cytoplasmic granules which overlie the nucleus and contain heparin and histamine, serotonin and leukotrienes. They have immunoglobulin E (IgE attachmenent sites. In the tissues they become mast cells.

Basophils: These are only occasionally seen in normal peripheral blood They have many dark cytoplasmic granules which overlie the nucleus and contain heparin and histamineIn the tissues they become mast cells. They have immunoglobulin E (IgE) attaclunent sites and their degranulation is associated with histamine release.

Monocytes: These are usually larger than other peripheral blood leucocytes and possess a large central oval or indented nucleus with clumped clu'omatin .The abndant cytoplasm stains blue and contains many fine vacuoles, giving a ground-glass appearance. Cytoplasmic granules are also often present .the monocyte precursors in the marrow (monoblasts and promonocytes) are difficult to distinguish from myeloblasts and monocytes.

Lymphocytes: The immune response depends upon two types of lymphocytes, B and T cells, which derive from the haemopoietic stem cell.

B-cells mature in the bone marrow and circulate in the peripheral blood until they undergo recognition of antigen.

In postnatal life, the bone marrow and thymus are the primary lymphoid organs in which lymphocytes develop. The secondary lymphoid organs arethe lymph nodes, spleen and lymphoid tissues of the alimentary and respiratory tracts.

2.1.5.4 Disorders of white cells

Terminology: leukocytosis: An absolute increase in the total number of circulating leukocytes.

leukopenia: An absolute decrease in the total number of circulating leukocytes.

Neutrophilia: An absolute increase in neutrophils can be found in:

1-Acute bacterial infections (often with left shift), e.g. abscesses, wound infections, meningitis, pneumonia, gonorrhoea, urinary tract infections.

1. Tissue damage, e.g. burns, trauma.
2. Snake envenomation.
3. Acute myocardial infarction.
4. Acute haemorrhage.
5. Malignant diseases.

6. Myeloid leukaemia.
7. Reactions to some drugs e.g. steroid therapy, and chemicals.
8. Metabolic disorders.
9. During pregnancy (normal) and delivery

Neutropenia: Common causes of a reduced neutrophil count are:

1. Bone marrow failure.
2. Viral infections, e.g. HIV disease, hepatitis, influenza.
3. Bacterial infections, e.g. typhoid fever, brucellosis, miliary tuberculosis, overwhelming septicaemia.
4. Splenomegaly.
5. Megaloblasticanaemia.
6. Drugs

Eosinophilia: An absolute increase in eosinophils can be found in:

1. Helminth infections, e.g. hookworm infection, strongyloidiasis, flilariasis, trichinosis, schistosomiasis, hydatid disease.
2. Allergic conditions, e.g. asthma, hay fever, urticaria, food allergies, drug allergies.
3. Skin diseases, e.g. psoriasis, dermatitis.
4. Pulmonary eosinophilia.
5. Hodgkins disease, lymphoma, malignancies.
6. Connective tissue diseases

Basophilia: An absolute increase in basophils can be found in:

1. Myeloproliferative disorders.
2. Some allergies.
3. Myxoedema

Lymphocytosis: An absolute increase in lymphocytes can be found in:

1. Infections in children, e.g. whooping cough, mumps, measles.
2. Bacterial infections, e.g. brucellosis, typhoid fever, chronic tuberculosis, syphilis.
3. Protozoal infections, e.g. malaria, toxoplasmosis.

4. Infectious mononucleosis.
5. Cytomegalovirus infection.
6. Lymphocytic leukaemia, lymphomas

Lymphopenia: Common causes of a reduced lymphocyte count are:

1. HIV/AIDS.
2. Severe bone marrow failure.
3. Hodgkins disease.
4. Some acute viral infections.

Monocytosis: An absolute increase in monocytes can be found in:

1. Chronic bacterial infections, e.g. tuberculosis, brucellosis, typhoid, bacterial endocarditis.
2. Protozoal infections, e.g. malaria, trypanosomiasis

Chronic myelomonocyticleukaemia.

2.1.6 Thrombopoiesis

2.1.6.1 Platelet production

Platelets are produced in the bone marrow by fragmentation of the cytoplasm of megakaryocytes, one of the largest cells in the body. The precursor of the megakaryocyte-the megakaryoblast-arises by aprocess of differentiation from the haemopoietic stem cell The megakaryocyte matures by endomitotic synchronous replication, enlarging the cytoplasmic volume as the number of nuclear lobes increase in multiples of two Mahlre megakaryocytes are extermely large, with an eccentric placed single lobu- Endomitotic synchronous nuclear Replication Simplified diagram to illustrate platelet production from megakaryocytes. lated nucleus and a low nuclear to cytoplasmic ratio. Platelets form by fragmentation of megakaryocyte cytoplasm, approximately each megakaryocyte giving rise to 1000-5000 platelets.

The time intervalfrom differentiation of the human stem cell to the production of platelets averages approximately 10 days. Thrombopoietin is the major regulator of platelet production and is constitutively produced by the liver and kidneys. Thrombopoietin increases the number and rate of mahuation of megakaryocytes

2.1.6.2Platelet antigens

Several platelet surface proteins have been fowld to be important antigens in platelet-specific autoimmwuty and they have been termed human platelet antigens (HPA). via c-Mpl receptor. Platelets also express ABO and human leucocyte antigen (HLA) class I but not class II antigens.

.2.1.6.3 Platelet function

The main function of platelets is the formation of mechanical plugs during the normal haemostatic response to vascular injury. Thrombocytopenia:

Abnormal bleeding associated with thrombocytopenia or abnormal platelet function is characterized by spontaneous skin purpura and mucosal haemorrhage and prolonged bleeding after trauma.

The main causes of thrombocytopenia are listed in follow:

2-1-6-4 Reduce production of platelet

Infections, e.g. typhoid, brucellosis.

- Deficiency of folate or vitamin B12.
- Aplastic anaemia.
- Drugs (e.g. cytotoxic, quinine, aspirin), chemicals (e.g. benzene), some herbal remedies, alcoholism.
- Hereditary thrombocytopenia (rare condition).

Increased desrtruction or consumptionof platelet:

- Infections, e.g. acute falciparum malaria, dengue, trypanosomiasis, visceral leishmaniasis.
- Disseminated intravascular coagulation (DIC).
- Hypersplenism.
- Immune destruction of platelets, e.g. idiopathic thrombocytopenic purpura (ITP), systemic lupus erythematosus (SLE), other connective tissue disorders, chronic lymphatic leukaemia, lymphomas and HIV/AIDS. Also exposure to drugs, e.g. quinine, mefloquine, penicillin, and some herbal remedie.

Thrombocytosis: Cause of an increase in platelete numbers include:

- Chronic myeloproliferative diseases, e.g. essential thrombocythaemia, polycythaemiavera, chronic myeloid leukaemia, myelofibrosis.

-Carcinoma (disseminated).

- Chronic inflammatory disease, e.g. tuberculosis.

-Haemorrhage.

- Sickle cell disease associated with a non functioning spleen or after splenectomy.

- Iron deficiency anaemia, associated with active bleeding [5].

2.2. Complete Blood Count (CBC)

The CBC, also known as a complete blood count, is test that provides information about certain cells in the blood .It is a very common and important test that is frequently ordered by a physician to check a patients general health status.

2-2-1: The CBC is a panel of tests which includes

WBC (White blood (leukocyte) cell count)-a mount of the actual number of white blood cells per volume of blood .white blood cells protect the body a gainst infection and their numbers can quickly increase when a person has a bacterial infection .Both increases and decreases can be significant.WBC types include: Neutrophils, Bands (young neutrophils), Lymphocytes, Monocytes, Eosinphils, and Basophils.

2.2.2: RBC (Red Blood Cell Count)- a count of the actual number of red blood cells per volume of blood .if the RBC count is low, the body may not be getting the oxygen it needs .If the RBC count is too high (polycythemia) it may cause thickening of the blood, which could increase the risk for blood clots. Hemoglobin- measures the amount of oxygen –carrying protein in the blood, Hemoglobin is what gives blood its red color.

2.2.3: Hematocrit- is the percentage of red blood cells in the blood. For example, a hematocrit of 36 means that 36% of the bloods volume is made of red blood

cells. Hematocrit and hemoglobin values can show if anemia or polycythemia is present.

2.2.4: MCV (Mean Corpuscular volume)- indicates size of red blood cell, MCH(Mean Corpuscular Hemoglobin)- indicates a mount of hemoglobin in an average red blood cell, MCHC(Mean corpuscular hemoglobin concentration)- measures the concentration of hemoglobin in red blood cell. MCV, MCH, and MCHC all help in diagnosing different type of anemia.

RDW(Red cell Distribution Width)- can be measured which shows if the cells are all the same or different sizes or shapes.

2.2.5: Platelet count- The platelet (thrombocyte) count is the number of platelets in a given volume of blood. Platelets are important in blood clotting. If there are too few platelets, uncontrolled bleeding may be a problem. If there are too many, there is a chance of a blood clot forming in a blood vessel.

2.2.6: Differential of CBC

The Differential is the identification of the 5 different White blood cell type that are present in blood, and in what amount. This is usually completed by a highly sophisticated Hematology instrument. These instrument can have complex measuring systems to accurately identify what white blood cell types are present. If there is any thing out of the ordinary, the instrument will indicate that further investigation is need. The differential will be completed manually. This requires that a blood smear (slide preparation) is made. A drop of blood is spread on a glass slide and special dyes are used to stain the cells. It is then reviewed under a microscope by a trained medical Technologist who evaluates the cell.

The WBC, RBC and Platelet cell number, size, and shapes are evaluated and recorded. This evaluation can help diagnose many blood disease like leukemia, malaria or sickle cell disease.

Part of differential are reported in both percent and a boslute values.

PERCENTAGE: 100cells are counted and the number of each type of white blood cell present is expressed as a percentage.

Absolute: Quantifies the real number of a specific cell type in thousands per cubic milliliter.

2-3 D-dimer

D-dimer is as fibrin degradation product (or FDP), asmall proteine fragment present in the blood after ablood clot is degrated by fibrinolysis .it is so named because it contain two D fragments of the fibrin protein joined by cross-link. [12]

the formation of blood lot or thrombus, ocures when the proteins of the coagulation caascade are activated. Ether by contact with damaged blood vessel wall and exposure to collgen in the tissue space (intrinsic pathway) oractivation of factor V11by tissue activating factors (extrinsic pathway) both pathway lead to the genration of thrombin, an enzyme thate turne the soluble blood protein fibrinogen in to fibrin which aggregates in to proteofibrils. Another thrombine-generated enzyme, factorX111.then crosslinks the fibrine proteofibrils at the D fragment site, leading to the formation an insoluble gel which serves as ascaffold for blood clot formation. [12]

D-dimer concentration may be determined by a blood test to help diagnose thrombosis.

Since its introduction in the 1990s,it has become an important test performed in patients with suspected thrmbotic disorder.

D-dimer are marker of fibrin breakdown, measurement is by immunoassay an not by aclot-based or color assay.

The d-dimer test has very good sensitivity but arather poor specificity.

Requires formation of d-dimer sequential action of thrombin, factor XIIIa and plasmin.

While a negative result practically rules out thrombosis ,positive result can indicate thrombosis but does not rule out other potential causes .its main use, therefore, is to exclude thromboebolic disease where the probability is low. In addition ,it is used in the diagnosis of the blood disorder disseminated intravascular coagulation. [12]

D-dimer are not normally present in human blood plasma, except when the coagulation system has been activated, for instance because of the presence of thrombosis DIT to aparticular epitope on the D-dimer assay depends on the binding of amonoclonal antibody to a particular epitopon the D-dimer fragment.[12]

Indication: D-dimer testing of clinical use when there is asuspicion of deep venous thrombosis (DVT), pulmonary embolism (PE) or disseminated intravascular coagulation (DIC)it is under investigation in the diagnosis of aortic dissection.

History: D-dimer was originally described in the 1970, and found its diagnostic application in the 1990.

D-dimer levels are raised in many systemic illnesses associated with fibrin formation and degradation.

3-2Elevated levels of D-dimer occur in most critically ill patient with sever infection, truma or nflamma disorder in addition to venous thromboemboli raised level of circulated in patients with.

1/ disseminated intravascular coagulation.

2/ vaso occlusive, sickle cell crisis.

3/ acute cerebrovasc accident.

4/ acute myocardial infarction.

5/ unstable angina .

6/ atrial fibrillation.

7/ pneumonia.

8/ vasculitis.

9/ superficial phlebitis.

10/ many cancers including lung, prostate ,cervical and colorectal note that only about 20 or less of patients admitted with these conditions will have abaseline D-dimerin the normal range. [13]

her factors fecting D-dimer els larger tend to produce ahigher levels of circulting D-dimer there is an increase in circulating D-dimer levels with age ,pregnancy

and smoking .D-dimer level may fail to increase if apatient has an acute venous thrombolism but impaired fibrinolytic activity.

D-dimer levels are reduced with initiation of heparine therapy and may be lowered by two*third in patientson oral anticoagulants. [13]

2-4. Preeclampsia

Preeclampsia is apregnancy complication characterized by high blood pressure and signs of damage to another organ system ,most often the liver and kidneys.

Left untreated, preeclampsia can lead to serious -even fetal -complication r your ribs on right [14]

2-4-1.Symptoms

preeclampsia sometimes develops with out any symptoms. high blood pressure may develop slowly, or it may have a sudden onset.

Monitoring your blood pressure is an important part of prenatal care because the first sign of preeclampsia is commonly arise in blood pressure .blood pressure that exceeds 140/90 millimeters on mercury (mmHg)or greater documented on two occasions ,at least four hours apart -is abnormal.

Other signs and symptoms of preeclampsia may include:

1-Excess protene in your urine or additional signs of kidney problems.

2-Sever headaches

3-Changes in vision, including temporary vision or loss of vision, blurred light sensitivity.

4-Upper abdominal pain, usually under your ribs on the right side.

5-Nausea or vomiting.

6-Decreased urine out put.

7-Decreased levels of platelets in your blood (thrompocytopenia).

8-Impaired liver function.

9-Shortness of breath, caused by fluid in your lungs sudden weight gain and swelling (edema) - particularly in your face an hands -may occur with preeclampsia . but these also occur in many normal pregnancies, so theyre not considered reliable signs of preeclampsia . [14]

Causes: The exact cause of preeclampsia involves several factors .experts believe it begins in the placenta -the organ that nourishes the fetus thought pregnancy. Early in pregnancy ,new blood vessels develop and evolve to efficiently send blood to the placenta.

in women with preeclampsia, these blood vessels don't seem to develop or function properly. There narrower than normal blood vessels and react differently to hormonal signaling, which limits the amount of blood that can flow through them.

1/Insufficient blood flow to the uterus.

2/Damage to the blood vessels.

3/A problem with the immune system.

4/Certain genes [14]

Other high blood pressure disorder during pregnancy: preeclampsia is classified as on of four high blood pressure disorder that can occur during pregnancy .the other three are:

1/Gestational hypertension: Women have high blood pressure but no excess protein in their urine or other signs of organ damage .some women of gestational hypertension eventually develop preeclampsia.

2/ Chronic hypertension :- High blood pressure that was present before 20 weeks of pregnancy.

3/Chronic hypertension with superimposed preeclampsia:

2-4-2 Risk factors of preeclampsia

Preeclampsia develops only as a complication of pregnancy .risk factor include:

1/ History of preeclampsia.

2/ Chronic hypertension.

3/ First pregnancy.

4/ New paternity.

5/ Age.

6/ Obesity .

7/ Multiple pregnancy.

8/Interval between pregnancies.

9/History of certain conditions.

10/In vitro fertilization [14]

4-5 Complications

The more severe your preeclampsia and the earlier it occurs in your pregnancy, the greater the risks for you and your baby. Preeclampsia may require induced labor and delivery. [15]

Delivery by cesarean delivery (C-section) may be necessary if there are clinical or obstetric conditions that require a speedy delivery. Otherwise, your doctor may recommend a scheduled vaginal delivery. Your obstetric provider will talk with you about what type of delivery is right for your condition. [15]

Complications of preeclampsia may include Fetal growth restriction

Preeclampsia affects the arteries carrying blood to the placenta. If the placenta doesn't get enough blood, your baby may receive inadequate blood and oxygen and fewer nutrients. This can lead to slow growth known as fetal growth restriction, low birth weight or preterm birth.

- **Preterm birth.** If you have preeclampsia with severe features, you may need to be delivered early, to save the life of you and your baby. Prematurity can lead to breathing and other problems for your baby. Your health care provider will help you understand when is the ideal time for your delivery.
- **Placental abruption.** Preeclampsia increases your risk of placental abruption, a condition in which the placenta separates from the inner awall of your uterus before delivery. Severe abruption can cause heavy bleeding, which can be life-threatening for both you and your baby.
- **HELLP syndrome.** HELLP — which stands for hemolysis (the destruction of red blood cells), elevated liver enzymes and low platelet count — syndrome is a more severe form of preeclampsia, and can rapidly become life-threatening for both you and your baby.

Symptoms of HELLP syndrome include nausea and vomiting, headache, and upper right abdominal pain. HELLP syndrome is particularly dangerous because it represents damage to several organ systems. On occasion, it may develop suddenly, even before high blood pressure is detected or it may develop without any symptoms at all.

- **Eclampsia.** When preeclampsia isn't controlled, eclampsia — which is essentially preeclampsia plus seizures — can develop. It is very difficult to predict which patients will have preeclampsia that is severe enough to result in eclampsia.

  Often, there are no symptoms or warning signs to predict eclampsia. Because eclampsia can have serious consequences for both mom and baby, delivery becomes necessary, regardless of how far along the pregnancy [14].
- **Other organ damage.** Preeclampsia may result in kidney, liver, lung, heart, or eyes, and may cause a stroke or other brain injury. The amount of injury to other organs depends on the severity of preeclampsia.
- **Cardiovascular disease.** Having preeclampsia may increase your risk of future heart and blood vessel (cardiovascular) disease. The risk is even greater if you've had preeclampsia more than once or you've had a preterm delivery. To minimize this risk, after delivery try to maintain your ideal weight, eat a variety of fruits and vegetables, exercise regularly, and don't smoke. [15]

2-4-3 Prevention

Researchers continue to study ways to prevent preeclampsia, but so far, no clear strategies have emerged. Eating less salt, changing your activities, restricting calories, or consuming garlic or fish oil doesn't reduce your risk. Increasing your intake of vitamins C and E hasn't been shown to have a benefit. [16]

Some studies have reported an association between vitamin D deficiency and an increased risk of preeclampsia. But while some studies have shown an

association between taking vitamin D supplements and a lower risk of preeclampsia, others have failed to make the connection.

In certain cases, however, you may be able to reduce your risk of preeclampsia with:

- **Low-dose aspirin.** If you meet certain risk factors — including a history of preeclampsia, a multiple pregnancy, chronic high blood pressure, kidney disease, diabetes or autoimmune disease — your doctor may recommend a daily low-dose aspirin (81 milligrams) beginning after 12 weeks of pregnancy.
- **Calcium supplements.** In some populations, women who have calcium deficiency before pregnancy — and who don't get enough calcium during pregnancy through their diets — might benefit from calcium supplements to prevent preeclampsia. However, it's unlikely that women from the United States or other developed countries would have calcium deficiency to the degree that calcium supplements would benefit them.

It's important that you don't take any medications, vitamins or supplements without first talking to your doctor.

Before you become pregnant, especially if you've had preeclampsia before, it's a good idea to be as healthy as you can be. Lose weight if you need to, and make sure other conditions, such as diabetes, are well-managed.

Once you're pregnant, take care of yourself — and your baby — through early and regular prenatal care. If preeclampsia is detected early, you and your doctor can work together to prevent complications and make the best choices for you and your baby. [16]

2-4-5 Preeclampsia Lab abnormalities

Definition: Proteinuria of: - >300 mg/24 h (mild preeclampsia).

- >5 g/24 h (severe preeclampsia).
- Urine dipstick >1+.
- Protein/creatinine ratio >0.3.
- Serum uric acid >5.6 mg/dL.

- Serum creatinine >1.2 mg/dL.
- Low platelets/coagulopathy.
- Platelet count <100.000/mm3.
- Elevated PT or aPTT.
- Decreased fibrinogen.
- Increased d-dimer.

A variant of severe preeclampsia and defined by the following:

- Hemolysis.
- Abnormal peripheral smear.
- Indirect bilirubin >1.2 mg/dL.
- Lactate dehydrogenase >600 U/L.
- Elevated Liver enzymes Serum AST >70 U/L.
- Low Platelets count <100.000/mm.

2-5: Previous study

Vasc health Risk Manage published online 2016 Nov 21.

1/ A study of the hematological picture and platelet function in preeclampsia –

ABSTRACT

Introduction: Preeclampsia – pregnancy specific condition associating pregnancy induced hypertension

and proteinuria – may present diverse hematological features, variating from normal laboratory

tests to severe thrombocytopenia (due to platelet activation and consumption), and/or anemia.(19)

Objectives: a theoretical and practical presentation of hematological picture that may appear in preeclampsia.

Materials and methods: We studied a number of 10 patients with preeclamptic pregnancies compared to 10 females with normal pregnancies, from Obstetrics-Gynecology Departments of Emergency University Hospital Bucharest, Elias University Emergency Hospital and "Prof. Dr. Panait-Sarbu" Clinical Hospital. For both cases and controls we studied clinical and laboratory parameters – especially hematological aspects. We particularly performed a complete study of the platelet surface markers by flowcytometry, in order to establish the functional status.(19)

Results and Discussions: Regarding the laboratory parameters, the CBC showed significant differences between the two studied groups only concerning platelet count – preeclamptic pregnancies presented slight thrombocytopenia, but with a significantly higher medium platelet volume; there were no differences in white blood count (all had slight leucocytosis with neutrophilia) or haemoglobin and erythrocytic.

Conclusions: Preeclampsia is associated with a degree of thrombocytopenia (which may become severe.(19)

2/Clin Lab. 2017 Nov 1;63(11):1897-1902. doi: 10.7754/ Clin. Lab. 2017.170705.

Jeon Y, Lee WI, Kang SY, Kim MH.

To evaluate modified complete blood count (CBC) indices as a predicting marker of preeclampsia (PE) from gestational hypertension (GH), we analyzed the neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and platelet to neutrophil ratio (PNR). PNR was a newly designed index in this study based on results of PE patients having a tendency toward higher neutrophil count and lower platelet count compared to normal pregnant women in previous studies.(20)

RESULTS:

NLR value of PE patients was significantly higher than GH patients ($p = 0.011$). PNR value was the most statistically significant index separating patients with PE and GH ($p < 0.001$). PLR value was lower in patients with PE compared to GH; however, statistical significance was low.(20)

3/SEEMA MAZHAR, NAGHMANA MAZHAR, AMBREEN ANWAR

Associate Professor (Haematology), Department of Pathology Allama Iqbal Medical College Lahore.

Objectives: The present study was designed to evaluate the usefulness of platelet count (PC) and mean platelet volume (MPV) in the prediction of preeclampsia.(20)

Study design: It is a cross-sectional prospective study.

Place of study: Pathology department Allama Iqbal medical college/Jinnah Hospital Lahore

Patients and Methods: A total number of 140 pregnant females in third trimester from gynecology and obstetrics department were included in the study. Eighty subjects were diagnosed cases of preeclampsia labeled as group I while in group II there were 60 healthy pregnant females. Complete blood count (CBC) was performed on sysmex kx-21 to see the platelet count and mean platelet volume.(20)

Results: Platelet count was found to be decreased in subjects with preeclampsia as compared to controls and a statistically significant difference was observed with a (P-value of <0.001) in pregnant females having preeclampsia than normal normotensive subjects. While mean paltelet volume was found to be increased in preaclampsia patient as compared to normal subjects (P-value of < 0.001.(20)

4/The Prediction of Preeclampsia and Its Association With Hemoglobin and ster of pregnencyHematocrit in first Trime.

Hamideh Pakniat,1 Farideh Movahed,1,* Atie Bahman,1 and Mahdi Azoor2

Received 2016 February 02; **Revised** 2016 June 09; **Accepted** 2016 June 12.

Abstract

Background: Hypertensive disorders in pregnancy are one of the most serious complications and their early diagnosis is one of the most important goals of prenatal care.(17)

Objectives: The objective of this study was to determine the association of first trimester Hemoglobin (Hb) and Hematocrit (Hct) with preeclampsia.(17)

Patients and Methods: This descriptive-analytic, prospective study was performedon1376, less than 12weeksof gestation, singleton pregnancies, visited for their prenatal care in health and medical clinics of the Qazvin province during years 2013 and 2014. At first, demographic data were recorded in a questionnaire and then all pregnant cases were referred to one of the three reference laboratories for their first trimester routine tests. After hemoglobin and hematocrit date collection, women were categorized in three groups: Hb < 11, Hb_ 12.49 and 11_Hb < 12.49, and based on Hct, two groups: Hct < 38% and Hct_ 38. The analysis was done by_2 (chi-square) and t-test with SPSS 16. Receiver operator characteristics (ROC) curve and Youden's index were utilized for finding the optimum cut off for each. P values of < 0.05 were considered significant.(17)

Results: Preeclampsia incidence was 5.1% in our study. Mean Hb was 12.38 _ 1.69 g/dL in the preeclampsia group and 11.8 _ 1.18 in the non-preeclampsia group, and mean Hct was 37.74_5.15% in the preeclampsia group and

35.45_3.58% in the preeclampsia group and 35.45_3.58% in the non-preeclampsia group, (P = 0.016) (P = 0.001). Furthermore, 43 out of 68 patients with preeclampsia (10.9%) had high hemoglobin (Hb_ 12.5 g/dL).We found a significant association between the 1st trimesterHb, Hct and preeclampsia (P < 0.001, P < 0.001). Assessed relative risk in high Hb group was 5.82 (3.14 - 10.18: CI 95%), and likewise 7.41 in high Hct group (Hct >38%) (4.41 - 12.044: CI 95%). According to Youden's Index, optimum cut-off for 1st trimester Hb was 12.65 and for Hct, this was 38.05%.(17)

Conclusions: The association of the 1st trimester high Hb and Hct with preeclampsia was revealed in this study, therefore it could be used as a prediction factor for early preeclampsia diagnosis.(17)

The publisher's final edited version of this article is available at Am J Perinatol

5/We evaluated the leukocyte differentials in women with normal pregnancies and in pregnancies complicated by preeclampsia (PE). A

retrospective study was performed in 240 women who were delivered at Louisiana State University Health Sciences Center– Shreveport, Louisiana, from January 1, 2002, to July 31, 2003. A total of 80 patients were studied in each group: normal pregnancy, mild PE, or severe PE. Leukocyte total and neutrophil, lymphocyte, monocyte, eosinophil, basophil, hemoglobin, and platelet counts were analyzed by analysis of variance and pairwise comparison. Data are presented as mean ± standard deviation. A p value <0.05 was set as statistically different. The total leukocyte count was significantly increased in women with severe PE compared with women with mild PE and normal pregnant controls:(18)

10.66 ± 3.70 (p < 0.0001) versus 9.47 ± 2.59 and 8.55 ± 1.93 ($1 \times 10^3/\mu L$), respectively. The increased total leukocyte count was mainly due to the increase in neutrophil numbers: 8.05 ± 4.01 (severe; p <0.0001) versus 6.69 ± 2.23 (mild) and 5.90 ± 1.79 (controls), respectively.

The total neutrophil count was further increased 48 hours after delivery in the group with severe PE. No statistical differences for monocyte and lymphocyte counts were observed between normal and PE groups. Increased neutrophil.(18)

Chapter Three

Materials and Methods

3. Materials and Methods

3.1. Study Design

A cross-sectional descriptive study conducted to evaluate the complete blood count and D-dimer in preeclampsia in women in Shendi town.

3.2. Study Area

The study was conducted in Shendi town which is located 172Km north to capital Khartoum, southern part of River Nile state, and covering an area of about 30Km2.

There are several general centers for different services and purposes; also there is Shendi University with various faculties like faculty of medicine and health science. Shendi has three pig hospitals, Elmek Nimer University hospital, Shendi Teaching Hospital and Military Hospital; all of them have different departments which provide good health services for the population.

3.3. Study Population

A total of 50 venous blood samples were collected from known preeclampsia patient as test group with different age and also 30 venous blood samples were obtained from pregnancy healthy individuals female with different age as control group.

3.3.1. Inclusion Criteria

All individuals known to have preeclampsia with different age.

3.3.2. Exclusion Criteria

All individuals have physiological changes and pathological change from other disease.

3.4 Study period

The study was conducted in period from April to July 2018.

3.5. Data collection tools

1. Structured Questionnaire.
2. Analytical laboratory tests of venous blood samples obtained by hematology analyzer and Ichroma.

3.6. Methods

3.6.1. Specimen collection

Approximately 2.5ml of venous blood was taken from study participants and transferred into an EDTA container. The sample was then sent as early to laboratory for analysis

3.6.2. Automated method

Blood cells are diluted in a buffered electrolyte solution. A measured volume of the sample passes through an aperture tube (e.g.100 micrometer meter in diameter) between two electrodes.

Pulse is proportioned to the volume of the cell which caused it. A threshold circuit ensures only those pulses that exceed the pre-set threshold level are counted. The cell count is determined from the total number of pulses obtained from a measured volume of blood.

3.6.3 Hematology analyzer: Mindray bc-3000 principle

The analyzer measures the number of cells and distinguishing between their types according to size using sheath flow DC detection. Electrical current is passed through solution, this methods measured the change in electrical resistance that occurs when blood cell pass through detection aperture. this instrument performs hematology analyses according to the RF/DC detection method.

3.6.4 Ichroma method

The sample type is human whole blood /plasma the test sample within 24 hours after collection.

The plasma was be separated from the clot by centrifugation within 3hours after the collection of whole blood.

Do not keep the sample in freezer, which could affect the test value of D-Dimer.

3.6.5 Test Procedure

1/Transfered 10ml of sample (Human whole blood /plasma/control) using a transfer pipette to a tube containing the detection buffer.

2/Selected the lid of detection buffer tube and mix the sample thoroughly by shaking it about 10times (the sample mixture must be used immediately).

3/Pipetted ou t 75 ml of asample mixure and dispense it into the sample well on the cartridge.

4/Leaved the sample /loaded cartridge at room temperature for 12 minutes

5/To scanned the sample loaded cartridge ,inserted it into the cartridge holder of the instrument for icroma tests. Ensure proper orientation of the cartridge befor the cartridge especially for this propose.

6/press selected button on the instrument for ichromas tesrs to.

3.7. Ethical Considerations

Procedure of blood sampling was explained to participants. All participants were informed about the research objectives and procedures during the interview period. A written valid consent was obtained from all participants.

Chapter Four

Results

4. Results

The data were compared by using statistical analysis performed with Statistical Package for Social sciences (SPSS-s)To compare means and standard deviation of the values of haematological variables.

Table (4-1) :Distribution of study group according to age

The age	Frequency	Percent
(17-24) years	9	18%
(25-30) years	6	12%
(31-35) years	12	24%
(36-40) years	14	28%
More than 40 years	9	18%
Total	**50**	**100%**

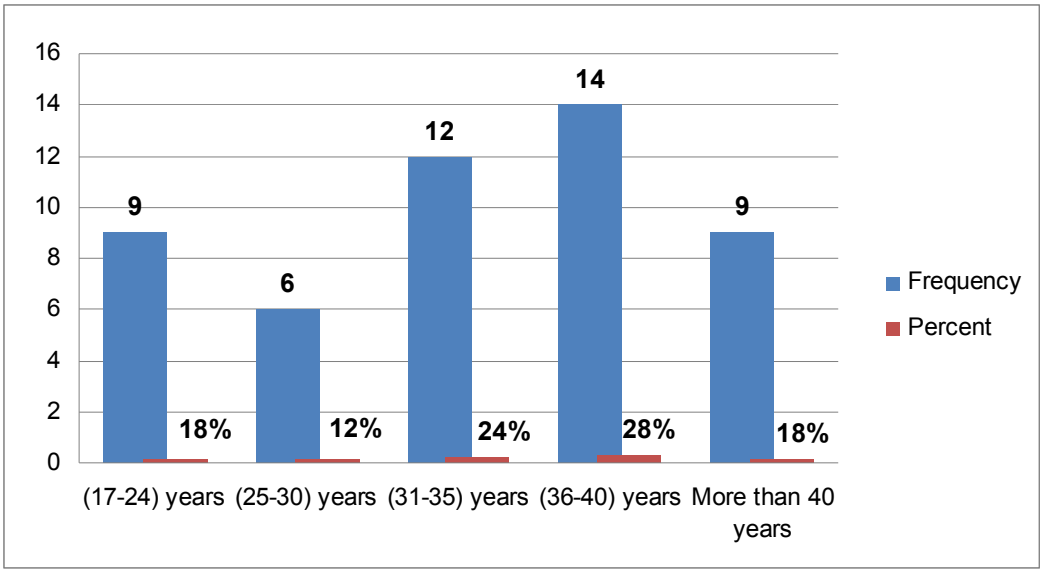

Figure (4-1) Show the frequency and percent of Age

Table (4-2) Distribution of study group according of the number of pregnant

Pregnant number	Frequency	Percent
(1-3) times	36	72%
(4-6) times	12	24%
(7-9) times	2	4%
Total	**50**	**100%**

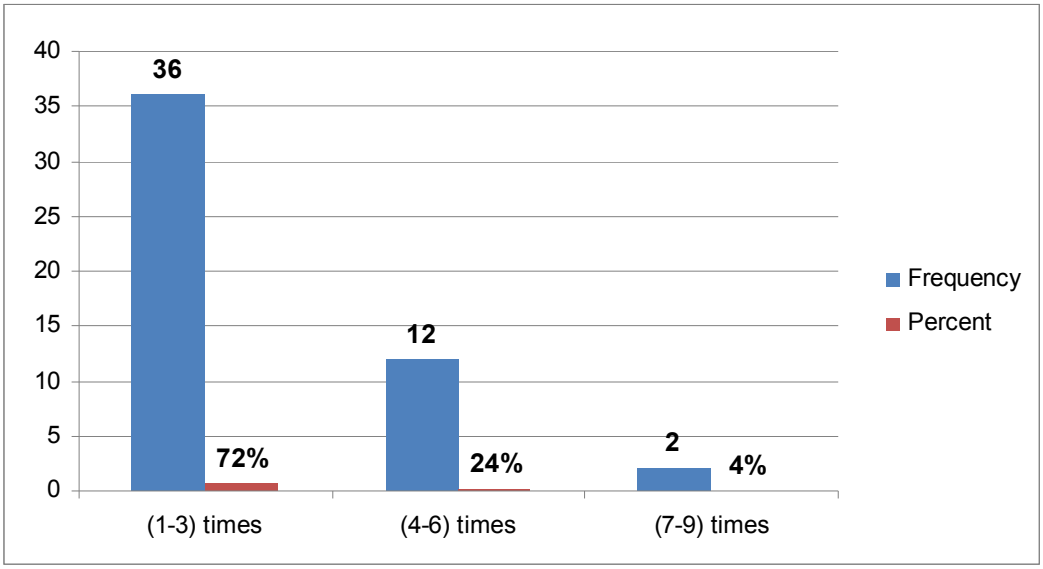

Figure (4-2) Show the frequency and percent of the pregnant number

Table (4-3) Distribution of study group according Gestational age

Gestational age	Percent	Frequency
Third trimester	47	94%
In 6 months	3	6%
Total	**50**	**100%**

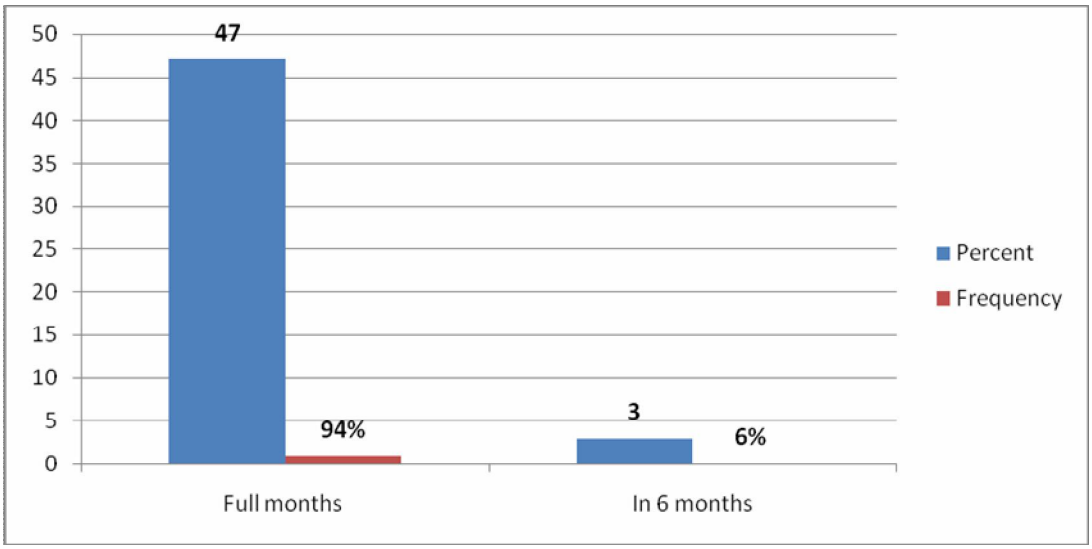

Figure (4-3) Show the frequency and percent of the Gestational age

Table (4-4) Mean of WBCs and differential in women with preeclampsia and control

Cells	Control	Test	P.value	The correlation
WBCs $x10^9$/UI	6.5×10^9	8.1×10^9	0.07	Not significant
Neutrophil%	52	68	0.00	Significant
Lymphocyte%	39	26	0.00	Significant
Monocyte%	8	7	0.340	Not significant
Eosinphil%	0.9	0.2	0.729	Not significant

Table (4-5) Mean of HB in women with preeclampsia and control

	No	Mean	P.value	Correlation
Test	50	14.0	0.001	Significant
Control	20	13.0		

Table (4-6) Mean of PCV in women with preeclampsia and control.

Sample	Mean	Sig. value	The correlation
Test	48.0	0.006	Significant
Control	45.0		

Table (4-7) Mean of RBCs indices in women with preeclampsia and control.

	Control	Sample	pv.value	The correlation
RBCs	3.7	4.8	0.055	Not significant
MCV	83.0	85.4	0.126	Not significant
MCH	27.0	28.0	0.290	Not significant
MCHC	33.4	33.9	0.06	Not significant

Table (4-8) Mean of PLT in women with preeclampsia and control.

Samples	Mean	Sig. value	The correlation
Test	236.0	0.1	Not Significant
Control	261.0		

Table (4-9) Mean of MVP in women with preeclampsia and control.

Samples	Mean	Sig. value	The correlation
Test	10.2	0.002	Significant
Control	9.4		

Table (4-10) Mean of D-dimer in women with preeclampsia and control

Samples	Mean	Sig. value	The correlation
Test	2180	0.111	Not Significant
Control	4140		

Chapter Five

Discussion

Conclusion

Recommendations

5.1 Discussion

A cross sectional descriptive study was conducted in Shendi to assess haematological parameters on women with preeclampsia, in period from April 2018 to July 2018.

The study include 50 women with preeclampsia in different age (17-24), (25-30), (31-35), (36-40) and more than 40 were (9,6,12,14,9)respectively.

Table (4-1)according to number of pregnancy were divided in to (1-3), (4-6), (7-9) were (36 ,12,2) respectively.

Table (4-2)according to gestational age of pregnancy divided in to third trimester and 6 month (47.3) respectively.

The result displayed in table (4-4) showed the mean of TWBCs count in women with preeclampsia was $8.0x10^9$/l and control was $6.0x10^9$/l, this results revealed that preeclampsia have no effect on TWBCs count (P.value 0.071). This result was disagreement with study conducted by Muneera A. Alsheeha Rafi SAlaboudi which found that preeclampsia have effect on TWBCs count increased(p.value 0.000).

Also the mean of Neutrophil in women with preeclampsia was 68% and control was 52% this results showed that preeclampsia was increased the neutrophil level (P.value 0.000), this results were in agreement with the finding reported by Mneera A.Alsheeha Rafia SAlaboudi (p. value 0.01).

The mean of lymphocyte in women with preeclampsia was 39% and control was 26% this result showed that preecalmpsia was decreased the lymphocyte level (P.value 0.000), this result were in agreement the finding reported by Muneera A.Alsheeha Rafia SAlaboudi (p.value 0.000).

Also table (4.4) showed the mean of monocyte in women with preclampsia was 8% and control was 7% this result that preclampsia no effect on monocyte. p.value (0.340).

The mean of eosinophile in women with preclampsia was 0.9% and control was 0.2%, this result that preeclampsia no effect on eosinophile p.value (0.729).

The mean of RBCs in women with preeclampsia was $4.0x10^{12}$ and control was $3.7x10^{12}$, this results showed that preeclampsia no effect on RBCs (P.value 0.055), this result was dis agreement with the finding reported by Preek lamptik Hastalarda Eritrosit indeksleri (p.value 0.000).

Furthermore preeclampsia no effect in RBCs indices (MCV: P.value (0.126), MCH: P.value (0.290) and MCHC: P.value (0.06), this findings were dis agreement with the finding reported by Preek lamptik Hastalarda Eritrosit indeksleri MCV(p,value 0.01), MCH (p.value 0.003) and MCHC (p.value0.012). Also result in table (4.13) showed association between preeclampsia and HB and PCV, P.value (0.001 and 0.006 respectively).this results were agreement with the finding reported by Preek lamptik Hastalarda Eritrosit indeksleri Hb (p.value 0.031) and PCV p.value (0.03).

The mean of platelet count in women with preeclampsis was $236x10^{9}$/l and control was $261x10^{9}$ /l, this results showed that preeclampsia no effect on platelet (P.value 0.1), and this result agreement the result conducted in Khartoum state at omdurman Maternity Hospital during peroid from March to June 2016 (p.value 0.1).

the mean of MVP in women with preeclampsia 10.2 and control 9.4 these result showed that preeclampsia increased the MVP (P.value 0.002). this results were agreement with the finding reported by in annals of haematology June 2006 publication by Temel ceyhan.(p.value 0.02).

The result illustrated in table (4.14)1revealed that preeclampsia was no effect on D-dimer (P.valu 0.111).

5.2 Conclusion

On the basis of this results the study it could be concluded that:

1- The most common age group women with preeclampsia was (36-40) years.

2- All women with preeclampsia wase in last few months of pregnancy (7,8,9) third trimester with high blood pressure and albumin in urine inspite of taking treatment of high blood pressure. and the majority of them on their first pregnancy.

3-preeclampsia effect on hematology profile by decreasing level of lymphocyte, increasing level of neutrophils and effect on MPV, Hb and PCV There is no association between preeclampsia and TWBCs, RBC indices and D-dimer.

5.3. Recommendations

On the basis of this results the study it could be recommended that:

1-Regular assessment of haematological parameter for women with preeclampsia to avoid the complications that result fom alteration in these parameter.

2- Further studies should be done in this topic with increasing sample size and adding of other parameter (PT and PTT).

3-Health education to all pregnant Idies to explain symptoms, signs and complication of the disease.

4-Further study to assess the situation of this disease and complication all over country.

Chapter Six

References

Appendices

6.1. References

1-Ciesla, B. (2007). *Hematology in practice*. Philadelphia: F.A. Davis Co.

2- Dacies J, (1995), pradical hematology eight edition, page 60 – 61.

3. Sirrjohn .Dacie " practical hematology eighth edition -1995, page 60 - 6.

4- Le Tao;Bhushan, Vikas, Vasan Niel. First Aid for the USMLE 2010 20th Anniversary p.1-23 .

.5- Hoffprand A.V, Pettit J.E., Moss P.A.H Essential Haematology. (2001), 4th Edition. Pages 1, 14, 17, 71, 83.

6- Text book of physiology by Dr. A. K. Jain reprint 2006-2007 3rd edition. P. 125

7-Michael Foller,Stephan M. Huber ,Florian Lang (August 2008) "Erythrocyte programmed cell death'.' P .(661-668).

.8- Ramnik sood, haematology for students and practitioners, Sixth edition 2010, page (255- 263).

9- Osman, M.M (2013). Normal Reference value of blood cell count and platelet of Khartoum North Area .*Alneelain medical Journal.* ***3:*** 100- 109.

10- Monica Cheesbrough, District laboratory practice in tropical countries. Part 2 (2007) 2nd Edition. Pages 299-313.

11- Krumbhaar EB (1919). "Role of the blood and the bone marrow in certain forms ofs gas poisoning". Fourth edition JAMA 72: 39–41

12- Moyer ,AV: U,S, preventive Services Task ,Force (Oct2 2012)S creening for coronary heart disease with electerocardiography :U.S preventive Services T ask Force recommendation statement :Annals of internal Medicine 157(7):512 - 8 doi 10.7326/0003-4819-157-7-20120020-00514.PMID 22847227.

13-Bertazzo ,S,et al Nano-analytical electron icroscopy reveal fundamental insights into human cardiovascular tissue .Nature Materials 12,576-583(2013).

14- (Kevin .Hanertty, P. Obstitrics Illustrated, Sixth Edition, (2003) page 57-64),(69-70),(224-235).

15- Cipolla M.L,. Cerebrovascular Iunction in pregnancy and eclampsia , Hypertension ,50,14-24,2007 .

16-Brewer J,,Owens N.Y,.Wallace K., Reeves A,A,. Morris R,. Khan M,. LaMarca B,. J ,N,. Jr ,. Posterior reversible eneephalopathy syndrome in 46-of 47 patente with eclampsia ,Am J. Obstet .Gynecol ,.208,,468 .,2013.

17-Makuyana D,Mahomed K,Shukusho FD,MajokoF.Liver and kidney function testes in normal andpre -eclamptic gestation comparison with non-gestation reference values Cent After JMed 2002 : 48:55:9

18-Kaya MG.inflamation and coronary artery disease .as a new biomarker neutrophil/lymphocyte ratio .Turk Kardiyol Dern Ars 2013:41:191-2

19-Ceyhan T,Beeyan C,Baser I,Kaptan K Gungor S,Ifran AThe effect of pre-eclampsia on complet blood count platelet count and mean platelet volum .Ann Hemmatol2006"85:320-2

20-Jaremo P,Lindahl TL ,Lennmarken C,Forsgren H,The use of platelte density and volum measurement to estimate the severity of pre-eclampsia Eur J Clin Invest 2003"30:1113-8

Appendix I

Evaluation of Complete blood count and D-dimer in women with preeclampsia in Shendi Locality River Nile State, Sudan.

Questionnaire

Personal data:

1- Identification number

2- Name……..

3- Age…….

4- Address……...……

5- Social economic:

1- High

2- Moderate

3-Low

6-Level education

1-Primary

2-Secondary

3-Post graduae

6- Clinical data:……

7-Number of pregnancy:.....

8-Gestational age:.....

9-Family history of same condition :.....

10-Previous history of preeclampsia:.....

11-Therapy:

-Yes

-No

12-Any other chronic disease\s……

CBC

D-dimer

6.2 Appendix II

إقرار بالموافقة

الإسم:----------

العمر :----------العنوان :----------

أوافق بمحض أرادتي في البحث العلمي المتعلق بدراسة التغييرات الدمويه لدي مـــرض تسمم الحمل في مستشفي الملك نمر الجامعي

سلوى محمد عثمان عبد الله

بعد أن شرح لي بأنه لا يترتب عليه أي أذي جسدي أو نفسي وأعلم أن المشاركة في هذا البحث لن تؤثر بأي حال من الأحوال في الرعاية الطبية التي اتلقاها كما أنه يحـــق لـــي بدون أبداء أسباب الإنسحاب من هذا البحث في أي مرحله من مراحله.

البحث بإشراف:

د/ أم كلثوم عثمان

التوقيع :---------- التاريخ :----------