بسم الله الرحمن الرحيم

Sudan University of Science and Technology

College of Graduate Studies

Platelet Count and Platelet Indices as Possible Predictors for Pre-eclampsia in Sudanese Pregnant Women in Aldamar Locality Maternity Hospitals

تعداد الصفائح الدموية ومؤشراتها كعوامل محتمله للتنبؤ بضغط الدم الجنيني لدى النساء الحوامل السودانيات بمستشفيات الولادة محليه الدامر

A thesis submitted for partial fulfillment for the requirement for master Degree (M.sc) in medical laboratory sciences (hematology and Immunohaematology)

Prepared by:

Ramla Kamal Abd Allah Ibrahim

BSc, Hematology and immunohaematology, Shendi University, 2014.

Supervised by:

Prof: Babiker Ahmad Mohammed

2017

بسم الله الرحمن الرحيم

قال تعالى:-

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

صدق الله العظيم

سورة النور- الآية (35)

Dedication

For the man who drinks from empty cup to give me a drop of love,,,
For the man who teaches me the way of life, happiness and his finger print in my life determine my way. thanks my GOD because you select for me the best father in world even for short period it is enough for me I am his daughter forever,,, For the man who want to see me the best one in the world so not just my research is for you but all my steps in the right way is because of you….

My Father

I could bring the star, or catch the moon or even gave them the sun, wouldn't just give them a little bit if what they do for me, for that I want to dedicate them this work hoping that will be proud of me,

My mother.

Acknowledgment

All thanks to Allah from the start

To the end.

I would like to thank my supervisor: **Dr: Babiker Ahmad Mohammed**

For his support and guidenss

I would like to thank all the family of Sudan University. I would like to thank my family, friends And all of people whose help me in this Research.

Abstract:

Pre-eclampsia is one of pregnency complications that is characterized by hypertension and proteinuria after the 20th week of gestation. The exact etiology of pre-eclampsia is un known, but its a common complication of pregnency that is associated with high maternal morbidity and mortality .

This is un analytical case control study carried out among 60 pregnant women with pre eclampsia (cases) matched in age with normal 60 pregnant women (control) at Atbara maternity hospitals , Aldamar maternity hospitals from May to September 2017.

The aim of the study was to determine the level of platelets count and platelets indicese among Sudanese pregnant women with pre-eclampsia compared with level among normotensive pregnant women and to identify whether there is any correlation between sevierity of pre-eclampsia and platelet count , mean platelet volume (MPV) , platelet distribution width (PDW) , and platelet large cell ratio (P-LCR) . Also to calculate lymphocyte to platelet and red cells to platelets ratios and correlated with degree of pre-eclampsia and to find out wether there is any association between gravidity , education , and family history of pre-eclampsia with the development of pre-eclampsia .

A short questionnaire was used to identify age ,education , occubation , gravida , parity , gestational age , history of hypertention , history of diabetes mellitus , family history of pre-eclampsia , other chronic or infectious disease , blood pressure and proteinuria .

Blood samples (2.5 ml) wre collected from the participents in EDTA anticogulant container . All samples were tested using haematology analyzer (Sysmex KX-21N model – Japan) . Data were analyzed using statistical package for social science software (SPSS) , and P-value was considered statistically significant at 0.05 .

Significant differences were found between the two studied groups with regard to platelet count, mean platelet volum (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR) (P.value 0.00) and between severe and mild case (p-value 0.02, 0.005, 0.008, 0.005) respectively .

The mean level of red blood cells to pletelet ratio (RPR) was found to be significantly high among pregnant women with severe preeclampsia (P value 0.002), wherreas, the difference between the means levels of platelet to lymphocyte ratio (PLR) of mild and severe type of preeclampsia was found to be insignificant (P value = 0.122).

This study suggested that, platelet count ,mean platelet volume (MPV), platelet distribution width (PDW) and platelets large cell ratio (P-LCR), and red blood cells to platelet ratio (RPR) can serve as early monitoring markers for the severity of pre-eclampsia (P.value0.02, 0.005, 0.008, 0.005, 0.002) respectively . It also revealed that primigravida and family history of pre-eclampsia were considered as one of the main risk factors for developing or experiencing pre-eclampsia (OR: 1.9, 17.7 respectively). Furthermore, educational level and family history of pre-eclampsia were found to be associated with developing pre-eclampsia (P-value =0.001 and 0.000 respectively).

المستخلص

ضغط الدم الجنيني هو أحد المضاعفات التي تحدث أثناء الحمل والذي يتميز بإرتفاع ضغط الدم ووجود فائض بروتين في البول بعد الإسبوع العشرين من الحمل . لايوجد سبب معروف ومحدد لحدوث المرض ولكنه من مضاعفات الحمل المعروفة والمرتبطة بمعدلات عالية من الإصبات والوفيات.

هذه دراسة تحليلية تم إجرؤها بين النساء الحوامل المصابات بضغط الدم الجنيني (الحالات) والنساء الحوامل الطبيعيات (المجموعة الضابطة) في مستشفى عطبرة للولادة ومستشفى الدامر للولادة في الفترة من مايو إلى أغسطس 2017.

الهدف من الدراسة هو قياس عدد ومؤشرات الصفائح الدموية لدى السودانيات المصابات بضغط الدم الجنيني ومقارنتها مع مستواها لدى الحوامل الطبيعيات , وكذلك تحديد ماإذا كانت هناك علاقة بين شدة المرض وعدد الصفائح الدموية, وتوصف حجم الصفيحة الدموية (MPV), عرض توزيع الصفائح الدموية (PDW) و(P–LCR), وربطها بشدة المرض .أيضا إكتشاف ما إذا كان هناك علاقة بين عدد الولادات , التعليم , وجود تاريخ عائلي للأصابة بالمرض .

اخذت 120 عينه من النساء الحوامل بعد اخطارهن بهذه الدراسه واخذت موافقتهن على المشاركه, 60 من الحالات المصابه بالمرض(الحالات) و60 امرأه حامل غير مصابات بالمرض (المجموعه الضابطه) وتم مقابله المجموعتين في الفئه العمريه .

استخدم استبيان مختصر لتحديد العمر ,السكن, مستوى التعليم, الوظيفه, عدد مرات الحمل , عدد الولدات, عمر الحمل , تاريخ الاصابه بضغط الدم , تاريخ الاصابه بمرض السكري, وجود تاريخ عائلي للاصابه بضغط الدم الجنيني, امراض اخري مزمنه او معديه, مقياس ضغط الدم ووجود فائض بروتين في البول.

تم سحب عينه دم (2.5 مل) في حاويه تحتوي على مانع تجلط (ثنائي الايثلين رباعي حمض الخل) من كل مشاركه. تم استخدام جهاز يعمل اتوماتيكيا لتحليل الدم الكامل (سسمكس) . تم تحليل البيانات احصائيا, وأخذت قيمه P للدلاله المعنويه عند 0.05 وجد ان هناك اختلاف ذو دلاله معنوية بين المجموعتين تحت الدراسه (الحالات المصابه والمجموعه الضابطه) فيما يتعلق بعدد الصفائح الدموية (PC) , متوسط حجم الصفيحه الدموية (MPV), عرض توزيع الصفائح الدموية (PDW) و (P–LCR) بنسبة معنوية (0.00)

وكذالك بين الحالات المعتدله والحالات الشديدة للمرض بنسبة معنوية (0.02,0.005,0.008,0.005) علي التوالي. وجد في هذه الدراسه ان هناك اختلاف ذو دلاله معنويه بين متوسط كريات الدم الحمراء الي الصفائح الدمويه (RPR) لدى الحالات الشديده المرض بنسبه معنويه(0.002) بينما لم يوجد اختلاف ذو دلاله معنويه بين متوسط نسبه الخلايا اللمفاويه للصفائح الدمويه (LPR).

اثبتت هذه الدراسه ان تعداد الصفائح الدمويه(PC) , متوسط حجم الصفيحه الدمويه(MPV) , عرض توزيع الصفائح الدموية(PDW) ونسبه كريات الدم الحمراء الى الصفائح الدمويه(P_LCR) يمكن ان تستخدم كمؤشرات للدلالة علي شده المرض بنسبة (0.02,0.005,0.008,0.002,0.005) علي التوالي .

اثبتت ايضا أن الحمل للمرة الاولي و وجود تاريخ عائلى لأصابه بالمرض تعتبر من العوامل الرئيسيه المهيئه للاصابه بالمرض لدي الحوامل في المستقبل بنسبه ارجحيه (1.9) (17.7) علي التوالي . علاوه علي ذالك وجد ان مستوي التعليم و وجود تاريخ عائلي للاصابة بالمرض له علاقه بحدوث المرض بنسبه معنوية (0.001, 0.000) علي التوالي. t

Table of Contents

Chapter One Introduction and Literature Review

Chapter Two: Material and Methodology

Chapter three: Results

Chapter four: Discussion, Content, and Recommendation

List of tables

List of figures

List of Abbreviations

Term	Abbreviation
5-HT	5-hydroxytryptamine
ADP	adenosine diphosphate
AIDS	Auto immune deficiency syndrome
ATP	adenosine triphosphate
CAMP	cyclic adenosine monophosphate
CBC	Complete blood count
CFU	colony-forming unit
DDAVP	diamino ,D-arginine ,vasopressin,
DIC	Disseminated Intracellular coagulation
DNA	Deoxyribonucleic acid
EDTA	Ethylene diaminate tetra acetic acid
FL	Femtoliter
Flt-L	FIt ligand
G-CSF	Granulocyte – colony stimulating factor
GEMM	granulocytes, erythrocytes, moenocytes and megakaryocytic
G PIIIa	glycoproteinIIIA
GP	glycoproteins
GM-CSF	Granulocyte –macrophage colony-stimulating factor
GMP	guanosine monophosphate
GP1a	glycoprotein la
GP1b	glycoprotein1b
GPIIb	glycoproteinIIb
HCG	human chorionic gonadotrophin
HELLP	Hemolysis elevated liver enzymes and low platelet

HIV	Human immunodeficiency virus
HLA	human leukocyte antigen
HPA-lA	Human platelet antigen-1A
HPA	Human platelet antigen
IL-1	Interleukin -1
IL-3	Interleukin 3
IL-5	Interleukin -5
ITP	Idiopathic thrombocytopenic purpura
Km	Kilometer
LD	Lower discriminator
L	Liter
M –CSF	macrophage colony-stimulating factor
MPV	Mean platelet volume
MW	molecular weight (MW
NO	Nitric oxide
PCT	Platelet –crit
PDGF	Platelet derived growth factor
PDW	Platelet distribution width
PG	Prostaglandin
PL	phospholipids
PLC-R	Platelet large cell ratio
PLR	Platelet lymphocyte ratio
RBCs	Red blood cell
RPL	Red blood cells to platelet ratio
SCF	stem cell factor
SLE	Systemic lupus erythromatous
SPSS	Statistical package for social science soft ware

TF	Tissue factor
TFP	Tissue factor pathway
TGF-β as	transforming growth factor-β
TNF	tumour necrosis factor
TPR	total peripheral resistance
TXA2	Thromboxane A2
TXA2	Thromboxane A2.
UD	Upper discrimination
VWF	von Will brand factor
WBCs	White blood cells
-γ IFN	γ-interferon

Chapter One

Introduction

Literature Review

1.1. Introduction

Pre-eclampsia is one of pregnancy complication that occur after the twentieth week of gestation (freitas et al ., 2013). the exact etiology of pre-eclampsia is un known ,but genetic predisposition and association with the presence of thrombophilia (tendency to clot) has been proposed(sibai,2010). Approximately 6% to 8% of all pregnancies are complicated by pre-eclampsia , most of them are less than 20 or greater than 30 years age (McCrae,2007). It is associated with high maternal morbidity and mortality, and it is common complication of pregnancy that causes intrauterine fetal growth retardation (Eiland et al.,2012). The disease affects multiple organ systems and it originates in the placenta and causes variable problems to both mother and fetus (Redman and Sargent,2005). HELLP syndrome is a variant of pre-eclampsia in which haemolysis , elevated liver enzymes, and low platelets are present .Women with pre-eclampsia who develop grandmal seizures have eclampsia (Fragento, 2006). Among the clinical signs and symptoms, decrease platelet count is an important character and is associated with HELLP syndrome (Schroeder, 2002), due to generalized endothelial cell activation, caused by enhanced vascular endothelial growth factor release, expression of adhesion molecules, lipid peroxidation, or activation of metalloproteases. This then leads to activation of platelets and coagulation cascade (Rodger et al., 2006). In Sudan, where pre-eclampsia and eclampsia are among the main causes of obstetric complication , there is extremely high maternal mortality (Ali and Adam, 2011). This high frequency of maternal morbidity and mortality needs improvement in obstetric care (Ali et al.,2012). Several aspects of pre-eclampsia in sudan were investigated (Elhaj et al.,2015). However ,there were no published research (to the best of our knowledge)on measurement of platelet count and indices in pre-eclamptic patients that carried out to find the role of platelet and platelet indices as predictors of it is severity . The aim of this study is to measure platelet count

and indices among pre-eclamptic women, and to determine their value in predicting the severity of pre-eclampsia for early intervention. Pregnancy is the period from conception to birth, occur after the egg is fertilized by sperm and then implantation in the of the uterus. It develops into placenta and embryo and later into fetus.

Pregnancy is status in which sign and symptoms vary from women to another, but the general and common sign is missed menstrual period and Worse, frequent urination, increase weight.

Pregnancy is measured in trimesters from the first day of your last menstrual period, totaling 40 weeks. The first trimester of pregnancy is1 week to12 week, or about 3 months. The second trimester is13 week to27 week. And the third trimester of pregnancy spans from28 week to the birth (Sheila Kitzinger., 1995).

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 a process of differentiation from the haemopoietic stem cell (Hoffbrand et al., 2006).

1.2 Literature review :

1.2.1 pre-eclampsia:

Pre-eclampsia is defined as the development of hypertension and proteinuria after the twentieth week of gestation. Specifically , systolic blood pressure of at least 140 mmHg or diastolic blood pressure of 90 mmHg must be present as well as proteinuria of at least 300 mg in a 24 –hour period . The presence of nondependent edema is no longer included in the definition of preeclampsia (Frageneto , 2006).

1.2.1.1 Patho physiology of preeclampsia :

The pathophysiological changes result in vascular lesions in uteroplacental vascular bed , peripheral vessel, and in various organ system, such as the

lungs, liver, brain, and kidneys. These pathophysiological abnormalities include:

1. Endothelial dysfunction
2. Inadequate maternal vascular response to placentation
3. Abnormal angiogenesis
4. Exaggerated inflammatory response with generalized vasospasm, activation of platelet, and abnormal haemostasis (Sibai, 2010) .

Although the cause of preeclampsia remains unclear, there is evidence that increase in circulating soluble fms-like tyrosine kinase 1, and decrease placental growth factor– the binding of circulating soluble fms-like tyrosine kinase 1 to placental growth factor and vascular endothelial growth factor- may have pathological role in developing preeclampsia (Levine et al.,2004) . Placental antiangiogenic factor are upregulated and disrupted in the maternal endothelial and cause :

1. hypertention
2. proteinuria
3. glomerular endotheliosis
4. HELLP (haemolysis, elevated liver enzyme level, and low platelet count) syndrome
5. cerebral edema (young et al., 2010).

1.2.1.2 Epidemiology of preeclampsia :

Systematic review by the World Health Organization as discussed by jeyabalan (2013) indicates that hypertensive disorders account for 16% of all maternal deaths in developed countries, 9% of maternal deaths in Africa and Asia, and 26% of maternal deaths in Latin America and the Caribbean.

The risks for the baby are poor growth and prematurity . In developing countries neonatal mortality and morbidity is higher than in developed one, due to limited access to neonatal intensive care of public hospital. 10%-15%

of maternal death are associated with pre-eclampsia and eclampsia, and perinatal mortality is high following pre-eclampsia, and higher following eclampsia (Duley, 2009).

1.2.1.3 Hematological changes during pregnancy:

Pregnancy place extreme stresses on the hematological system and an understanding of the physiological changes that result on obligatory in order to interpret any need for therapeutic intervention. These changes are:

- **physiological anemia**

Decrease in hemoglobin (Hb) concentration due to increased blood plasma volume by around 1250 ml, or 45% above normal.

- **iron deficiency anemia**

Up to 60 mg iron is required for the increase in red cell mass and a further 300mg for the fetus. Despite an increase in iron absorption, few women avoid depletion of iron reserves by the end of pregnancy (Hoffbrand et al., 2006).

- **Folate deficiency**

Serum folate level decrease to about half the normal range due to increased folate requirements,along with poor diet, this leads to development of megaloblastic anemia (Hoffbrand et al., 2006).

- **Thrombocytopenia**

The platelet count falls by approximately 10% in an uncomplicated pregnancy. In approximately 7% of women this fall is more sever and can result in thrombocytopenia (platelet count $<140\times10^9$ C/L) and this known as incidental thrombocytopenia (Hoffbrand et al., 2006).

The haematologist is usually consulted in one of three scenarios that cause thrombocytopenia during pregnancy:

1. Pre-existing thrombocytopenia--- most commonly, immune thrombocytopenia.

2. Decreasing platelet count or newly discovered thrombocytopenia in pregnancy, which may or may not be related to pregnancy?
3. Acute onset of thrombocytopenia in the setting of severe preeclampsia, the HELLP syndrome (haemolysis, elevated liver enzymes, low platelets) or acute fatty liver of pregnancy (Rajasekhar et al., 2013).

- **Haemostasis and thrombosis in pregnancy**

Pregnancy leads to hypercoagulable state with consequent increased risk of thromboembolism and disseminated intravascular coagulation (DIC) due to change in concentration of procoagulant, anticoagulant, and anti-fibrinolytic factors. There is an increase in plasma factor VII, VIII, X, vWF, and fibrinogen, and in addition to the increase in procoagulant factor, there is a concurrent decrease in the anticoagulants proteins and antithrombin as well as a decrease in the activity of the fibrinolytic system, most likely due to an increase in plasminogen activator inhibitors so fibrinolysis is suppressed (Hoffbrand et al., 2006: Rodger et al., 2006).

1.2.1.4 Classification of hypertensive disorders during pregnancy:

The hypertensive disorders of pregnancy is classified in to :

- Chronic hypertension which include patient with hypertension preceding but exacerbated by pregnancy.
- Preeclampsia-eclampsia .
- preeclampsia superimposed on chronic hypertension : in which a sudden increase in proteinuria or a sudden increase in blood pressure in a women with previously well controlled hypertension or in a women with elevated blood pressure and proteinuria prior to 20 weeks of gestation .
- Chronic hypertension: in which hypertension persists for more than 12 weeks postpartum.

- Gestational hypertension: which develop after 20 weeks of pregnancy but not associated with proteinuria (McCrae,2007).

1.2.1.5 Risk factors for preeclampsia:

Common risk factors are:

- Null parity.
- African- American race.
- Age more than 40 years.
- Preeclampsia with previous pregnancy.
- Diabetes.
- Multiple gestations.
- Lupus.
- Chronic renal disease.
- Obesity. (Fragento, 2006).

1.2.1.6 Criteria for severe pre-eclampsia :

- Systolic blood pressure of at least 160 mmHg, or diastolic blood pressure at least 110 mmHg on two occasions at least 6 hours apart.
- Proteinuria of at least 5g in a 24 hours period .
- Oliguria.
- Pulmonary edema.
- Impaired liver function.
- Visual or cerebral disturbances.
- Epigastric or right upper quadrant pain.
- Thrombocytopenia.
- Intrauterine growth restriction (Fragento, 2006).

For the diagnosis of mild pre-eclampsia, systolic blood pressure between 140 and 160 mmHg and diastolic blood pressure between 90 and 110 mmHg, and proteinuria > 1+ or 2+ on a urine dipstick was considered significant (Ramin, 2002).

1.2.1.7 Complication of preeclampsia and HELLP:

- Acute renal failure
- Pulmonary edema
- Abruptio plcentae
- Hypertensive encephalopathy
- Postpartum hemorrhage
- Wound or intra abdominal hematomas
- Liver hematoma with possible rupture
- DIC and multi organ failure, including liver, kidneys and lungs
- Neurologic like eclampsia
- Ischemia, infarcts, edema, and hemorrhage can also occur, as can cardiorespiratory arrest (Queenan et al., 2010).

1.2.1.8 Prevention and treatment of preeclampsia:

There is one single strategy that is of benefit in preventing the development of the disease, once the diagnosis of preeclampsia has been made, treatment options are limited, delivery of the fetus and placenta remain the only curative treatment (Norwitz et al., 2002).

Magnesium sulfate administered to preeclampsia to preeclampsia parturient for seizure prophylaxis.

Recent studies have demonstrated that it is more effective in preventing seizures than other drugs, including phenytoin and diazepam. While magnesium sulfate is administered to prevent seizures, it does produce other beneficial effects. A sustained decrease in systemic vascular resistance and an increase in cardiac index occur in preeclampsia patient receiving magnesium sulfate. This can lead to improved uteroplacental perfusion.

Parturient with severe hypertension will require antihypertensive therapy. Most obstetricians recommend treatment for systolic blood pressure > 160 to 170 mmHg or diastolic blood pressure > 105 to 110 mmHg. Intravenous hydralazine and labetalol are the most common antihypertensive agents used in pre-eclamptic patients (Fragento, 2006).

1.2.2 Pregnancy:-

1.2.2.1 DEFINATION:-

Pregnancy is the period from conception to birth , occur after the egg is fertilized by sperm and then implantation in the of the uterus. It develops into placenta and embryo and later into fetus (Edward Arnold., 2006).

1.2.2.2 Sign and symptoms:-

1-Amenorrhea:

An overdue menstrual period remains, for most women with a regular menstrual cycle, the first suggestion of pregnancy. Pregnancy is the commonest cause of amenorrhea but other causes such as disturbances in the hypothalamic-pituitary-ovarian axis or recent use of the contraceptive pill may be responsible.

2-Nausea or sickness:

Many women suffer some gastric upset in the early months of pregnancy, from nausea and anorexia to repeated vomiting, especially in the morning. The cause is unknown and raised levels of both estrogen and human chorionic gonadotrophin (HCG) in the circulation have been blamed. Gastric motility is reduced, and in early pregnancy, the lower esophageal sphincter is relaxed.

3-Bladder symptoms:

Increased frequency of micturition in the second and third months is due to combination of increased vascularity and pressure from the enlarging uterus. Near term, frequency may again appear due mainly to pressure of the fetal head on the bladder.

4-Breast changes:

The earliest symptoms and signs increased vascularity and a sensation of heaviness, almost of pain appear at 6weeks. By 8 weeks the nipple and surrounding area the primary areola have become more pigmented.

5-Uterine changes:

Although no longer commonly undertaken, uterine enlargement may be detected on bimanual examination at seven to eight weeks (Edward Arnold., 2006).

1.2.2.3 Insemination – the First Step in Pregnancy:-

After sexual intercourse millions of sperm swim through the cervix into the uterus and then up into the two fallopian tubes, which connect each of a woman's ovaries to her uterus. When an egg is released by one of the ovaries and is penetrated by a sperm cell, insemination has taken place and conception begins. The fertilized egg, now called a zygote, will have a full set of 46 chromosomes and the ability to become a whole new human being.

Implantation of the Fertilized Egg:-

After insemination, the zygote takes about five days to travel down the fallopian tube into the uterus (Kevin and Hanretty., 2003).

1. 2.2.4 The Timeline of Pregnancy:-

Pregnancy is measured in weeks from the first day of the mother's last period until childbirth. Pregnancy is also divided into a first trimester that includes weeks 1 through 12, a second trimester of weeks 13 through 26, and a third trimester of weeks 27 until childbirth.

- **5 Weeks into Pregnancy: Fetal Development:**

By this time the baby's brain, spinal cord, heart, and gastrointestinal system have already begun to form, the embryo will start to develop arm and

leg buds. The heart is beating regularly and blood is starting to move through rudimentary blood vessels.

- **8 Weeks into Pregnancy: Fetal Development:**

At the end of six weeks, the fetal heartbeat may be seen and heard during a special test called a vaginal ultrasound By seven weeks every one of the embryo's essential organs has started to form. By the end of eight weeks the embryo begins to look like a little human and becomes a fetus. The fetus has begun to develop facial features and is the size of a bean.

- **12 Weeks into Pregnancy: Fetal Development:**

The fetus' face is now well formed, and the liver is actively making red blood cells. The arms and leg buds have now become longer and are recognizable limbs. Genitals appear to differentiate the sex of the fetus, the head makes up about half of its body size and the fetus will close its eyes now until about week 28.

- **16 Weeks into Pregnancy: Fetal Development:**

At 16 weeks you can almost see through the fetal skin, and a very fine growth of hair, muscles and bones are coming together to form the skeletal system. The fetus starts to move and make sucking motions with its mouth. The liver and pancreas have formed, and the intestines have started to make the first bowel movement.

- **20 Weeks into Pregnancy: Fetal Development:**

By 20 weeks, the fetus is making itself known. What the mother felt as a slight fluttering at 18 weeks is now regular movement. The fetus can actually hear noises outside the womb. The heartbeat is loud enough to be heard with a stethoscope. Eyebrows and eyelashes have appeared and tiny nails have surfaced on the fingers and toes. The fetus is now about 8 inches long and 12 ounces in weight.

- **24 Weeks into Pregnancy: Fetal Development:**

At 24 weeks the fetus is well on its way to being the little person that will emerge at birth. It is so attuned to its environment that the mother may feel the fetus move suddenly when it is startled by a loud noise. The eyes are now completely formed, and the all-important air sacs are beginning to form in the lungs. The fetus has even developed its own unique fingerprints and footprints.

32 Weeks into Pregnancy: Fetal Development:

By 32 weeks the fetus should weigh approximately four pounds and be about 11 or 12 inches long. At this point, if a mother were to give, a baby could survive with the help of medical technology. The lungs make rhythmic movements as they practice breathing air. the eyes may start to blink open and shut .

- **36 Weeks into Pregnancy: Fetal Development:**

The fetus is now a baby getting ready for birth. Its skeletal system is still soft, but the baby has started to store calcium and iron. The skin begins to look like normal infant skin as the baby begins to gain weight and body fat. At 16 to 19 inches and 5 to 6 pounds, the baby will typically assume a head down position inside the womb in preparation for childbirth.

- **37 Weeks to Childbirth:**

After 38 weeks the infant is considered full term. The mother may actually notice a decline in baby movement because her little one has begun to run out of space in the womb. The fine lanugo hair has been replaced with normal scalp hair. The mother’s body pumps some final protective antibodies in through the placenta. The lungs are ready to take their first breath. Fetal development is complete. Childbirth is about to begin (Kevin and Hanretty ., 2003).

1.2.2.5 Biochemistry changes during pregnancy:-

Pregnancy is associated with normal physiological changes that assist the nurturing and survival of the fetus. Biochemical parameters reflect these adaptive changes and are clearly distinct from the non-pregnant state. The woman's renal function, carbohydrate and protein metabolism, and particularly the hormonal pattern are affected. It is critical to appreciate both normal and abnormal changes as laboratory results can influence the management of both mother and child (Edward Arnold., 2006).

1.2.2.6 Complication of pregnancy:-

Pregnancy is a normal event in life and as the majority of the population does not have medical disorder most women will remain medically fit and well for the duration of their pregnancy.

1-Heart disease:-

Is a more but potentially serious medical condition that complication approximately 1% of all pregnancies (Kevin and Hanretty ., 2003).

2-Hypertension:-

May complicate (5–7) % of all pregnancies risk factors for developing supper imposed pregnancy included hypertension renal disease. Maternal age (40 years) – diabetes connection tissue disease(Kevin and Hanretty ., 2003).

3-Diabetes mellitus:-

May complicate a pregnancy either because the women has preexisting insulin dependent diabetes before have pregnancy begin or she may be develop an impaired glucose tolerance during the causes of her pregnancy.

Approximately 1 – 2% of women will develop gestational diabetes during pregnancy (Kevin and Hanretty ., 2003).

4-Thyroid disorder:-

During pregnancy the production of thyroid binding globulin by the liver double as the result of estrogenic stimulation.

Hyperthyroidism in the mother occur in 1 even 500 pregnancies, in the majority of cases the condition has been diagnosed before pregnancy and 90% of case are secondary to and raves disease.

Hypothyroidism women treated with radioactive iodine will frequently by using thyroxin supplements and the dose should be check in early pregnancy to ensure appropriate level of FT4(thyroxine) and FT3(triiodothyronine) are available, 20% of patient who we hypothyrodic during pregnancy will remain so postally (Kevin and Hanretty ., 2003).

5-Adrenal disorder:-

Cushing's syndrome. All adrenal disease is rare in pregnancy, most common with Cushing syndrome are infertile and in the few reported cases of pregnancy as high incidence of the preterm delivery and still birth is described Addison syndrome.

Is usually an auto immune process, occasionally the disease may be present as crisis and fluid replacement inadequate treatment patient the pregnancy usually continues normally (Kevin and Hanretty ., 2003).

6-Respiratory disorder:-

Asthma is reversible bronchial airway obstruction a common complaint that may complicate up to 2% of pregnancies (Kevin and Hanretty ., 2003).

7-Haematological disorder:-

Anemia in pregnancy most commonly due to lack of haemoglobin production because of low lead of essentional precursors such as iron and foliate, less commonly it may be to chronic blood loss or haemolysis.

Thrombocytopenia the incidence of thrombocytopenia is a surprisingly common condition and may be present to some degree in 7 – 8% of pregnancy population.

A number of pregnancy complication have been associate with epilepsy including both anti partum and post partum hemorrhage, preeclampsia, preterm delivery and low birth weight.

Up to one- fifth of pregnancy will experience migraine, although 70% of migraine suffers feel that their migraine improves during pregnancy (Kevin and Hanretty ., 2003).

8-Gastro intestinal disorder:-

Acute fatty of pregnancy this is a very serious disorder of liver function occur in approximately 1 in 10.000 pregnancy.

The condition typically is noted in primiparous women and develop in the third trimester or within a few days of still birth.

Cholestosis of pregnancy is an uncommon condition of pregnancy occurring in approximately 1: 2000 pregnancies (Kevin and Hanretty ., 2003).

9-Skin disease:-

There are extensive physical change to the skin during pregnancy, increase pregnant during pregnancy, increase pigmentation usually especially on the face, areola, axillae and abdominal midline.

Preexisting skin condition such as eczema or psoriasis some time improve during pregnancy, perhaps because of increase level of corticosteroid (Philip and Baker ., 2008).

10-Renal disease:-

In very severe case of acute renal failure particularly when pregnancy related due to anti partum haemorrhage the is chemical insult to the kidney may exceed their regenerative capacity there is renal cortical necrosis and no recovery of renal function (Willialm Mershel ., 2008).

1.2.3 Platelets:-

1.2.3.1 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 a process of differentiation from the haemopoietic stem cell .

The megakaryocyte matures by endomitotic synchronous replication (i.e. DNA replication in the absence of nuclear or cytoplasmic division) enlarging the cytoplasmic volume as the number of nuclear lobes increase in multiples of two.

A pichlre of mature polyploid megakaryocytes.Very early on invaginations of plasma membrane are seen, called the demarcation membrane, which evolves through the development of the megakaryocyte into ahighly branched network At a variable stage in development, most commonly at the eight nucleus stage, the cytoplasm becomes granular .Mature megakaryocytes are 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 interval from differentiation of the human stem cell to the production of platelets averages approximately 10 days.

Tlhrombopoietin is the major regulator of platelet production and is constitutively produced by the liver and kidneys. Thrombopoietin increases the number and rate of maturation of megakaryocytes. Platelet levels start to rise 6 days after the start of therapy and remain high for 7-10 days. Unfortlmately, thrombopoietin is not available for routine clinical practice. Platelets also have receptors for thrombopoietin and remove it from the circulation. Therefore, levels are high in thrombocytopenia as a result of marrow aplasia and vice versa.

The normal platelet count is approximately 250 x 10^9 c/L (range 150-400 x 10^9 c/L) and the normal platelet lifespan is 7-10 days. Up to one-third of the marrow output of platelets may be trapped at any time in the normal spleen (Sheila Kitzinger., 1995).

1.2.3.2 Platelet structure:-

Platelets are extremely small and discoid, 3.0 x 0.5 11m in diameter, with a mean volume 7-11 fL.

The ultrastructure of platelets is represented in the granules are discharged into the open canalicularsystem.

Platelets are also rich in signalling and cytoskeletal proteins which support the rapid switch from quiescent to activation that follows vessel damage(Sheila Kitzinger., 1995).

1.2.3.3 Platelet antigens:-

Several platelet surface proteins have been found to be important antigens in platelet-specific autoimmunity and they have been termed human platelet antigens (HPA). In most cases, two different allelesexist, termed a or b alleles.

Platelets also express ABO and human leucocyte antigen (HLA) class I but not class II antigens (Sheila Kitzinger., 1995).

1.2.3.4 platelet function:-

The main function of platelets is the formation of mechanical plugs during the normal haemostatic response to vascular injury. In the absence of platelets, spontaneous leakage of blood through small vessels may occur. The immobilization of platelets at the sites of vascular injury requires specific platelet vessel wall (adhesion) and platelet-platelet (aggregation) interactions.

The blood flow conditions determine the specific receptor ligand interactions.

Platelet adhesion and platelet activation Following blood vessel injury, platelets adhere to tissue exposed subendothelial matrix proteins via specific adhesive glycoprotein (GP) (Sheila Kitzinger., 1995).

1.2.3.5 Platelet aggregation:-

It is characterized by cross-linking of platelets through active GPII /IIIa receptors with fibrinogen bridges. A resting platelet has about 50-80000 GPII/IIIa receptors, which do not bind fibrinogen, VWF or other ligands. Stimulation of a platelet leads to an increase in GPII/IIIa molecules, due to binding of a-granule membrane (rich in receptors) with the plasma membrane, activation of surface-exposed GPII/IIIa , enabling platelet cross-linking with fibrinogen bridges. Binding brings about molecular conformational changes resulting in a firm connection and further activation of the platelet, Platelet release reaction and amplification Primary activation by various agonists induces intracellular signalling, leading to the release of a and 0- granules. a-Granule contents play an important role in platelet aggregate formation and stabilization and, in addition, the ADP released from dense granules plays a major positive feedback role in promoting platelet activation. TXA2 is the second of the two major platelet positive feedback loops important in secondary amplification of platelet activation to firm a stable platelet aggregate.

It is formed de /laVa upon activation of cytosolic phospholipase A (PLA2) which is the rate limiting step.

This liberates arachidonic acid from the membrane phospholipids, and is metabolized by cycloxogenase to TXA2. It is a labile substance and lowers platelet cyclic adenosine monophosphate (cAMP) levels and initiates the release reaction .

Thromboxane A2 not only potentiates platelet aggregation, but also has powerful vasoconstrictive activity. The release reaction is inhibited by substances that increase the level of platelet cAMP.

One such substance is the prostaglandin prostacyclin (PGI2) which is synthesized by vascular endothelial cells. It is a potent inhibitor of platelet aggregation and prevents their deposition on normal vascular endothelium (Sheila Kitzinger., 1995).

1.2.3.6 Clot formation and retraction:-

The highly localized enhancement of ongoing platelet activation by ADP and TXA2 results in a platelet plug large enough to plug the area of endothelial injury. In this platelet plug the platelets are completely degranulated and adherent to each other.

This is followed by clot retraction which is mediated by GPIIb/IIIa receptors which link the cytoplasmic actin filaments to the surface bound fibrin polymers (Sheila Kitzinger., 1995).

1.2.3.7 Platelet procoagulant activity:-

After platelet aggregation and release, the exposed membrane phospholipid (platelet factor 3) is available for two reactions in the coagulation cascade.

Both phospholipid-mediated reactions are calciumion dependent. The first (tenase) involves factors IXa, VIlla and X in the formation of factor Xa.

The second (prothrombinase) results in the formation of thrombin from the interaction of factors Xa, Va and prothrombin (II). The phospholipid surface forms an ideal template for the crucial concentration and orientation of these proteins (Sheila Kitzinger., 1995).

1.2.4 Disorder of platelet function:

Disorders of platelet function are suspected in patients who show skin and mucosal haemorrhage and in whom the bleeding time is prolonged despite a

normal platelet count. These disorders may be hereditary or acquired (Sheila Kitzinger., 1995).

1.2.4.1 Hereditary disorder:

Rare inherited disorders may produce defects at each of the different phases of the platelet reactions leading to the formation of the haemostatic platelet plug (Sheila Kitzinger., 1995).

1-Thrombasthenia (Glanzmann's disease):

This autosomal recessive disorder leads to failure of primary platelet aggregation because of a deficiency of membrane GPIIb (gene on chromosome 17). It usually presents in the neonatal period and, characteristically, platelets fail to aggregate in *vitro* to any agonist except ristocetin (Sheila Kitzinger., 1995).

2-Bernard-Soulier syndrome:

In this disease the platelets are larger than normal and there is a deficiency of GPIb (chromosome 23).

There is defective binding to VWF, defective adherence to exposed subendothelial connective tissues and platelets do not aggregate with ristocetin. There is a variable degree of thrombocytopenia) (Sheila Kitzinger., 1995).

1.2.4.2 Acquired disorder:

1-Anti platelet drugs:

Aspirin therapy is the most common cause of defective platelet function. It produces an abnormal bleeding time and, although purpura may not be obvious, the defect may contribute to the associated gastrointestinal haemorrhage. The cause of the aspirin defect is inhibition of cyclo-oxygenase with impaired thromboxane A2 synthesis.

There is consequent impairment of the release reaction and aggregation with adrenaline and adenosine diphosphate (ADP), After a single dose the defect

lasts 7-10 days, i.e. the life of the platelet. Aspirin is contraindicated in patients with gastrointestinal or genitourinary bleeding, retinal bleeding, peptic ulcer, haemophilia or severe hypertension (Sheila Kitzinger., 1995).

2-Hyperglobulinaemia:

Hyperglobulinaemia associated with multiple myeloma or Waldenstrom's disease may cause interference with platelet adherence, release and aggregation (Sheila Kitzinger., 1995).

3-Uraemia:

This is associated with various abnormalities of platelet function. Heparin, dextrans, alcohol and radiographic contrast agents may also cause defective Function (Sheila Kitzinger., 1995).

4-Thrombocytopenia:

Abnormal bleeding associated with thrombocytopenia or abnormal platelet function is characterized by spontaneous skin purpura and mucosal haemorrhage and prolonged bleeding after trauma (Sheila Kitzinger., 1995).

- **The main causes of thrombocytopenia are listed in follow**:

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.
- Leukaemias, lymphoma, myeloma, myelofibrosis, carcinoma.
- Hereditary thrombocytopenia (rare condition).

Increased desrtruction or consumption of 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 erythromatous (SLE), other connective tissue disorders, chronic lymphatic leukemia, lymphomas and HIV/AIDS. Also, exposure to drugs, e.g. quinine, mefloquine, penicillin, and some herbal remedies (Sheila Kitzinger., 1995).

Thrombocytosis:

Causes of an increase in platelet numbers include:

- Chronic myeloproliferative diseases, e.g. essential thrombocythaemia, polycythaemia vera, 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 (Cheersebrought ., 2000).

1.2.5 The effect of pre-eclampsia on platelet count and indices:

The platelet activation is major cause of accelerated platelet clearance in this disorder, and this argument is supported by increased plasma level of the platelet α- granule proteins thromboglobulin and platelet factor 4, as well as the increased level of β- thrombpxane A2 metabolites in the urine of preeclamptic patient. The activation of coagulation system and generation of thrombin leads to platelet activation with accelerated clearance of activated platelet. The platelet contact with exposed subendothelium underlying the injured placental vasculature, increased level of von Willebrand factor (vWF), as well as adhesive proteins such as fibronectin also cause platelet activation. Patient with preeclampsia also display microangiopathic hemolytic anemia due to red cell fragmentation, due to shearing of red cell

on fibrin strands in the microvasculature or placental circulation (McCrae, 2007). Platelet when activated increase number and size of pseudopodia which in turn increase the size of platelet leading to large platelets formation. The mean platelet volume (MPV), and platelet distribution width (PDW) are platelet indices that increased during platelet activation (Vagdatli et al., 2010). The MPV is measured by clinical hematology analyzers and it is used as marker for platelet function and activation, and it is increased in certain vascular risk factor states, such as hypercholestrolaemia, diabetes mellitus, and preeclampsia. An elevated MPV predicts a poor outcome following myocardial infarction and the development of pre-eclampsia (Bath Butterworth, 1996). The PDW is calculated by the hematology analyzers, by measuring the width of the size distribution curve (in femtolitre (fl)) at the 20% level when the peak distribution curve is taken as 80% or 100% (Briggs et al., 2007). The automated blood count shows an increased MPV and PDW when there is increased platelet consumption or destruction and low MPV when there failure of bone marrow output (Bain, 2006).

1.2.6 previous and relevant studies :

Boriboonhirunsarn et al study showed that MPV in severe pre eclamptic women is statistically greater than in normal pregnant women (Boriboonhirunsarn et al.,1995).

A previous longitudinal study in Turkey provided evidence that mean platelet volume (MPV)gradually increased in pregnant women affected by pre-eclampsia compared to women with normal pregnancies (Dundar et al.,2008).

Other study in Brazil found that lower platelets count were observed in sever pre-eclampsia compared to normal pregnant and non pregnant women (Freitas et al.,2013).

A study was conducted among normal and pre-eclamptic pregnancies, and they found that there was increase in mean platelet volume (MPV)in patient with pre-eclampsia and suggested that mean platelet volume (MPV) my serve as early monitoring marker for the severity of pre-eclampsia (Han et al.,2014).

Recently study was conducted in Korea and the research found that, as the desease progressed, there was decrease in platelet count, and increase in mean platelet volume (MPV) and platelet distribution width (PDW). Also they suggested that PDW can serve as a candidate marker for predicting the severity of pre-eclampsia (Yang et al.,2014).

On the other hand some studies disagreed with the above studies, they found that there were no prognostic significance of complete blood count (CBC), platelet count, and mean platelet volume (MPV) on the presence and/or severity of pre-eclampsia (Ceyhan., 2006).

Another study in Turkey found that, increase mean platelet volume (MPV) was not a significant predictor for pre-eclampsia, and did not differ both between mild and severe pre-eclampsia, and normotensive pregnant women (Altinbas et al., 2012).

Duckitt and Harrington (2005) in their study proved that nulliparity and family history of pre-eclampsia were strong risk factor almost increasing the risk of pre-eclampsia .

The mean platelet volume (MPV) and platelet to lymphocyte ratio (PLR) did not show statistically significant difference between patients with severe pre-eclampsia (PE), healthy pregnant and non- pregnant women (Yavuzcan et al., 2014).

1.3 objectives:

1.3.1 General objective:

To determine the platelets count and platelets indices among Sudanese women with pre-eclampsia compared with the level among normotensive pregnant women in some Atbara maternity hospitals.

1.3.2 Specific objective:

1. To measure platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR) in pregnant women with pre-eclampsia and correlated it with those in pregnant women without pre-eclampsia .
2. To identify whether there is any correlation between severity of pre-eclampsia and platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR).
3. To calculate lymphocyte/platelet and red cell/platelet ratios and correlate it with the degree of pre-eclampsia .
4. To find out the possible association between age, education, and family history of pre-eclampsia with the development of pre-eclampsia.

1.4 Justification:

Pre-eclampsia is an obstetric disorder that is associated with maternal and prenatal morbidities. Timely accurate diagnosis of the disease is the very important and helpful in preventing the poor outcome of the disease.

Sudan is one of the developing countries, where pre-eclampsia is one of the main causes of obstetric complication with high maternal morbidities and mortality. Because of the important of the disease for both mother and babies along with the significant increase in the affected individuals among pregnant ladies, a reliable predictor for pre-eclampsia will play an important role in early prevention and intervention.

This study was conducted to determine the changes in platelets count and indices among pre-eclamptic women and to verify their value in predicting the severity of pre-eclampsia for early intervention, since they are simple and routinely done tests, with lower cost and greater accessibility in clinical laboratory.

Chapter Two

Material and Methodology

2.1. Study design:-

A case-control study, conducted in Aldamar locality during the period from May to September 2017 that aimed to determine the changes in platelet count and indices among pre-eclamptic women and to verity their value in predicting the severity of pre-eclampsia for early intervention.

2.2. Study area:-

The study was done in Aldamar locality which is located in the north of sudan and north of the capital khartoum and for about 300km, and to the north of shendi for about 157km, located in the east side of the River Nile, most of population are farming.

2.3. Inclusion criteria:-

Any pregnant lady diagnosis with preeclampsia having high blood pressure and protein urea included in this study.

2.4. Study population sampling:-

Patient with pre-eclampsia investigated for platelet and platelet indices, according to design of study the sample (case) selected by a simple random sampling method (probability sampling).sixty samples of patient (case (pregnant with preeclampsia)) matched by sixty samples as controls (pregnant without preeclampsia).

2.5. Sample collection:

2.5 ml of venous blood was taken from adult and transferred into an EDTA container. The sample was then sent as early as possible (maximum 3 to 6 hours) to Modern Medical Analysis Centre for analysis. For haematological parameters a standard coulter gram use for diagnosis was done on the hematological analyzer (Sysmex).

2.6. Ethical consideration

Informed consent was attached to each questionnaire to be obtained from the patient verbally. There was full commitment precaution sample taken and privacy and confidentiality.

2.7. Data collection tools:-

Informations from pregnant women were collected by performed questionnaire.

2.8. Data collection technique:-

Fresh venous in EDTA container are taken to platelet and indices count.

2.9. Principle and procedure of the method used:

Automated blood count (Sysmex KX-21N model – Japan)**:**

Principle:

The blood is well mixed (though not shaken) and placed on a rack in the analyzer. This instrument has many different components to analyze different elements in the blood. The cell counting component counts the numbers and types of different cells within the blood. The results are printed out or sent to a computer for review. Blood counting machines aspirate a very small amount of the specimen through narrow tubing. Within this tubing, there are sensors that count the number of cells going through it, and can identify the type of cell; this is flow cytometry. The two main sensors used are light detectors, and electrical impedance. One way the instrument can tell what type of blood cell is present is by size. Other instruments measure different characteristics of the cells to categorize them. Because an automated cell counter samples and counts so many cells, the results are very precise. However, certain abnormal cells in the blood may be identified incorrectly, and require manual review of the instrument's results and identifying any abnormal cells the instrument could not categorize.

In addition to counting, measuring and analyzing red blood cells, white blood cells and platelets, automated hematology analyzers also measure the amount of hemoglobin in the blood and within each red blood .

Equipment:

- Syringe
- Cotton
- EDTA container
- Dettol
- Blood sample
- Hematological analyzer

Principle of:

PLT count

PLT (10^9/L) is measured directly by counting the platelets passing through the aperture.

MPV

Based on the PLT histogram, this analyzer calculates the mean platelet volume (MPV,fL).

PDW

Platelet distribution width (PDW) is the geometric standard deviation (GSD) of the platelet size distribution. Each PDW result is derived from the platelet histogram data and is reported as 10 (GSD).

PCT

This analyzer calculates the pct as follows and expresses it in %.

Where the PLT is expressed in 10^9/L and the MPV in fL.

PCT = PLT x MPV/10000

Method

Blood samples were drawn into a test tube containing EDTA and then mixed gently. RBCs count, HCT, Hb concentration, haematimetric indices (MCV, MCH, and MCHC), RDW, WBCs and platelets counts were measured by

using an automatic blood cell counter (Mindray -3000 analyzers). The assay was performed according to the instructions provided by the manufacturer. The analyzer was controlled by normal control, abnormal high and abnormal low.

Chapter three

Results

Chapter three

3- Results:

This case-control study involved sixty pregnant women with pre-eclampsia (cases) and other disease free pregnant women (control) who attended three maternity hospitals in Atbara city.

The study showed that the average systolic blood pressure among cases was found to be 165mmHg compared with 112mmHg among controls. Average diastolic blood pressure was found to be 103 mmHg among cases compared with 74 mmHg among controls, with an overall average of diastolic pressure of 89mmHg.Thirty(25%) of the cases showed protein urea level of (+++),whereas 13(10.8%) of them showed a level of(++++).

Table 3.1 : Distribution of study sample according to age.

Cross tabulation		Type	
		Case (pregnant with preeclampsia)	Control (healthy pregnant)
Age group (years)	15-20	20(33%)	7(11%)
	21-26	20(33%)	18(30%)
	27-32	15(25%)	23(38%)
	32-38	5(8%)	12(20%)
Study population= 120(100%)			

Distribution of the participants of the two groups (case and controls) according to their ages, showed that 20(33%) and 7(11%) of them were found to have been falling in the age group (15-20) years ,whereas 20(33%) and 18(30%) of them were found to have been falling in the age group (21-26) years, whereas 15(25%) and 23(38%) of them were found to have been falling in the age group (27-32) years, whereas 5(8%) and 12(20%) of them were found to have been falling in the age group (33-38) years in case and control respectively with an overall average age of 26 years and standard deviation , as a measure of variability (dispersion), of 26 years as seen in table (3.1.).

Table 3.2 : Distribution of the two study groups according to the potential risk factors .

Cross tabulation		Case (Pregnant with preeclampsia)	Control (Healty pregnant)
Educational level	Basic	33 (55%)	11 (18.3%)
	Secondary	11 (18.3%)	18 (30%)
	University	16 (26.7%)	31 (51.6%)
Gravidity	1-2	46 (76.7%)	19 (31%)
	3-5	14 (23.3%)	41 (69%)
Parity	None	35 (58.3%)	24 (40%)
	1-2	17 (2803%)	14 (23.3%)
	3-4	8 (13.4%)	22 (36.7%)
Family history of preeclampsia	Yes	32 (53.3%)	1 (1.7%)
	No	28 (46.7%)	59 (98.3%)
Study population = 120 (100%)			

According to their level of education it was noticed that 33(55%) and 11(18%) of case and control respectively having basic education with an illiteracy rate 21.7% shows the distribution of the participants of two groups (case and control) according to the potential risk factor 32(53%) ,1(1.7%) respectively , where cases showed a lower level of education less than the controls , 46(76%) were have gravid 1to 2 ,whereas 14(23.3%) were having gravid 3to 5 ,with an overall average gravid of 3, with slight differences in gravid among both cases and controls , 35(58.3%) ,24(40%) of cases and control respectively were found to have zero parity (primigravida), whereas 17(28.3%) ,14(23.3%) of case and control were having parity 1to2 and 1 to3 r respectively and 8(13.4), 22(36.6%) of case and control were having parity

3to 4 and 4to 5 respectively ,parity 1 to 2 were grater among cases compared with control . It was found that family history of pre eclampsia was present among 32(53.3%) of the families of cases compared with1(1.6%)among the families of the controls. table (3.2)

Table 3.3 : The effect of preeclampsia on complete blood count .

T-test		Mean	Std Deviation	P-value
TWBCS ($X10^3$/uL)	Case (Pregnant with preeclampsia)	12.7	4.2	0.000**
	Control (Healthy Pregnant)	7.7	2.1	
RBCs ($x10^6$ /uL)	Case (Pregnant with preeclampsia)	4.3	0.7	0.445
	Control (Healthy Pregnant)	4.2	0.5	
HGB (g/dL)	Case (Pregnant with preeclampsia)	11.2	2.1	0.141
	Control (Healthy Pregnant)	11.6	1.3	
HCT (%)	Case (Pregnant with preeclampsia)	32.8	5.6	0.270
	Control (Healthy Pregnant)	33.7	3.5	
MCV (fL)	Case (Pregnant with preeclampsia)	76.9	6.4	0.001**
	Control (Healthy Pregnant)	80.5	5.0	
MCH (Pg)	Case (Pregnant with preeclampsia)	26.3	3.2	0.003**
	Control (Healthy Pregnant)	27.8	2.2	
MCHC (g/dL)	Case (Pregnant with preeclampsia)	34.0	2.0	0.101
	Control (Healthy Pregnant)	34.6	1.5	

PLT (x102	Case (Pregnant with preeclampsia)	185.5	78.1	0.000**
	Control (Healthy Pregnant)	257.7	66.6	
RDW-SD (FL)	Case (Pregnant with preeclampsia)	45.4	4.7	0.001**
	Control (Healthy Pregnant)	42.9	3.8	
RDW-CV (%)	Case (Pregnant with preeclampsia)	16.2	2.8	0.000**
	Control (Healthy Pregnant)	14.1	1.4	
PDW (FL)	Case (Pregnant with preeclampsia)	15.5	3.5	0.000**
	Control (Healthy Pregnant)	12.6	2.0	
MPV (FL)	Case (Pregnant with preeclampsia)	10.8	1.1	0.000**
	Control (Healthy Pregnant)	9.8	1.0	
P-LCR(%)	Case (Pregnant with preeclampsia)	32.8	8.6	0.000**
	Control (Healthy Pregnant)	24.1	7.0	

*T- Test P. value < 0.05 that's considered statistically significant.

A vast number of significant differences between the two means of platelets count ($x10^3$ /uL),platelet distribution width (PDW(fl)), means of platelet volume (MPV(fl)),and platelet large cell ratio (P-LCR(%)) between cases and control was highly significant (P-value = 0.00) as seen in table 3.3

Table 3.4 : The effect of the grade of preeclampsia on complete blood count.

T-test	Preeclampsia	Mean	Std. Deviation	P-value
TWBCS ($X10^3$/uL)	Mild	13.1	5.2	0.574
	Severe	12.5	3.7	
RBCs ($x10^6$ /uL)	Mild	4.2	0.7	0.760
	Severe	4.3	0.8	
HGB (g/dL)	Mild	11.0	1.9	0.669
	Severe	11.3	2.2	
HCT (%)	Mild	32.6	5.5	0.842
	Severe	32.9	5.7	
MCV (fL)	Mild	77.0	5.8	0.978
	Severe	76.9	6.8	
MCH (Pg)	Mild	26.1	2.6	0.711
	Severe	26.4	3.6	
MCHC (g/dL)	Mild	33.8	1.5	0.508
	Severe	34.2	2.2	
PLT (x102	Mild	216.1	56.9	0.020**
	Severe	167.8	83.7	
RDW-SD (FL)	Mild	43.6	3.9	0.016**
	Severe	46.5	4.7	
RDW-CV (%)	Mild	15.3	2.0	0.041**
	Severe	16.8	3.0	
PDW (FL)	Mild	14.0	2.9	0.008**
	Severe	16.4	3.5	
MPV (FL)	Mild	10.3	1.0	0.005**
	Severe	11.1	1.1	
P-LCR(%)	Mild	28.7	8.0	0.005**
	Severe	35.1	8.2	

***T- Test P. value less than 0.05 that's considered as statistically significant.**

Among severe and mild cases (P value 0.02, 0.008, 0.005,0.005) respectively , as seen in table 3.4 .

Table 3.5: Univariate analysis for individual factors in the studied groups (case and control) .

Cross tabulation		Type		Pearson Ch-Square Value	P-Value
		Case	Control		
Educational level	Basic	33 (55%)	11 (18.3%)	1.30	0.000**
	Secondary	11 (18.3%)	18 (30%)		
	University	16 (26.7%)	31 (51.6%)		
Family history of preeclampsia	Yes	32 (53.3%)	1 (1.7%)	0.89	0.004**
	No	28 (46.7%)	59 (98.3%)		
Age group (Years)	15-20	20(33%)	7(11%)	4.03	0.181
	21-26	20(33%)	18(30%)		
	27-32	15(25%)	23(38%)		
	32-38	5(8%)	12(20%)		

*Chi square P value < 0.05 that's considered statistically significant

Chi square test, as nonparametric test of association, showed that educational level and family history of pre-eclampsia as independent variables, were found to be associated with the developing pre-eclampsia as dependent variable, P-values were highly significant(P value = 0.000 and 0.004 respectively) as seen in table 3.5.

Table 3.6: Univariate analysis for individual factors according to the degree of pre-eclampsia .

Cross tabulation		Preeclampsia		Chi square value	P value
		Mild	Severe		
Age group (Years)	15-20	10(16.6%)	10(16.6%)	0.572	0.363
	21-26	9(15%)	11(18.3%)		
	27-32	8(13.4%)	7(11.7%)		
	32-38	4(6.7%)	1(1.7%)		
Family history of preeclampsia	Yes	17(28.3%)	15(25%)	0.809	0.813
	No	14(23.3%)	14(23.3%)		
Educational level	Basic	15(25%)	18(30%)	0.279	0.155
	Secondary	5(8.3%)	6(10%)		
	University	11(18.8%)	5(8.3%)		

*Chi square value > 0.05 that's considered statistically insignificant.

Age, educational level, and family history of pre-eclampsia were not associated with the degree of pre eclampsia as shown in table 3.6.

Table 3.7 : Differences between means of platelet to lymphocyte ratio and red blood cell to platelet ratio in the studied cases.

Variable	Degree of preeclampsia	N	Mean	Std. Deviation	P-value
PLR	mild	22	102.9	40.6	0.122
	Severe	38	82.3	52.9	
RPR	Mild	22	20.7	5.9	0.002**
	Severe	38	31.9	15.8	

*T –test P. value < 0,05 that's considered statistically significant.

For red blood cell to platelet ratio(RPR), the difference between the means levels of mild and severe type of pre-eclampsia was found to be significant(P-value = 0.002) ,Red blood cell to platelet ratio (RPL) was found to weekly correlated with the degree of pre- eclampsia as shown in table 3.7.

Table 3.8 : Differences between percentages of platelet count and indices in the cases and control .

Cross tabulation		Type		Chi square value	P value
		Case	Control		
PLT ($x10^3$ /uL)	Normal	44(73.3%)	59(98.3%)	23.720	0.000**
	Low	16(26.7%)	1(1.7%)		
PDW (fL)	Low	1(1.7%)	1(1.7%)	12.131	0.002**
	Normal	45(75%)	59(98.3%)		
	High	14(23.3%)	0		
MPV (fL)	Low	3(5%)	5(8.3%)	6.274	0.044**
	Normal	43	54(90%)		
	High	14(23.3%)	1(1.7%)		
P-LCR (%)	Low	0	4(6.7%)	7.883	0.019**
	Normal	48(80%)	56(93.3%)		
	High	12(20%)	0		
Study population = 120 (100%)					

*Chi square P value < 0.05 that's considered statistically significant.

Apllication of Chi square test among cases and controls as regarding the platelets count($x10^3$/uL), mean platelet volume (MPV(fl)) platelets distribution width (PDW(fl)), and platelets large cell ratio(P-LCR(%))as a

test of significance of differences between percentages ,the following results were obtained , as shown in table(3.8). There was a significant difference between cases and controls regarding platelet count .Cases showed a high percentage of low platelets count than controls, P-value (0.000) which is highly significant.

The difference in percentages between cases and controls regarding platelets distribution width (PDW) was quite significant. High PDW (fL) was greater among cases than control. None of the controls has shown high PDW (fL).

Mean platelets volume (MPV(fl)) was significantly among cases than controls.

Platelets large cell ratio (P-LCR (%)) was significantly among cases compared with controls where none of the controls had shown any high P-LCR (%).

Table 3.9 : The association of the degree of pre-eclampsia and platelet count and indices.

Cross tabulation		Preeclampsia		Chi square value	P value
		Mild	Sever		
PLT ($x10^3$ /uL)	Normal	20(33.3%)	18(30%)	11.375	0.001**
	Low	2(3.3%)	20(33.3%)		
PDW (fL)	Low	1(1.7%)	0	3.522	0.172
	Normal	19(31.7%)	29(48.3%)		
	High	2(3.3%)	9(15%)		
MPV (fL)	Low	1(1.7%)	0	5.400	0.067
	Normal	21(35%)	32(53.3%)		
	High	0	6(10%)		
P-LCR (%)	Low	1(1.7%)	0	5.400	0.067
	Normal	21(35%)	32(53.3%)		
	High	0	6(10%)		

*Chi square P value < 0.05 that's considered as statistically significant.

Table 3.9 showed significant differences between the percentages of severe pre-eclampsia and low platelet count ,P-value(0.001).Those with severe pre-eclampsia showed low level of platelets count.

Table 3.10 : The association of family history of preeclampsia and the studied disease.

Cross tabulation		Type		Total
		Case	Control	
Family history of preeclampsia	Yes	37 (30.8%) A	5 (4.2%) B	42 (35%) A+B
	No	23 (19.2%) C	55 (45.8%) D	78 (65%) D+C
Total		60 (50%) A+C	60 (50%) B+D	120 (100%) A+B+D+C
Odds Ratio = ((a*d)/(c*b)) =17.7 CIM (6.173-50.724)				

Table 3.11 : The association of gravidity and the studied disease.

Cross tabulation		Type		Total
		Case	Control	
Gravidity	Primigravida	28 (23.3%) A	19 (15.8%) B	47 (39.2%) A+B
	multigravida	32 (26.7%) C	41 (34.2%) D	73 (60.8%) C+D
Total		60 (50%) A+D	60 (50%) A+D	120 (100%) A+B+C+D
Odds Ratio = ((a*d)/(c*b)) =1.9 CIM (0.898-3.972)				

Risk factors (Family history of preeclampsia and Gravidity): Case (Pregnant with preeclampsia) more likely to be exposed than Control (Healthy pregnant) with odd ratio 17.7 and 1.9, respectively.

Computation of odds ratio(OD) among cases and controls in regard to family history of pre-eclampsia and gravidity, revealed that those with family history of pre- eclampsia were more likely to develop the disease almost 18 times as those of no family history of pre-eclampsia ,and primigravida ladies were more likely to develop the disease almost twice as multigravida one , as shown on table 3.10 and 3.11.

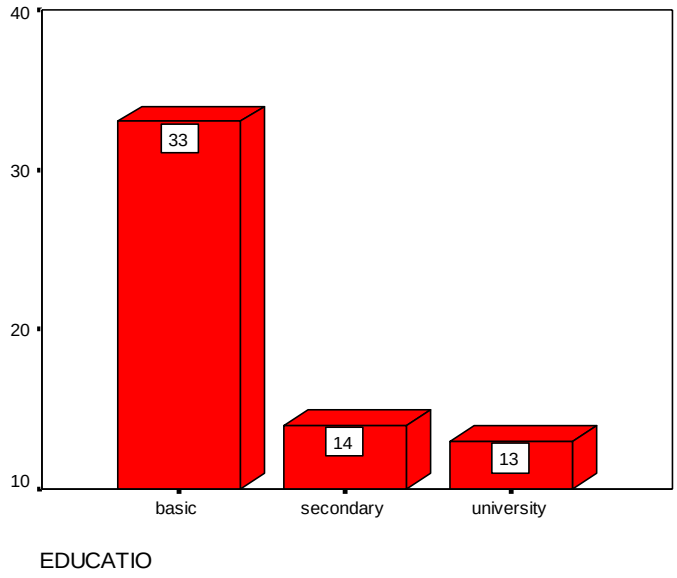

Figure 3.1: Distribution of the study sample according to educational level.

According to their level of education it was noticed that 33(55%) and 11(18%) of case and control respectively having basic education with an illiteracy rate 21.7%

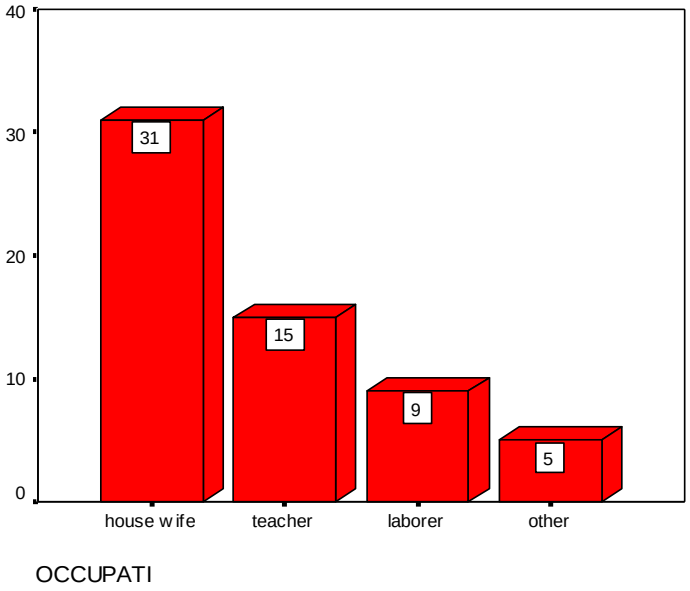

Figure 3.2: Distribution of the study sample according to occupation.

The results showed that 31(51.7%) of the participants in the case group (n=60) were house wives, whereas 15(25%)of them were teachers

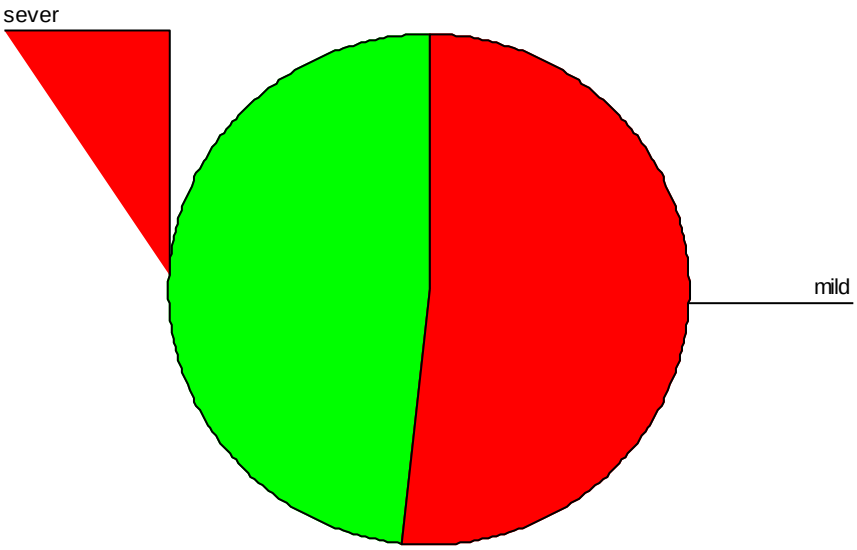

Figure 3.3: Distribution of pre-eclampsia patients according to degree of preeclampsia.

Sever pre-eclampsia was shown by 38 (63.3%) of cases(n = 60),whereas the mild type was seen among the rest

Chapter four

Discussion, Content, and Recommendation

4.1 Discussion:

This case-control study involved 120 Sudanese pregnant women (60 with preeclampsia and 60 diseases free) who attended three maternity hospitals in Atbara State during the study period.

The outcome of this study is that primigravida women had twice time chance to develop pre-eclampsia than multigravida women (Odd ratio 1.9). Family history of pre-eclampsia was present among the families of 53.3% of the cases compared with only 1.7% of the control.

Family history of pre-eclampsia was considered as one of the main predisposing factor of developing or experiencing pre-eclampsia in the future and that was statistically proved in this study where the computed odds ratio , as a risk factor was found to be very high (17.7).

These findings agreed with controlled cohort studies which showed that the risk of pre-eclampsia was increased in women with nulliparity (odds ratio 2.91 ,1.28 to 6.61) and family history of pre-eclampsia (odds ratio 2.9 ,1.7 to 4.93) (Duckitt and Harrington, 2005). Proteinuria at the rang of (++-+++) was present among all cases where level of proteinuria of (+++) was dominant among cases (50%) . Zhuang et al (2015) found that 84% of cases had proteinuria >= 0.3g/24hour (P value 0.000) which prove that proteinuria is an important diagnostic criterion for preeclampsia . In this study it was found that the difference between the two means of mean platelet volume (MPV) among the cases and control was highly significant (P value 0.000). On contrast, a study done in Turkey found that increased mean platelet volume (MPV) was not significant predictor for pre-eclampsia and did not differ between mild and severe pre-eclampsia, and pre-eclampsia, and normotensive pregnant women (Altinbas et al., 2012).

Whereas this study agreed with another study which provided evidence that MPV gradually increases in pregnant women affected by pre-eclampsia compared to women with normal pregnancies (Dundar et,2008).

Interestingly there was significant difference the two means of platelets distribution width(PDW) among the cases and control(P-value 0.000) and among the sever and mild case (P-value 0.008).

This similar to study done in Korea which suggested that PDW can serve as a candidiate marker for predicting the severity of eclampsia (Yang et al.,2014).

The same study proved that as the disease progresses, there is decrease in platelet count which agrees with this study in which there was significant difference between the two mean of platelet count among cases and control(P-value 0.00) and among severe and mild cases(P-value 0.002), but this was not found in literature review, whereas, the difference between the means levels of platelet to lymphocyte ratio (PLR) of mild and severe type of pre-eclampsia was found to be in significant (P-value 0.122).

This agrees with Yavuzcan et al (2014) who found that PLR is not an effective marker for sever PE (P-value =0.098).

Pre-eclampsia was found to be weakly and negatively associated with platelets count. Weak positive correlations were found between pre-eclampsia and both mean platelets volume (MPV) and platelets large cell ratio (P-LCR).so ,low platelets count can be considered as an indicator for severe pre- eclampsia .

This agrees with a study in brazil which found that lower platelets counts were observed in severe pre-eclampsia compared to normal pregnant and to non pregnant women (Freitas el al .,2013). On the other hand this study agreed with (Boriboomhirunsarn et al.,1995) who suggested that MPV in severe preeclamptic women is statistically greater than in normal pregnant women also this study agreed with (Han et al .,2014) who found that there was an increase in the mean platelet volume MPV in patient with pre-eclampsia and suggested that mean platelet volume(MPV) may serve as an early monitoring marker for the severity of pre-eclampsia.

4.2 Conclusion:

1-Primigrvida ladies were more likely to develop pre-eclampsia than multigravida ones.

2-Family history of pre-eclampsia was found to be associated with development of pre-eclampsia.

3- The difference between the two means of platelets count, mean platelets volume (MPV), platelet distribution width(PDW),and platelets large cell ratio (P-LCR) , for cases and control were found to be highly significant .

4-Aweak correlation was found between the degree of pre-eclampsia and platelet count(negative), mean platelet volume and platelet large cell ratio (positive).

5-Age, educational level and family history of pre-eclampsia were not associated with degree of pre-eclampsia.

6-The mean level of red blood cells to platelets ratio (RPR) was found to be significantly high among pregnant women with severe pre-eclampsia while platelet to lymphocyte ratio (PLR) was not.

4.3 Recommendations:

1. More prenatal care should be taken specially with primigravida women and pregnant women who have family history of the disease.
2. In women with pre-eclampsia, the platelet count can be used as a valid measurement tool to predict the progress of the disease.
3. Measurement of platelet count and indices (MPV, PDW and P-LCR) should be done as a useful marker for the prediction of pre-eclampsia**.**
4. Further community – based studies with large sample size are recommended to verify these findings.
5. Follow up for pre-eclamptic women after delivery should be taken and also for there babies .Neonatal intensive care should be found in all public hospital .

Reference:

Ali A.A. and Adam I. (2011). Lack of antenatal care , education , and high maternal mortality in Kassala Hospital , Eastern Sudan during 2005-2009. J Matern Fetal Neonatal Med **.** 24 (8): 1077-8.

Ali A.A., Okud A., Khojali, A., and Adam I . (2012) . High incidence of obstetric complication in Kassala Hospital Eastern sudan . Journal of Obstet Gynaecol . 32 (2) : 148-9.

Altinbas S., Togrul C ., Orhan A ., Yucel M. And Danisman N. (2012) . Increased MPV is not a significant predictor for pre- eclampsia during pregnancy. Journal of clinical Labrotory Analysis. 26(5) : 403-6.

Bain B.J. (2006). Blood Cell – A practical Guide. 4th Ed. Malden :Blackwell: 242.

Bath P.M. and Butterworth R .J. (1996) . platelet size : measurement , physiology and vascular disease . Blood coagulation and fibrinolysis : an international journal in haemostasis and thrombosis, 7(2) : 157-61.

Boriboonhirunsarn D., Atisook R., and Taveethamsathit T. (1995). Mean platelet volume of normal pregnant women and severe preeclamptic women in Sirirajb Hospital . Journal of Medical association of Thailand. 78(11): 5869.

Briggs C ., Harrison P . and Machin S. J (2007). Continuitg develelopments with the automated platelet count . International Journal of laboratory Hematology . 29(2): 77-91.

Ceyhan T ., Beyan C ., Baser I., Kaptan K., Gungor S . and Ifran A.(2006) . The effect of pre-eclampsia on complete blood count , platelet count and mean platelet volume .Annals of Hematology . 85(5): 320-22.

Dacie J.V and Lewis S.M . (1995). Practical Haematology. 8th Ed. New York: Churchill. Livingstone: 12.

Duckitt K . and Harrington D . (2005). Risk Factors for pre-eclampsia at antenatal booking : systemic review of controlled studies. BMJ (Clinical research ed .). 330 (7491): 565.

Duley L. (2009). The Global impact of pre-eclampsia and Eclampsia . Seminars in perinatology. 33(3): 130-37.

Dundar O ., Yoruk P ., Tutuncu L ., Erikci A.A ., Muchcu M., Ergur A.R., Atay V . and Mungen E . (2008) . Longitudinal Study of platelet size changes in gestation and predictive power of elevated MPV in development of pre-eclampsia . prenatal diagnosis .28(11):1052-6.

Eiland E ., Nzerue C . and Faulkner M. (2012). Preeclampsia 2012 . Journal of pregnancy , 2012: 586578.

Elhaj E . T . Adam I., Alim A., Elhassan E.M. and Lutfi M.f. (2015) . Thyroid Function /Antabodies in Sudanese Patients with preeclampsia . Front Endocrinol(Lausanne). 6:87.

Fragento R.Y . (2006) The High risk obstetric patient in : Braveman F . R.(ed). Obstetric and Gynecologic Anesthesia : The requisites . Philadelphia : Elsevier Mosby: 79-80.

Freitas L.G., Alpoim P.N., Komastsuzaki F., Carvalho M.d.and Dusse L.M.(2013). Preeclampsia : are platelet count and indices useful for its prognostic? Hematology (Amsterdam, Netherlands). 18(6) : 360-4 Available at : http://www.ncbi.nlm.nih.gov/pubmed/23676885.

Han L., liu X ., Li H., Zou J., Yang Z., Han J., Huang W., Yu L., Zheng Y. And Li L. (2014) . Blood coagulation parameters and platelet indices:

changes in normal preeclamptic pregnancies and predictive values for preeclampsia PLoS One, 9(12) : e 114488.

Harmening D.M. (2005). Modren Blood Banking and transfusion practices. 5th Ed. Philadelphia: F.A.Davis company: 14.

Hoffbrand A.V ., Moss P.A.H, and pettit J.E. (2006). Essential Hematology. 5th Ed .Malden : Blackwell: 269, 352-4.

Hoffbrand A.V ., Catousy D ., Tuddenham E.G.D. and Green A.R. (2011) Postgraduate Haematology. 6th Ed . Oxford , UK:wiley-Blackwell : 773.

Hubbard J.D. (2010) . Aconcise Review of Clinical Laboratory Science. 2nd Ed. Philadelphia: Lippincott Williams and Wilkins:52-9.

Jeyabalan A . (2013) . Epidemiology of preeclampsia: Impact of obesity. Nutrition Reviews. 71(1):18-25.

Levine R.L., Maynard S.E., Qian C., Lim K.H., England L.J., Yu K.F., Schisterman E.F., Thadhani R., Sachs B.P., Epstein F.H., Sibai B.M., Sukhatme. V.P.and Karumanchi S.A. (2004). Circulating angiogenic factors and the risk of preeclampsia. The New England journal of medicine. 350(7):672-83.

McCrae K. R. (2007) Thrombocytopenia in pregnancy. In : Michelson A.D.(ed). Platelet. 2nd ED. London:Elsevier:928-30.

Norwitz E . R. Hsu C.D. and Repke J.T (2002). Acute complication of preeclampsia . Clinical Obstetrics and gynecology , 45(2):308-29.

Provan D ., Singer C.R.J., Baglin T. And Lilleyman J. (2004). Oxford Handbook of Clinical Haematology. 2nd Ed. New York: Oxford University Press: 370.

Queenan J.T., Hobbins J.C. and Spong C.Y.(2010). Protocol for High – Risk Pregnancies: An Evidence Based Approach . 5th Ed. London: Wiley – Blackwell:422.

Rajasekhar A., Gernsheimer T., Stasi R. And James A.H. (2013). Clinical Practice Gide on Thrombocytopenia in pregnancy. Washington, DC: American society of heamtology :2.

Ramin S.M. (2002). ACOG practice bullttin. Diagnosis and management of preeclampsia and eclampsia . Number 33, January 2002. American College of Obstetricians and Gynaecologsts . International Journal of Gynaecology and Obstetrics, 77(1): 67-75. Available at:

http://WWW.ncbi.nlm.nih.gov/pubmed/21860314\nhttp://WWW.ncbi.nlm.nih.gov/pubmed/12094777

Redma n C.W. and Sargent I.L.(2005). Latest advances in understanding preeclampsia. Science (New York, N.Y.). 308(5728): 1592-4.

Rodger L.B., Frenkel E ., Baker W. And Sorode R. (ed) (2006) Haematological Complications in Obstetrics, Pregnancy, and Gynaecology, New York: Cambridge University Press:495.

Schroeder B.M. (2002) ACOG practice bulletin. Diagnosis and management of preeclampsia . Am Fam Physician. 66(2): 330-1.

Shaughnessy D.O., Makris M . and lillicarp D. (2005). Practical Haemostasis and thrombosis. Malden: Black well:3.

Sibai B.M. (2010). Preeclampsia. In: Queenan J. T., Hobbins J. C. And Spong C. Y. (ed) . Protocol for High –Risk Pregnancies. 5th Ed . West Suuex, UK: Welly-Blackwell: 414.

Sysmex Corporation (2004). Automated Haematology analyser: Operator Manual. Kobe, Japan: Sysmex Corporation.

Vagdatli E., Gounari E., Lazaridou E., Katsibourlia E ., Tsikopoulou F. And Labrianou I. (2010). Platelet distribution width: A simple , practical and specific marker of activation of coagulation . Hippokratia. 14(1): 28-32.

Yang S W., Cho S.H., Kwon H.S., Sohn I.S. and Hwang H.S. (2014). Significance of the platelet distribution width as a severity marker for the development of preeclampsia.

Yavuzcan A., Caglar M., Ustum Y., Dilbaz S., Ozdemir I., Yildiz E., Ozbilgec S., and Kumru S. (2014). Mean Platelet Volume , neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in severe preeclampsia. Ginekol Polska . 85(3): 197-203.

Young B.C. Levine R.J. and Karumanchi S. A . (2010). Pathogenesis of preeclampsia. Annual review of pathology. 5: 173-192.

Zhuang X., Chen Y.Y., Zhou Q. And Lin J.H.(2015). Qualitative Analysis of Diagnostic Value of 24-h Proteinuria for preeclampsia. Chinese Medical Journal. 128(22): 2998-3002.

Appendices

Appendix I :

Sudan University of Science and Technology College

of Graduate Studie

Questionnaire

Platelets Count and Indices as possible Predictors for Pre-eclampsia in Sudanese Women in Atbara town Maternity Hospitals

1- Serial Sample No:

2- Age:

3- Education:

Basic

Secondary

University

4- Occupation:

House Wife

Teacher

Labourer

Others

5- Gravid:

6-Parity:

7-Gestational Age:

First trimester

Second trimester

Third trimester

8- History of Hypertension:

Yes

No

9- History of Diabetes mellitus:

Yes

No

10- Other Chronic or Infectious Diseases:

Yes

No

11- Family History of Preeclampsia:

Yes

No

12- Blood Pressure: .....

13- Proteinuria: .....

Appendix II

Reference range:

WBC ($x10^3$ /uL)	4.0 - 10.0
RBC (x 10^6 /uL)	3.8 - 4.8
HB (g/dl)	12.0 – 15.0
HCT (%)	36 – 46
MCV (FL)	83 – 101
MCH (pg)	27 – 32
MCHC (g/dl)	31.5 – 34.3
PLT ($x10^3$ /uL)	140 – 400
LYMPHOCYTE (%)	20 – 40
MXD (%)	2 – 10
NUTROPHEL (%)	40 – 80
ABSOLUTE LYMPHOCYTE ($x10^3$ /uL)	1.0 – 3.0
ABSOLUTE MXD ($x10^3$ /uL)	0.2 – 1.0
ABSOLUTE NUTROPHEL ($x10^3$ /uL)	2.0 – 7.0
PDW-SD (FL)	39 – 46
PDW-CV (%)	11.6 – 14.0
PDW (FL)	9.4 – 18.1
MPV (FL)	8.5 – 12.4
P-LCR (%)	14.3 – 44.0