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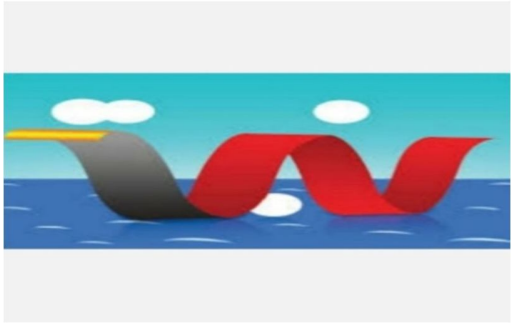

MEASUREMENT OF COAGULATION PARAMETERS & D-DIMER AMONG SUDANESE PREGNANT WOMEN WITH PREECLAMPSIA IN KHARTOUM STATE IN 2022.

"*A thesis submitted in partial fulfillment of the degree of MBBS*"

BY

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Dedication

I dedicate this work

To my Dear parents

To my sisters and brothers and

To all precious people in my life with endless love

Acknowledgments

- First and last my thanks to Allah for lightning my way and made me able to finish this work.

-I am grateful to supervisor ***Dr. Makarim Mohammed Zain*** *who was the real supporter from the beginning*

-I am greatly indebted to my colleagues who are the contributor in bringing this work to the light.

Thank you.

List of abbreviations

APC	Anticoagulant Property Of Activated Protein C
APTT	Thromboplastin Partial Activated
BT	Bleeding Time
CT	Clotting Time
DI-D	DimeR-D
DIC	Disseminated Intravascular Coagulation
HELLP	Hemolysis, Elevated Liver Enzymes And Low Platelets
P M	Preeclampsia Mild
PE	eclampsia-reP
PDW	Width Distribution Platelets
PIH	Hypertension Induced Pregnancy
PT	Time Prothrombin
SP	preeclamsia Severe
TAT	Complex Antithrombin-Thrombin

ABSTRACT

Background: Preeclampsia affects 5%–7% of all pregnancies globally and is the leading cause of maternal and fetal death and morbidity. The mechanisms responsible for the pathogenesis of preeclampsia are unclear. In this study we aimed to measure coagulation parameters and D-dimer level among Sudanese pregnant women with Preeclampsia.

Patients and Methods: case control hospital-based study Conducted at Omdurman Military Hospital. Khartoum, Sudan, study include two groups s ixty were women healthy twenty and group Cases were eclampsia-pre with women and questionnaire, interviewing direct using collected data ،control as included were D.dimer and INR APTT, PT, patients. all from collected was sample blood .(26 vs) programe ware soft SPSS using analyzed Data assessed.

Results: out of total over one third 31 (38.8%) of patients within age group 20-30 years, followed by 22(28.3%) within age group 31-40 years. No significant difference in age group between cases and controls. According to parity, 23(38.3 %) of cases were Primigravida, 20(33.3%) were multipara, and 17(28.3%) were Grand multipara. Compared to control group 12(60%) of control group were multipara. (P value= 0.00). There was significant difference in mean PT (cases 23.34±21.4, vs controls control:18.99±1.37), (P value=0.036). INR was significantly higher among cases group **(**1.17±0.18 vs 1.10±0.10), (P value =0.00). D. dimer was significantly higher among cases (mean±SD) (5595.4 ±2442.0 vs 3240.6± 724.6). There was Statistically insignificant differences in PT, APTT, and INR according to preeclampsia severity. (P value>0.05). D. dimer significantly incresed with severity of preeclampsia (P value =0.041).

Conclusion: Prothrombin time, INR, and D. dimer were significantly higher among preeclampsia group, and increased with preeclampsia severity.

ملخص الأطروحة

الخلفية: تصيب مقدمات الارتعاج 5٪ - 7٪ من جميع حالات الحمل على مستوى العالم وهي السبب الرئيسي لوفيات ومراضة الأم والجنين. الآليات المسؤولة عن التسبب في تسمم الحمل غير واضحة. هدفت هذه الدراسة إلى قياس معاملات التخثر ومستوى D-dimer بين النساء السودانيات الحوامل المصابات بمقدمات الارتعاج.

المرضى والطرق: دراسة حالة التحكم في المستشفى أجريت في مستشفى أم درمان العسكري. تضمنت الدراسة في الخرطوم ، السودان ، مجموعتين ، ستين امرأة مصابة بمقدمات الارتعاج ، كانت مجموعة الحالات وعشرين امرأة سليمة ضابطة ، وجمعت البيانات باستخدام استبيان المقابلات المباشرة ، وتم جمع عينة الدم من جميع المرضى. تم تقييم PT و APTT و INR و D. تم تحليل البيانات باستخدام برنامج برمجيات) SPSSمقابل 26).

النتائج: من إجمالي أكثر من الثلث 31 (38.8٪) من المرضى ضمن الفئة العمرية 20-30 سنة ، يليهم 22 (28.3٪) ضمن الفئة العمرية 31-40 سنة. لا يوجد فرق كبير في الفئة العمرية بين الحالات والضوابط. وفقًا للتكافؤ ، كانت 23 (38.3٪) من الحالات من Primigravida ، و 20 (33.3٪) متعددة الحبيبات ، و 17 (28.3٪) من الحالات الكبرى. مقارنة بالمجموعة الضابطة 12 (60٪) من مجموعة التحكم كانت متعددة الأبراج. (قيمة P = 0.00). كان هناك فرق كبير في متوسط) PTالحالات 23.34 ± 21.4 ، مقابل التحكم في الضوابط: 18.99 ± 1.37) ، (قيمة P = 0.036). كان INR أعلى بشكل ملحوظ بين مجموعة الحالات (1.17 ± 0.18 مقابل 1.10 ± 0.10) ، (قيمة P = 0.00). كان D. dimer أعلى بكثير بين الحالات (يعني ± 2442.0 ± 5595.4) (SD مقابل 3240.6 ± 724.6). كانت هناك فروق ذات دلالة إحصائية في PT و APTT و INR وفقًا لشدة تسمم الحمل. (قيمة P< 0.05). D. dimer بشكل كبير مع شدة تسمم الحمل (P قيمة = 0.041).

الخلاصة: كان زمن البروثرومبين و INR و D. dimer أعلى بشكل ملحوظ بين مجموعة تسمم الحمل ، وزاد مع شدة تسمم الحمل

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CHAPTER ONE

INTRODUCTION

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1.1 Introduction:

Preeclampsia is a prenatal hypertension condition that accounts for 2% to 8% of all disorders connected to pregnancy worldwide. In high-income countries, it causes 16% of maternal mortality, compared to 9% to 26% in low-income nations. New-onset hypertension is the medical term for preeclampsia. [1] Systolic blood pressure of 140 mm Hg or higher, or diastolic blood pressure of 90 mm Hg or higher, on two separate occasions that are at least four hours apart, or shorter interval timing of systolic blood pressure of 160 mm Hg or higher, or diastolic blood pressure of 110 mm Hg or more, all of which must be identified after 20 weeks of gestation..[2]

The earliest appearance of preeclampsia often emerges in near-term pregnancies. Proteinuria, signs of end-organ damage like thrombocytopenia, impaired liver function, severe persistent right upper quadrant or epigastric pain, excluding all other alternative diagnoses, new-onset headache unresponsive to all forms of management, pulmonary edema, or renal insufficiency with abnormal lab values are additional significant findings that may or may not be a part of the clinical presentation. Preeclampsia can also be classified as mild or severe, with the distinction being made depending on how it presents and other clinical factors that will be discussed in more detail.[3,4]

Etiology:

Preeclampsia's underlying etiology is not well understood, despite the fact that clinical presentation, diagnostic criteria, and therapy are all well understood and often used. The hypothesis of aberrant placentation leading to severe maternal physiological dysfunction is a commonly accepted cause of preeclampsia. Despite these challenges, it has been demonstrated that defective placentation, which

causes aberrant spiral artery remodeling, placental ischemia, hypoxia, and oxidative stress, is the well-supported etiologic origin of preeclampsia..[3,5]

Epidemiology

Preeclampsia and eclampsia account for greater than 50,000 maternal deaths yearly worldwide. Like hypertensive disorders, the incidence of preeclampsia is correlated to ethnicity and race, most prevalent among African-American and Hispanic patients, making up around 26% of maternal death among this population.[3,6]

Preeclampsia has a number of risk factors and predictors. In-vitro fertilization or other forms of assisted reproductive technology, maternal comorbidities (chronic hypertension, chronic kidney disease, diabetes mellitus, thrombophilia, obstructive sleep apnea, obesity with a pre-pregnancy BMI greater than 30), family history, history of placental abruption or preeclampsia in a previous pregnancy, or intrauterine fetal growth restriction are some of these. [7,8]

Pathophysiology

Preeclampsia develops as a result of aberrant placentation, which causes the placental vasculature to undergo extensive abnormal remodeling, which has long-lasting pathophysiologic repercussions. Preeclampsia is a multisystem disorder that can potentially worsen end-organ dysfunction and severe hypertension. [9]

Release of distress markers, such as antiangiogenic and pro-inflammatory factors, facilitates an imbalance of increased competition with binding sites for angiogenic and essential growth factors as vascular sclerosis and abnormal arteriole remodeling of the placenta cause progressive placental ischemia. This has negative impacts on several organ systems, most notably the cardiovascular, renal, and

hepatic systems. It also leads to aberrant artery development and insufficient vascular accommodation.[10,11]

History and Physical

Although preeclampsia normally manifests as a history of symptoms and physical manifestations, there are a few unusual presentations that might occur. The most typical preeclampsia manifestations will be covered in this part, along with those that, when present, call for additional research and diagnostic testing. [12]

The most typical history findings in patients with preeclampsia are patient complaints of a new-onset headache not answerable by any other alternative diagnosis (i.e., history of headaches or migraines) that is unresponsive to medicine. Additional complaints of visual disturbance may or may not be made in conjunction with this complaint. Patients may also complain of epigastric or right upper quadrant pain along with any accompanying nausea or vomiting. Other possible symptoms include shortness of breath and swelling that appears to be getting worse despite already existing pregnancy-related symptoms. [13]

Patients who present with any single feature or combination of these history findings should undergo a thorough physical exam. This begins with an evaluation of vital signs, more specifically, blood pressure. Patients with a systolic blood pressure of 140 mmHg or greater, or a diastolic pressure of 90 mmHg or greater, should increase suspicion for preeclampsia. In patients at greater than 20 weeks gestation, blood pressure readings on two measurements at least 4 hours apart should be evaluated with further diagnostic workup.[14]

Recent reevaluation of diagnostic blood pressure readings had expanded to include sustained severe hypertensive readings within minutes of repeat readings to allow

for timely intervention with antihypertensive therapy. These blood pressure readings include systolic pressure of 160 mmHg or greater or diastolic of 110 mmHg or more. Regardless of the presence of other diagnostic criteria, preeclampsia with severe characteristics should be diagnosed in patients who have previously been diagnosed with gestational hypertension and who come with blood pressures in this severe range. If patients report having trouble breathing, auscultation and lung percussion should be done to check for pulmonary abnormalities. In order to check for tenderness, the right upper quadrant and epigastric regions should also be palpated. The overall presence of edema should be assessed, paying particular attention to any dependent (gravity-related) edema in the lower limbs or independent edema in the hands or face.[3]

Evaluation

Patients who exhibit preeclampsia signs and symptoms should receive prompt diagnostic testing after a thorough history and physical examination. The laboratory testing for pregnancy-induced hypertension comprises:[15]

- Urinalysis to evaluate the presence of proteinuria (either with a urine dipstick result of 2+ or greater if other methods are not readily available, a 24-hour urine collection sample significant for 300mg or greater, or a urine protein to creatinine ratio significant for 0.3 or greater).[16]

- Complete blood count to evaluation for thrombocytopenia (defined as a platelet count of less than 100 K/mm),

- Complete metabolic panel to assess for impaired liver function (with liver enzymes greater than two times the upper limit of normal), and renal insufficiency

(defined as a serum concentration of 1.1 mg/dL or greater, or levels two times greater than baseline). [16]

Severity of pre-eclamsia:

Although PE may develop gradually, it often starts abruptly after 20 weeks of pregnancy. The disorder may range from mild to severe. Mild PE occurs in 75% of the cases whereas severe PE occurs in 25%.[24]

Mild PE can be defined as the presence of hypertension (blood pressure $\geq$140/90) on 2 occasions at least 6 hours apart, but without evidence of any organ damage in the patient.

Severe PE is defined as PE with the presence of one or more of the following symptoms or signs:

- Systolic blood pressure of 160 mm Hg or higher or diastolic blood pressure of 110 mm Hg or higher on 2 occasions at least 6 hours apart
- Proteinuria of more than 5 g in a 24-hour collection or more than 3+ on 2 random urine samples collected at least 4 hours apart
- Pulmonary edema or cyanosis
- Oliguria (<400 mL in 24 hours)
- Persistent headaches
- Epigastric pain and/or impaired liver function
- Thrombocytopenia
- Oligohydramnios (low amniotic fluid level), decreased fetal growth, or placental abruption

Eclampsia: If preeclampsia-associated seizures develop and cannot be attributable to any other disorder, then the disorder is called eclampsia. [24]

Treatment / Management

Early identification and intervention, with an emphasis on effective blood pressure management and seizure prevention, are the first steps in the management of preeclampsia. Beta-blockers like labetalol or calcium-channel blockers like nifedipine can be used to lower blood pressure. [25]

A fetal evaluation should also include non-stress tests, biophysical profiles, and ultrasound measurements of the amniotic fluid index and the estimated baby weight. Delivery vs expectant treatment in preeclamptic individuals may also be significantly influenced by fetal condition. [26]

The delivery of the fetus is ultimately the only cure for preeclampsia. The dangers of expectant management persist (see "Complications" section), even if continuous observation is permitted for preterm gestations in patients with either well-controlled gestational hypertension or preeclampsia without severe symptoms in the context of normal antepartum testing. Serial ultrasound, weekly antepartum tests, close monitoring of symptoms, blood pressure, and laboratory results should all be used when expectant management is applied to stable patients. According to ACOG, individuals diagnosed with prenatal hypertension or preeclampsia at 37 0/7 weeks gestation should deliver rather than have expectant management.[27]

Additionally, it is advised that patients with severe preeclampsia who have been diagnosed at or after 34 0/7 weeks of pregnancy have their babies once the mother has stabilized, rather than delaying the procedure to allow for steroid therapy. When preeclampsia with severe characteristics is discovered in patients fewer than 34 weeks gestation, expectant treatment may be used when sufficient stabilization of the maternal and fetal well-being has been established. [28]

While neonatal and maternal outcomes may benefit from delivery or expectant management, informed decision-making regarding benefits and risks must be discussed with the patient. Antepartum admission with close monitoring of maternal and fetal conditions may be employed with a low threshold for delivery if maternal or fetal deterioration is suspected. Findings that indicate expeditious delivery after stabilization regardless of gestational age can be described as fetal and maternal factors.[28]

Fetal factors include abnormal antepartum testing, sustained reversed end-diastolic flow of the umbilical artery. Maternal factors are uncontrolled blood pressure, continued headaches/visual disturbance or right upper quadrant/epigastric pain despite repeated medical management, myocardial infarction, stroke, pulmonary edema, HELLP syndrome, eclampsia, or suspicion of placental abruption or bleeding with no other diagnosis. Delivery before 34 0/7 weeks gestation if indicated should prompt the administration of antenatal steroids for fetal lung maturation, but this should not delay delivery. [28]

Infusions of labetalol, hydralazine, and oral immediate-release nifedipine are used to stabilize blood pressure in the severe range. Intravenous magnesium sulfate therapy is the first option for individuals with preeclampsia with severe characteristics when trying to prevent seizures.[29]

Complications:

In preeclamptic patients who are in the late preterm period, delaying delivery of the fetus increases the risk of severe hypertension, which can lead to serious complications like eclampsia, HELLP syndrome, pulmonary edema, myocardial infarction, acute respiratory distress syndrome, stroke, renal and retinal injury, and fetal complications like fetal growth restrictions, placental abruption, or fetal or maternal death.[3,30]

With the start of medical therapy for adequate blood pressure control, there are frequently encountered problems. These include fetal cardiac tracing anomalies utilizing labetalol, hydralazine, or nifedipine, as well as tachycardia, hypotension, headaches, and other symptoms. Respiratory depression and cardiac arrest are two additional adverse effects and complication concerns associated with the use of magnesium sulfate for seizure prophylaxis. Therefore, it is advised that patients receiving magnesium sulfate medication undergo routine physical examinations every 4 to 6 hours and regular laboratory testing of serum magnesium levels.[3]

2.1. Rational :

Preeclampsia is a serious complication among pregnant, resulting in high morbidity and mortality which still obscure and no clear pathogenesis. Maternal mortality is extremely high in Sudan coagulation status could a good predictor for onset and clinical degree of PE, also there is no published data on this study in our country.

Objective :

General objective:

To measure coagulation parameters and D-dimer level among Sudanese pregnant women with Preeclampsia.

Specific objective :

-To measure D-dimer among pregnant women with preeclampsia compared with normal pregnant women as a control group.

-To measure prothrombin time (PT), Activated partial thromboplastin time (APTT) among pregnant women with preeclampsia compared with normal pregnant women

-To find out the correlation of the results of coagulation parameters and D-dimer between pregnant women with preeclampsia and control.

CHAPTER TWO

LITERATURE REVIEW

Literature review:

Chaware SA, et al; study evaluated coagulation profile in 120 patients with Pregnancy induced hypertension. These patients were categorized as mild, severe preeclampsia and eclampsia. Coagulation parameters such as PT, a PTT, BT, CT, FDPs and platelet count were studied in these patients along with control group of 45 healthy pregnant females. Study showed significant alteration of coagulation profile depending on severity of the disease. All results were statistically analysed.[31]

A study by *Mathur S. et al;* was undertaken at Department of Obstetrics and Gynecology, NIMS Medical College and Hospital, Rajasthan for the period of 1 year on 100 patients diagnosed with PIH. revealed that, the mean BT, CT were in normal range in all patients of PIH; but CT was significantly higher in Eclampsia (E) group than PE &GTN. Mean CRT was poor in patients with E group and normal in patients of PE & GTN group. Mean platelet counts & serum fibrinogen levels found to be decreased with severity of PIH. Prolonged mean PT & aPTT were observed in patients with E. Conclusion: Inclusion of coagulation profile with routine investigations leads to early prediction of severity of PIH and subsequent complications. [32]

Bhutani N, et al; evaluate a total of 150 cases comprising 75 control groups and 75 cases group (pregnancy-induced hypertension). Hematological parameters like platelet count, MPV, PDW and coagulation parameters like PT and APTT were studied in these patients. The hematological parameter - Platelet count was markedly reduced in patients with preeclampsia compared to normal pregnant patients. MPV, PDW, PT and APTT were increased which is statistically significant. The abnormalities about hematological and coagulation parameters in

preeclampsia are the prognostic markers used as an additional diagnostic criterion for preeclampsia in rural hospitals. [33]

An observational retrospective case-control study conducted by *Lefkou E, et al;* total of 84 women divided into three groups, the healthy pregnant (HP) group (n=35), the mild preeclampsia (MP) group (n=34) and the severe preeclampsia (SP) group (n=15). All women were assessed with classic coagulation tests (aPTT and PT) fibrinogen levels and hemogram. Women with preeclampsia - mild or severe- showed significant increase of TFPI, TFa and TMa levels as compared to healthy pregnant women. No significant difference of TFPI, TFa was observed between MP and SP groups. In contrast, TMa levels were significantly increased in SP as compared to MP group. The ratio TFa/TFPI was also lower in SP as compared to MP-group. Women in MP or SP group had similarly shorter PPL clotting time as compared to HP group. D-dimer levels were increased in women with preeclampsia as compared to the HP group. D-Dimer levels were significantly higher in SP as compared to MP group. Prothrombin time was found to be increased in cases as compared to that in the controls. The mean value of prothrombin time in mild preeclampsia was 13.24±0.80 seconds and in severe preeclampsia it was seconds 14.77±0.96 and in pregnant controls 12.23±0.59 seconds ($p<0.05$ and $p<0.001$ respectively). The mean prothrombin time was found to increase with increasing severity of disease ($p<0.001$). The mean activated partial thromboplastin time were increased in mild preeclampsia and was 32.64±1.83 seconds and in severe preeclampsia it was 35.59±1.53 seconds and in pregnant controls 29.53±1.62 seconds ($p<0.001$). The activated partial thromboplastin time was found to increase with increasing severity of disease ($p<0.001$). The antithrombin III decreased in severe SP and MP or compared to

pregnant controls (76.33±4.32 and 88.06±9.68 versus 95.40±0.36 respectively; p<0.001). This decrease is more pronounced in SP compared to MP (p<0.001). [34]

A nested, prospective cohort, analytical case–control study was conducted by *Rodríguez□Peña Y, et al;* among women with pre-eclampsia between March 2017 and March 2018. There were 132 patients with pre-eclampsia, of which 44 were classed as controls and 88 were classed as having severe pre-eclampsia (case group). Cohort characteristics included: age between 18 and 45 years (mean 28.0 ± 6.3 years); presence of gestational hypertension (10.6%), chronic arterial hypertension (9.0%); and gestational diabetes (5.3%). In the case group, levels of D-dimer were significantly higher than in controls (19.3% vs 2.3%, odds ratio [OR] 10.30, 95% confidence interval [CI] 1.32–80.14, *P*=0.004) as well as significant in the unconditional logistic regression model adjusted for maternal age, parity, gestational age, and comorbidities (OR 10.02, 95% CI 1.28–78.68, *P*=0.028). [35]

Jhansi K, et al; study evaluated total of 120 women were divided into two groups: 60 women without PE (control group) and 60 women with PE in a prospective observational case–control study conducted in a rural tertiary care setting in India. from January 2019 to December 2019, The participants in this study ranged in age from 18 to 38 years old, with an average age of 26.38 ± 4.38 years. The average age of the women in the case group was 26.42 + 3.92 years, while the average age of the women in the control group was 27.38 ± 4.52 years. Most of the patients were between the ages of 31 and 40 (51.67%) years. The mean gestational age in the case group was 26.60 ± 2.19 weeks, while it was 26.73 ± 2.39 weeks in the control group. Early screening of pregnant women for high D-dimer levels and lipid profile can play a significant role in reducing the morbidity and mortality of both mother and fetus. [36]

CHAPTER THREE

PATIENTS AND METHODS

PATIENTS AND METHODS

3.1. Study design:

Case – control hospital based study

Study area:

Conducted at Omdurman Military Hospital. Khartoum, Sudan.

3.2. Study population:

Known Sudanese pregnant women diagnosed with preeclampsia.

3.3. Inclusion criteria :

- Among Sudanese women's diagnosed with preeclampsia.
- 20- 41+3 weeks (third trimester) of gestation.
- Not known hypertensive.

3.4.Exclusion criteria:

- Pre-existing medical disorders
- Diabetes Mellitus
- Renal disease
- Any coagulopathies.
- On anticoagulant therapy.

3.5. Data collection:

Data was collected using direct interviewing questionnaire.

3.6. Semple collection :

2.7 ml venous blood samples was collected in tri-sodium citrate

3.7. Sample size:

60 samples of Sudanese pregnant women diagnosed with preeclampsia – the second group include 20 subjects who comprised the control group (normal pregnant women)

3.8. Methods:

Sample technic is Randomizer sample

Coagulation profile :

Platelet poor plasma (p.p,p) is prepared for coagulation study (PT, APTT, INR) and D-dimer level by using XRC full automated coagulation analyzer.

3.9. Data analysis:

Results obtained was analyzed by the computerized program of statistical package of social studies (SPSS) Statistical package for the social sciences

3.10. Ethical consideration:

Approval was taken from the faculty of Medicine Napata College Ethical Committee

Consent was taken from each patient before being enrolled in the study.

Each patient was informed about the nature of the study.

CHAPTER FOUR

RESULTS

RESULTS

Table 1: Age group of patients among cases and controls groups

age		Group		Total
		Cases	Control	
<20	Count	17	1	18
	%	21.3%	1.3%	22.5%
20-30	Count	21	10	31
	%	26.3%	12.5%	38.8%
31-40	Count	14	8	22
	%	17.5%	10.0%	27.5%
>40	Count	8	1	9
	%	10.0%	1.3%	11.3%
Total	Count	60	20	80
	%	75.0%	25.0%	100.0%

P value=0.074

Sixty women with pre-eclampsia were enrolled in this study (as Cases) and twenty healthy women were included (as control), about one third 31 (38.8%) of patients within age group 20-30 years, followed by 22(28.3%) within age group 31-40 years, and 18(23.3%) within age group less than 20years. No significant difference in age group between cases and controls. **Table (1)**

Table 2: Education level of patients among cases and controls groups

Education level		Group		Total
		Cases	Control	
Illiterate	Count	4	0	4
	%	5.0%	0.0%	5.0%
Primary school	Count	19	6	25
	%	23.8%	7.5%	31.3%
Secondary school	Count	26	8	34
	%	32.5%	10.0%	42.5%
University and above	Count	11	6	17
	%	13.8%	7.5%	21.3%
Total	Count	60	20	80
	%	75.0%	25.0%	100.0%

P value=0.504

Regarding education, the Majority 34(42.5%) of patients had secondary school level, 25(31.3%) had primary school level, 17(21.3%) had university level, and 4(5.0%) were illiterate. No significant difference in education level between cases and controls. **Table (2)**

Table 3: Antenatal care visits of patients among cases and controls groups

ANC		Group		Total
		Cases	Control	
Regular	Count	29	0	29
	%	48.3%	0.0%	36.3%
Irregular	Count	23	3	26
	%	38.3%	15.0%	32.5%
No	Count	8	17	25
	%	13.3%	85.0%	31.3%
Total	Count	60	20	80
	%	100.0%	100.0%	100.0%

P value =0.000

Most of cases 29(48.3%) were regularly attended antenatal care, and 23(38.3%) attended irregularly the ANC, while 17(85%) of controls had no ANC visits. (P value=0.00). **Table (3)**

Table 4: Parity of patients among cases and controls groups

Parity		Group		Total
		Cases	Control	
PG	Count	23	1	24
	%	38.3%	5.0%	30.0%
1-5	Count	20	12	32
	%	33.3%	60.0%	40.0%
>5	Count	17	7	24
	%	28.3%	35.0%	30.0%
Total	Count	60	20	80
	%	100.0%	100.0%	100.0%

P value =0.000

According to parity, 23(38.3 %) of cases were Primigravida, 20(33.3%) were multipara, and 17(28.3%) were Grandmultipara. Compared to control group 12(60%) of control group were multipara. (P value= 0.00) **Table (4)**

Table 5: Gestational age of patients among cases and controls groups

Gestation age	Cases	Controls
Mean ±SD weeks	37.066±2.3	38.65±1.039
P value = 0.016		

the mean gestation age was significantly higher among control group 38.65±1.039 compared to mean gestation age among cases 37.0±2.3 weeks (range 29-40 weeks). (P value=0.016) **Table (5)**

Table 6: blood pressure of patients among cases and controls groups

Blood pressure (Mean ±SD)	**Cases**	**Controls**
Systolic	167.23±19.5	119.9±2.02
Diastolic	111.2±12.8	80.4±2.5
P value = 0.000		

The mean systolic/diastolic blood pressure was 167.23/111.26 ±19.5/12.9 (with range 114-196/71-128) among cases which significantly higher than control 119.9/80.4 ±2.02/2.5. **Table (6)**

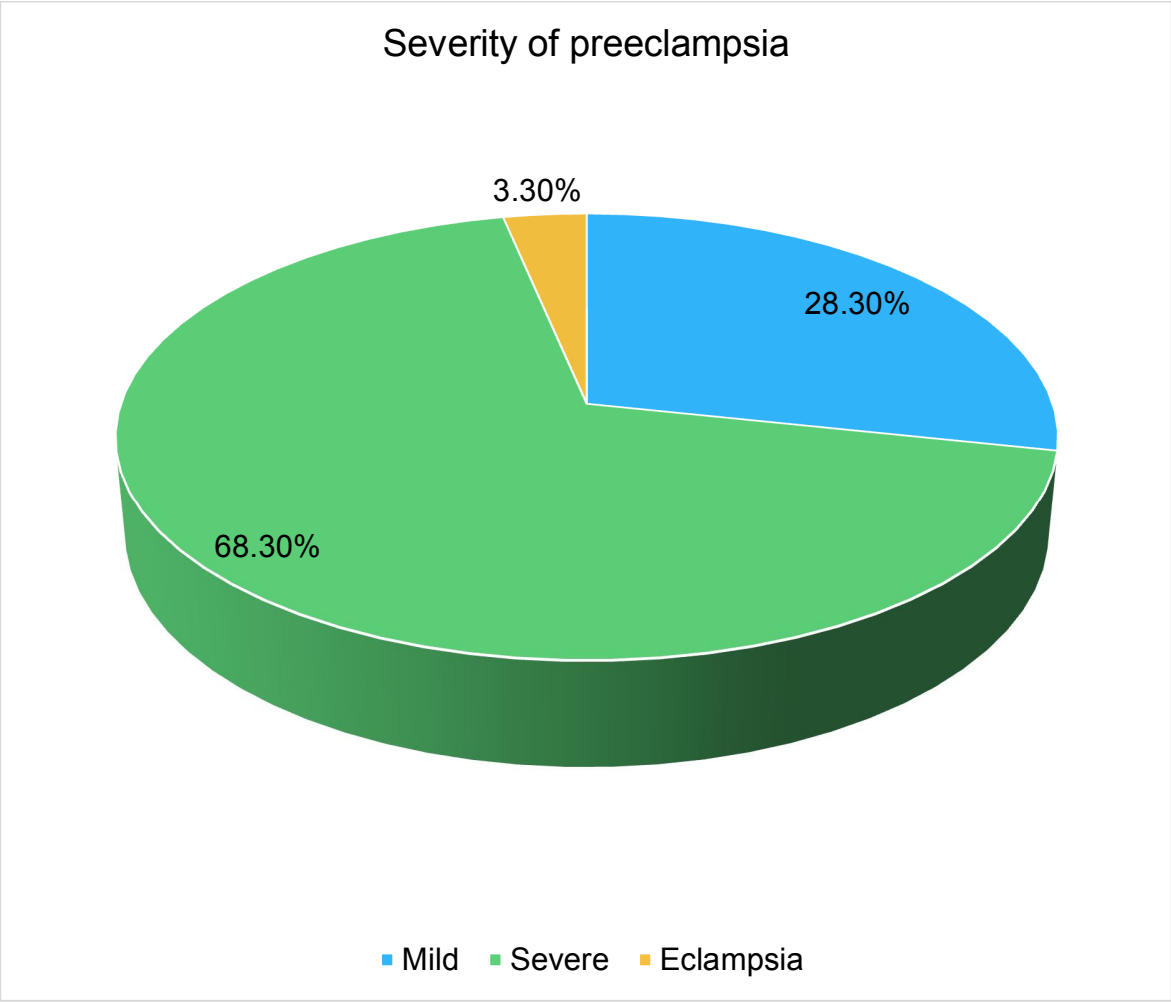

Figure 1: Severity of preeclampsia among patients (cases group) (n=60)

The majority 41(68.3%) of patients had severe preeclampsia, 17(28.3%) had mild preeclampsia and 2 (3.3%) had eclampsia. **Figure (1)**

Table 7: Coagulation parameters of patients among cases and controls groups

Coagulation parameter	Group		P value
	Cases	Controls	
PT	23.34±21.4	18.99±1.37	0.036
PTT	43.13±3.9	36.89±7.9	0.492
INR	1.17±0.18	1.10±0.10	0.00

There was no significant difference in mean PT (cases 23.34±21.4, vs controls control:18.99±1.37), (P value=0.36), and mean APTT between (cases 43.13±3.9 and controls 36.89±7.9) (P value =0.492). INR was significantly higher among cases group (mean±SD)**(** 1.17±0.18) compared to control group (1.10±0.10), (P value =0.00). **Table (7)**

Table 8: D. dimer of patients among cases and controls groups

	Cases	Controls
D-dimer (Mean±SD)	5595.4 ±2442.0	3240.6± 724.6
P value =0.000		

D. dimer was significantly higher among cases (mean±SD) (5595.4 ±2442.0) compared to controls (3240.6± 724.6). **Table (8)**

Table 9: Coagulation parameters of patients and severity of preeclampsia cross tabulation

Coagulation parameters	Severity of preeclampsia			P value
	Mild	Severe	Eclampsia	
PT	18.20±1.13	20.72± 1.9	24.67±1.9	0.04
PTT	42.28±3.2	43.50±4.3	42.75±1.4	0.39
INR	1.17±0.18	1.17±0.19	1.15±0.14	0.39

There was Statistically insignificant differences in PT, APTT, and INR according to preeclampsia severity. (P value>0.05). **Table (9)**

Table 10: Severity of preeclampsia and D. dimer cross tabulation

	Severity of preeclampsia		
	Mild	Severe	Eclampsia
D. dimer	4133.58±1516.52	6142.04±2465.87	6815.00±4504
P value =0.041			

D. dimer significantly incresed with severity of preeclampsia (P value =0.041). **Table (10)**

Table 11: Severity of preeclampsia and parity cross tabulation

Parity		Severity			Total
		Mild	Severe	Eclampsia	
Pg	Count	0	21	2	23
	%	0.0%	35.0%	3.3%	38.3%
1-5	Count	5	15	0	20
	% l	8.3%	25.0%	0.0%	33.3%
>5	Count	12	5	0	17
	%	20.0%	8.3%	0.0%	28.3%
Total	Count	17	41	2	60
	%	28.3%	68.3%	3.3%	100.0%

P value=0.000

Severity of preeclamsia was associated significantly with parity, eclampsia patients were primigravidum, and majority of grandmultipara patients had mild preeclampsia. (Pvalue=0.00) **Table (11)**

CHAPTER FIVE

DISCUSSION

CONCLUSION

RECOMMENDATIONS

Chapter five

Discussion

Hypertensive disorders are the most important cause of maternal and perinatal morbidity and mortality**.** In this study sixty women with pre-eclampsia were enrolled in this study (as Cases) and twenty healthy women were included (as control).

In present study, we found significant difference in mean PT (cases 23.34±21.4, vs controls 18.99±1.37), (P value=0.036). In addition to that we also reported significant association between PT and preeclampsia severity. (P value=0.04). this is consistent with *Bhutani N, etal;* [33] study which revealed that the mean prothrombin time of patients with mild preeclampsia it was 17.61 ± 2.88 s and in severe eclampsia it was found to be 18.88 ± 0.0 s. 57.14% of gestational hypertension, 83.33% of mild preeclampsia cases and all cases of severe eclampsia had prolonged prothrombin time with significant P-value <0.0001. Our study data correlated well with the following statistically significant studies for PT. Study by *Priyadarshini et al.* [37] observed the mean prothrombin time of 15.27 s in patients with preeclampsia and found it to be 13.72 s in cases with normal pregnancy. The increase in PT in severe eclampsia cases was found to be statistically significant. Similarly study by *Mushtaque T et al.* [38] study revealed the mean prothrombin time in three study groups for normal pregnancy, non-severe PIH and severe PIH patients were 10.9 s, 10.1 s and 9.8 s respectively, with significant P-value less than 0.0001 In a study conducted by *Mishra et al.* [39] it was observed that the mean PT was found to be significantly increased with p value of <0.05 in severe preeclampsia and eclampsia study groups. Moreover, *Mathur S. et al;* [32] study documented mean prothrombin time of patients with preeclampsia patients was

16.9 secs and eclampsia patients was 27.6 secs. About 58.7% of the patients with preeclampsia and all the patients of eclampsia had prolonged prothrombin time. *Shetty et al.* [40] studied haematological changes in pregnancy-induced hypertension and observed that the 28.57% cases of mild PIH and 82.86% of severe PIH had prolonged PT (>14 s). The PT in severe PIH was found to be significantly prolonged ($P < 0.05$). Sudanese study by *Abdulla et al.* [41] studied PT in 100 PIH cases and found that 50% of cases have prolonged PT with significant p value of (0.000) indicating that a highly significant difference in prothrombin time occurs between cases and their control.

This study showed that the mean APTT among cases 43.13±3.9 and controls 36.89±7.9) was not associated with preeclampsia (P value =0.492). on other hand INR was significantly higher among cases group (mean±SD) (1.17±0.18) compared to control group (1.10±0.10), (P value =0.00). In addition to that we also reported insignificant differences in PT, APTT, and INR according to preeclampsia severity. (P value>0.05). In contrast *Bhutani N, et al* [33] stated the mean APTT for normal pregnancy, gestational hypertension and mild preeclampsia and severe eclampsia were 25.76 ± 2.99 s, 33.55 ± 2.44 s,38.79 ± 2.52 s and 41.85 s respectively, with significant P-value <0.0001. also *Mathur S. et al;* [32] The mean APTT among the patients was 35.8 secs in patients with preeclampsia and 51.2 secs in patients with eclampsia. The APTT was prolonged in 50% of the patients with preeclampsia and all the patients with eclampsia. *Mushtaque T et al.* [38] study revealed the mean APTT for normal pregnancy, Non severe PIH and severe PIH patients were 26.68 s, seconds 26.71 and 26.25 s respectively, with P value less than 0.005 was statistically significant. this variation may due to small size of control group in our study which may affect in the significance of different value.

In present study D. dimer was significantly higher among cases (mean±SD) (5595.4 ±2442.0) compared to controls (3240.6± 724.6). and significantly increased with severity of preeclampsia (P value =0.041). Similarly, *Lefkou E, et al;* [34] found that in the case group, levels of D-dimer were significantly higher than in controls (19.3% vs 2.3%), in similar context *Jhansi K, et al;* [37] study found patients with plasma D-dimer >0.5 g/ml had significantly higher mean systolic and diastolic blood pressures than those with plasma D-dimer 0.5 g/ml (P = 0.026). The majority of preeclamptic women (68.4%) with plasma D-dimer >0.5 g/ml had systolic blood pressure <160 mm Hg, compared to 44.2% of those with plasma D-dimer <0.5 g/ml (P = 0.034). Nearly 84% of pre-eclamptic women with plasma D-dimer >0.5 g/ml had severe proteinuria, compared to 48.6% of pre-eclamptic women with plasma D-dimer <0.5 g/ml (P = 0.027). The study finds that the plasma D-dimer level can be simply employed in pre-eclamptic patients to screen for hypercoagulable states, which has both preventative and therapeutic implications. The link between preeclampsia and high D-dimer levels (>0.5 g/ml) was investigated in this study, where high D-dimer levels were found in 38 (63.33%) of the women in the case group (preeclampsia), but only in 08 (13.33%) of the women in the control group (normotensive). The P = 0.025 is significant, indicating that there is a link between preeclampsia and high D-dimer levels (>0.5 g/ml). The current investigation found that preeclamptic women's D-dimer levels were considerably higher than normal controls, which is consistent with the findings of *Tacoosian et al* [42] *and Kucukgoz Gulec et al.* [43] found that D-dimer levels were significantly higher in the study group than in the control group and that they were also significantly higher in patients with severe preeclampsia than in those with mild preeclampsia.

Limitation of the study:

The major limitation of this study was small sample of control participants, also we didn't assess the clotting, and bleeding time which are completed the coagulation profile.

Conclusion

The majority of patients (cases group) had severe preeclampsia.

There was significant elevation in PT, and INR among cases compared to controls group. While APTT was not significantly different.

D. dimer was significantly higher among cases compared to controls, and significantly incresed with severity of preeclampsia.

There was Statistically insignificant differences in PT, APTT, and INR according to preeclampsia severity.

Recommendations

1. Further controlled studies with large sample size and study more coagulation parameters should be conducted.
2. Prothrombin time, INR, and D.dimer screening during pregnancy should be adopted as indicators of preeclampsia.

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Measurement of coagulation parameters & D-dimer among Sudanese pregnant women with preeclampsia in Khartoum state.

Questionnaire:

1. **Agree** ☐ **Disagree** ☐
2. **age** :

< 20 ☐ 20-30 ☐ 30-40. ☐ > 40 ☐

3. **Educational level :**

Illiterate ☐ primary ☐ secondary ☐ university and above ☐

4. **Attended Antenatal care**

Regular ☐ Irregular ☐ No ☐

5. **Parity:**

PG ☐ 1 – 5 ☐ >5 ☐

6. **Gestational age weeks**:…….
7. **blood pressure** :

Systolic ☐ diastolic ☐

8. **Had preeclampsia:**

Yes ☐ No ☐

9. **if yes severity:**

Mild ☐ severe ☐ eclampsia ☐

10. **coagulation profile** :

PT: …… PTT:…… INR:……

11. **Plt count**: ……
12. **D-dimer:** ……..