RESEARCH ARTICLE

Chinese Journal of Medical Research
Chinese J Med Res 2022; 5(1): 13-17

ISSN(e): 2618-091X
ISSN(p): 2663-8053

Impact of Preeclampsia on Coagulation Profiles among Sudanese Pregnant Females Attending Wad Medani Maternity Hospital, Gezira State, Sudan

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Received: January 29, 2022; Accepted: March 06, 2022

Abstract

Background: Preeclampsia (PE) is a serious multi-systemic problem associated with pregnancy complications resulting in maternal mortality. It is associated with endogenous coagulative pathways, consuming platelets, and subsequently activating thrombopoiesis and fibrinolysis. **Aim:** The purpose of this study was to assess the Prothrombin Time (PT), International Normalize Ratio (INR), Activated Partial Thromboplastin Time (APTT), and platelet count in pregnant women who were preeclamptic. **Design and Methods:** From October 2020 to March 2021, a case-control hospital-based study was conducted at Wad Medani Maternity Hospital in Sudan. This study included 100 pregnant women (50 with preeclampsia as cases (32.20 ± 3.21 years) and 50 pregnant women with normal blood pressure as controls (30.68 ± 2.85 years). All participants had 4 milliliters of venous blood drawn (2 ml in EDTA containers and 2 ml in Trisodium citrate containers). The platelets count was determined using Mindray BC 3000 Automated Hematology Analyzer. A Coatron M4 coagulometer was used to evaluate coagulation profiles. The data was analyzed using the SPSS computer program (version 22.0). **Results:** The study results showed that the means of PT, INR, APTT, and platelets count were (15.18 ± 1.94 sec, 1.18 ± 0.23, 40.28 ± 3.30 sec, and 144.40 ± 31.80 × 10^9/L respectively) versus controls (13.92 ± 0.76 sec, 0.97 ± 0.06, 31.80 ± 2.72, and 269.40 ± 72.50 × 10^9/L respectively) with highly statistically significant differences (*P-value* = 0.000 for all) between them. There were no significant differences in PT, INR, APTT, and PLTs count between mild preeclamptic females and severe preeclamptic females. 58% of cases have thrombocytopenia (< 150 × 10^9 /L). The thrombocytopenia was a highly associated with the severity of preeclampsia (*P-value* = 0.000). **Conclusion:** The study concluded that PT, INR, and APTT were significantly increased in preeclamptic females. Furthermore, pregnant women with severe preeclampsia are associated with thrombocytopenia. For measuring and forecasting the risk of severe preeclampsia, coagulation profiles and platelet counts should be included.

Keywords: Severe preeclampsia, Preeclamptic females, PT, INR, APTT, Platelets count.

INTRODUCTION

The most prevalent medical consequence of pregnancy is hypertension, which is a leading cause of maternal morbidity and mortality [1,2].

Preeclampsia (PE) is a dangerous multi-systemic pregnancy condition that affects 2 – 7% of healthy nulliparous women worldwide [3,4]. The risk is significantly higher in women carrying twins (14%), as well as those who have had preeclampsia in the past (18%). Preeclampsia affects 1.8 percent to 16.7% of pregnant women in impoverished nations like Sudan [5].

Preeclampsia is a major cause of maternal death in Africa, as well as a primary cause of poor pregnancy outcomes under the category "hypertensive illnesses of pregnancy" [6]. As a result, it is regarded as one of the most serious health issues related with pregnancy, as well as one of the leading causes of maternal mortality, particularly in underdeveloped nations where the incidence and rates of negative consequences are higher [1,2]. PE is characterized by high blood pressure (>140/90 mmHg), proteinuria (>0.3 g/d), edema, and other clinical findings that can begin as early as the 20th week of pregnancy and last up to 6 weeks after delivery [7,8].

Normal pregnancy causes changes in the platelets, coagulation,

and fibrinolytic system and it is associated with hypercoagulable state result from more likely due to hormonal change, maternal inflammatory reactions, and immune dysfunction. Pregnancy-induced hypertension can cause a range of hematological problems in women [9].

The regulation of uteroplacental circulation and organ perfusion in pregnant females depend on the balance of coagulation and anticoagulation. A typical pregnant lady needs an appropriate increase in blood coagulation to prevent postpartum hemorrhage and other problems [10]. The super hypercoagulable state of women with PE can cause metabolic problems, various organ malfunctions, and possibly endanger the lives of both the mother and the fetus [11].

This hypercoagulability is more at the time of delivery with the release of thromboplastin substance due to placental expulsion [9]. PE can activate thrombopoiesis and fibrinolysis by triggering multiple abnormalities in the endogenous coagulative pathways and consuming platelets and FIB [10]. The predominant mode for treating hypertensive disorder in pregnancy includes antihypertensive, anticonvulsants, and the interruption of pregnancy [12]. As a result, coagulative and fibrinolytic state is an excellent predictor of PE occurrence and severity [10].

MATERIALS AND METHODS

The study was conducted at Wad Medani Maternity Hospital in Sudan, from October 2020 to March 2021 as a case-control hospital-based study. According to inclusion and exclusion criteria, samples were taken at random from 50 preeclamptic pregnant females as cases and 50 normotensive pregnant females as controls.

The Researches and Ethics Committees (REC) of the Ministry of Health, Gezira State, Sudan, provided ethical approval and consent the study. Each participant signed an informed consent form.

A clean venipuncture technique was used to obtain a 4 ml venous blood sample (2 ml in K_2EDTA anticoagulant containers and 2 ml in trisodium citrate container). The PPP was extracted using centrifugation of blood at 1200 – 2000 rpm for 15 minutes [13]. Coagulation profiles were measured using a Coatron M4 Coagulometer. The platelets count was measured using the Mindray BC 3000 Plus Cell Counter. SPSS computer program (v 22.0) was used for data analysis.

RESULTS

This study included 50 preeclamptic females with mean age 32.20 years; and 50 normotensive pregnant females with mean age 30.68 years. 76% women in the third trimester compared to 24% in the second trimester (Table 1).

Preeclampsia had been diagnosed in 12% of instances; 72% of patients had no family history of preeclampsia; and 50% of cases had severe preeclampsia (Table 2).

The means of PT, INR, APTT, and PLTs count (15.18 ± 1.94 sec, 1.18 ± 0.23, 40.28 ± 3.30 sec, and 144.40 ± 31.80 × 10^9/L respectively) versus controls (13.92 ± 0.76 sec, 0.97 ± 0.06, 31.80 ± 2.72, and 269.40 ± 72.50 × 10^9/L respectively) giving highly statistically significant differences (*P-value* = 0.000 for all) between them (Table 3).

The means of PT, INR, APTT, and PLTs did not differ significantly between mild preeclamptic females and severe preeclamptic females (Table 4).

There were no significant differences in PT, INR, APTT, and PLTs count between second and third trimester among preeclamptic females (Table 5).

58% of cases have thrombocytopenia (< 150 × 10^9 /L) compared to 42% with normal platelet count. Furthermore, 52% of cases had abnormal platelets morphology (Giant and aggregated platelets) in the peripheral blood picture. Thrombocytopenia is highly significant associated with the severity of preeclampsia (*P-value* = 0.000) (Table 6).

Table 1: Demographic data of study preeclamptic females and control

Demographic data	Preeclamptic females (N = 50)	Control (N = 50)
Age/years	32.20 ± 3.21	30.68 ± 2.85
Age group (years)		
Less than 30 years	22 (44 %)	27 (54 %)
More than 30 years	28 (58 %)	23 (46 %)
Weight	71.10 ± 5.70	67.84 ± 5.63
Tribes		
Middle tribes	13 (26 %)	14 (28 %)
Northern tribes	14 (28 %)	15 (30 %)
Eastern tribes	15 (30 %)	14 (28 %)
Western tribes	8 (16 %)	7 (14 %)
Educational level		
Un-educated	2 (4 %)	-
Primary level	13 (26 %)	15 (30 %)
Secondary level	25 (50 %)	20 (40 %)
University level	10 (20 %)	15 (30 %)
Economical status		
Low status	12 (24 %)	20 (40 %)
Medium status	25 (50 %)	20 (40 %)
High status	13 (26 %)	10 (20 %)
Trimester		
Second	12 (24 %)	5 (10 %)
Third	38 (76 %)	45 (90 %)

Table 2: Clinical findings of preeclamptic females

Clinical findings	Cases (N = 50)
Preeclampsia severity	
Mild	25 (50 %)
Severe	25 (50 %)
Pervious history	
Yes	6 (12 %)
No	44 (88 %)
Family history	
Yes	14 (28 %)
No	36 (72 %)
Recurrent miscarriage	
Yes	10 (20 %)
No	40 (80 %)

Table 3: Comparison of coagulation profiles and platelets count between preeclamptic females and control

Parameters	Preeclamptic females (N=50)	Controls (N=50)	*P-value*
PT/ sec	15.18 ± 1.94	13.92 ± 0.76	**0.000**
INR	1.18 ± 0.23	0.97 ± 0.06	**0.000**
APTT/ sec	40.28 ± 3.30	31.80 ± 2.72	**0.000**
PLTs count × 10^9/L	144.40 ± 31.80	269.40 ± 72.50	**0.000**

Table 4: Comparison of coagulation profiles and platelets count between Mild and severe preeclamptic females

Parameters	Mild preeclampsia (N=25)	Severe preeclampsia (N=25)	*P-value*
PT/ sec	15.03 ± 1.95	15.34 ± 1.96	0.576
INR	1.20 ± 0.26	1.18 ± 0.20	0.664
APTT/ sec	40.61 ± 7.24	39.90 ± 6.03	0.710
PLTs count × 10^9/L	166.60 ± 18.30	122.30 ± 26.80	0.379

Table 5: Comparison of coagulation profiles and platelets count between trimesters

Parameters	2nd trimester (N=12)	3rd trimester (N=38)	*P-value*
PT/ sec	15.68 ± 2.96	14.96 ± 2.13	0.493
INR	1.20 ± 0.29	1.18 ± 0.23	0.223
APTT/ sec	41.23 ± 5.11	39.83 ± 7.26	0.959
PLTs count × 10^9/L	149.80 ± 26.80	142.70 ± 33.40	0.588

Table 6: Association between thrombocytopenia and severity of preeclampsia

Parameters	Thrombocytopenia (PLTs <150×10^9/L)	Normal (PLTs >150×10^9/L)	*P-value*
Mild	6	19	**0.000**
Severe	23	2	

DISCUSSION

Hemostasis changes during pregnancy, with a rise in most clotting factors, a decrease in natural anticoagulants, and a decrease in fibrinolytic activity. Hypercoagulability develops as a result of these alterations, which are most likely caused by hormonal changes and raise the risk of thromboembolism [14].
PE is a multisystem illness with an unknown origin that is defined by aberrant vascular responses and is linked to increased systemic vascular resistance, platelet aggregation, coagulation system activation, and endothelial cell dysfunction [15].

In late pregnancy, normal pregnancy generates a physiological hypercoagulable state in the mother. PE can cause thrombopoiesis and fibrinolysis by triggering complicated abnormalities in the endogenous coagulative pathways and consuming platelets and fibrinogen [10].

The study included 16 cases in the second trimester and 34 in the third trimester. 25 cases had a mild form of preeclampsia and 25 had a severe form of preeclampsia.

The means of PT, INR and APTT were significantly increased in cases compared with control (*P-value* = 0.000, 0.000, and 0.000 respectively). Biochemical changes consistent with intravascular coagulation and less often erythrocyte destruction may complicate preeclampsia and especially preeclampsia. Changes in coagulation profile that occur in normal pregnancy include the biochemical adaptation especially the hematological changes that occur in response to pregnancy are profound. The levels of many blood coagulation factors are increased during pregnancy and preeclampsia.

When compared to control, the means of PT, INR, and APTT were substantially higher in preeclamptic females (*P-values* = 0.000 for all). Preeclampsia, especially preeclampsia, might be complicated by biochemical abnormalities associated with intravascular coagulation and, less frequently, erythrocyte destruction. The biochemical adaptation, particularly the hematological alterations that occur in response to pregnancy, are significant changes in the coagulation profile that occur in normal pregnancy. During pregnancy and preeclampsia, the levels of numerous blood coagulation factors rise.

There were no variations in means of coagulation profiles according to severity of preeclampsia. This study finding agrees with a study done by Han *et al.,* [10].

The mean platelet count was significantly decreased in cases compared with control (*P-value* = 0.000). This study results similar to previous studies [16-20]. The preeclampsia-related vascular changes that lead to platelet consumption in the repair of vessel damage, platelet contact with the injured endothelium activates the coagulation system, which can increase both platelet consumption and production in the bone marrow, improve thrombopoiesis, and produce younger platelets that are larger than older platelets. Despite the mean of platelet count was decreased in severe compared with mild preeclampsia but was insignificant. Furthermore, 29 (58%) of cases have thrombocytopenia (< 150 × 10^9 /L) compared to 21 (42%) with normal platelets count. From 29 cases with thrombocytopenia; 23 (79.3%) cases with severe preeclampsia (thrombocytopenia in severe preeclampsia was 4 folds than in mild preeclampsia) (*P-value* = 0.000) (Table 6). Furthermore, 52% of cases had abnormal platelets morphology (Giant and aggregated platelets) in the peripheral blood picture. There was a highly significant link between thrombocytopenia and preeclampsia severity. This result agrees with the study done in Southern Asia which demonstrated that the platelet count decreased significantly with the severity of preeclampsia [21]. But this result differs from the result obtained from a study done in the United Kingdom which showed there was no significant variation in platelet count according to preeclampsia severity [16]. Platelet consumption and aggregation, followed by secondary regeneration, may be the source of this consequence. However, the beginning of PE, particularly severe PE, is characterized by complicated coagulative pathway abnormalities, both endogenous and external with subsequent feedback activation of thrombopoiesis and fibrinolysis.

CONCLUSION

The study concluded that thrombocytopenia is mainly associated with severe than mild. In addition, women with preeclampsia had significantly increased coagulation profiles (PT, INR, and APTT) levels and low platelet count than normal pregnant women. So, platelet count along with coagulation profiles (PT, INR, and APTT) should be used as prognostic markers of preeclampsia. Furthermore, thrombocytopenia is a marker for assessing and predicting the risk of severe preeclampsia.

Conflict of Interest

No competing interests exist.

Funding and support

Nil.

Author Contributions

All authors contributed to conception of research, the data analysis and manuscript writing.

Acknowledgements

Wad Medani Maternity Teaching Hospital and Faculty of Medical Laboratory Sciences, University of Gezira were thanked for helping.

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