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Research Article

Activated Partial Thromboplastin Time (APTT) and Prothrombin Time (PT) Level among Sudanese women with Recurrent Miscarriage

Maab Gazi Mohammed Nasr[1] Maye M. Merghani[4], Nihad Elsadig Babiker*,[1,2,3]

[1] *Faculty of Medical Laboratory Sciences, National University, Sudan*

[2] *Darfur University College, Sudan*

[3] *National Center of Neurological Sciences, Sudan*

[4] *Nahda College, Sudan*

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*Address for Correspondence:

Nihad Elsadig Babiker, Faculty of Medical Laboratory Sciences, National University, Sudan

Abstract

Background: Miscarriage is that the commonest complication of pregnancy, defined as rate of pregnancy loss in women with a missed menstrual period and positive urine pregnancy and it is occurrence of three consecutive pregnancy losses during the primary trimester.

Material and methods: This study was an analytical case – control study conducted at the research laboratory of the National university, Khartoum, Sudan during the period July to November, 2021 and aimed estimate activated partial thromboplastin time(APTT) and Prothrombin time (PT) level among Sudanese women with recurrent miscarriage**.** 50 patients attending obstetrics and gynecology unit at Ibrahim Malik teaching hospital and diagnosed with recurrent spontaneous abortion during the mentioned period were selected as cases group. In addition to that, 50 apparently healthy women with no history of abortion and without any other risk factor related to abortion were selected as control group. From each participant 5ml of venous blood samples were dispensed into sterile containers with tri-sodium citrate anticoagulant container for APTT and PT measurement. The tests were performed using semiautomatic device.

Results: In the present study revealed highly significant increase in PT and APTT in case when compared to control. Also PT, APTT, and INR in cases compared with the age group the result revealed that; there was an insignificant difference (P.value ≤ 0.05). In addition, also there were insignificant differences of these parameters when compared with the number of miscarriage and the history of any disease.

Conclusion: In conclusion, Prothrombin time and activated partial thromboplastin time can be use as predictive parameter for further miscarriages in cases of recurrent miscarriage. There is no explanatory cause in women with prolonged PT and APTT.

Keywords: recurrent miscarriage, pregnancy, thromboplastin , PT and APTT

INTRODUCTION

Miscarriage is that the commonest complication of pregnancy, defined as rate of pregnancy loss in women with a missed menstrual period and positive urine pregnancy and it is occurrence of three consecutive pregnancy losses during the primary trimester. The Clinical miscarriages divided to; early clinical pregnancy losses (<12 weeks), and late clinical pregnancy losses (between 12-21 weeks). [1,2]

Purported causes of recurrent miscarriage are multiple ranging from genetic environmental, infectious, metabolic, and endocrine to purely anatomic ones. The best defined causes are parental chromosomal abnormalities, metabolic abnormalities, and anatomic abnormalities. [2]

Coagulation is a dynamic processand normal coagulation pathway represents a balance between the pro-coagulant pathway that is responsible for clot formation and the mechanisms that inhibit the same beyond the injury site. [3]

The hemostatic system consists of blood vessels, platelets, and the plasmacoagulation system including the fibrinolytic factors and their inhibitors. When a blood vessel is injured, three mechanisms operate locally at the site of injury to control bleeding: vessel wall contraction, platelet adhesion and aggregation (platelet plug formation), and plasmatic coagulation to form a fibrin clot. All three mechanisms are essential for normal hemostasis. [4]

Abnormal bleeding usually results from defects in one or more of these three mechanisms. For a better understanding of the pathogenesis of pathological bleeding, it is customary

to divide hemostasis into two stages (i.e., primary and secondary hemostasis). Primary hemostasis is the term used for the instantaneous plug formation upon injury of the vessel wall, which is achieved by vasoconstriction, platelet adhesion, and aggregation. The fibrin formation is not required for hemostasis at this stage. Primary hemostasis is, however, only temporarily effective. Hemorrhage may start again unless the secondary hemostasis reinforces the plateletplug by formation of a stable fibrin clot. Finally, mechanisms within the fibrinolytic system lead to a dissolution of the fibrin clot and to a restoration of normalblood flow. [4]

Recurrent Miscarriage, as well as a complex and multifactorial reproductive health problem that affects people all over the world. The etiology of most types of recurrent miscarriage unknown.The coagulation function in a large series of reproductive-age women diagnosed as Recurrent Miscarriage

In Sudan, to our knowledge there is no published data addressing the association of PT and APTT level as a risk for recurrent miscarriage among Sudanese women. However, the result of such study could improve the management of treatment protocol, for those having higher PAI-1 concentration. The study aimed to explore the association between PT and APTT level and recurrent miscarriage, in order to evaluate whether they could be used as early predictive factors for recurrent miscarriage.

MATERIAL AND METHODS

This study was an analytical case – control study, conducted at the research laboratory of the national university, Khartoum, Sudan during the period July toNovember, 2021. All patients attending obstetrics and gynecology unit at Ibrahem Malikteaching hospital and diagnosed with unexplained recurrent spontaneous abortion (more than three recurrent abortions) during the aforementioned period were included as cases. In addition to that, apparently healthy women with no history of abortion at reproductive age and without any other risk factor related to abortion were selected as control group.

From each participant 5ml of venous blood was withdrawn with minimal stasis from the ante-cubital vein using a dry sterile disposable syringe and needle. Blood samples were dispensed into sterile containers with tri-sodium citrate anticoagulant container forAPTT and PT**.** The coagulation tests (PT and APTT) were performed using semiautomatic device (coagulometer machine).

The participants were interviewed with questionnaires; the questions were about demographic data and clinical information along with other data required in the study. SPSS16.0 statistical software (SPSS Inc., USA) was used for statistical analysis. Data was expressed as means with standard deviations (SD). The statistical analysis was performed by the analysis of variance. A value of $P < 0.05$ was Considered statistically significant. This study was approved by the ethical committee of national university. A written informed consent was obtained from all participants before sample collection.

RESULTS

Socio- demographic data

In the present study 50 women were selected as cases and apparently 50 women were selected as control group. The most affected age group was 25-34 year (58.1%), followed by 35-40 years (30%) and 18-24 (12 %) (Table3.1). The frequency of the miscarriage number was; three time about 44% and more than three time about 56%. in addition, all of the cases their pregnancy outcome is miscarriage, also about 8% had a history of diabetes Miletus, 12% had thyroid disease and only about 8% had a history of genetic disease. For the risk factor only about 4% was smoker. All of the cases are taken folic acid during pregnancy and all of them were diagnosed as unexplained causes of miscarriage (table 3.2)

Table (3.1) Sociodemographic data of the Cases

Sociodemographic data		Frequency	Percent
Age (years)	18-24	6	12.0
	25-34	29	58.0
	35-40	15	30.0
	Total	50	100.0
Miscarriage how many	3	22	44.0
	> 3	28	56.0
	Total	50	100.0
What is the outcome of the pregnancies	Miscarriage	50	100.0
History of any diseases	DM	4	8.0
	Thyroid problem	6	12.0
	No	40	80.0
	Total	50	100.0
Any family history of genetics or inherited disease from (female side)	Yes	4	8.0
	No	46	92.0
	Total	50	100.0
Social background of patient	Smoking	2	4.0
	No	48	96.0
	Total	50	100.0

Table (3.2) Frequency of treatment and diagnosis of miscarriage

		Frequency	Percent
Any previous treatment taken	Yes	10	20.0
	No	40	80.0
	Total	50	100.0
In the pregnancy folic acid taken	Yes	50	100.0
Suggestion of cause	No	48	96.0
	DM	2	4.0
	Total	50	100.0
Diagnosis recurrent miscarriage	Unexplained	49	98.0
	Couldn't remember diagnosis	1	2.0
	Total	50	100.0

Hematological Result

For the PT, APTT, and INR when compared between case and control group there was highly significant differences (p. v= 0.000) (table 3.3) (fig1).

Also PT, APTT, and INR in cases compared with the age group the result revealed that; there was in significant differences (P. value ≤ 0.05) (table 3.4). In addition, also there was in significant differences of these parameters when compared with the number of miscarriage and the history of any disease (table 3.5, 3.6).

Table (3.3) Comparisons of PT, INR and APTT between case and control

Parameters	Case (n=50)	Control (n=50)	P. value
PT (seconds)	19.9 ± 6.1	14.0 ± 2.1	0.000
INR	1.5 ± 0.4	1.4 ± 0.2	0.539
APTT (seconds)	42.1 ± 5.1	33.8 ± 6.7	0.000

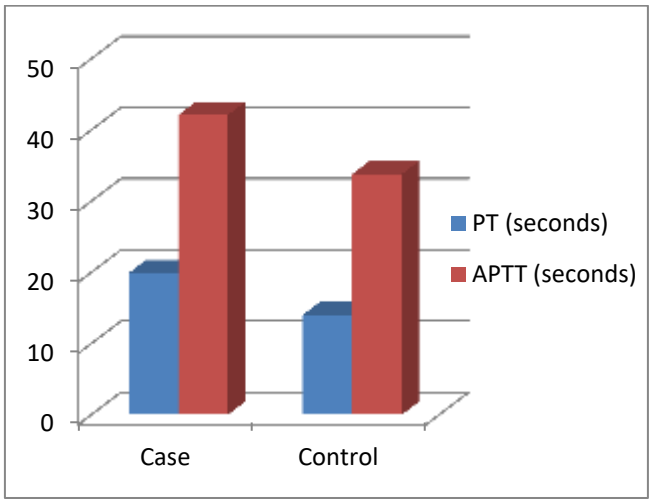

Figure (3.1) Descriptive of hematological parameters in case and control

Table (3.4) Comparisons of PT, INR and APTT according to age of cases

Parameters	Age of patients			P. value
	18-24 (n=6)	25-34 (n=29)	35-40 (n=15)	
PT (seconds)	17.2 ± 6.7	20.3 ± 6.2	20.2 ± 5.7	0.509
INR	1.4 ± 0.6	1.5 ± 0.4	1.5 ± 0.4	0.716
APTT (seconds)	39.8 ± 5.6	42.9 ± 5.2	41.5 ± 4.8	0.358

Table (3.5): Comparisons of PT, INR and APTT according to frequency of miscarriage

Parameters	Frequency of miscarriage		P. values
	3 times (n=22)	>3 times (n=28)	
PT (seconds)	19.3 ± 6.5	20.4 ± 5.8	0.544
INR	1.5 ± 0.5	1.5 ± 0.4	0.699
APTT (seconds)	40.7 ± 5.2	43.2 ± 4.9	0.094

Table (3.6): Comparisons of PT, INR and APTT according to history of any diseases

Parameters	History of any diseases			P. value
	DM (n=4)	Thyroid problem (n=6)	No (n=40)	
PT (seconds)	19.9 ± 7.2	25.4 ± 8.1	19.1 ± 5.3	0.054
INR	1.6 ± 0.4	1.8 ± 0.6	1.5 ± 0.4	0.125
APTT (seconds)	42.3 ± 5.9	42.7 ± 6.5	42.0 ± 4.9	0.957

DISCUSSION

Recurrent miscarriage one of common gynecological distressing condition affecting around 1% of couples tying to conceive it can be very frustrating for both clinicians and patients as, despite intensive workup.[5]

This study includes 100 participants, divided as 50 women suffering from recurrent miscarriage as case and 50 healthy women as control. The results of the demographic data show that, age group was 25-34 year (58.1%), followed by 35-40 years (30%) and 18-24 (12 %). 56.0% of case had mischarge more than three time and 40% three time. also about 8% had a history of diabetes Miletus, 12% had thyroid disease and only about 8% had a history of genetic disease. For the risk factor only about 4% was smoker. Just 20% of cases searching for treatment. All of the cases are taken folic acid during pregnancy and all of them were diagnosed as unexplained causes of miscarriage.

In attempt to answer the question "Can use prothrombin time and activated partial thromboplastin time were a predictive parameter for further miscarriages in cases of recurrent miscarriage? Our result revealed that highly significant increase the mean of APTT value in case (42.1 ± 5.1) compared to control (33.8 ± 6.7) (P=0.000) this results in a similar manner to study done by Nilay Karaca and Lebriz Hale Aktün in Turkey which revealed prolonged APTT in patients[6]. In other hand this result opposite to study done by Aysha Ali *el al*, in Indian population which revealed that significant shortened in mean APTT values of cases were 27.01 and the control was 31.01 (p=0.001) [7] also the same result obtained by Mayumi Ogasawara *el* al, in Japan which showed a shortened APTT before conception is associated with further miscarriages. [8] Furthermore, result of PT value revealed highly significant increase in case (19.9 ± 6.1) compared to control (14.0 ± 2.1) (P=0.000), the results of Mayumi Ogasawara el al, in Japan showed insignificant difference in PT value.

Do the patients' demographic data and the risk factors of recurrent miscarriage affect the level of PT and APTT? The present study demonstrated insignificant difference in PT and APTT level according to age of patients (P ≥ 0.05). Moreover, insignificant difference in PT and APTT level in spite of frequent miscarriage (P ≥ 0.05). Finally, the results again revealed insignificant difference in PT and APTT level in spit the history of any disease (P ≥ 0.05).

The present study revealed a high association between elevated APTT and PT values with recurrent miscarriage.

CONCLUSION

In conclusion, Prothrombin time and activated partial thromboplastin time can be use as predictive parameter for further miscarriages in cases of recurrent miscarriage. There is no explanatory cause in women with prolonged PT and APTT.

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