World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Measurement of coagulation profiles (PT and APTT) among pregnant women with recurrent abortion in Sudan

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World Journal of Advanced Research and Reviews, 2022, 15(03), 473–479

Publication history: Received on 21 August 2022; revised on 25 September 2022; accepted on 27 September 2022

Article DOI: https://doi.org/10.30574/wjarr.2022.15.3.0956

Abstract

Background: Abortion is a very serious problem that affects in health and life of many ladies during childbearing, and research in recent years has shown a link between blood clotting and miscarriage, blood clotting poses a danger to the mother and her baby. Hemostatic disorders in abortion are rare, but when they occur, they can lead to serious complications, and increased blood loss is usually due to incomplete abortion, laceration, perforation, or uterine anatomy rather than coagulation disorder. Severe hemorrhage can induce consumptive coagulopathy. Prothrombin time and activated partial thromboplastin time are preliminary tests of coagulation profile to detect Haemostatic disorders, this study aimed to evaluate the coagulation profile PT and APTT in recurrent abortion and if it is useful to determine the incidence of abortion in women.

Methods and Results: This was a case control study conducted in Khartoum state hospitals (Sudan) during the period of June to August (2019) to measure PT and APTT among ladies with recurrent abortion. The study included 100 samples (50 abortion-50 control), and the diagnosis was based on manual methods. The age group for abortion was between 20 to 45 years old, and the mean age was (32.96) years. In < 30 years the frequency of abortion was 19 (38%) and in > 30 years were 31 (62%). The correlation done between age group and abortion was shows significant results (P value 0.003). And also, the correlation between abortion and PT, APTT was highly significant (P value < 0.005). The frequency of abortions that occurred in the first (64%) was higher than second trimester (36%).

Conclusion: The present study demonstrates a highly significant elevation in PT and APTT in the abortion group compared with the normal group and results were affected by age and month of abortion. The results obtain indicated that measurement of PT, APTT were necessary when evaluating female with recurrent miscarriages, seems to be a predictive parameter for miscarriage.

Keywords: Recurrent abortion; PT; APTT; Measurement of coagulation profile; Pregnant women

1. Introduction

1.1. Abortion (Miscarriage)

Recurrent abortion is defined as ≥2 consecutive pregnancy losses Abortion is a very serious problem that affects in health and life of many ladies during childbearing, and research in recent years has shown a link between blood clotting and miscarriage, blood clotting poses a danger to the mother and her baby. Hemostatic disorders in abortion

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are rare, but when they occur, they can lead to serious complications, and increased blood loss is usually due to incomplete abortion, laceration, perforation, or uterine anatomy rather than coagulation disorder. Severe hemorrhage in itself can induce consumptive coagulopathy. Prothrombin time and Activated partial thromboplastin time are preliminary tests of coagulation profile to detect Haemostatic disorders, this study aimed to evaluate the coagulation profile PT and APTT in recurrent abortion and if it is useful to determine the incidence of abortion in women [1].Recurrent Pregnancy loss (RPL) represents a major health problem, with approximately 15-20 % of all clinically recognized pregnancies resulting in pregnancy loss, it affects approximately 1% to 2% of women. and may be caused by various factors, including genetics, chromosomal abnormalities, thrombosis, immunological disorders, environmental factors, nutritional factors, psychological stress, or maternal infections; however, as many as 50% of RPL cases are idiopathic. Pregnancy complications are still challenge for Gynecologists as knowledge of pathogenesis is still limited. The determination of predisposing factors for the development of recurrent `miscarriage is useful to determine the incidence of abortion in women [2].

1.2. Normal pregnancy

Normal pregnancy is during changes within the coagulation and fibrinolytic systems. These include increases in several clotting factors (I, II, VII, VIII, IX and XII), a decrease in protein S levels, and inhibition of fibrinolysis. As gestation progresses, there's also a big fall within the activity of activated protein C, a very important anticoagulant. While these physiological changes could also be important for minimizing intrapartum blood loss, they entail an increased risk of thromboembolism during pregnancy and therefore the post-partum period [3]. Plasma concentrations of the procoagulants change significantly during normal pregnancy. There are increases in prothrombin (factor II), factor VII, factor X, factor XII [4.5]and factor VIII Prekallikrein levels show a rise during normal pregnancy [6]. But at the onset of labor prekallikrein levels drop and those of kallikrein rise [7]. Early studies on factor XII showed no changes during normal pregnancy, but in later studies levels were shown to be increased in the third trimester. Levels of high-molecular-weight kininogen have also been shown to rise in pregnancy. Results for factor XI have been reported: Philips et al and Beller and Ebert reported that factor XI levels fall gradually, reaching average levels of between 60 and 70% at term–thus conflicting with the findings of Condie who reported that levels of factor XI remain static or show a slight increase [8,9]. Prominent changes occur in pregnancy within the factor VIII complex, with VIII, von Willebrand factor antigen and ristocetin cofactor all significantly increasing. Initially, factor VIII and von Willebrand factor increase in parallel but the ratio of von Willebrand factor antigen to factor VIII coagulant activity changes in the last trimester. This divergence may reflect the selective effect of thrombin on factor VIII coagulant activity [10] Factor VII showed a substantial rise (74%) [5] but none of the other vitamin-K-dependent factors (prothrombin, factor IX or factor X) showed the same magnitude of rising. Several studies have shown marked increases in levels of fibrinogen in normal pregnancy. Allowing for plasma volume increases, the total fibrinogen circulating is twice the non-pregnant amount [6]. Animal studies suggest that the rise is due to increased synthesis. Hormonal changes alone would not appear to be sufficient to account for the full increase in fibrinogen. Factor XIII has been reported to fall in normal pregnancy [10].

1.3. Prothrombin time

The PT test is employed to watch patients taking certain medications likewise on help diagnose clotting disorders. A sample of the patient's blood is obtained by venipuncture. The blood is decalcified (by collecting it into a tube with oxalate or citrate ions) to stop the clotting process from starting before the test. The blood cells are separated from the liquid a part of the blood (plasma) by centrifugation. The PT test is performed by adding the patient's plasma to some source of Tissue Factor (e.g.: a protein, thromboplastin, from homogenized brain tissue) that converts prothrombin to thrombin. The mixture is then kept during a warm water bath at 37 °C for one to 2 minutes. Salt (excess quantities of ionized calcium) is added to the mixture to counteract the sodium citrate and permit clotting to start out. The test is timed from the addition of the salt until the plasma clots [11]. This point is termed the Prothrombin Time [12]. The prothrombin test specifically evaluates the presence of things VII, V, and X, prothrombin, and fibrinogen. A prothrombin time within the 11 -15 second range (depending on the source of thromboplastin used) indicates that the patient has normal amounts of the above clotting factors (27. A protracted prothrombin time indicates a deficiency in any of things VII, X, V, prothrombin, or fibrinogen. it should mean that the patient contains a naphthoquinone deficiency (vitamin K may be a co-factor within the synthesis of functional factors II (prothrombin), VII, IX, and X) or disease (the liver is that the site of synthesis of the protein factors). The prothrombin time of patients receiving a vitamin K-competing coumarin drug like warfarin (anticoagulation therapy employed in deep venous thrombophlebitis) also will be prolonged, usually within the range of 1 and one half to 2 times the conventional PT time [13].

1.4. Activated partial thromboplastin time

The activated partial thromboplastin time (APTT) could be a test performed to research bleeding disorders and to watch patients taking an anticlotting drug like heparin which inhibits factors X and thrombin, while activating anti-thrombin [13]. The APTT test uses blood which is decalcified to stop clotting before the test begins. The plasma is separated by centrifugation. (Ionized) Calcium and activating substances are added to the plasma to start out the intrinsic pathway of the coagulation cascade. The substances are kaolin (hydrated aluminum silicate) and cephalin. Kaolin serves to activate the contact-dependent clotting factor, and cephalin substitutes for platelet phospholipids [11]. The partial thromboplastin time is that the time it takes for a clot to make, measured in seconds. Normally, the sample will clot in 35 seconds. PTT measures the integrity of the intrinsic system (Factors XII, XI, VIII, IX) and customary clotting pathways. Increased levels during a person with a bleeding disorder indicate a plasma protein is also missing or defective. At this time, further investigation is required and warrants the employment of sensitive assays for specific coagulation factors, disease decreases the assembly of things, increasing the PTT [13]. We hypothesized a strong association between hemostatic changes and pregnancy complications, circulatory homoeostasis depends on the equilibrium between vasoconstricting and vasodilating forces regulating blood pressure, as well as the equilibrium between procoagulant and fibrinolytic factors regulating blood rheology [14].

Objectives

- General objectives
  - To measure PT and APTT among Sudanese ladies with abortion in Khartoum state hospitals.
- Specific objectives
  - To measure PT and APTT among Sudanese ladies with abortion compared with normal pregnancy as the control group.
  - To study the association between PT and APTT with the month of abortion.
  - To study the association between PT and APTT with age.

2. Material and methods

2.1. Study group

This is across sectional study conducted in maternity hospitals in Khartoum state, the study included 50 female samples with abortion and 50 females without abortion as control.

2.2. Sample Collection

1.8 ml of venous blood sample was collected in Tri sodium citrate container. The ratio of the blood to citrate was 9:1 then Centrifuged for 15 minutes at 4000 RPM to separate platelet poor plasma and tested within 2 hours by manual method.

2.3. Methods

2.3.1. Prothrombin time

Centrifuge anticoagulated blood at 4000 rpm for 15 minutes to preparation platelet poor plasma (PPP). Pre warm the reagent, control sample and the tested plasma in water bath at 37 °C. Take 200ul(0.2ml) of thromboplastin is added to 100ul(0.1) of PPP(mix well) and start stop watch immediately.Stop the watch as soon as the first fibrin strand is visible & records the time.

2.3.2. Activated partial thromboplastin time

Centrifuge anticoagulated blood at 4000 rpm for 15 minutes to preparation platelet poor plasma (PPP). Pre warm the reagent, control sample and the tested plasma in water bath at 37 °C. Add 100ul of patient PPP in test tube in water bath. Add 100ul of APTT reagent and incubate for 1 min (varies according to reagent used). Add 100ul of cacl2 and start the stopwatch immediately. Stop the watch as soon as the first fibrin strand is visible & records the time.

2.4. Data analysis

The data was computerized and analysed using statistical package for social science (SPSS). p-value less than 0.05 assigned statistically significant.

2.5. Ethical consideration

All information was obtained from participants was kept as highly security data. A consent form was taken from all participants, they were provided with information about the study and any risk that may arise especially when the collection technique was applied. The study was approved by the Ethics Committee at Maternity Hospital (Sudan).

3. Results

The study included 100 samples, 50 samples from recurrent abortion and 50 samples as controls. The age group in abortion was between 20 to 45 years old, the mean age was (32.96 yrs.). In less than 30 years the frequency was 19(38%) and more than 30 years was 31 (62%) (table 3.1). Most of abortion occurred in first and second trimester, frequency was 64% and 36% subsequently, (figure 3.1).

The results of PT in recurrent abortion group shows 58% higher than normal and 48% within normal range (figure 3.2), while APTT shows 76% higher than normal and 24% within the normal range (table 3. 2 and 3). The correlation done between age group and abortion which was shows a significant difference (P value 0.003). And also the correlation between abortion and PT, APTT was highly significant (P value < 0.005) (table 3.4).

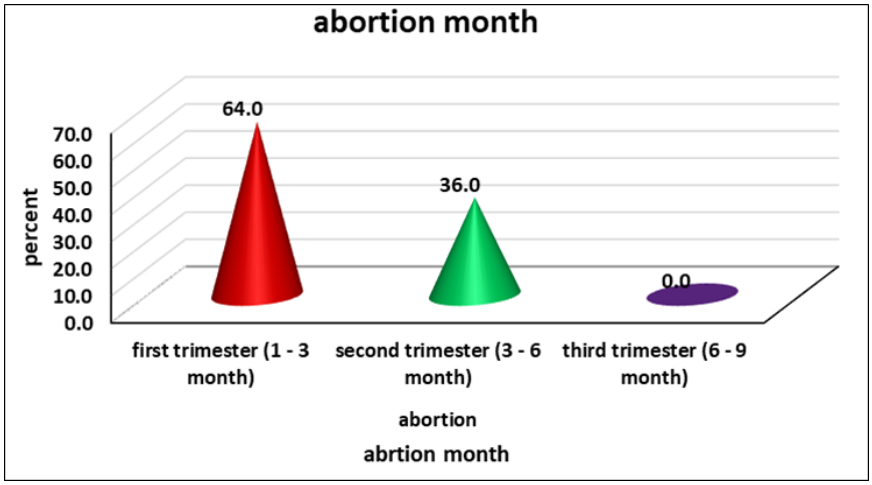

Figure 1 Frequency of gestational period of abortion

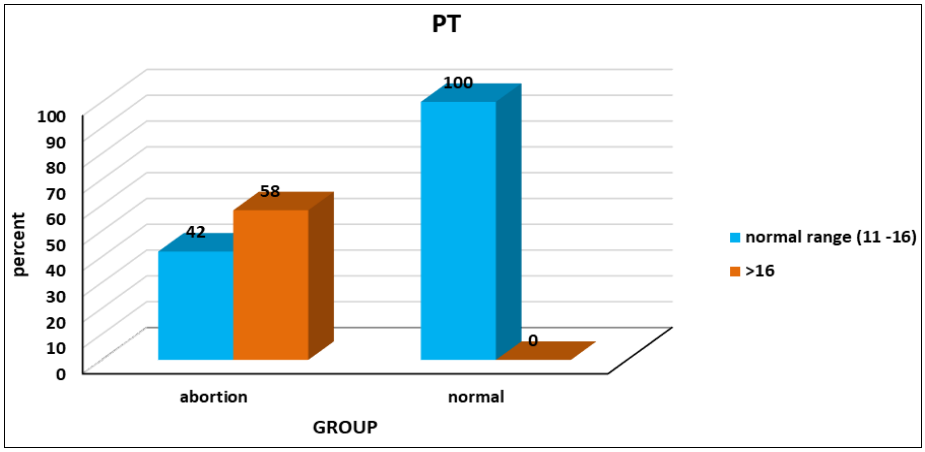

Figure 2 Prothrombin time between the study groups

Table 1 Age frequency between the study group

Study group	Abortion group	Normal group
< 30 years	38%	56%
> 30 years	62%	44%
Total	100%	100%

Table 2 Activated partial thromboplastin time between the study groups

Group	APTT range	Frequency	Percent
Abortion	Within normal range (28 - 40)	12	24
	Higher than normal (>40)	38	76
	Total	50	100
Normal	Normal (28 - 40)	50	100
	Higher than normal	0	0
	Total	50	100

Table 3 Mean and SD of PT and APTT in the study group

Group		age	PT	APTT
Abortion	Mean	32.96	18.98	47.28
	N	50	50	50
	Std. Deviation	5.311	10.397	12.309
Normal	Mean	30.60	14.30	33.34
	N	50	50	50
	Std. Deviation	5.414	1.644	4.284
Total	Mean	31.78	16.64	40.31
	N	100	100	100
	Std. Deviation	5.465	7.770	11.539

Table 4 Measurement of association between the study groups

Variables correlated	P. value
age * Group	0.003
abortion * Group	0.0001
PT * Group	0.002
APTT * Group	0.0001
Significance level	P. value is significant if it is < 0.05

4. Discussion

Recurrent pregnancy loss is defined by the consecutive loss of two or more pregnancies with the same partner. Recurrent pregnancy loss (RPL) or recurrent miscarriage (RM) affects from 1-5% of the reproductive age couples. This diagnosis is both emotionally challenging and confusing for most couples, as the definitive diagnosis using conventional evaluations is found in fewer than half of the couples experiencing repeated loss [15.16], This study was carried out in hospitals in Khartoum state. The preliminary investigations obtained from this study revealed that the PT and PTT levels in Sudanese abortion ladies and normal ladies comparing with age, abortion group were highly significant which was agreed with several studies. The months of abortion in first trimester frequency was (64%), and in second trimester (36%) and third trimester no abortion was occurred. Also this study indicates significant increase in PT and PTT in abortion group when compared with control group, which was agreed with study done in 2012 by Jevara and Esam which was shows 5% had prolonged prothrombin time [17], while disagreed with the study done in 2016 by Ali and in 2015 by Ibeh, et al which was shows the means of the APTT were significantly lower in the first second and third trimesters compared with controls [18,19].Our study indicates that significance in PT and PTT with age group (p-value=0.0030) when comparing with control, also age was significant between abortion group higher in more than 30 years of age. Also, our studies are disagreeing with study conducted among Sudanese women with recurrent pregnancy loss showed no significant change in PT and PTT [20]. This evaluation may be useful in the Improvement of gynecological care of women with recurrent pregnancy loss and accurate knowledge of all significant complications in these women regarding coagulation disorders and formulate a plan to diagnosis and treatment of these conditions.

5. Conclusion

This study revealed that PT and APTT results affected by age of females and month of abortion (shows prolongation) and PT, APTT seem to be predictive parameter for miscarriage.

Recommendation

Recommended to do further studies with large sample size, including other coagulation profiles. Like fibrinogen level, D. dimer and factor V leiden and Prothrombin gene mutation.

Compliance with ethical standards

Acknowledgments

We would like to thank all the pregnant women involved in the study

Disclosure of conflict of interest

The authors declared that no competing interests exist.

Statement of ethical approval

The ethical approval was obtaining from College of Medical Laboratory Science, University of Science and Technology IRB committee.

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