ORIGINAL ARTICLE

Prothrombin Time and Activated Partial Thromboplastin Time in Pregnant Women Attending Antenatal Clinic at Nnamdi Azikiwe University Teaching Hospital (Nauth), Nnewi, Nigeria – A Cohort Study

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ABSTRACT

Background: Normal pregnancy is associated with major changes in many aspects of hemostasis, all contributing to maintain placental function during pregnancy and to prevent excessive bleeding during delivery. Most of these changes in blood coagulation create a state of hypercoagulability. The purpose of this study was to evaluate the values of prothrombin time (PT) and activated partial thromboplastin time (APTT) during normal pregnancy. **Methods:** This was a cohort study carried out at the antenatal clinics of Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria, from January to December, 2016. This research was carried out on 160 apparently healthy pregnant women who presented for booking for antenatal care in their first trimester. Their ages ranged from 20 to 40 years. Similarly, 160 age-matched females consisting of health science students and the staff of NAUTH, constituted the control group. These pregnant women were followed up till the last trimester, but only 140 subjects completed the study. Blood samples collected for PT and APTT were analyzed using standard laboratory methods. **Results:** The mean value of PT in the control subjects (14.68 ± 1.07) was significantly increased when compared with the first trimester (12.86 ± 1.29), second (11.74 ± 1.41), and third (10.96 ± 1.50) (F = 300.9, *P* = 0.000). The mean value of APTT in the control subjects was also significantly increased compared with the first trimester (30.10 ± 4.49), second (29.33 ± 4.59), and third (28.33 ± 4.76) (F = 24.1, *P* = 0.000). When compared among the trimesters, the mean value of PT was significantly shortened from the first (12.86 ± 1.29) to the third (10.96 ± 1.50) (F = 93.4, *P* = 0.000). There was also a significant shortening of APTT from the first trimester (30.10 ± 4.49) to the third (28.33 ± 4.76) (F = 7.6, *P* = 0.001). **Conclusion:** This study has shown that pregnancy shortens PT and APTT. This effect helps to prevent excessive maternal bleeding during delivery. Therefore, early evaluation of these parameters is encouraged to monitor pregnancy and prevent pregnancy complications.

Key words: Activated partial thromboplastin time, Nigeria, Nnewi, pregnancy, prothrombin time

INTRODUCTION

The hemostatic balance tilts in the direction of hypercoagulability which helps to reduce bleeding complications during delivery.[1] The changes in the coagulation system during normal pregnancy are consistent with a continuing low-grade process of intravascular coagulation.[2] The hormones which are necessary for the maintenance of pregnancy, that is, estrogen and progesterone increase several folds and these, especially estrogen stimulate hepatocytes thereby increasing the production of virtually all coagulation factors. Evaluation of levels of certain coagulation factors occur in practically all healthy pregnant women which are most likely the result of small amounts

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of pro-coagulant factors such as tissue thromboplastin, which could cause direct and slow systemic activation of the coagulation cascade.[3] Changes in coagulation system could be due to increased synthesis or increased activation by coagulation factors. These changes serve to protect the mother from hazard of bleeding imposed by placentation and delivery, but they also carry the risk of an exaggerated response, localized, or generalized.[4]

According to a research,[5] the prothrombin time (PT), which assesses the factors in the extrinsic pathway, was reduced when compared with the value in non-pregnant controls. He showed that the mean PTs in the first, second, and third trimesters of pregnancy showed that production of these coagulation factors increases as pregnancy advanced as there was statistically significant reduction in PT from the first to the third trimesters of pregnancy. Significant difference was also noticed in the activated partial thromboplastin time (APTT) with Kaolin among the pregnant and control subjects, which shows that levels of factors in the intrinsic pathway are also increased in normal pregnancy. There was no statistically significant difference in the result of APTT in various trimesters of pregnancy. This may probably be due to the fact that the estrogen-induced stimulation of factors VIII and IX production is much less that for the extrinsic pathway factors. The very high prevalence of shortened PT and APTT during the third trimester of pregnancy and labor when chances of bleeding is highest seem to be common.[6] Therefore, the aim of this study was to longitudinally determine the values of PT and APTT during normal pregnancy at Nnewi, Nigeria. The findings will encourage early evaluation and management of pregnancy to prevent bleeding and other pregnancy complications.

MATERIALS AND METHODS

Study area

The research was conducted between January and December, 2016 at the antenatal clinics of Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi.

Subjects

One hundred and sixty (160) apparently healthy pregnant women who presented for booking for antenatal care in their first trimester (3rd month) visit were enrolled for the study of which only 140 subjects completed the study. Their age range was between 20 and 40 years. The control group constituted of 160 age-matched non-pregnant females, comprising students in the faculty of health science and staff of NAUTH. The pregnant women were followed-up till the last trimester. During the second trimester (5th month), 156 pregnant women were followed-up, but only 140 completed the study in the third trimester (8th Month). Pregnant women who could not complete the research study had still birth, miscarried changed address, or was not interested in the study again. Results were compared between pregnant women and the control subjects, and comparisons were also made among the trimesters.

Sample collection

Four milliliters (4 mls) of blood was collected from each subjects by means of hypodermic syringe and needle, and 2 mL was aliquoted into plain tubes and used for screening for HIV I and II, Hepatitis B surface Antigen (HBsAg), Hepatitis C Virus, and Venerable Disease Research laboratory qualitatively, while the remaining 2 mL was put into sodium citrate anticoagulant bottles.

Hematological assay

The PT and APTT tests were determined using the Dia-Pt and APTT kits by Diagon Ltd., Hungary. The same tests were conducted on the non-pregnant females at NAUTH laboratories. Pregnancy test was conducted on the non-pregnant females to confirm that there was no pregnant.

The blood pressure was measured using a sphygmomanometer at all trimesters. The weight and height were measured and used to calculate the body mass index, which was expressed as weight (kg)/height (m^2). This study was approved by the Ethics Review Committee of NAUTH and informed consent was obtained from the pregnant women before recruiting them for the study.

Statistical analysis

The statistical analysis was performed using the Statistical Package for the Social Sciences versions 2010. Students unpaired two-tailed *t*-test was used to determine whether a parameter from two different groups differ significantly or not. Comparisons with regard to trimester were analyzed using one–way analysis or variance and statistical significance was calculated using *Post hoc* test to analyze the result of the experimental data. $P < 0.05$ was considered to be statistically significant.

RESULTS

The table 1 showed the mean level of PT in the control subjects (14.68 ± 1.07) was significantly increased when compared with the first trimester (12.86 ± 1.29), second (11.74 ± 1.41) and third (10.96 ± 1.50) (F = 300.9, P = 0.000). The mean value of APTT in the control subjects was also significantly increased compared with the first trimester (30.10 ± 4.49), second (29.33 ± 4.59) and third (28.33 ± 4.76) (F = 24.1, P = 0.000).

Table 2 showed the mean level of PT was significantly shortened from the first trimester (12.86 ± 1.29) to the third trimester (10.96 ± 1.50) (F = 93.4, P = 0.000). There was a significant shortening in APTT from the first trimester (30.10 ± 4.49) to the third (28.33 ± 4.76) (F = 7.6, P = 0.001).

Table 1: Mean PT and APTT in non-pregnancy females (control), first, second, and third trimesters

Control/trimester	PT (s)	APTT (s)
Control *n*=160	14.68±1.07	32.09±4.72
First trim *n*=160	12.86±1.29	30.10±4.49
Second trim *n*=156	11.74±1.41	29.33±4.54
Third trim *n*=140	10.96±1.50	28.33±4.76
F (*P*-value)	300.9 (0.000)*	28.33 (0.000)*
	Post hoc	
C versus 1st	0.000*	0.000*
C versus 2nd	0.000*	0.000*
C versus 3rd	0.000*	0.000*
1st versus 2nd	0.000*	0.338*
2nd versus 3rd	0.000*	0.127
1st versus 3rd	0.000*	0.001*

*Significant at $p<0.05$. PT: Prothrombin time, APTT; Activated partial thromboplastin time

Table 2: Mean Prothrombin Time and Activated Partial Thromboplastin Time in First, Second, Third Trimesters and Non-Pregnancy Females (Control)

Trimester	PT (s)	APTT (s)
First trim *n*=160	12.86±1.29	30.10±4.49
Second trim *n*=156	11.74±1.41	29.33±4.54
Third trim *n*=140	10.96±1.50	28.33±4.76
F (*P*-value)	93.4 (0.000)*	7.6 (0.001)*
	Post hoc	
1st versus 2nd	0.000*	0.212
2nd versus 3rd	0.000*	0.071
1st versus 3rd	0.000*	0.000*

*Significant at $P<0.05$. PT: Prothrombin time, APTT: Activated partial thromboplastin time

DISCUSSION

During pregnancy, the coagulation system undergoes significant changes, for example, hormonal changes. These changes help in maintaining placental function during pregnancy, protects from fetal hemorrhage during delivery, but at the same time predisposes to thromboembolism.[7] Thrombophilia predisposes a woman to an increased risk of developing both early and late complications in pregnancy. This includes recurrent miscarriages and late placental vascular-mediated problems (fetal loss, preeclampsia, placental abruption, and intrauterine growth restriction.[8] In this study, the profile showed that PT significantly shortened in pregnancy compared with the non-pregnant female controls. This is in agreement with the study of,[8] who showed that PT is shortened in pregnancy than in the non-pregnant controls. It is also consistent with the work done by Hellgren in 2003. There was reduced PT during pregnancy compared to non-pregnancy according to Durotoye *et al*.[5] It was reported that PT as being significantly shortened in pregnancy compared with control.[3] It has been shown that prolongation of PT in the face of what was otherwise called a hypercoagulable state.[9,10] It has been shown that PT remains unchanged in pregnancy.[11] It was shown that there is a high prevalence of shortened PT (22.5%) and APTT (37.6%), in pregnancy.[6]

Different values of PT by various authors may be associated with the sensitivities of the reagents and techniques employed. However, variability in PT results from different researchers have been traced to the differing sensitivities of the thromboplastin reagents used, concentration of citrate anticoagulation, and method of analysis.[12] APTT was also shortened in pregnancy as compared to the non-pregnant females, and it is in line with.[1,13] This shows that levels of factors (FV, FViii, Fix, and Fxii) in the intrinsic pathway are also increased in normal pregnancy.[5,14] The study of[13] also showed that the APTT were significantly lower in the first, second, and third trimester compared with controls. Both PT and APTT were shortened to protect the mother from the hazard of bleeding imposed by placentation and delivery. This is similar to the work of[15] who showed shortened PT and APTT in all trimesters compared with controls. The reason might be to maintain placental function and prevent maternal bleeding in every stage of the pregnancy. There was a significant decrease in PT from the first to the third trimester. This is in line with the work done by[16] who stated that the mean PT in the subjects in the first, second, and third trimesters of pregnancy showed that production of the coagulation factors increases as pregnancy advanced as there was statistically significant reduction in PT from the first to the third trimesters. There was significant difference in the levels of APTT when compared among the trimesters. This also agrees with the study of[17,18] who followed the same pattern. This might be due to increased synthesis or increased activation by coagulation factors.

CONCLUSION

The study has concluded that pregnancy shortens Prothrombin and APTT. In other words, it results to a transient hyper-coagulable state. This aids in preventing excessive maternal bleeding during delivery. Therefore, early evaluation of these parameters is encouraged to monitor pregnancy and prevent complications in pregnancy.

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