INTRODUCTION

In order to ensure that thrombin generation is limited and localised to prevent thrombosis after minor injury, coagulation inhibitors play a vital role\textsuperscript{[1,2]}. The natural coagulation inhibitors can be of endothelial or hepatic group, based on their synthetic sites\textsuperscript{[1]}. Antithrombin III, heparin, heparin co-factor II, antitrypsin and tissue-factor pathway inhibitor (TFPI) are inhibitors of serine proteases of the coagulation cascade such as thrombin, Xa and TF-VIIa\textsuperscript{[2]}\textsuperscript{[2]}. Antithrombin III accounts for about 60\% of plasma anticoagulant activities and it plays its inhibitory role by not only complexing with thrombin but also by inhibiting the clotting factors XIIa, XIa, IXa and Xa in the presence of heparin sulphate on the endothelial cell surface\textsuperscript{[2-5]}\textsuperscript{[2]-\textsuperscript{5]}.

Protein C, TM (thrombomodulin), protein S, C4b binding protein and APC (activated protein C) inhibitor are all components of the protein C system\textsuperscript{[2]}\textsuperscript{[2]}. Activation of this system occurs when thrombomodulin binds to thrombin to form activated protein C (APC) which rapidly degrades factors VIIIa and Va on the phospholipid surface of activated platelets and prevents the appropriate tenase and prothrombinase complexes, a reaction that increases 10-20 folds.

ABSTRACT

AIM: In order to ensure that thrombin generation is limited and localised to prevent thrombosis after minor injury, coagulation inhibitors play a vital role. The study assessed protein C and antithrombin III levels in pregnant women in Kano, North-Western Nigeria.

MATERIALS AND METHODS: A total of two-hundred and fifty apparently healthy subjects (150 pregnant and 100 non-pregnant women), aged 17-40 years were recruited for the study in Aminu Kano Teaching Hospital, Kano between August 2010 and October 2011. Blood samples collected were analysed for Protein C and antithrombin III activities using standard laboratory procedures.

RESULTS: There was significantly lower value of proteins C activity in pregnant women compared to non-pregnant women \((P<0.05)\) while the values of antithrombin III in pregnant and non-pregnant women showed no statistically significant difference \((P>0.05)\). Different and fluctuated values of Protein C activities and antithrombin III activities with regard to first, second and third trimesters respectively, showed no significant differences \((P>0.05)\). Maternal age and parity had no significant influences on protein C and antithrombin III activities.

CONCLUSION: Pregnancy is associated with significantly lower value of protein C activity while antithrombin level remained stable and unchanged. Gestational age, maternal age and parity showed no influences in protein C and antithrombin III activities. It is recommended that protein C activity be assessed in pregnant women to avoid thromboembolism.

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Key words: Protein C; Antithrombin III; Activities; Healthy Nigerian women

when protein C combines with its co-factor protein S\(^{[14]}\).

Antithrombin concentration varies with race, age, sex and methodology used\(^{[5,10]}\). Conflicting reports have been made on the levels of antithrombin III in pregnancy as reduced activity was documented by earlier author\(^{[12]}\), increased activity was reported by During et al.\(^{[13]}\) while majority of the studies reported no significant changes\(^{[14-16]}\). Earlier researcher documented reduced protein C activity during pregnancy\(^{[17]}\) while other studies showed stable and unchanged levels of protein C during pregnancy\(^{[18-20]}\).

The study was to determine protein C and antithrombin III levels in pregnancy as extremely scanty information on these naturally occurring anticoagulants is available in Nigeria.

**MATERIALS AND METHODS**

A total of two-hundred and fifty apparently healthy subjects (150 pregnant and non-pregnant women), aged 17-40 years were recruited for this study in Aminu Kano Teaching Hospital (AKTH), Kano between August 2010 and October 2011. Ethical approval and consent were obtained from the ethical committee of AKTH, Kano and the subjects respectively. Pregnant and non-pregnant women with histories of recurrent miscarriages, liver disease, renal disease, diabetes and hypertension and non-pregnant women who are on oral contraceptives were excluded from the study.

4.5 mL of venous blood sample was collected from each subject and mixed with 0.5 mL of 32.0 g/L trisodium citrate solution in the plain container. Blood samples in the citrated containers were centrifuged at 2,500 g for 15 minutes and the plasma separated into plastic containers for the determination of protein C and antithrombin III activities.

Protein C and antithrombin III activities were assayed according to the instructions of TECChrom kits with reference numbers C1100-012 and C1000-010 respectively, manufactured in Germany and the clotting times determined using Cormay KG coagulometer manufactured in Poland.

**Statistical analysis**

The mean values and standard deviations of the parameters in the pregnant and non-pregnant women were assessed using student’s \(t\)-test while the differences with regard to gestation period, maternal age and parity were assessed using one-way analysis of variance (ANOVA). \(P\)-value of \(\leq 0.05\) was considered significant.

**RESULTS**

Table 1 shows protein C and antithrombin III levels in pregnant and non-pregnant women. Pregnant women showed significantly lower value of protein C activity (55.4±29.0%) compared to non-pregnant women (86.0±32.7%) \((P<0.05)\) while the values of antithrombin III in pregnant and non-pregnant women showed no statistically significant difference \((P=0.05)\).

Changes in protein C and antithrombin III activities with gestation period (trimester) are summarised in table 2. Different and fluctuated values of protein C activities (52.9±28.4%, 60.0±31.4% and 51.3±26.1%) and antithrombin III activities (85.58±14.88%, 79.64±19.73% and 85.34±12.01%) with regard to first, second and third trimesters respectively, showed no statistically significant difference \((P>0.05)\).

Table 3 indicates the effects of maternal age on protein C and antithrombin III activities. Different values of protein C activities (61.4±35.0%, 53.7±30.0%, 60.3±26.9% and 45.2±23.1%) and antithrombin III activities (78.34±22.96%, 82.7±15.26%, 85.37±13.47% and 74.81±18.14%) with regard to age-groups 17-22 years, 23-28 years, 29-34 years and 35-40 years respectively, showed no statistically significant differences \((P>0.05)\).

**DISCUSSIONS**

Deficiencies of naturally occurring anticoagulant proteins such as antithrombin III, protein C and protein S produce favourable medium for thrombus generation which has been linked to thromboembolic disease\(^{[17,23]}\). This study has shown significantly lower value of protein C activity in pregnant women compared to the control subjects. This is in line with the previous authors\(^{[11,12,14]}\) but disagrees with other researchers who reported no significant change\(^{[23]}\). Inconsistent reports of protein C levels during pregnancy by various authors might be associated with different sensitivities and specificities of protein C reagents.
used, and assay techniques employed. The study further showed the stability of protein C levels within the gestation period which is consistent with other studies\textsuperscript{[6,12,13]}; however, protein C deficiency has been associated with venous thromboembolism\textsuperscript{[26,27]}. Maternal age and parity had no significant effects on protein C activity within the period of pregnancy but showed significance when compared to non-pregnant status. However, maternal age of 35-40 years showed the least protein C level which could make an advanced maternal age a risk factor to thrombosis.

This study has further demonstrated that antithrombin III level showed no significant difference in pregnant women. This finding agrees with the majority of the earlier studies\textsuperscript{[6,12,13]} but disagrees with the significantly lower value reported by Essien\textsuperscript{[11]} likely due to the variation of sensitivities and specificities of antithrombin III reagents used. This study has further confirmed the earlier studies that gestational age had no effect on antithrombin III activity\textsuperscript{[6,27]}. Maternal age and parity showed no influences on antithrombin III level during pregnancy in this study. However, variation in antithrombin III levels in pregnancy as reported by various authors\textsuperscript{[6,12,13]} could be associated with methodology employed, poor storage of citrated plasma and reagents and sample size.

In conclusion, pregnancy is associated with significantly lower value of protein C activity while antithrombin III level showed no significant difference. Gestational age, maternal age and parity showed no influences on protein C and antithrombin III activities. It is recommended that protein C activity be assessed amongst other routine tests for pregnant women since its deficiency has been linked to thromboembolism.

**CONFLICT OF INTERESTS**

The author has no conflicts of interest to declare.

**REFERENCES**


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