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Relationship between Natural Coagulation Inhibitor and Obstetrics History in Predicting Thromboembolic Events during Pregnancy

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: There is a low level of information on natural coagulation inhibitors in this environment and whether the early detection of its deficiencies could serve as a risk assessment tool for thromboembolic events in pregnancy. This study aims to determine the relationship between natural coagulation inhibitors and obstetrics history in predicting thromboembolic events during pregnancy.
Methods: The study was a comparative cross-sectional hospital-based study conducted among one hundred and fifty pregnant women and age-matched healthy non-pregnant control. Obstetrics history was obtained via questionnaire and other information was extracted from case notes. Blood specimens were obtained for laboratory assessment of natural coagulation inhibitors (Protein C, S, and antithrombin III) at various trimesters of pregnancy. Data were analyzed using SPSS version 23.
Results: All NCIs decreased across the three trimesters of pregnancy but only the mean protein S and antithrombin III decreased with statistical significance (p = 0.001). Protein C, S, and antithrombin III did not show a statistically significant association when correlated with obstetrics histories.
Conclusion: Although this study demonstrated a progressive decrease in the levels of NCIs across various trimesters of pregnancy, the use of NCIs as predictive tools for thromboembolic events in women with past bad obstetrics histories was not established but rather for risk assessment during pregnancy regardless of past obstetrics history.

Keywords: NCIs; protein C; protein S; antithrombin III; Nigeria.

1. INTRODUCTION

Pregnancy is recognized as a hypercoagulable state that protects women from potentially catastrophic hemorrhage during placentation and the post-partum period [1]. Normal pregnancy has been associated with alteration of the homeostatic system which has been linked to an increased risk of thromboembolic complications [2,3].

The incidence of venous thromboembolism (VTE) during pregnancy has been estimated to be approximately 1 per 1000 deliveries and this is 5.5-6 times higher than the general female population of childbearing age [1]. Several investigators have reported an association between thrombophilia and adverse pregnancy outcomes caused by uteroplacental thrombosis. Other groups, however, have failed to confirm this association [4].

Protein S and protein C deficiencies have been found in the general population including pregnant women. Also, antithrombin III deficiency is associated with recurrent miscarriages [5,6]. Several reports have regarded platelet count, prothrombin time and activated partial thromboplastin time, and clotting factors assay as markers for thromboembolic disorder in pregnancy [7,8].

Normal pregnancy is associated with significant changes in venous stasis, endothelial damage, and enhanced coagulation (Virchow triad), shifting the equilibrium towards a hypercoagulable state [9]. These include increasing concentrations of most clotting factors, decreasing concentrations of some of the natural anticoagulants, and reducing fibrinolytic activity [9]. Indeed, there is a significant decrease in protein S activity and a progressive increase in resistance to activated protein C in the second and third trimesters of pregnancy [10].

The maternal mortality ratio has remained unacceptably high, despite all efforts to curb the trend in Nigeria and in most developing countries [5,11]. Several studies from different parts of Nigeria have reported different figures, ranging from 532-2989 per 100,000 live births [9]. Several efforts have been made to reduce maternal death from postpartum hemorrhage (PPH) over some years now and these have yielded positive results with maternal death from PPH reducing drastically [9,12].

Other causes of maternal death are frequently undiagnosed or under-diagnosed and these deaths are sparingly reported, and even when reported, autopsies are rarely done to establish the cause of such mortality [11]. However, most of these deaths result from thromboembolic disease in pregnancy [11]. Approximately 50% of

women with venous thrombo-embolic (VTE) disorders detected during pregnancy or puerperium have an underlying hereditary thrombophilia in addition to other acquired risks [13].

However, there is a paucity of information on the level of natural coagulation inhibitors in this environment and whether the early detection of its deficiencies could serve as a risk assessment tool for thromboembolic events in pregnancy, therefore, this study aimed to find any relationship between natural coagulation inhibitor and obstetric history in predicting thromboembolic events during pregnancy.

2. METHODOLOGY

2.1 Study Design

The study was a comparative cross-sectional hospital-based study conducted among pregnant women attending booking clinics and antenatal clinics at LAUTECH Teaching Hospital, Ogbomoso.

The study included a total of seventy-five (twenty-five in each trimester of pregnancy) normal pregnant women between 15- 49 years. Seventy-five age-matched healthy non-pregnant women were recruited as control.

2.2 Sample Size Calculation

The minimum sample size for patients was calculated using the statistical formula that compares two prevalences [14]. The minimum sample size derived was 24.55. To enhance the power of this study, a sample size of 75 was considered for both subjects and controls with a total sample size of 150 participants.

2.3 Study Instrument

A semi-structured questionnaire was used as the survey instrument to seek information on the subject's socio-demographic characteristics, pregnancy history, and risk factors for thromboembolism. A reliability test was done on the questionnaire at the state general hospital by interviewer-administered method.

2.4 Procedures

Study group subjects with normal pregnancy were recruited from the antenatal clinic, booking clinic, and labor ward while control subjects were recruited from nonpregnant women. This was done using a simple random sampling method in which each member of the population has an equal probability of being chosen.

Blood specimens (5mls) were collected in EDTA bottles analysis of Protein C, Protein S, and Antithrombin III assays using the enzyme-linked immunosorbent assay technique.

2.5 Data Analysis

The statistical analysis was carried out using Statistical Package for Social Science (SPSS) version 23. A multivariate analysis was done. Mean and standard deviation were used to report baseline continuous variables while frequency and proportions were used to report categorical variables. Pearson's chi-squared, and student T-test were used to compare variables as appropriate. Regression analysis was modeled to assess the independent correlation between natural anticoagulants and obstetric histories.

3. RESULTS

The mean ages of the subjects and control group were 32.6±4.6 and 34.5±6.9 years respectively. There was no statistically significant difference between the 2 groups (p=0.508).

The majority of participants in the subjects and control group have had a history of two to three pregnancies before (study: 56%, control: 58.7%) respectively. 37.7% of the subjects and 34.5% of the control group had previous miscarriages respectively.

The proportion of subjects with a history of high blood pressure during pregnancy was almost similar across groups with 5.3% of subjects and 6.9% of the control groups respectively. Two (3.8%) of the subjects and none of the control group had a history of intrauterine fetal death (p = 0.155). Histories of unilateral leg swelling, and complications associated with placenta e.g. abruptio placenta, placenta previa, and breathlessness before/after delivery were not also significantly different between the two groups.

There was a significant difference in mean protein C across age groups of subjects in the first-trimester group (t=4.768, p-value = 0.000). Among subjects in the second trimester, there was a significant difference in Antithrombin III

across age groups of subjects, p-value = 0.035. However, none of the NCI differed significantly by age and religion of subjects in the third trimester, p-value > 0.05.

Table 1. Socio-demographic characteristics of subjects

Variables	Control group n (%)	Subjects n (%)	χ^2	p-value
Age (Years)				
20 - 24	7 (9.3)	9 (12.0)	5.287	0.508
25 - 29	23 (30.7)	26 (34.7)		
30 - 34	34 (45.3)	30 (40.0)		
35 – 39	6 (8.0)	9 (12.0)		
40 – 44	1 (1.3)	1 (1.3)		
45 – 49	4 (5.4)	0 (0.0)		
Mean ± SD	34.5 ± 6.9	32.6 ± 4.6		
Religion				
Christianity	62 (82.7)	53 (70.7)	3.091	0.082
Muslim	13 (17.3)	22 (29.3)		
Marital Status				
Married	63 (84.0)	74 (98.7)	10.247	*0.006
Single	10 (13.3)	1 (1.3)		
Widowed	2 (2.7)	0 (0.0)		
Ethnicity				
Yoruba	75 (100)	70 (93.3)	5.172	0.075
Igbo	0 (0.0)	2 (2.7)		
Others	0 (0.0)	3 (4.0)		
Level of education				
Primary education	0 (0.0)	1 (1.3)	3.934	0.140
Secondary education	4 (5.3)	10 (13.3)		
Tertiary education	71 (94.7)	64 (85.3)		

χ^2: Chi-square statistic, p-value < 0.05 indicates significance

Table 2. Comparison of Gynaecological history between subjects and controls

Variables	Control group n (%)	Subjects n (%)	χ^2	p-value
No of pregnancies				
0	17 (22.7)	0 (0.0)	21.064	*<0.0001
1	0 (0.0)	22 (29.3)		
2 – 3	44 (58.7)	42 (56)		
> 3	14 (18.7)	11 (14.7)		
Previous miscarriage				
Yes	20 (34.5)	20 (37.7)		0.873
No	38(65.5)	33 (62.3)		
Number of miscarriages				
One	14 (70.0)	15 (75.0)		0.915
Two	4 (20.0)	3 (15.0)		
Three	4 (10.0)	2 (10.0)		
High blood pressure in pregnancy				
Yes	4 (6.9)	4 (5.3)		0.993
No	54 (93.1)	71 (94.7)		
Need for cervical cerclage				
Yes	0 (0.0)	3 (5.7)		0.341
No	58 (100)	50 (94.3)		
Intrauterine fetal death				
Yes	0 (0.0)	2 (3.8)		0.436
No	58 (100)	51 (96.2)		

Variables	Control group n (%)	Subjects n (%)	χ^2	p-value
Delivery before 37 weeks				
Yes	6 (10.3)	10 (18.9)		0.314
No	52(89.7)	43 (81.1)		
Intrauterine growth restriction				
Yes	2 (3.7)	1 (1.9)		1.000
No	56 (96.6)	52 (98.1)		

χ^2: Chi-square statistic, p-value < 0.05 indicates significance

Table 2. Continued

Variables	Control group n (%)	Cases n (%)	χ^2	p-value
Unilateral swelling of limbs				
Yes	0 (0.0)	1 (1.3)	0.000	1.000
No	58 (100)	74 (98.7)		
Complications associated with placenta				
Yes	0 (0.0)	1 (1.3)	2.0743	0.1498
No	58 (100)	52 (98.7)		
Breathlessness before/after delivery				
Yes	6 (8.0)	1 (1.3)	2.0743	0.1498
No	52(92.0)	52 (98.7)		

*χ^2: Chi square statistic, *p-value < 0.05 indicates significance*

There was no significant difference in mean protein C, Protein S, and Antithrombin across age and religion of respondents among control subjects, p-value > 0.05.

Fig. 1 shows the relationship between plasma levels of coagulation inhibitors among pregnant women in different gestation ages. Protein C, Protein S, and antithrombin III all declined with gestational age.

The mean protein C decreased from the first to the third trimester (first: 1094.1 ± 276.7pg/ml, second: 1064 ± 241.2pg/ml, third: 1043.8 ± 218.0pg/ml). These differences were not significant (p=0.769).

The mean protein S among subjects in the first trimester was 5.7 ± 0.7ng/ml and 4.8 ± 0.7ng/ml in both the second and third trimesters. These differences were statistically significant (p=0.001).

The mean antithrombin III decreased from the first trimester to the third trimester (first: 603.5 ± 56.4 ng/ml, second: 570.8 ± 57.6ng/ml, third: 530.0 ± 48.1ng/ml). These differences were statistically significant (p=0.001).

Among subjects in the first trimester, the mean protein C was significantly higher in subjects with delivery <37 weeks p-value = 0.019. The mean protein C did not differ by no of pregnancy, previous miscarriage, and high BP, p-value >0.05.

Protein S differed significantly by no of pregnancy and was higher among subjects with previous miscarriage, p-value <0.05. Antithrombin III does not differ by any obstetric parameter, p-value >0.05. Table 4a.

Among subjects in the second trimester, the mean Protein C and protein S did not differ by obstetrics parameters, p-value > 0.05. However, the mean antithrombin III differed significantly by the number of previous pregnancies, p-value <005. Table 4b.

Among subjects in the third trimester, protein C and protein S did not differ by any of the obstetrics parameters, p-value > 0.05. However, antithrombin III was significantly higher among subjects with unilateral swelling of limbs and problems with the placenta, p-value < 0.05. Table 4c.

Among controls, the mean protein C differed significantly by the number of pregnancies, p-value = 0.014. Also, the mean protein C was significantly higher among subjects with previous miscarriage and delivery < 37 weeks, p-value < 0.05. Similarly, protein C was higher among subjects with breathlessness before or after delivery, p-value < 0.05.

Table 3. Socio-demographic characteristics and NCI in test subjects

Trimester group	Variables	Protein C Mean ± SD	F/t (p-value)	Protein S Mean ± SD	F/t (p-value)	Antithrombin III Mean ± SD	F/t (p-value)
First trimester	**Age (Years)**						
	Less than 30	998.8 ± 274.7	2.287 (*0.032)	5.7 ± 0.83	0.731 (0.472)	597.2 ± 56.6	0.678 (0.504)
	30 and above	1237 ± 221.4		5.9 ± 0.40		613.0 ± 57.8	
	Religion						
	Christianity	1109.0 ± 287.5		5.9 ± 0.6	0.660 (0.516)	615.40 ± 49.3	0.855 (0.402)
	Islam	1084.1 ± 287.5	0.216 (0.831)	5.7 ± 0.8		595.60 ± 61.1	
	Age (Years)						
	Less than 30	1102.5 ± 230.1		4.9 ± 0.7		600.0 ± 58.4	2.237 (*0.035)
	30 and above	1038.3 ± 252.8		4.8 ± 0.8		515.3 ± 49.8	
Second trimester	**Religion**				0.038 (0.970)		
	Christianity	1005.9 ± 216.4	0.644 (0.526)	4.8 ± 0.8		570.3 ± 59.5	0.092 (0.927)
	Islam	1368.8 ± 76.6		5.2 ± 0.6		573.3 ± 54.6	
	Age (Years)						
	Less than 30	1058.5 ± 228.8	5.976 (*0.001)	4.78 ± 0.9	0.883 (0.386)	523.0 ± 46.1	0.586 (0.564)
	30 and above	1034.0 ± 218.2		4.9 ± 0.6		534.7 ± 50.5	
Third trimester	**Religion**						
	Christianity	1014.5 ± 211.8	0.270 (0.790	4.8 ± 0.7	0.392 (0.698)	529.3 ± 50.4	0.188 (0.853)
	Islam	1258.3 ± 145.1		5.1 ± 0.8		535.0 ± 33.6	
			1.915 (0.068)		0.646 (0.525)		

**t: t-statistic, F: F statistic, p-value < 005 indicates significance*

Table 4a. Relationship between NCI and obstetrics history of test subjects in the first trimester

Trimester group	Variables	Protein C Mean ± SD	F/t (p-value)	Protein S Mean ± SD	F/t (p-value)	Antithrombin III Mean ± SD	F/t (p-value)
First Trimester	**No of Pregnancy**						
	0-1	988.57 ± 315.66	0.762	5.87 ± 0.44	4.725 (0.020)*	602.57 ± 45.27	1.736
	2	1162.50 ± 273.32	(0.479)	5.27 ± 0.81		577.00 ± 70.16	(0.199)
	>3	1113.20 ± 257.83		6.15 ± 0.51		625.40 ± 46.25	
	Previous Miscarriage						
	Yes	1113.20 ± 257.83	0.277	6.15 ± 0.51	2.421 (0.024*)	625.40 ± 46.26	1.637
	No	1081.33 ± 298.86	(0.785)	5.52 ± 0.70		588.93 ± 59.28	(0.115)
	High BP in pregnancy						
	Yes	1205.00 ± 0.00	0.583	5.98 ± 0.00	0.429 (0.672)	555.00 8± 0.00	-1.285
	No	1084.43 ±2 86.94	(0.566)	5.76 ± 0.72		607.748 ± 56.93	(0.212)
	Intrauterine foetal death						
	Yes	840.01 ± 0.00	-0.925	4.97 ± 0.00	-1.208 (0.239)	609.01 ± 0.00	0.097
	No	1104.68 ± 277.48	(0.360)	5.82 ± 0.69		603.29 ± 57.63	(0.924)
	Delivery < 37 weeks						
	Yes	1318.34 ± 88.81	2.517	5.74 ± 0.40	-0.176 (0.862)	620.01 ± 50.50	0.815
	No	1023.80 ± 279.05	(0.019)*	5.80 ± 0.74		5988.33 ± 55.77	(0.424)
	Unilateral swelling of limbs	0.00 ± 0.00	NA	0.00 ± 0..00	NA	0.00 ± 0.00	NA
	Yes	1094.09 ± 276.74		5.77 ± 0.70		603.52 ± 56.43	
	No						
	Problems with Placenta						
	Yes	0.00 ± 0.00	NA	0.00 ± 0..00	NA	0.00 ± 0.00	NA
	No	1094.09 ± 276.74		5.77 ± 0.70		603.52 ± 56.43	
	Breathlessness before/after delivery						
	Yes	0.00 ± 0.00	NA	0.00 ± 0..00	NA	0.00 ± 0.00	NA
	No	1094.09 ± 276.74		5.77 ± 0.70		603.52 ± 56.43	

t: t-statistic, F: F statistic, p-value < 0.05 indicates significance, NA: Means could not be compared because of incomparable sample sizes

Table 4b. Relationship between NCI and obstetrics history of test subjects in the second trimester

Trimester group	Variables	Protein C Mean ± SD	F/t (p-value)	Protein S Mean ± SD	F/t (p-value)	Antithrombin III Mean ± SD	F/t (p-value)
Second Trimester	**No of Pregnancy**						
	0-1	1066.92 ± 251.61	0.428 (0.657)	4.81 ± 0.65	0.586 (0.565)	593.85 ± 65.07	4.324 (0.026)*
	2	1126.67 ± 250.17		5.12 ± 1.13		571.67 ± 22.29	
	>3	995.00 ± 232.87		4.65 ± 0.53		519.83 ± 28.02	
	Previous Miscarriage						
	Yes	1002.50 ± 145.00	-0.548 (0.589)	4.76 ± 0.05	-0.242 (0.811)	529.25 ± 38.37	-1.624 (0.118)
	No	1075.71 ± 256.41		4.86 ± 0.08		578.67 ± 57.92	
	High BP in pregnancy						
	Yes	0.00 ± 0.00	NA	0.00 ± 0.00	NA	0.00 ± 0.00	NA
	No	1064.00 ± 241.18		4.84 ± 0.77		570.76 ± 57.63	
	Intrauterine foetal death						
	Yes	1370.00 ± 0.00	1.314 (0.202)	5.07 ± 0.00	0.300 (0.767)	493.00 ± 0.00	-1.405 (0.173)
	No	1651.25 ± 227.61		4.84 ± 0.75		574.00 ± 56.5	
	Delivery < 37 weeks						
	Yes	790.00 ± 0.00	-1.168 (0.255)	4.12 ± 0.00	-0.985 (0.355)	510.00 ± 0.00	-1.080 (0.291)
	No	1075.42 ± 239.37		4.88 ± 0.75		573.29 ± 57.44	
	Unilateral swelling of limbs						
	Yes	0.00 ± 0.00	NA	0.00 ± 0.00	NA	0.00 ± 0.00	NA
	No	1064.00 ± 241.18		4.84 ± 0.75		570.76 ± 56.63	
	Problems with Placenta						
	Yes	0.00 ± 0.00	NA	0.00 ± 0.00	NA	0.00 ± 0.00	NA
	No	1064.00 ± 241.18		4.84 ± 0.75		570.76 ± 56.63	
	Breathlessness before/after delivery						
	Yes	0.00 ± 0.00	NA	0.00 ± 0.00	NA	0.00 ± 0.00	NA
	No	1064.00 ± 241.18		4.84 ± 0.75		570.76 ± 56.63	

t: t-statistic, F: F statistic, p-value < 0.05 indicates significance, NA: Means could not be compared because of incomparable sample sizes

Table 4c. Relationship between NCI and obstetrics history of test subjects in the third trimester

Trimester group	Variables	Protein C Mean ± SD	F/t (p-value)	Protein S Mean ± SD	F/t (p-value)	Antithrombin III Mean ± SD	F/t (p-value)
Third Trimester	**No of Pregnancy**						
	0-1	981.43 ± 235.21	1.264 (0.302)	4.94 ± 0.97	0.079	535.71 ± 41.43	0.525
	2	1142.50 ± 220.44		4.80 ± 0.66	(0.925)	515.38 ± 49.61	(0.599)
	>3	1008.50 ± 197.58		4.82 ± 0.68		537.70 ± 53.26	
	Previous Miscarriage						
	Yes	991.67 ± 194.18	-0.664 (0.513)	4.69 ± 0.44	-0.597	553.33 ± 46.35	1.388
	No	1060.26 ± 227.43		4.89 ± 0.81	(0.556)	522.63 ± 47.66	(0.178)
	High BP in pregnancy						
	Yes	1170.00 ± 98.99	0.848 (0.405)	4.66 ± 0.55	-0.371	516.50 ± 30.41	-0.406
	No	1032.83 ± 223.27		4.86 ± 0.75	(0.714)	531.17 ± 49.67	(0.688)
	Intrauterine foetal death	0.00 ± 0.00	NA	0.00 ± 0.00	NA	0.00 ± 0.00	NA
	Yes	1651.25 ± 227.61		4.84 ± 0.75		574.00 ± 56.5	
	No						
	Delivery < 37 weeks						
	Yes	1025.00 ± 0.00	-0.156 (0.877)	4.78 ± 0.47	-0.159	560.33 ± 56.08	1.173
	No	1046.36 ± 223.36		4.86 ± 0.77	(0.875)	525.86 ± 46.89	(0.253)
	Unilateral swelling of limbs	1220.00 ± 0.00	0.819 (0.421)	5.15 ± 0.00	0.415	625.00 ± 0.00	2.164
	Yes	1036.46 ± 219.56		4.84 ± 0.74	(0.682)	526.04 ± 44.81	(0.041)*
	No						
	Problems with Placenta	1220.00 ± 0.00	0.819 (0.421)	5.15 ± 0.00	0.415	625.00 ± 0.00	2.164
	Yes	1036.46 ± 219.56		4.84 ± 0.74	(0.682)	526.04 ± 44.81	(0.041)*
	No						
	Breathlessness before/after delivery						
	Yes	795.00 ± 0.00	-1.174 (0.253)	4.25 ± 0.00	-0.828	531.00 ± 0.00	0.021
	No	1054.17 ± 216.35		4.87 ± 0.74	(0.416)	529.96 ± 49.26	(0.984)

t: t-statistic, F: F statistic, p-value < 0.05 indicates significance, NA: Means could not be compared because of incomparable sample sizes

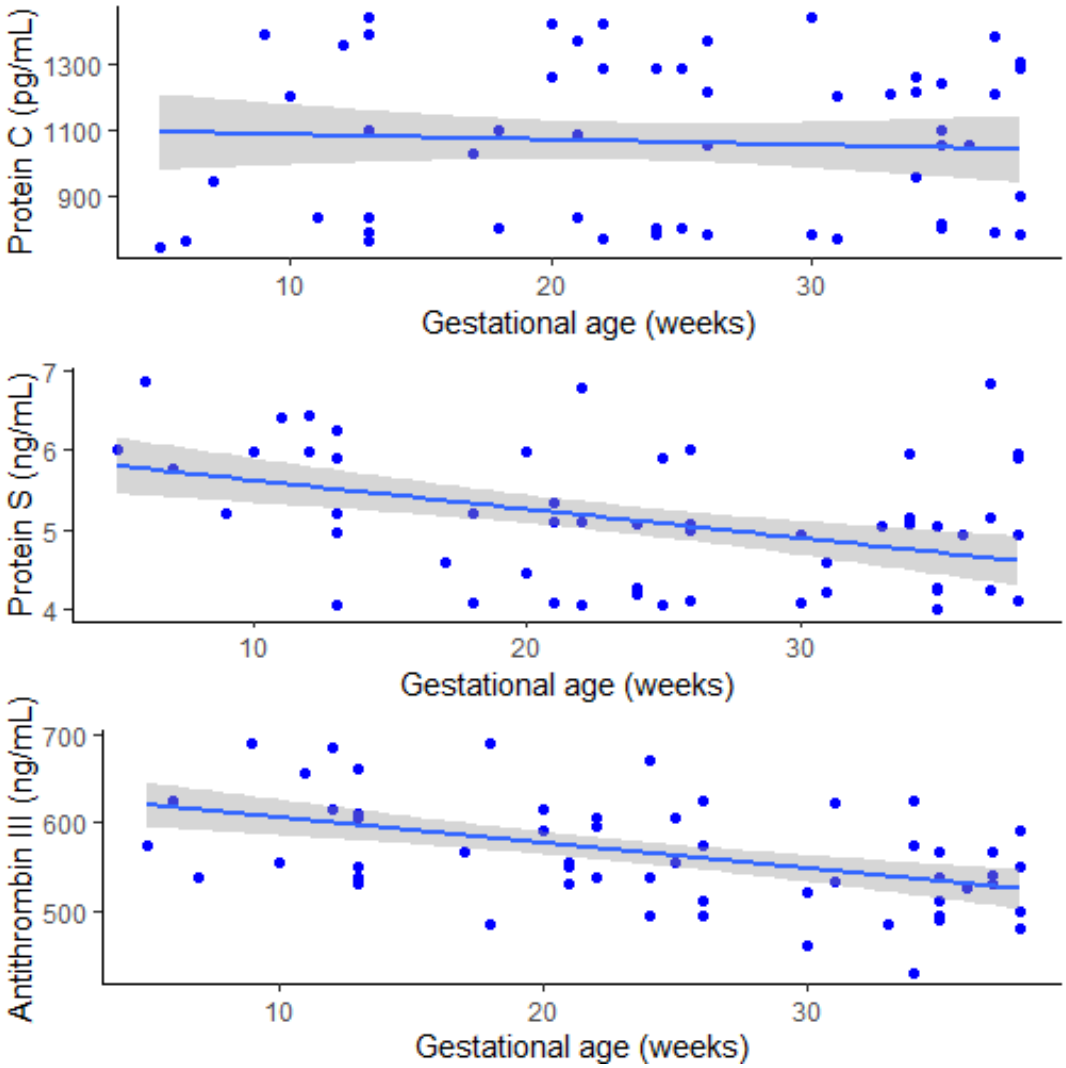

Fig. 1. Relationship between plasma levels of natural coagulation inhibitors among pregnant women with gestational age

Protein S differed significantly by the number of pregnancies, high BP in pregnancy and delivery < 37 weeks, p-value < 0.05. Also, protein S was higher among subjects with breathlessness before or after delivery, p-value < 0.05. Antithrombin III was significantly higher among subjects with delivery < 37 weeks, p-value < 0.05.

4. DISCUSSION

The majority of participants in the subjects and control group have had a history of two to three pregnancies and less than half of both subjects and control have had a previous history of miscarriages. Only a few had high blood pressure in pregnancy and a minority had a history of the use of cervical cerclage and intrauterine fetal death. There was no significant difference in the history of intrauterine growth restriction between the subjects and the control group. Histories of unilateral leg swelling, and complications associated with placenta e.g. abruptio placenta, placenta previa, and breathlessness before/after delivery were not also significantly different between the two groups.

The study observed that levels of coagulation inhibitors among pregnant women declined with gestational age with varying patterns. This is in keeping with the hypercoagulable state of pregnancy and increased consumption of the NCI as the pregnancy progressed to the third trimester. Nwagha et al. reported the same pattern with protein C [11]. Other reports by

Imoru et al. and Ajayi et al. showed different patterns and fluctuated values for protein C and antithrombin III at different gestation periods with no statistical significance [9,15].

The mean protein C was significantly higher in subjects with delivery <37 weeks in the first trimester while Protein S differed significantly by the number of pregnancies and was higher among subjects with previous miscarriages. In the second trimester, the mean Protein C and Protein S did not differ by obstetrics parameters. However, the mean Antithrombin III differed significantly by the number of previous pregnancies. In the third trimester, protein C and protein S did not differ by any of the obstetrics parameters. However, antithrombin III was significantly higher among subjects with limb swelling and a history of placenta problems.

It has been reported that antithrombin III deficiency is associated with recurrent miscarriages [5,6]. Normal pregnancy is associated with significant changes in venous stasis, endothelial damage, and enhanced coagulation (Virchow triad), shifting the equilibrium towards a hypercoagulable state [9]. These include increasing concentrations of most clotting factors, decreasing concentrations of some of the natural anticoagulants, and reducing fibrinolytic activity [9]. Indeed, there is a significant decrease in protein S activity and a progressive increase in resistance to activated protein C in the second and third trimesters of pregnancy [10].

Deficiencies of naturally occurring anticoagulant proteins such as antithrombin III, protein C, and protein S produce a favorable medium for thrombus generation which has been linked to thromboembolic disease. Inconsistent reports of protein C levels during pregnancy by various authors might be associated with different sensitivities and specificities of assay techniques.

5. CONCLUSION

This study did not demonstrate the levels of NCIs as predictive tools for thromboembolic events in pregnancy among women with past bad obstetric history because the difference in NCI levels in both control and test subjects has no statistically significant association. However, it was established that there is a progressive decrease in NCI levels across various trimesters which could be a significant risk factor for thromboembolic events.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

ETHICAL APPROVAL

Approval was obtained from the ethical committee of the LAUTECH Teaching Hospital (LTH) Ogbomosho, Oyo State Nigeria.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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