ISSN: 2536-7153

SJMLS

Sokoto Journal of Medical Laboratory Science 2023; 8(2): 26 - 36

SJMLS - 8 (2) - 003

Some Coagulation Parameters, Fibrinogen, Protein C and Antithrombin III among Pregnant Women Visiting the Antenatal Clinic in University of Calabar

Okoli, Adaku O. [1], Okpokam, Dorathy C.* [1], Ada-Kooffreh, Mbang [2], Akwiwu, Euphoria C. [1], Udo, Atim [3]
Department of Haematology and Blood Transfusion Science, University of Calabar, Calabar, Nigeria [1], Department of Internal Medicine, University of Calabar Teaching Hospital, Calabar, Nigeria [2], Department of Obstetrics and Gynaecology, University of Calabar, Calabar, Nigeria [3].
Author for Correspondence *: +2348023552406/oghalove@gmail.com.
https://dx.doi.org/10.4314/sokjmls.v8i2.3

Abstract

Haemostatic changes in pregnancy are significant, essential and have the potential to cause adverse pregnancy outcomes. The aim of this study was to assess and provide information on some coagulation parameters (PT, APTT, TT), fibrinogen (FIB), Protein C (PC), and Antithrombin III (AT III) of pregnant women attending University of Calabar Teaching Hospital. This cross-sectional case study included one hundred and twenty (120) pregnant women (subjects), aged 18 – 45 years, alongside sixty (60) age-matched non-pregnant women (controls). Ethical clearance and informed consent (well-structured questionnaire) from all subjects were obtained. Citrated and serum samples were used. PT, APTT and TT were assayed using the One-Stage Quick method respectively, FIB was assayed using Clauss method, while PC and ATIII were assayed using ELISA technique. Age distribution of the subjects indicated that 52.5% of pregnant women were 19-28 years, 30.8% were 29–38 year and 16.7% were 39–48 years. Pregnant women with tertiary education had the highest (58.3%), followed by secondary (29.2%) and primary education (12.5%). It was observed that FIB (4.40g/l), PC (3715.83 pg/ml) and AT III (1346.65ng/ml) showed significant increase when compared with non-pregnant women ($P< 0.001$). Also, APTT and TT showed significant differences ($P<0.05$) in age ranges, while TT and PC were significantly decreased ($P<0.05$) in Multiparous 4 and Multiparous 3 when compared with Primiparous and Nulliparous among pregnant women based on parity respectively. PT and FIB (13.88 secs and 4.71g/L) were significantly increased in 3rd trimester when compared with the 1st and 2nd trimester (13.12 secs, 13.19 secs) and (4.18g/L and 4.29g/L) respectively. FIB and ATIII are significantly high; PC activity was significantly low, while multigravidity has an influence on protein C, among pregnant women. Health care givers should be aware of the pregnancy induced changes to aid the proper management and monitoring of pregnant women with bleeding or other thromboembolic disorders in this locality.

Keynote: *Coagulation profiles, Protein C, Antithrombin III, Pregnant women, Calabar*

Introduction

Pregnancy is the fertilization and development of one or more offspring known as embryo or foetus in woman's uterus or the state of carrying a developing embryo or foetus within the female body (Blessing *et al.,* 2017). Childbirth typically occurs around 40 weeks from the start of the last menstrual period (LMP) (Abman, 2011). An embryo is the developing offspring during the first eight weeks following fertilization, after which, it becomes a foetus until birth. It is conventionally divided into three trimesters, each roughly three months long (Eunice *et al.,* 2013). Normal pregnancy is associated with major changes in the coagulation and fibrinolytic system which contribute to maintain placental function during pregnancy and to prevent excessive bleeding during delivery (Gresele, 2008). This phenomenon protects women from haemorrhage during delivery but predisposes her to thromboembolism both during pregnancy and in puerperium.

Pregnancy is a state of hypercoagulation which is likely an adaptive mechanism to reduce the risk of haemorrhage during and after the delivery process. Unfortunately, because of the hypercoagulable state, thromoboembolism is one of the leading causes of death associated with pregnancy (Domenico *et al.,* 2005). Hypercoagulability states as a pre-existing condition in pregnancy include both acquired ones such as antiphospholipid antibodies, and congenital ones including factor *V. Leiden,* prothrombin mutation, protein C and S deficiencies and antithrombin III deficiency (Domenico *et al.,* 2005).

Haemostasis in normal pregnancy involves a complex network of interactions with positive and negative feedback loops, integrating blood vessels, platelets, coagulation factors, coagulation inhibitors and fibrinolysis and has evolved to maintain the integrity of the vasculature (Pannala *et al.,* 2013). Coagulation, which is an important part of haemostasis is the process by which blood forms clot. It involves cessation of blood loss from a damaged vessel. The damaged blood vessel is covered with platelet and fibrin containing clot to stop bleeding and repair of haemorrhage or obstructive clotting (David *et al.,* 2009). Venous thromboembolism remains the major cause of maternal mortality in the developed world. Estimates of the incidence of pregnancy associated venous thromboembolism vary between one in 1000 and two in 2000 deliveries (Ingrid and Helga, 2002). Conflicting reports have been made on the level of antithrombin III in pregnancy as reduced activity was documented by earlier author (Essien 1997). Increased activity was reported by (During and Schwarzlos, 1990) while majority of the studies reported no significant change (Ghanavatti-Abbassi *et al.,* 2009; Sarkar and Sogani, 2013). Earlier researchers documented reduced protein C and S activity during pregnancy (Oruc *et al.,* 2000), while other studies showed stable and unchanged levels of protein C and protein S during pregnancy (Faught *et al.,* 1995).

Another study showed that haemostatic mechanism also involves decreased levels of anticoagulant protein S and Protein C as well as enhanced thrombin generation and decreased fibrinolytic activities (Dati *et al.,* 2009). Haemostatic failure because of various complications of pregnancy is an important cause of maternal mortality.

So far, published data is scarce from our locality concerning the level of hypercoagulability or thromboembolism among pregnant women and some natural anticoagulant such as protein C, Antithrombin III, fibrinogen and some coagulation parameters such as thrombin time (II) prothrombin time (PT) and activated partial thromboplastin time (APTT).

Materials and Methods

Study design

This study was a cross-sectional case study.

Study area/location

The test subjects were recruited from among pregnant women attending Antenatal Clinic at University of Calabar Teaching Hospital. Non-pregnant women recruited from Calabar metropolis were monitored as the controls. Pregnancy test was done by using a dipstick method to certify the control individuals as non-pregnant. Informed consent and pretest counselling were obtained using a structured questionnaire. Participants were between the age range of 18 to 45 years for both pregnant women and non-pregnant women.

Subjects selection/scope of the study

A total number of one hundred and eighty (180) subjects between 18 to 45 years were included in this study. Ethical clearance with the Reg. number (UCTH/HREC/33/553) was obtained from the Health Research Ethical Committee of the University of Calabar Teaching Hospital before commencement of the study and informed consent was obtained from all subjects recruited.

A. Inclusion and exclusion criteria

All pregnant women attending UCTH Antenatal Clinic who gave their consent were included. Pregnant subjects and non-pregnant controls with present and past medical history of underlying pathologies such as liver disease, congenital bleeding disorder, renal disease, diabetes, and those on anticoagulants therapy were excluded.

B. Sample collection/handling

The subjects were informed about the project and its benefits to them before commencing the procedures. After the questionnaire was completed and signed by the pregnant women to give their consent, 4.5mls of venous blood sample was drawn from each pregnant woman. The blood was dispensed (2.25ml) into a plain sample bottle containing 0.25ml (250µl) of 3.13 percent in-sodium citrate anticoagulant which was centrifuged at 3000rpn for 10 minutes and the remaining into a plain sample container. Platelet poor plasma (PPP) was obtained and was used to determine some haemostatic parameters. The remaining 2.25ml of blood was dispensed into a plain sample bottle, allowed to clot and was centrifuged at 3000rpm for 10 minutes to obtain serum which was used to assay natural anticoagulants (Protein C and Antithrombin III).

C. Research methodology used in the study

(a) Prothrombin time estimation
The prothrombin time (PT) was done using the Quick One Stage method using Helena reagent. LOT NO: HL-2-P-3038 Rev. 4.
Reference range for PT is 10 – 14 seconds.

(b) APTT estimation
The APTT was done using Quick One Stage method using Helena Reagent. LOT NO: HL-2-P-1787 Rev. 8.
Reference range for APTT is 26 – 45 seconds.

(c) Thrombin – Time estimation
Thrombin time estimation was based on Quick One Stage technique. Helena kit was used. LOT No: HL-2-0444P Rev. 15
Reference range for thrombin time estimation is 9 – 13 seconds.

(d) Fibrinogen estimation
Fibrinogen was assayed using a Claus technique principle-based Biosystems reagent. COD No: 61002.
Reference Range is 2.0-4.0glL.

(e) Protein C estimation
Protein C test was done using Enzyme Linked Immunosorbent Assay (ELISA). Elabscience kit was used. Catalog No: E-EL-H1167.
Reference range of protein C = 62.5-4000pg/ml.

(f) Antithrombin III estimation
Antithrombin III test was done using Enzyme Linked Immunosorbent Assay (ELISA). Elabscience kit was used. Catalog No: E-EL-H0432.
Reference range of Antithrombin III =31.25-2000ng/ml.

Statistical tools

The data collected was recorded on an excel spread sheet and later subjected to analysis using statistical software SPPS version 20.0. Statistical analysis included.

1. Frequency, percentages, and chi-squared tests.
2. One way analysis of variance (ANOVA) was used followed by the post hoc to compare the mean ± SD of fibrinogen, Protein C, Antithrombin III, fibrinogen and some coagulation parameters of pregnant when there are more than two groups.
3. Student – Test analysis was used to compare the parameters of the pregnant women and non-pregnant women (control) in the group. Differences were considered significant at $p<0.005$.

Results

Table 1 shows the demographic variables of the study groups based on age, educational level, occupation, gestational age, parity, marital status, use of contraceptives before this index pregnancy, use of anticoagulant, other health conditions and drugs were highlighted. The classification of pregnant women into different women into different age shows that the ages of 19-28 years constitute the highest percentages of pregnancy (52.5 percent) followed by age 29-38 years (30.8 percent) while the age 39-48years (16.7 percent) has the least. The different educational level in pregnant women shows that 70 (58.3 percent), 35 (29.2 percent) and 15 (12.5 percent) of 120 pregnant women were with tertiary level, secondary level and primary level respectively, the tertiary level constituted the highest and primary level the lowest percentage in this group. The classification of pregnant women into different occupations namely, civil servants, business, housewife and students respectively, were revealed. The result showed that 60 (50.0 percent), 36 (30.0 percent), 10 (8.3 percent) and 14 (11.7 percent) of 120 pregnant women were civil servant, business women, housewives and students respectively. The result observed that civil servants constituted the highest percentage in this group whereas, housewives

were observed to be the lowest. The results observed for marital status were 113 (94.1 percent), 5 (4.2 percent), 0 (0) and 2 (1.7 percent), for married, single, widow and divorced respectively. Married women constituted the highest number whereas, widows constituted the lowest number. Distribution of subjects based on their gestational age revealed that 47 (39.2 percent), 40 (33.3 percent) and 33 (27.5 percent) for 2nd trimester, 3rd trimester and 1st trimester respectively. The second trimester was observed to have the greatest number of representations compared to 3rd trimester and 1st trimester. The classification of pregnant women into parity was shown as follows; 45 (37.5 percent), 30 (25.0 percent), 26 (21.7 percent), 11 (9.1 percent) and 8 (6.7 percent), for nulliparous, primiparous, multiparous (2), multiparous (3) and multiparous (4) respectively. First timers constituted the highest numbers while those with four children have the lowest number. The classification of pregnant women into different usage of contraceptives before the index pregnancy revealed that 105 (87.5 percent), 6 (5.0 percent), 5 (4.2 percent) and 4 (3.3 percent) for those without contraceptive, oral, implant and injectable contraceptive before the index pregnancy. Those without contraceptives have the highest percentage and injectables have the lowest. The classification of pregnant women into different health conditions shows that 114 (95.0 percent), 4 (3.3 percent), 2 (1.7 percent) and 0 (0 percent) have no health condition, ulcer, high blood pressure (HBP) and others (HIV, Hepatitis and Syphilis). The classification of pregnant women into different medication shows 87 (72.5 percent), 15 (12.5 percent), 12 (10.0 percent), and 4 (3.3 percent), for pregnant women on routine drugs (folic acid, B complex, Calcium), those on no medication, on pregnant care supplement and on omeprazole. Pregnant women on routine drugs constituted the highest number.

Table 2 shows the comparison of some coagulation parameters, Fibrinogen (FIB), Protein C (PC), Antithrombin III (AT III) of pregnant subjects and non-pregnant controls in University of Calabar Teaching Hospital (UCTH). The mean PT, APTT, TT, FIB, PC and AT III were taken into consideration; however, no significant difference was observed with PT, APTT and TT parameters. The FIB and AT III showed statistical significance increase ($P<0.05$) in pregnant women (4.40±0.32g/L and 1346.65±14.98ng/ml) when compared to the non-pregnant women (3.41±0.06g/L and 1284.60±26.82ng/ml). Protein C revealed significant decrease ($P<0.05$) in pregnant women (3715.83±7.88pg/ml) when compared to non-pregnant women (3754.0±5.96pg/ml).

PT, APTT, TT, FIB, PC and AT III of pregnant women based on age is shown in Table 3. There was a significant difference in FIB and AT III among the pregnant women when age was considered, while other parameters show no significant changes. The APTT and TT was significantly increased ($P<0.05$) in age range 29-38years (37.03±0.52secs and 11.32±0.26secs) when compared with age range 19-28years (34.98±0.50secs and 10.62±0.15secs). However, PT, FIB, PC and AT III were all statistically non-significant ($P>0.05$) when compared based on age group.

Table 4 shows some coagulation parameters, Fibrinogen, Protein C and Antithrombin III of pregnant women based on parity. There was a significant difference in TT and PC among the pregnant women when parity was considered, while other parameters show no significant changes. The TT significantly decreased ($P<0.05$) based on parity 4 (9.62±0.56secs) when compared to parity 2 (11.34±0.26secs). Protein C revealed significant increase ($P<0.05$) in parity 1 (3755.23±15.7pg/ml), when compared to parity 3 (3669.18±25.44pg/ml). However, PT, APTT, FIB and AT III are all statistically non-significant ($P>0.05$) when compared to the different parity in the study.

Table 5 shows some coagulation parameters, PT, APTT, TT, FIB, PC and AT III of pregnant subjects. There was a significant difference in PT and FIB among the pregnant women when trimester was considered, while other parameters show no significant changes. There was a statistically significant rise ($P<0.05$) in PT and FIB of subjects in the 3rd trimester (13.88±0.19secs and 4.71±0.05g/L) when compared with 1st and 2nd trimester (13.12±0.16secs and 13.19±0.18secs) and (4.18±0.05 and 4.29±0.03). Meanwhile, APTT, TT, PC and AT III were statistically not significant ($P>0.05$) when compared to different trimesters in the group.

Table 1: Demographic variables of the pregnant women and non-pregnant women

Variable	Pregnant women N=120	Non-pregnant women N=60
Age range (years)		
19-28	63(52.5)	15(25.0)
29-38	37 (30.8)	34(56.7)
39-48	20(16.7)	11(18.3)
Educational level		
Primary	15 (12.5)	10(16.6)
Secondary	35 (29.2)	16 (26.7)
Tertiary	70 (58.3)	34 (56.7)
Occupation		
Civil servant	60(50.0)	22(36.7)
Business	36(30.0)	15(25.0)
House wife	10(8.3)	5(8.3)
Students	14(11.7)	18(30.0)
Marital status		
Married	113 (94.1)	35(58.3)
Single	5(4.2)	25(41.7)
Widowed	0(0)	0(0)
Divorced	2(1.7)	0(0)
Gestational age		
1st Trimester	33 (27.5)	0(0)
2nd Trimester	47 (39.2)	0(0)
3rd Trimester	40 (33.3)	0(0)
Parity		
Nulliparous	45(37.5)	25(41.7)
Primiparous	30(25)	8(13.3)
Multiparous	26(21.7)	11(18.3)
Multiparous	11(9.1)	10(16.7)
Multiparous	8(6.7)	6(10.0)
Other health conditions		
No illness	114(95.0)	60(100)
Ulcer	4(3.3)	0(0)
High blood pressure	2(1.7)	0(0)
HIV, hepatitis, diabetes, syphilis, asthma	0(0)	0(0)
Use of contraceptive before this index pregnancy		
Non	105(87.5)	60(100)
Oral contraceptives	4(3.3)	0(0)
Implant	6(5.0)	0(0)
Injectable	5(4.2)	0(0)
Medication		
None	15(12.5)	60(100)
Pregnant care supplement	12 (10.0)	0(0)
Routine drugs	87 (72.5)	0(0)
Omeprazole	4 (3.3)	0(0)

Table 2: Comparison of some coagulation parameters, fibrinogen, Protein C and Antithrombin III among the pregnant subjects and the non-pregnant controls

Parameters	Pregnant Women (N=120)	Non-Pregnant Women (N=60)	P-Values
PT [sec]	13.39±0.11	11.38±0.14	0.830
APTT [sec]	35.75±0.36	31.70±0.43	0.502
TT [sec]	10.83±0.12	11.47±0.15	0.700
FIB [g/l]	4.40±0.32	3.41±0.06	0.001
PC [pg/ml]	3715.83±7.88	3754.03±5.96	0.001
AT 111 [ng/ml]	1346.65±14.98	1284.60±26.82	0.001

Values are expressed as T-test values $p<0.001$ as statistically significant.

Table 3: Some coagulation parameters, fibrinogen, Protein C, and Antithrombin III of pregnant subjects based on age

Parameters	19-28 years (n=63)	29-38 years (n=37)	39-48 years (n=20)	P-Values
PT [secs]	13.48±0.16	13.43±0.16	13.1±0.28	0.459
APTT [secs]	34.98±0.50	37.03±0.52*	36.13±1.06	0.039
TT [secs]	10.62±0.15	11.32±0.26*	10.77±0.28	0.035
FIB [g/l]	4.37±0.04	4.38±0.62	4.56±0.07	0.099
PC [pg/ml]	3703.21±11.09	3729.05±10.28	3713.18±21.37	0.321
ATT111 [ng/ml]	1315.22±24.76	1389.78±9.21	1362.72±38.11	0.078

Values are expressed as one way ANOVA values; $p<0.05$ as statistically significant
*=Significant with age range 19-28
a=Significant with age range 29-38
b=Significant with age range 39-48

Table 4: Some coagulation parameters, fibrinogen, Protein C, and Antithrombin III of the pregnant subjects based on parity.

Parameters	Nulliparous (0) (n = 45)	Primiparous (n = 30)	Multiparous (2) (n = 26)	Multiparous (3) (n = 11)	Multiparous (4) (n = 8)	P-Value
PT (sec)	13.73±0.18	13.13±0.21	13.42±0.22	12.91±0.31	13.00±0.38	0.907
APTT (sec)	35.96±0.52	35.10±0.89	35.81±0.79	36.09±0.79	35.75±0.31	0.089
TT (sec)	10.76±0.21	10.83±0.17	11.34±0.26	10.72±0.33	9.62±0.56[b]	0.027
FIB (g/L)	4.35±0.52	4.51±0.06	4.44±0.85	4.31±0.09	4.33±0.08	0.271
PC (pg/ml)	3506.9±13.10	3755.2±15.70	3709.4±15.02	3669.2±25.44[a]	3699.5±28.05	0.033
AT III (ng/ml)	1351.4±22.25	1376.3±24.29	1339.4±39.25	1246.8±66.94	1376.3±33.62	0.243

Values are expressed in one way ANOVA values; $p<0.05$ statistically significant
*= Significant with Nulliparous
a=Significant with primiparous
b=Significant with mutiparous(2)

Table 5: Some coagulation parameters, fibrinogen, Protein C, and Antithrombin III of pregnant subjects based on trimester

Parameters	1st Trimester (n=33)	2nd Trimester (n=47)	3rd Trimester (n=40)	P-Value
PT (secs)	13.12±0.16	13.19±0.18	13.88±0.19*[a]	0.006
APTT (secs)	36.33±0.58	35.02±0.57	35.70±0.77	0.367
TT (secs)	10.63±0.31	11.02±0.11	10.83±0.22	0.437
FIB (secs)	4.18±0.05	4.29±0.03	4.71±0.05*[a]	0.001
PC (pg/ml)	3721.03±14.28	3720.47±12.03	3702.63±15.28	0.566
AT III (ng/ml)	1352.29±30.13	1339.99±25.09	1351.56±23.59	0.928

Values are expressed as one way ANOVA values $p<0.05$ statistically significant
*=Significant with 1st trimester
a=Significant with 2nd trimester
b=Significant with 3rd trimester

Discussion

One hundred and twenty (120) pregnant women between the ages of 18-45 years and sixty (60) age-matched non-pregnant women were recruited for this study. There were significant differences between the age groups parity and gestational periods (trimester) of pregnant subject and non-pregnant controls. The difference in the ages and parity represent a selection bias as the study was conducted in a Teaching Hospital and this resulted in most of the control subject being Business women and University students. Demographic profile of pregnant women and non-pregnant women from the demographic profile of the pregnant women, it was revealed that the almost all the pregnant women and non-pregnant women had formal education. Majority had university education as their least educational qualification, majority of the subjects (pregnant women were civil servants, traders (business women), Housewives and students.

In this study, prothrombin time assesses the extrinsic pathway of coagulation and is sensitive to factor VII, X, V, II and fibrinogen. Also activated partial thromboplastin time assesses the intrinsic pathway of coagulation and is sensitive to deficiencies of factor I, II, VII, IX, X, XI, XII. The result of this study revealed that mean prothrombin time of pregnant women showed no statistically significant difference when compared with non-pregnant women (controls). There is no significant difference when comparing maternal age, parity of the pregnant women. PT increased slightly in the third trimester when compared with the first trimester. This could be because of physiological changes. This indicates that pregnancy is not likely to have any adverse effect on prothrombin time. This finding is consistent with an earlier report by Cerneca *et al.* (1997) who recorded no change in the mean prothrombin time value among pregnant women while there was a statistically significant difference when compared trimester with the control group. Our finding is consistent with the earlier reports (Temal *et al.,* 2007; Buseri *et al.,* 2008) who reported an increased prothrombin time values among pregnant women.

Activated partial thromboplastin time of pregnant women recorded no significant different when compared with non-pregnant women. Parity and trimester stage do not have any influence on APTT. There was a statistically significant increase when comparing the maternal age of 29-38 years to 19-28 years. This might be attributed to the physiological changes in the maternal haemostatic system arising from the concentration of foetal haemoglobin in the maternal circulation. On the other hand, mean thrombin time of pregnant women was not significantly different when compared with non-pregnant women. There was no significant different when comparing the trimester stage of the pregnant women. TT is slightly increased in maternal age of 29 – 38 years compared to age range of 19-28 years. This study also revealed that TT is slightly increased in multigravida women compared to parity group 4 where TT value is decreased. This finding is inconsistent with other studies which indicated that TT is slightly decreased in pregnancy and that this increase was because of increased thrombin generation in pregnancy and as a result a gross elevation of fibrinogen concentration (Dacie and Lewis, 2010). Thrombin time is a function of fibrinogen concentration in plasma.

This study also indicated a statistically significant higher fibrinogen concentrations among the pregnant subject compared to the non-pregnant controls ($P< 0.001$). The finding from this study is consistent with previous report (Awodu and Enosolease, 2003) who indicated that pregnancy exerts a significant increase in fibrinogen. Finding from this study is also in agreement with previous reports by Amilo *et al. (*2013), which indicated a significant increase in fibrinogen concentration during pregnancy. Pregnancy is known to be a procoagulable state; therefore, it is not surprising that this study and other studies have observed an increase in fibrinogen, the precursor of fibrin beginning in early pregnancy (O'Riordan and Higgins, 2003). Fibrinogen is an acute-phase protein. The increase in fibrinogen seen among pregnant women may be due to the inflammatory state of pregnancy it was observed during this study that trimester affects coagulation. The fibrinogen of pregnant women in the third trimester was

significantly higher than that of the first and second trimester (P<0.05). This study indicated that the level of fibrinogen rose significantly from the first trimester to third trimester. This result is consistent with an earlier report of Cernaca *et al.* (1997) which indicated that the level of fibrinogen rose significantly from the second to third trimester recorded similarly, Choi and Pai (2002) observed a similar increase in fibrinogen from first to third trimester and reported that the highly elevated fibrinogen concentration was markedly seen in the third trimester. These changes result in a state of hypercoagulability and are likely due to hormonal changes and increase the risk of thromboembolism (Hui and Lili, 2012). Previous report indicates that fibrinogen level is obviously elevated in late pregnancy as compared with the non-pregnant women (control group similarly most blood coagulation factors including fibrinogen has been shown to be increased during pregnancy (Domenico *et al.*, 2005; Okwesili *et al.,* 2016).

Finding from this study is an agreement with previous report by Hui and Lili, (2012), which indicated that during normal pregnancy the haemostatic balance changes in the direction of hypercoagulability with increase in fibrinogen thus decreasing bleeding complications in connection with delivering. Their control of 58 women with singleton pregnancies observed that the level of fibrinogen is higher in early pregnancy than those in non-pregnant controls. In this present study, the fibrinogen levels were significantly higher among pregnant women compared to non-pregnant women.

When comparing mean PC of pregnant women with non-pregnant women there was a significantly lower value of protein C activity in pregnant women compared to non-pregnant woman (P<0.05). This report agrees with a previous report (Imoru and Fiekumo, 2015) but disagrees with previous study who reported no significant difference. The values of Antithrombin III changes in pregnant and non-pregnant women showed no statistically significant difference (P>0.05). This is in line with a previous study which reported no significant change. Szecsi *et al*. (2010) reported that the difference in protein C levels reported during pregnancy reported by various authors might be associated with different sensitivities and specificities of protein C reagents used, and assay techniques employed.

Maternal age had no significant influence on protein C activities. Different and fluctuated values of protein C activities with regards to first, second and third trimesters respectively, showed no significant different (P > 0.05). This study also revealed that antithrombin III showed no significant difference in pregnant women. This finding is consistent with the earlier studies by During and Schwarzolos (1990); Ghanavatti *et al.* (2009) but disagrees with the significantly lower value reported by Essien (1997) probably due to the variation of sensitivities and specificities of Antithrombin III reagent used. This study also confirmed the earlier studies that trimester stage, maternal age and parity have no influence on Antithrombin III level during pregnancy. However, variation in AT III levels in pregnancy as reported by various authors (Essien, 1997) could be associated with methodology employed or poor storage of reagent and samples.

Conclusion

Protein C activity was significantly low while fibrinogen and antithrombin III levels were markedly and significantly raised in this study. Maternal age and trimester showed no influence on protein C and antithrombin III, while multigravidity has influence on protein C only.

There should be immediate checks of some haemostatic parameters and natural anticoagulants since pregnancy is associated with a lot of changes. Obstetricians and health care givers should be made aware of the pregnancy induced changes. This is to ensure they make informed decision in diagnosis, management and monitoring of pregnant women.

Acknowledgement: The authors wish to acknowledge the staffs and the pregnant women attending the Department of Obstetrics and Gynaecology, for providing the enabling environment for assessing our subjects and for the pregnant women cooperation in getting the

samples. We would also like to thank the Department of Haematology and Blood Transfusion Science for the use of their Laboratory facilities, both of the University of Calabar Teaching Hospital.

Conflict of interest: The authors have no conflict of interest.

Source of funds: It was Self-funded by authors.

References

Abman, S.H. (2011). *Foetal and neonatal physiology.* (4th ed.). Philadelphia: Elsevier/Saunders. 46-47.

Amilo, G.I., Anokwute, M.U., Chukwuanukwu, P.C., Onyenekwe, C.C., Ifediata, C. and Ezeah, S.C. (2013). Fibrinogen concentration and thrombin levels in pregnant women in Nnewi, Anambra State, Southeastern Nigeria. *Journal of Biology and Agricultural Health;* **3(7)**: 14.

Awodu, O.A. and Enosolease, M.E. (2003). Activated thromboplastin time in women with recurrent spontaneous abortions. *Annals of Biomedical Science;* **2(1)**: 42-46.

Blessing, D.B., Abdulrahman, Y., Muktar, Y., Isaac, Z., Frank, U., Imoru, M., Okwesili, A., Aliyu, I.B., Festus, U.O., Kwaifa, I.B., Aliyu, I.B., Osaro, Erhabor and Daniel, N.D. (2017). Thrombin levels among pregnant women of African Descent in Sokoto, Northwestern Nigeria. *Journal of Nursing and Health Care;* **1(2)**: 55-78.

Buseri, F.I., Jeremiah, Z.A. and Kalio, F.G. (2008). Influence of pregnancy and gestation period on some coagulation parameters among Nigerian antenatal women. *Research Journal of Medical Sciences;* **2(6)**: 275-281.

Cerneca, F., Ricci, G., Simeon, R., Malisamo, M., Alberico, S. and Guaschono, S. (1997). Coagulation and fibrinolysis changes in normal pregnancy. Pregnancy induce a hypercoagulable state combined with reactive fibrinolysis. *European Journal of Obstetrics and Gynaecology Reproductive Biology;* **73**: 31-36.

Choi, J.W. and Pai, S.H. (2002). Tissue plasminogen activator levels change with plasma fibrinogen concentrations during pregnancy. *Annals of Haematology;* **81(11)**: 611-615.

Dacie, J.V. and Lewis, K. (2010). The role of plasma proteins in whole blood viscosity in textbook of practical haematology. (11th ed.). 233-309.

Dati, F., Pelzer, H. and Wagner, C. (2009). Changes in the haemostatic relevance of markers of haemostasis activation in obstetrics/gynecology and pediatrics. PMID: 98340II.

David, L., Nigel, K., Michael, M. and Denise, O.S. (2009). *Practical haemostasis and thrombosis.* London: Wiley-Blackwell. 1-5.

Domenico, P., Gabriele, C. and Michela, F. (2005). Haemostatic changes in normal pregnancy. 10.

During, R. and Schwarzlos, G. (1990). Antithrombin III level in normal pregnancy and patients with pregnancy induced hypertension. *Zentralbl Gynakology;* **112(6)**: 351-354.

Essien, E.M. (1997). Changes in antithrombin II level in pregnancy labour and in women on the contraceptive pill. *African Journal of Medicine Science;* **6(3)**: 109-113.

Eunice Kennedy National Institute of Child Health and Human Development (2013). Pregnancy condition information.

Faught, W., Sarner, P., Jones, G. and Ivey, B. (1995). Changes in protein C and protein S levels in normal pregnancy. *American Journal of Obstetrics and Gynaecology;* **172**: 147-150.

Ghanavatti-Abbassi, M., Greer, L.G., Cunningham, F.G. (2009). Pregnancy and laboratory studies: A reference table for clinicians. *Obstetrics and Gynaecology*; **1114(6)**: 1326-1331.

Gresele, P. (2008). *Platelets in haematologic and cardiovascular disorders: A clinical handbook.* Cambridge, United Kingdom: Cambridge University Press.

Hui, C. and Lili, M. (2012). Changes in coagulation and haemodynamics during pregnancy: A prospective longitudinal study of 58 cases. *Archive Gynaecology and Obstetrics;* 1231-1236.

Imoru, M. and Fiekumo, I.B. (2015). Protein C and antithrombin III activities in Healthy Nigeria women. *International Journal of*

Haematology Research-Medical Science; **1(1)**: 23-55.

Ingrid, P. and Helga, G. (2002). Thrombosis during pregnancy: Risk factor, diagnosis and treatment. *Pathophysiology and Thrombin Haemostasis;* **2(1)**: 34-56.

O'Riordan, M.N. and Higgins, J.R. (2003). Haemostasis in normal and abnormal pregnancy. *Best Practice Research in Clinical Obstetrics and Gynaecology;* **17(3)**: 385-396.

Okwesili, A., Ibrahim, K., Nnadi, C., Barnabas, B., Abdulrahaman, Y., Buhari, H., Udomah, F. A., Imoru, M., Egenti, B.N. and Erahabor, O. (2016). Fibrinogen levels among pregnant women of African descent in Sokoto North Western Nigeria. *Frontiers in Biomedical Sciences;* **1(2)**: 7-11.

Oruc, S., Saruc, M., Koyuncu, F.M. and Ozdemir, E. (2000). Changes in the plasma activities of protein C and during pregnancy. *Australian Journal of Obstetrics and Gynaecology;* **40(4)**: 448-450.

Pannala, S., Inayatulla, K. and Puli, S.H. (2013). Estimation of prothrombin time in pregnancy compared with normal controls. *Journal of Evolution of Medical and Dental Sciences;* **2**: 72.

Sarkar, P.D. and Sogani, S. (2016). Association of antithrombin III and platelet count with pregnancy induced hypertersion. *International Journal of Reproduction, Contraception, Obstetrics and Gynaecology;* **2(3)**: 398-401.

Szecsi, P.B., Maja, J., Anna, K., Malane, R.A., Nina, P.C. and Steen, S. (2010). Haemostatic reference intervals in pregnancy. *Thromb Haemost*;**103(4)**:718-727.

Temal, C., Cirkel, U. and Eller, T. (2007). Establishing reference values of coagulation parameters in pregnant women. *Journal of Thrombin Haemostasis,* 5(2): 597.

Citation: Okoli, Adaku O., Okpokam, Dorathy C., Ada-Kooffreh, Mbang, Akwiwu, Euphoria C., Udo, Atim. Some Coagulation Parameters, Fibrinogen, Protein C and Antithrombin III among Pregnant Women Visiting the Antenatal Clinic in University of Calabar. ***Sokoto Journal of Medical Laboratory Science*; 8(2): 26 - 36**. https://dx.doi.org/10.4314/sokjmls.v8i2.3