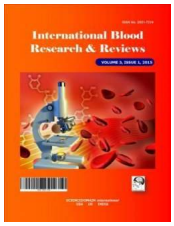

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Assessment of Some Fibrinolytic Parameters during Pregnancy in Northern Nigeria

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Authors' contributions

This work was developed in collaboration by the both authors. Author IM designed the study, wrote the protocol, managed the literature searches and analysed the data while author OIA contributed to the literature searches and the analysis of the data. Both authors read and approved the final manuscript.

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ABSTRACT

Aim: The study was undertaken to assess the fibrinolytic activity during pregnancy and to determine the effects of maternal age, gestation period and parity on fibrinolytic parameters in Northern Nigeria.
Materials and Methods: 150 pregnant and 100 non-pregnant women, aged 17-40 years, were recruited for the research in Aminu Kano Teaching Hospital, Kano between August 2010 and October 2011. Blood samples collected were analysed for the plasma levels of fibrinogen, d-dimer and Fibrin Degradation Products (FDP) using standard laboratory methods.
Results: Pregnant women had significantly higher values of fibrinogen concentration, d-dimer and FDP of 3.46±0.35 g/L, 0.78±0.82 µg/mL and 10.17±15.08 µg/mL respectively compared to 3.12±0.3g/L, 0.45±0.78 µg/mL and 2.8±7.63 µg/mL, in non-pregnant women (P<0.05). D-dimer values for the first, second and third trimesters showed statistically significant differences (P<0.05) while fibrinogen levels showed no significant effects within the gestation period (P>0.05). Maternal

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age and parity had no significant influences on fibrinogen concentration, d-dimer and FDP levels (P>0.05).
Conclusion: Changes in fibrinolytic parameters in this study are associated with increased levels of fibrinogen, d-dimer and FDP during pregnancy, irrespective of maternal age and parity, and these changes can be linked to increased fibrinolytic activity during pregnancy. It is recommended that plasma fibrinogen, d-dimer and FDP levels be determined during pregnancy to prevent the risk of thrombosis that the pregnant women are prone to.

Keywords: Assessment; fibrinolytic parameters; pregnancy; Northern Nigeria.

1. INTRODUCTION

Fibrinolysis is a normal body process where fibrin clot, the product of coagulation, is broken down by plasmin at various sites leading to the production of circulating fragments or soluble fibrin degradation products (FDP) that are cleared by other proteinases or by kidney and liver [1-3].

Normal pregnancy is associated with changes in all aspects of haemostasis, including increase in concentrations of most clotting factors such as coagulation factors V, VII, VIII, IX, X, XII, fibrinogen and von-Willebrand factor and decreasing concentrations of some of the natural anticoagulants with diminishing fibrinolytic activity [4-6]. These changes have been associated with increased risk of thromboembolism during pregnancy and puerperium [4].

Increased fibrinogen concentration during pregnancy documented by previous authors [6-8] has been associated with increase in fibrinogen synthesis due to its utilization in the utero-placental circulation or as a result of hormonal changes such as increasing progesterone levels [6] while increased d-dimer level observed by earlier authors [9-11] has been associated with increased fibrinolysis following fibrin formation, increased coagulation activation and thrombin generation or combination of both [12-14].

The study of some fibrinolytic parameters (fibrinogen, d-dimer and FDP) during pregnancy was necessitated to further clarify the general concept of reduced fibrinolytic activity during pregnancy that is in dispute by earlier authors [15-18].

2. MATERIALS AND METHODS

This study was conducted on two-hundred and fifty apparently healthy subjects (150 pregnant and 100 non-pregnant women), aged 17-40 years in Aminu Kano Teaching Hospital (AKTH), Kano between August 2010 and October 2011. Ethical approval and consent were obtained from AKTH 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 on oral contraceptives were excluded from the study.

A venous blood sample (4.5 mL) collected from each subject was mixed with 0.5ml of 3.2% trisodium citrate solution in a plain container. Blood samples in the citrated containers were centrifuged at 2500 rpm for 15 minutes and the plasma separated into plastic containers for the determination of fibrinogen, d-dimer and FDP.

Plasma fibrinogen concentration was determined by modified Clauss method (Catalogue number 050-500 and manufactured by PZ Cormay, Poland). D-dimer and FDP were performed according to the manufacturer's instructions using Latex agglutination kits of catalogue numbers 150-700 and 00541 respectively manufactured from PZ, Poland and Diagnostica stago, France respectively.

2.1 Statistical Analysis

The mean values and standard deviations of the parameters in pregnant and non-pregnant women were assessed using Student's t-test while differences with regard to gestational age, maternal age and parity were analyzed using one-way analysis of variance (ANOVA). The differences were considered significant when the p values were ≤ 0.05.

3. RESULTS

3.1 Fibrinolytic Parameters in Pregnant Women

The fibrinolytic parameters (fibrinogen, d-dimer and FDP) were estimated in pregnant and non-pregnant women. The mean values of plasma

fibrinogen, d-dimer and FDP in pregnant and non-pregnant women are shown (Table 1). Pregnant women were found to show significantly higher values of fibrinogen concentration, d-dimer and FDP compared to non-pregnant women ($p < .05$).

3.2 Changes of Fibrinolytic Parameters with Gestation Period

Mean values of plasma fibrinogen, d-dimer and FDP for first, second and third trimesters are shown (Table 2). Values of fibrinogen concentration and FDP for the first, second and third trimesters showed no significant differences ($p > .05$) while d-dimer values increased significantly with increasing gestation period ($p < .05$).

3.3 Influences of Maternal Age on Fibrinolytic Parameters

Effects of maternal age on fibrinogen concentration, d-dimer and FDP are displayed (Table 3). The varied mean values of fibrinogen concentration, d-dimer and FDP for different age groups (17-22 years, 23-28 years, 29-34 years and 35-40 years) showed no significant differences ($p > .05$).

3.4 Effects of Parity on Fibrinolytic Parameters during Pregnancy

Effects of 0, 1-2 and ≥3 parity on fibrinogen concentration, d-dimer and FDP are shown (Table 4). The different mean values of fibrinogen, d-dimer and FDP with regard to 0, 1-2 and ≥3 parity, showed no significance ($p > .05$).

4. DISCUSSION

It has been generally documented that there is diminished fibrinolytic activity during pregnancy but this common reports seem to be questionable [15-18].

This study has shown significantly higher value of fibrinogen concentration in pregnancy compared to non-pregnant women and this is in line with the widely documented reports fromprevious authors [6-9,19,20]. The study has further confirmed the earlier finding on increase in fibrinogen level as pregnancy progresses [10,21,22] but there was no significant change in the fibrinogen level within the gestation period which agrees with the report of Buseri et al. [19]. However, increased fibrinogen concentration during pregnancy has been linked to assisting the prevention of post-partum haemorrhage through deposition of 5-10% of the

Table 1. Fibrinolytic parameters in pregnant and non-pregnant women

Parameter	Non-pregnant women (control)	Pregnant women
Number of subjects	100	150
Fibrinogen concentration (g/L)	3.12±0.3	3.46±0.35*
D-dimer (µg/mL)	0.45±0.78	0.78±0.828*
FDP (µg/mL)	2.8±7.63	10.17±15.08*

**P <0.05, pregnant women compared to the control group*

Table 2. Changes of fibrinolytic parameters with gestational age

Parameter	First trimester (n=24)	Second trimester (n=66)	Third trimester (n=60)
Fibrinogen concentration (g/L)	3.4±0.80	3.6±0.88	3.6±0.72
D-dimer (µg/mL)	0.36±0.4*	0.88±0.82	0.75±0.88
FDP (µg/mL))	4.32±8.29	11.36±19.16	10.73±10.72

**P <0.05, first trimester compared to second and third trimesters*

Table 3. Effects of maternal age on fibrinolytic parameters during pregnancy

Parameter	17-22 years	23-28 years	29-34 years	35-40 years	*P* value
Number of subjects	24	67	48	11	
Fibrinogen concentration (g/L)	3.6±0.79	3.5±0.70	3.8±0.87	3.2±0.85	>0.05
D-dimer (µg/mL)	1.08±0.92	0.64±0.67	0.84±0.94	0.7±0.88	>0.05
FDP (µg/mL)	10.1±10.23	10.07±20.61	11.51±14.91	16..36±24.05	>0.05

Table 4. Parity influence on fibrinolytic parameters during pregnancy

Parameter	0 Parity	1-2 Parity	≥3 Parity	*P* value
Number of subjects	42	51	57	
Fibrinogen concentration (g/L)	3.6±0.85	3.7±0.71	3.5±0.84	>0.05
D-dimer (µg/mL)	1.12±0.79	1.30±1.02	1.10±0.91	>0.05
FDP (ug/mL)	14.29±22.98	22.83±38.07	17.59±14.36	>0.05

total circulatory fibrinogen at the placental site [23,24]. There was no parity influence on fibrinogen level during pregnancy in this study and this is consistent with the earlier report [22] but the effect of maternal age on fibrinogen concentration during pregnancy documented by the previous author [22] is in contrary to our finding in this study. However, the divergent view expressed by Durotoye et al. [22] may be associated with the wider age groups considered in their study.

Significantly increased d-dimer level during pregnancy was observed in this study and this is in agreement with the earlier findings [10,11,25-27]. This study further revealed that the d-dimer levels increased significantly in the second and third trimesters of pregnancy and these are consistent with the reports of previous authors [10,11,28-30] which showed progressive rise in the d-dimer concentrations of up to 600 ng/mL. There was no influence of maternal age on the d-dimer level during pregnancy in this study and this is in line with the report of Jeremiah et al. [30]. This observation in this study, may be associated with increased fibrinolysis from the second trimester of pregnancy probably due to increased fibrin formation to prevent thrombosis. However, elevated d-dimer level has been associated with increased fibrinolytic activity as a result of coagulation activation and thrombin generation [12-14].

The study has further confirmed earlier reports on increased fibrin degradation products during pregnancy [17,31-33]. The study further revealed that there was no effect of gestational age on FDP level. However, increased FDP level has been associated with increased fibrinolysis [33] probably to neutralize the effect of increased fibrin formation during pregnancy.

Maternal age and parity showed no significant effects on fibrinogen concentration, d-dimer and FDP levels in this study.

5. CONCLUSION

In conclusion, changes in fibrinolytic parameters in this study have been associated with increased levels of fibrinogen, d-dimer and FDP during pregnancy, irrespective of maternal age and parity. The altered parameters in this study can be linked to increased fibrinolytic activity probably to neutralize or counterbalance increased intravascular coagulation during pregnancy to reduce thrombosis. It is recommended that plasma fibrinogen concentration, d-dimer and FDP levels be included amongst ante-natal tests to aid in monitoring pregnant women who are prone to thrombosis while innovative approach to unravel mechanism of fibrinolytic status in pregnancy should include the measurement of some parameters such as tissue plasminogen activator (tPA), plasminogen, plasminogen activator inhibitor type 1 (PAI- 1) amongst others, since tPA has been observed to primarily initiate fibrinolysis in the vascular system, and its low level in the blood with increased PAI-1 has been associated with an increased risk of arterial thrombosis [34-36].

CONSENT

We declare that written informed consent was obtained from every pregnant woman or control subject studied.

ETHICAL APPROVAL

Ethical approval was obtained from the ethical committee of Aminu Kano Teaching Hospital, Kano to carry out the research.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Walker JB, Neisheim ME. The molecular weights, mass distribution, chain

composition and structure of soluble fibrin degradation products released from fibrin clot perfused with plasmin. Journal of Biological Chemistry. 1999;274:5201-5212.
2. Lijnen HR. Elements of the fibrinolytic system. Ann N Y Acad Sci. 2001;936: 226-236.
3. Cesarman-Naus G, Hajjar KA. Molecular mechanism of fibrinolysis. British Journal of Haematology. 2005;129:307-321.
4. Prisco D, Ciuti G, Falciani M. Haemostatic changes in normal pregnancy. Haematologica reports. 2005;1:1-5.
5. Simioni P, Campello E. Haemostatic changes in pregnancy. Reviews in Health Care. 2013;4:3s. Available:http://journals.edizioniseed.it/index.php/rhc/article/view/878 (Accessed 10 Nov, 2013)
6. Kametas N, Krampt E, McAuliffe F, Rampling MW, Nicolaides KH. Haemorrheological adaptation during pregnancy in a Latin American population. European Journal of Haematology. 2001; 66:305-311.
7. Salawu L, Durosinmi MA. Erythrocyte rate and plasma viscosity in health and disease. Nigerian Journal of Medicine. 2001;10:11-13.
8. Imoru M, Emeribe AO. Haemorrheologic and fibrinolytic activities in pregnant women: Influence of gestational age and parity. African Journal of Biotechnology. 2009;8:6641-6644.
9. Uchikova EH, Ledjev II. Changes in haemostasis during normal pregnancy. European Journal of Obstetrics and Gynaecology and Reproductive Biology. 2005;119:185-188.
10. Kline JA, Williams GW, Hernandez-Nino J. D-dimer concentrations in normal pregnancy: New diagnostic thresholds are needed. Clinical chemistry. 2005;51(5): 825-829.
11. Reger B, Peterfalvi A, Litter I, et al. Challenges in the evaluation of D-dimer and fibrinogen levels in pregnant women. Thromb Res. 2013;131:183-187.
12. Bellart J, Gilabert R, Fontcuberta J, Borrell M, Miralles RM, Cabero L. Fibrinolysis change in normal pregnancy. Journal of Perinatal Medicine. 1997;25:368-372.
13. Kjellberg U, Anderson NE, Rossen S, Tengborn L, Hellgren M. APC resistance and other haemostatic variables during pregnancy and puerperium. Thrombosis and Haemostasis. 1999;81:527-531.
14. Eichinger S. D-dimer testing in pregnancy. Pathophysiology of Haemostasis and Thrombosis. 2004;33:327-329.
15. Howie PW. Blood clotting and fibrinolysis in pregnancy. Postgrad Med J. 1979; 55(643):362-366.
16. Maki M, Soga K, Seki H. Fibrinolytic activity during pregnancy. Tohoku J Exp Med. 1980;132(3):349-354.
17. Stirling Y, Woolf L, North WRS, Seghatchian MJ, Meade TW. Haemostasis in normal pregnancy. Thrombosis and Haemostasis. 1984;52:176-182.
18. Holmes VA, Wallace JMW. Haemostasis in normal pregnancy: A balancing act? Biochemical society transactions. 2005;33 (2):428-432.
19. Buseri FI, Jeremiah ZA, Kalio FG. Influence of pregnancy and gestation period on some coagulation parameters among Nigerian antenatal women. Research Journal of Medical Sciences. 2008;2:275-281.
20. Szecsi PB, Lorgensen M, Klainbard A, Anderson MR, Colov NP, Stender S. Haemostatic reference intervals in pregnancy. Thrombosis and Haemostasis. 2010;103:718-727.
21. Greer IA. Haemostasis and Thrombosis in pregnancy. In: Bloom AL, Forbes CD, Thomas DP, Tuddenham EGD (editors). Haemostasis and Thrombosis (3rd ed), Churchill Livingstone, Edinburgh. 987-1015.
22. Durotoye IA, Babatunde AS, Olawumi HO, Olatunji PO, Adewuyi JO. Haemostatic parameters during pregnancy in Ilorin, Nigeria. The Tropical Journal of Health Sciences. 2012;19(2):18-22.
23. Kobayashi T, Asahina T, Machara K, Itah M, Kanayama N, Terao T. Congenital afibrinogemia with successful delivery. Gynae and Obstet Inv. 1996;42(1):66-69.
24. Hellgren M. Hemostasis during normal pregnancy and puerperium. Thrombosis and Haemostasis. 2003;29:125-130.
25. Van Wersch JWJ, Ubachs JMH. Blood coagulation and fibrinolysis during normal pregnancy. Eur J Clin Chem Clin Biochem. 1991;29:45-50.
26. Bremme K, Ostlund E, Almqvist I, Heinonen K, Blomback M. Enhanced Thrombin generation and fibrinolytic activity in normal pregnancy and the puerperium. Obstet Gynaecol. 1992;80(1): 132-137.

27. Morse M. Establishing a normal range for D-dimer levels through pregnancy to aid in the diagnosis of pulmonary embolism and deep vein thrombosis. Journal of Thrombosis Haemostasis. 2004;2:1202-1204.
28. Nolan T, Smith R, Devoe L. Maternal plasma D-dimer levels in normal and complicated pregnancies. Obstet Gynecol. 1993;81:235-238.
29. Francalanci I, Comeglio P, Allessandrello Liotta A, Cellai AP, Fedi S, Paretti E, et al. D-dimer plasma levels during normal pregnancy measured by specific ELISA. Intl J Clin Lab Res. 1997;27:65-67.
30. Jeremiah ZA, Adias TC, Opiah M, George SP, Mgbere O, Essien EJ. Elevation in D-dimer concentrations is positively correlated with gestation in normal uncomplicated pregnancy. International Journal of Women's Health. 2012;4:437-443.
31. Woodfield DG, Cole SK, Allan AGE, Cash JD. Serum fibrin degradation products throughout normal pregnancy. Brit Med J. 19684:665-8.
32. Yuasa S, Ishizawa M, Yuki Y, Minoura T, Fujita N, Takahashi H, et al. Coagulation and fibrinolysis in pregnancy. Rinsho Byori. 1992;40(12):1287-1291.
33. Higgins JR, Walshe JJ, Darling MRN, Norris L, Bonnar J. Haemostasis in the uteroplacental and peripheral circulations in normotensive and pre-eclamptic pregnancies. American Journal of Obstetrics and Gynaecology. 1998;179: 520-526.
34. Hamsten A, Walldius G, Szamosi A, Blomback M, De Faire U, Dahlen G, et al. Plasminogen activator inhibitor in plasma: Risk factor for recurrent myocardial infarction. Lancent. 1987;2:3-9.
35. Jansson JH, Nilsson TK, Olofsson BO. Tissue plasminogen activator and other risk factors as predictors of cardiovascular events in patients with severe angina pectoris. Eur Heart J. 1991;12:157-161.
36. Chandler WL, Jascur ML, Henderson PJ. Measurement forms of tPA in plasma. Clinical Chemistry. 2000;46:38-46.

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