Fibrinogen Levels Among Pregnant Women of African Descent in Sokoto North Western Nigeria

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Citation

Abstract
Haemostatic changes in pregnancy are significant and essential, and have the potential to cause adverse pregnancy outcome. The aim of this study is to determine the effect of pregnancy on the fibrinogen (FIBC) levels of 100 consecutively-recruited pregnant women of African descent in Sokoto North Western Nigeria aged 18-34 with a mean age 25.52 ± 4.92 years. Fifty age-matched non-pregnant women were monitored as controls. The FIBC levels was significantly higher among the pregnant subjects (2.79 ± 0.78 g/L) compared to the non-pregnant controls (1.37 ± 0.16 g/L) (p<0.001). The mean FIBC levels of the pregnant subjects was significantly higher (p=0.05) among pregnant women in the third trimester (3.31 ± 0.56 g/L) compared to the second (2.42 ± 0.57 g/L) and first trimester (2.19 ± 0.71 g/L). The results conclude that the fibrinogen levels is significantly higher among pregnancy when compared with non-pregnant control women. Trimester plays a significant role in the FIBC levels of pregnant women. It may be necessary to routinely monitor the FIBC level during pregnancy.

1. Introduction

Pregnancy is the fertilization and development of one or more offspring, known as an embryo or foetus, in a woman's uterus. Normal pregnancy is accompanied by major changes in the haemostatic mechanism especially an increase in the level of coagulation factors (fibrinogen, V, VIII, and X) and a noticeable decrease in fibrinolytic activity [1]. Such changes have been interpreted as a physiological development to provide effective haemostasis and preservation of the maternal blood during parturition [2]. Pregnancy is a risk factor for venous thrombosis. Venous thromboembolism is an important cause of maternal morbidity and mortality. In normal pregnancy there is a marked increase in the procoagulant activity in maternal blood characterized by elevation of factors VII, X, VIII, fibrinogen and von Willebrand factor, which is maximal around term [3]. Increase in the blood level of these coagulation factors is maximal in the 3rd trimester of pregnancy [4].
Normal fibrinogen activity usually reflects normal blood clotting ability. Significantly decreased fibrinogen activity may be due to decreased or dysfunctional fibrinogen. Reduced fibrinogen activity and antigen levels may impair the body's ability to form a stable blood clot. Chronically low levels may be related to decreased production due to an inherited condition such as afibrinogenemia or hypofibrinogenemia or to an acquired condition such as end-stage liver disease or severe malnutrition. Acutely low levels are often related to consumption of fibrinogen such as may be seen with DIC and abnormal fibrinolysis. Reduced fibrinogen levels may also occur following rapid, large-volume blood transfusions (dilutional coagulopathy). It is not known to what extent pregnancy affect the fibrinogen of pregnant women of African descent in Sokoto North Western Nigeria. In Nigerian reference values derived from non-pregnant women are routinely used for pregnant women. The aim of this study was to investigate the fibrinogen level of pregnant women in Sokoto, North Western Nigeria.

2. Materials and Methods

2.1. Study Area

This study was conducted in the Specialist Hospital Sokoto State. Sokoto state is located in the extreme Northwest of Nigeria, near to the confluence of the Sokoto River and the Rima River. The metropolitan city of Sokoto covers an area of 60.33 km. It is in the dry Sahel surrounded by sandy savannah with an annual average temperature of 28.3°C (82.9°F). The warmest months are February to April, the rainy season is from June to October, during which showers are a daily occurrence. From late October to February, during the 'cold season', the climate is dominated by the Harmattan wind blowing Sahara dust over the land. Sokoto State has a projected population of 3.7 million people based on 2006 census. The State is made up of two major ethnic groups namely, Hausa and Fulani [6].

All the citrated samples collected were analyzed at the Haematology Department of Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto. It is among the Hospitals that were established in May 1980 as a second generation teaching hospitals along with Calabar, Port Harcourt, Ilorin, Maiduguri and Jos. The hospital started operating at the Specialist hospital, Sokoto. It has witnessed different kinds of transformations in recent years which have translated into the provisions of tertiary health care service to the entire Northwest region.

2.2. Sample Size Estimation

Blood samples from pregnant women obtained will be compared to that of non-pregnant women as controls.

\[ n = \frac{Z^2 pq}{d^2} \]

Where \( n \) = minimum required sample size

\( Z \) = standard normal deviation (1.96)  
\( p \) = proportion of success or prevalence =50%  
\( d \) = precision tolerable margin of error (0.05)  
\( n \) = \( (1.96)^2 \times 0.5(1-0.5) ÷ (0.5)^2 \)

Minimum sample size = 384

50% was used as the prevalence (P) due to the fact that no prevalence value was found in previous researches.

2.3. Study Population

The study population comprised of adult pregnant visiting the antenatal clinic in Specialist Hospital Sokoto. The control participants were age-matched, non-pregnant women residing in Sokoto metropolis. Subjects and control participants were aged 18-40 years.

2.4. Study Design

This is a case control study designed to include 100 pregnant women as the subjects and 50 non-pregnant women as controls.

2.5. Inclusion Criteria

All consenting adults (≥ 18 years) pregnant (subjects) without any history of bleeding disorders or oral anticoagulants use were included from the study. Control participants were non-menopausal and non-menstruating.

2.6. Exclusion Criteria

All women who did not meet the inclusion criteria are excluded from this study. Menopausal and menstruating women are excluded as control. Pregnant subjects with bleeding disorders, underlying coagulation disorders, pregnancy-related problem, patients on anticoagulants therapy and patients that refused to give a verbal informed consent were excluded.

2.7. Sample Collection

For each subject a tourniquet was applied around the arm, the antecubital fos was disinfected with cotton wool soaked in methylated spirit. About 4.5mls of venous blood was collected using a 5mls syringe into sodium citrate anticagulated tube. The blood was centrifuged to obtain citrated plasma. The citrated plasma was used for the determination of fibrinogen and thrombin concentration.

2.8. Determination of Fibrinogen Concentration

2.8.1. Principle

During the process of coagulation, the enzyme thrombin converts soluble fibrinogen into insoluble fibrin. The time required for this conversion is proportional to the
concentration of fibrinogen in plasma.

2.8.2. Procedure
1. One in ten dilutions (1/10) of the test and standard fibrinogen plasma (Diagnostic Reagents Ltd., UK) was made in imidazole buffer.
2. Two hundred microlitres (200µl) of diluted plasma was warmed at 37°C for two minute.
3. Hundred microlitres (100µl) of thrombin reagent was added to the plasma dilutions and the clotting time was then measured.

2.9. Reference Range for Fibrinogen
The normal range for fibrinogen using the Clauss technique is: 1.7-4.0g/L

2.10. Statistical Analysis
Data obtained was entered manually into computer statistical software (SPSS version 20.0). Results were expressed as mean ± standard deviation. Student t-test was used to compare means difference of FIBC between pregnant and non-pregnant women.

3. Results
The fibrinogen concentration (FIBC) levels of 100 consecutively-recruited pregnant women and 50 non-pregnant women (as controls) were studied. The mean age and range of pregnant subjects were aged 25.52 ± 4.92 years and 18 to 34. The mean of FIBC observed among the pregnant subjects and control participants was 2.788 g/L and 14.35 seconds respectively. Table 1 show the mean fibrinogen levels of pregnant subjects and the non-pregnant controls. The mean of FIBC levels observed among the pregnant subjects was compared against the non-pregnant controls. The FIBC higher among the pregnant subjects (2.79 ± 0.78 g/L) seconds compared to the non-pregnant controls (1.37 ± 0.16 g/L) (p=0.001). Table 2 show the mean fibrinogen levels among the pregnant subjects based on trimesters. The mean fibrinogen level was significantly higher (p=0.05) among pregnant women in the third trimester (3.31 ± 0.56 g/L) compared to the second (2.42 ± 0.57 g/L) and first trimester (2.19 ± 0.71 g/L).

4. Discussion
Haemostatic abnormalities have been associated with various complications of pregnancy. This research work was carried out to assess the fibrinogen concentration among pregnant women in Sokoto North Western Nigeria. This study indicated a statistically significant higher fibrinogen concentration among the pregnant subjects compared to the non-pregnant controls (p=0.001). Finding from this study is consistent with previous report [6] who indicated that pregnancy exert a significant increase in fibrinogen. Finding from this study is also in agreement with previous reports [7-11] 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 in beginning in early pregnancy [12-14]. 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 also observed during the course of this research 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 to the third trimester. This result is consistent with an earlier report [15] which indicated that the level of fibrinogen rose significantly from second to third trimester recorded. Similarly, Choi and colleagues [16] 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 [4, 7, 17]. Previous report indicates that fibrinogen level is obviously elevated in late pregnancy as compared with the control group [18]. Similarly most blood coagulation factors including fibrinogen has been shown to be increased during pregnancy [19].

Haemostasis abnormalities have been associated with various complications of pregnancy [6]. These changes in haemostatic system are considered to be in preparation for the maintenance of the placental function which occurs during pregnancy. These substances stimulate clot formation...
to stop maternal blood loss. As placental blood flow is up to 700ml/min considerable haemorrhage can occur if clotting fails. Pregnancy is a complex physiological process with many physiological changes as seen in increased coagulation factors and decreased anticoagulation factors. During pregnancy there are significant changes in coagulation in the direction of coagulability, thus decreasing bleeding complications in connection with delivery [20].

Finding from this study is in agreement with previous report 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 delivery [20-26]. Previous report by Hui and colleagues [27] on their cohort 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 controls. This finding indicates that the haemostatic reference intervals being used which are generally based on samples from non-pregnant women may not be correct, is not relevant to pregnant women and can potentially hinder the accurate diagnosis and treatment of haemostatic disorders during pregnancy. This observation is consistent with previous reports which suggest that gestational age-specific reference values are essential for the accurate interpretation of a subset of haemostatic tests during pregnancy, delivery, and puerperium [28-30]. Elevated markers of coagulation and fibrinolytic system activation indicate increased thrombin activity and increased fibrinolysis following fibrin formation throughout pregnancy. These changes exceed the biological variability in most cases. Haemostatic reference intervals are generally based on samples from non-pregnant women. Thus, they may not be relevant to pregnant women, a problem that may hinder accurate diagnosis and treatment of haemostatic disorders during pregnancy.

5. Conclusion

This study has shown that pregnancy has a significant effect on the Fibrinogen levels of women of African descent. It may be necessary to routinely monitor the fibrinogen level of pregnant women of African descent.

Recommendations

Finding from this study is a wakeup call on the need to routinely monitor haemostatic parameters of pregnant women. There is need to develop haemostatic reference intervals for pregnant women in the area. Current reference intervals being used are generally based on samples from non-pregnant women. This may hinder the accurate diagnosis and treatment of haemostatic disorders during pregnancy. It is recommended that pregnant women with haemostatic complications should be under the management and care of a qualified obstetrician to mitigate the possible negative effect during pregnancy and delivery. There is also the need to provide the necessary facilities and trained Medical Laboratory Scientist to facilitate the effective diagnosis and monitoring of haemostatic disorders associated with pregnancy.

References


