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# Evaluation of Some Hemostatic Changes in Pregnant Women Attending FMC keffi, Nasarawa State, Nigeria

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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:** The term "Haemostasis" has its origins in the Greek words "Haem," signifying blood, and "stasis," meaning a standstill. It refers to the process responsible for stopping bleeding, thereby preventing blood from escaping through damaged blood vessels.
Pregnancy brings about significant anatomical and physiological changes in the expectant mother's body, aimed at nurturing and accommodating the developing fetus. These changes commence after conception and impact every organ system in the body.
During pregnancy, there is an elevation in several clotting factors, accompanied by a reduction in fibrinolytic and anticoagulant activities, notably protein S. While this adaptation serves to minimize bleeding risks during delivery, it simultaneously heightens the risk of thrombosis. Generally, a normal pregnancy is considered a state of increased blood clotting propensity, likely evolved as a protective mechanism to mitigate the potential hazards of acute hemorrhage during childbirth.

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**Aim:** This study was aimed to determine the hemostatic changes in pregnant women attending FMC Keffi, Nasarawa state.
**Materials and Methods:** Blood samples were collected from 75 confirmed pregnant women attending Federal Medical Center Keffi and 25 apparently non-pregnant controls. Prothrombin time (PT) and activated partial thrombin time (APTT) were performed using manual methods and D-dimer was determined using the Finecare Wondfo method.
**Results:** The results show statistically nosignificant difference ($p>0.05$) in the mean of PT and APTT, International Normal Ratio (INR) of pregnant women and control subjects respectively. On the other hand, the results also show a significant difference ($p< 0.05$) in the means of d-dimer of pregnant women and control subjects respectively.
**Conclusions:** No significant statistical difference was observed, indicating pregnant women have normal PT, APTT, INR and increased D-dimer.

*Keywords: Hemostasis; Lymphocytes; PT; APTT; INR; D-dimer.*

## 1. INTRODUCTION

The term "Haemostasis" originates from the Greek words "Haem," signifying blood, and "stasis," meaning a standstill. “It describes the process that halts bleeding, preventing blood from escaping damaged blood vessels. This marks the initial phase of wound healing, often involving the transformation of liquid blood into a solid state. The intactness of blood vessels plays a pivotal role in moderating blood clotting. Endothelial cells in undamaged vessels prevent blood clotting through the release of heparin-like molecules and thrombomodulin, inhibiting platelet aggregation via nitric oxide and prostacyclin” [1]. “However, when endothelial injury occurs, these cells cease the secretion of coagulation and aggregation inhibitors and instead release Von Willebrand factors, initiating the maintenance of haemostasis after injury.

Normal haemostasis relies on close interactions between blood vessels, platelets, clotting factors, anticoagulants, and the fibrinolytic system. When a blood vessel sustains injury, platelets adhere to exposed collagen, leading to platelet activation and the formation of initial platelet aggregates. Von Willebrand factor (VWF) in circulation also binds to exposed collagen, aiding platelet adhesion. Blood coagulation pathways revolve around thrombin generation, which cleaves fibrinogen to create fibrin, the structural framework stabilizing platelet aggregates at sites of vascular injury” [2]. Inhibitory anticoagulant pathways confine the haemostatic response to the injury site, regulating thrombin generation and crucially contributing to controlled haemostatic plug formation.

“During pregnancy, significant anatomical and physiological changes occur in the pregnant mother's body to nurture and accommodate the developing fetus, starting after conception and affecting every organ system” [3]. “In most women experiencing uncomplicated pregnancies, these changes resolve after childbirth with minimal lingering effects. Understanding the normal physiological changes in pregnancy helps distinguish them from abnormal adaptations” [3].

Plasma volume progressively increases throughout a typical pregnancy [4], with most of this 50% increase happening by 34 weeks' gestation and correlating with the baby's birth weight. “Because plasma volume expands more than red blood cell mass, there is a decrease in haemoglobin concentration, haematocrit, and red blood cell count. However, mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC) usually remain unchanged. Platelet count tends to drop progressively during normal pregnancy but typically stays within the normal range. In some women (5–10%), platelet count may reach levels of 100–150 × 109 cells/l by term, even without any pathological processes. Hence, a woman is generally not considered thrombocytopenic during pregnancy until her platelet count falls below 100 × 109 cells/l” [3].

“Pregnancy induces changes in the coagulation system, resulting in a physiological hypercoagulable state (preparing for haemostasis after delivery)” [5]. Concentrations of specific clotting factors, particularly VIII, IX, and X, increase. Fibrinogen levels rise significantly, up to 50%, and fibrinolytic activity decreases. Concentrations of endogenous anticoagulants such as antithrombin and protein S decrease. Consequently, pregnancy alters the balance within the coagulation system, favoring clotting and predisposing pregnant and postpartum women to venous thrombosis. This

elevated risk is present from the first trimester and for at least 12 weeks after delivery. In vitro coagulation tests (activated partial thromboplastin time - APTT, prothrombin time - PT, and thrombin time - TT) remain normal unless affected by anticoagulants or a coagulopathy.

## 2. MATERIALS AND METHODS

In this study, one hundred (100) participants were recruited using stratified random sampling technique, out of which, 75 (75%) of them were pregnant women with the mean age of 28.92 ± 7.51 years, and 25(25%) were control subjects with the mean age of 27.60 ± 6.27 years. Blood sample was collected for Prothrombin time (PT), activated partial thrombin time (APTT), International Normal Ratio (INR) and D-dimer level determination. “PT was determined using a kit fromSpectrum company, Plasma is combined with a thromboplastin and calcium chloride reagent at a temperature of 37 degrees Celsius, and the elapsed time for a clot to form is recorded. This clotting time, measured in seconds, is then converted into the International Normalized Ratio (INR). Typically, this conversion is performed by consulting a table provided by the reagent manufacturer or by using a formula” (Cheesbrough, 2006).

“The activated partial thromboplastin time (APTT) was determined using a kit from the Spectrum company. In this process, kaolin (a surface activator) and a platelet substitute (phospholipid) were incubated with citrated plasma at 37 degrees Celsius for the specified duration according to the test method. Calcium chloride (CaCl2) was subsequently introduced, and the time taken for the mixture to clot was measured” (Cheesbrough, 2006). The INR is derived from the prothrombin time (PT), which is calculated as the ratio of the patient's PT to a control PT that has been standardized to the potency of the thromboplastin reagent developed by the World Health Organization.

## 3. RESULTS

Data collected from both subjects and controls were analyzed using Statistical Package for Social Sciences (SPSS version 23.0 software) to calculate mean, standard deviation, ttest, Karl Pearson correlation of coefficient and pvalues. (P-value ≤ 0.05) were considered statistically significant while (P-value >0.05) were considered not statistically significant. Table 1 shows ademographic data of the study subjects. It shows the age, Trimester and Blood pressure of the study subjects and controls. The mean age of the participants was 28.92 ± 7.51. The pregnant women were also grouped according to trimester. Equal number 25 (33.3%) of the participant were in their first, second and third trimester each.

Table 2 Shows the Comparison of Hemostatic Parameters in pregnant women and Controls subjects. The table revealed that there is no significant difference (p>0.05) in the mean of PT (12.12±1.12 vs 11.96±0.74), PTTK (28.07±4.29 vs 26.28±4.03), INR (1.02±0.11 vs 0.99±0.07) of pregnant women and control subjects respectively. On the other hand, the table also shows a significant difference (p< 0.05) in the means of FDP (3.42±2.10 vs 2.31±1.10) of pregnant women and control subjects respectively.

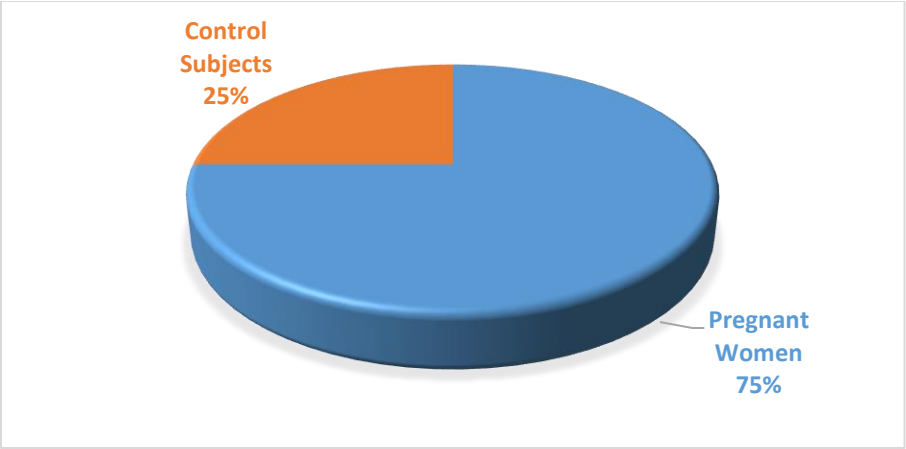


**Fig. 1. Pie Chart showing the percentage distribution of study subjects**

**Table 1. Socio-Demographic Data of Pregnant Women and Control subjects**

| Parameters | | Pregnant Women | Controls |
|---|---|---|---|
| Age (years) | | 28.92 ± 7.51 | 27.60 ± 6.27 |
| Trimester | First | 25(33.3%) | 8(32%) |
| | Second | 25(33.3%) | 8(32%) |
| | Third | 25(33.3%) | 9(36%) |
| Blood Pressure | 120/80 | 36(48%) | 17(68%) |
| | 130/80 | 29(39%) | 4(16%) |
| | 140/80 | 9(12%) | 4(16%) |
| | 150/80 | 1(1%) | 0(0%) |

*All values are expressed as mean ± standard deviation*

**Table 2. Comparison of hemostatic parameters in pregnant women and controls subjects**

| Variables | Pregnant Women | Controls | p-value | Remarks |
|---|---|---|---|---|
| PT | 12.12±1.12 | 11.96±0.74 | 0.42 | NS |
| PTTK | 28.07±4.29 | 26.28±4.03 | 0.06 | NS |
| INR | 1.02±0.11 | 0.99±0.07 | 0.34 | NS |
| FDP | 3.42±2.10 | 2.31±1.10 | 0.00 | S |

*All values are expressed as mean ± standard deviation. NS- Not Significant and S- Significant*

Table 3 Shows the Changes in Prothrombin time (PT) according to trimesters among pregnant women. The result shows an insignificant increase in the average PT among pregnant women as pregnancy progresses from first (11.92±1.19), second (12.36±1.11) and third trimester (12.08±1.04) respectively (p-value = 0.18).

**Table 3. Changes in prothrombin time according to trimesters among pregnant women**

| Trimester | Number | Mean ± SD | p-value | Remarks |
|---|---|---|---|---|
| First | 25 | 11.92±1.19 | | |
| Second | 25 | 12.36±1.11 | 0.18 | NS |
| Third | 25 | 12.08±1.04 | | |

*All values are expressed as mean ± standard deviation. NS- Not Significant and S- Significant*

Table 4 Shows the Changes in Partial Thromboplastin time with Kaolin (PTTK) according to trimesters among pregnant women. The result shows a significant increase in the average PTTK among pregnant women as pregnancy progresses from first (27.00±3.42), second (27.20±4.66) and third trimester (30.00±4.19) respectively (p-value = 0.03).

Table 5 Shows the Changes in International Normalize Ratio (INR) according to trimesters among pregnant women. The result shows an insignificant increase in the average INR among pregnant women as pregnancy progresses from first (1.00±0.11), second (1.04±0.11) and third trimester (1.01±0.10) respectively (p-value = 0.36).

**Table 4. Changes in partial thromboplastin time with kaolin according to trimesters among pregnant women**

| Trimester | Number | Mean ± SD | p-value | Remarks |
|---|---|---|---|---|
| First | 25 | 27.00±3.42 | | |
| Second | 25 | 27.20±4.66 | 0.03 | S |
| Third | 25 | 30.00±4.19 | | |

*All values are expressed as mean ± standard deviation. NS- Not Significant and S- Significant*

**Table 5. Changes in International Normalize Ratio according to trimesters among pregnant women**

| Trimester | Number | Mean ± SD | p-value | Remarks |
|---|---|---|---|---|
| First | 25 | 1.00±0.11 | | |
| Second | 25 | 1.04±0.11 | 0.36 | NS |
| Third | 25 | 1.01±0.10 | | |

*All values are expressed as mean ± standard deviation. NS- Not Significant and S- Significant*

Table 6 Shows the Changes in Fibrin Degradation Product (FDP) according to trimesters among pregnant women. The result shows a significant increase in the Mean± S.Dvalues of FDP among pregnant women as pregnancy progresses from first (1.44±0.31), second (4.05±1.97) and third trimester (4.78±1.80) respectively (p-value = 0.00).

## 4. DISCUSSION

This research was designed to assess hemostatic changes in pregnant women. A total of 100 women participated in the study: the

average hemostatic parameters (PT, PTTK, INR, and FDP) of 75 pregnant women (the test group) were determined and compared with those of the control group, which consisted of 25 non-pregnant women. Mean hemostatic parameters (PT, PTTK, INR, and FDP) for both groups are presented in Table 3. The data in Table 3 indicates that there is no statistically significant difference in the mean PT, PTTK, and INR values between pregnant women and the control group.

**Table 6. Changes in Fibrin Degradation Product according to trimesters among pregnant women**

| Trimester | Number | Mean ± SD | p-value | Remarks |
|---|---|---|---|---|
| First | 25 | 1.44±0.31 | | |
| Second | 25 | 4.05±1.97 | 0.00 | S |
| Third | 25 | 4.78±1.80 | | |

*All values are expressed as mean ± standard deviation. NS- Not Significant and S- Significant*

It has been reported that during pregnancy, the hemostatic balance tends to shift towards hypercoagulability to reduce the risk of bleeding complications [6]. However, this finding contradicts the previous studies by Hellgren [7], Durotoye et al. [8], and Avwioro et al. [9], which all reported statistically significant differences in mean PT values between normal, uncomplicated pregnant women and healthy non-pregnant women. The study also evaluated changes in hemostatic parameters across trimesters among pregnant women, as presented in Tables 4, 5, and 6.

The data in Table 3 shows that in the first and second trimesters, the mean PT slightly increased from 11.92±1.19 to 12.36±1.11, which was not statistically significant. “However, as pregnancy progressed to the third trimester, a statistically significant decrease in PT was recorded, with the third trimester showing a PT of 12.08±1.04. This change is explained by the hemostatic balance shifting more towards hypercoagulability as pregnancy advances, aiming to reduce bleeding complications during delivery” [6].

Table 4 reveals that in the first, second, and third trimesters, the mean PTTK slightly increased from 27.00±3.42 to 30.00±4.19, which was statistically significant. Table 6 displays that in the first and second trimesters, the mean INR slightly increased from 1.00±0.11 to 1.04±0.11, which was not statistically significant. However, in the third trimester, a statistically significant decrease in INR was observed, with a value of 1.01±0.10.

Furthermore, Table 5 shows that in the first, second, and third trimesters, the mean FDP slightly increased from 1.44±0.31 to 4.78±1.80, which was statistically significant. According to Soma-Pillay et al. [10], pregnancy is associated with significant changes in the hemostatic profile, including increased levels of fibrinogen and clotting factors due to rising estrogen levels. These changes lead to a prothrombotic state during pregnancy.

In conclusion, this study indicates that prothrombin time decreases during normal pregnancy when compared to non-pregnant control groups. Additionally, it shows that prothrombin time decreases significantly as pregnancy progresses toward term, although the mean PT values in both subjects and controls remained within the normal range. This finding aligns with previous studies, suggesting that increased coagulation activity during pregnancy serves as a protective mechanism during childbirth.

## 5. CONCLUSION

Disorders of hemostasis are not uncommon in pregnancy, and they may have a significant impact on the patient. An understanding of the common causes and treatment of hemostatic changes in pregnant women will inform the management of major hemorrhage during delivery.

This research observed no significant statistical difference in PT, APTTand INR between the test and control group. However, there was significant statistical difference in PT between the pregnant women and the normal controls.

## 6. RECOMMENDATION

It is therefore recommended that Hemostatic test should be included as part of routine antenatal Haematology test. This will help provide evidence-based data for proper management of pregnant with regard to coagulation disorders associated with pregnancy such as bleeding and thrombosis.

## CONSENT

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

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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