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Assessment of Selected Haemostatic Parameters among Pregnant Women at Different Parities

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Abstract

Coagulation pattern in pregnancy is postulated to be impacted by gestational age and parity. The study sets out to assess the prothrombin time (PT), activated partial thromboplastin time (APTT) and platelets count (PLT) in pregnant women and investigate the impact of parity on these haemostatic parameters. A total of 150 participants were recruited into this study comprising of 75 pregnant with different parity and varying trimester and 75 non-pregnant women. 4.5ml of venous blood sample was collected into 1/10 volume of 3.8% sodium citrate anticoagulant bottle and 4ml of venous blood sample was collected into ethylenediamine tetraacetic acid (EDTA) anticoagulant bottle from each participant after obtaining written informed consent. Blood samples were spun and separated in the laboratory. PT, APTT and PLT were analyzed immediately using Quick's test, Tilt-tube method, improved Neubauer hemocytometer method respectively. Data were analyzed using SPSS 20.0 and taken to be significant at $p<0.05$. Prothrombin time in pregnant women (15.76 ± 2.91) was significantly prolonged compared with non-pregnant participants (13.03 ± 2.01) in this study ($p<0.05$). APTT on the other hand was lower among pregnant women (23.71 ± 5.23) than non-pregnant women (34.86 ± 2.86) $p<0.05$. There was no significant difference between the platelets count among the two groups. Higher parity showed significant association with prolonged PT and shortened APTT. Pregnancy exhibits modulatory effects on haemostatic parameters with noticeable impact on PT and APTT. Increased parity appears to be an independent factor to this effect.

Keywords: Parity**;** Prothrombin time; Activated Partial Thromboplastin Time; Platelet count; Coagulation pattern.

1. Introduction

Maternal physiological changes occur in the three trimesters of pregnancy with alterations in the hematological parameters. Normal pregnancies are hypercoagulable; nevertheless, even minor deviations from normal levels can result in a life-threatening syndrome known as Disseminated Intravascular Coagulation. Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) are useful screening tests for extrinsic and intrinsic coagulation pathways, respectively. Platelet count is also crucial, as any thrombocytopenia that goes undetected might lead to maternal hemorrhage [1].

Hormone levels fluctuate during pregnancy, particularly during the third trimester when estrogen and progesterone levels peak, leading to hypercoagulability in pregnant women. Abnormal hypercoagulability during pregnancy can lead to thrombotic and bleeding diseases, endangering the health and possibly lives of pregnant women and fetuses. As a result, routine coagulation tests are essential for pregnant women to evaluate their coagulation and fibrinolytic systems [2].

Pregnancy is associated with several changes in the coagulation system, including an increase in clotting factors such as fibrinogen, factors VII, VIII, and X, and Von Willebrand factor. These changes are thought to be adaptive, ensuring that the mother does not bleed excessively during childbirth [3].

Pregnancy is considered a procoagulant state, meaning that there is an overall increase in coagulation factors and a decrease in fibrinolysis (the process of breaking down blood clots). This shift in the coagulation balance not only helps prevent excessive bleeding during childbirth but also increases the risk of thrombosis. Pregnancy is associated with several physiological changes that can affect APTT. These include an increase in plasma volume, changes in hormone levels (such as increased estrogen and progesterone), and alterations in the coagulation system to prevent excessive bleeding during childbirth (formation of blood clots) [4].

This study investigates variations in selected haemostatic parameters among pregnant women at different parities. The aim is to understand how these changes can impact maternal health and inform clinical management. The study assessed the platelet count (PT), prothrombin time (PT) and activated partial thromboplastin time (APTT) in nulliparous and multiparous women. By comparing these parameters, the study was able to identify significant differences and explore potential influencing factors. This research is crucial for understanding maternal-fetal physiology and improving healthcare interventions.

2. Materials and Methods

2.1. Study Area

This study was carried out in University of Medical Sciences Teaching Hospital (UNIMEDTH). UNIMEDTH is located in Ondo city which can be found in Ondo West local Government, Ondo State. It is about 48km from the state capital, Akure. It lies between longitudes 4”30 and 6” east of the Greenwich Meridian, 5”45 and 8”15” North of the Equator.

2.2. Study Design

This is a cross sectional and experimental study to assess selected haemostatic parameters among pregnant women at different parities in University of Medical Sciences Teaching Hospital, Ondo City (UNIMEDTH). This study was carried out within one year, it is a probability simple randomized study whereby each participant has equal chance of participating in the study without bias and it also involved test and control specimens.

2.3. Study Population

The study population involves pregnant women at University of Medical Sciences Teaching Hospital, Ondo City (UNIMEDTH). The written and verbal consents of the participants were sought and a total of 75 blood samples were collected from pregnant women with different parity at different trimesters as the test group in this study while 75 blood samples were collected from age-matched non-pregnant individuals to serve as control.

2.4. Ethical Approval

Ethical approval was sought and obtained from the Ethical Review Committee of the UNIMED Teaching Hospital, Ondo.

2.5. Sampling Technique

2.5.1. Sample size Determination

The sample size was determined using the sample size formula for population less than 0,000

Sample Size (S) = $\frac{a^2bc}{d^2}$ [5]

a=1.96 at 95% confident interval [5]

b= 11% = 0.11 [6]

c= 1- 0.11= 0.89

d= 0.05 degree of accuracy [5]

S= $\frac{1.96^2\times0.11\times0.89}{0.05^2}$S= 150

Sample size of 150 was considered in this study.

2.5.2. Sampling of Subjects

A total of 75 age-matched non-pregnant women were selected who served as control subjects. Randomized probability sampling method was employed for this study on pregnant women in the hospital and also the control subjects. Whole blood samples were collected from the both subjects and control groups and analyzed in the laboratory to assess the prothrombin time, activated partial thromboplastin time and platelets count.

2.5.3. Sample Collection

Eight (8) ml whole blood sample was collected by venipuncture from the cubical vein of the participants in an aseptic environment with 4ml each dispensed into Ethylene Diamine Tetra Acetic acid (EDTA) anticoagulated bottle and 1/10 volume of 3.8% Sodium citrate anticoagulated bottles and mixed properly. The specimens were properly labeled with participant’s identification number and participant name.

2.6. Preparation of Samples

The sodium citrated blood was centrifuged at low speed of 3000 revolutions per minute (rpm) for 15 minutes to obtain platelet poor plasma. Blood samples collected in the sodium citrate bottles and EDTA bottles were analyzed immediately for prothrombin time, activated partial thromboplastin time and platelet count.

2.7. Laboratory Analysis of Specimen

Quality control was carried out on each batch of prothrombin and activated partial thromboplastin reagents (Agappe product), expiry date, LOT number, manufacturer's address, manufacturing date, temperature limits were stated on the reagent pack. Reagents were stored at 2-8ºC.

2.7.1. Prothrombin Time

Principle: Activation of the coagulation system in a plasma sample in the presence of tissue factor (apoprotein and phospholipid) and $CaCl_2$ leads to the formation of a stable clot. The time from activation to formation of a stable clot is recorded in seconds, and represents the PT.

Procedure (Quic k's test)

The method of Ignjatovic [7] was adopted in this analysis. A water bath was pre-warmed and the temperature was stabilized at 37°C and a stopwatch (timer) was gotten prior to starting the test.

The tubes and reagent used for testing were pre-warmed at 37°C in the water bath for 10 minutes.

0.1 ml of test or control plasma was pipetted into the test tube and incubated at 37°C for 3 minutes.

0.2 ml of the pre-warmed prothrombin reagent was pipetted into the test tube and the timer was started simultaneously.

The reaction tube was tilted back and forth (under water as much as possible) in the 37°C water bath, and was continually observed for clot formation. Immediately upon formation of a clot, the timer was stopped and the result was recorded.

2.7.2. Activated Partial Thromboplastin Time

Principle: Activation of the coagulation system in a plasma sample in the presence of a platelet substitute (silica), activator of factor XII, and $CaCl_2$ leads to the formation of a stable clot. The time from activation to formation of a stable clot is recorded in seconds, and represents the APTT. The absence of the tissue factor from this reaction mixture has led to the use of the term "partial."

2.7.3. Procedure (Tilt-Tube Method)

A water bath was pre-warmed and the temperature was stabilized at 37°C. The tubes and reagents used for testing were pre-warmed at 37°C in the water bath for 10 minutes. A 0.1 ml aliquot of test or control plasma was pipetted into the test tube. Thereafter, 0.1 ml of the pre-warmed APTT reagent was pipetted into the test tube. The test tube was mixed well and incubated at 37°C for 3 minutes. Then 0.1 ml of pre-warmed calcium chloride ($CaCl_2$) solution (reagent 1) was pipetted into the tube and the time was started simultaneously. The reaction tube was tilted back and forth (under water as much as possible) in the 37°C water bath, and was continually observed for clot formation. Immediately upon formation of a clot, the timer was stopped and the result was recorded [7].

2.8. Platelets Count

Principle: Whole blood is diluted 1 in 20 in a solution of ammonium oxalate reagent, a diluent which hemolysis red blood cells leaving the platelets to be counted.

2.8.1. Procedure (Improved Neubauer Hemocytometer Method)

A 0.38 ml aliquot of ammonium oxalate was pipetted into a clean test tube. A 0.02ml portion of blood sample collected in the EDTA bottle was pipetted into the clean test tube containing ammonium oxalate solution. The test tube was mixed well and incubated for 5 minutes to ensure lysis of red cells. The grid area of the Neubauer counting chamber was cleaned and a cover slip was affixed to the Neubauer chamber until Newton's rings were seen. A Pasteur pipette was used to fill one of the grids of the counting chamber with the mixture. The platelet cells were viewed and counted microscopically and the result was recorded [1].

2.9. Collection of Data and Data analysis

An interviewer-administered questionnaire was used to obtain demographic information, such as age, gravidity status, parity level and gestational age, which could lead to variation in the clotting profile of pregnant women and the data collected were statistically analysed using SPSS (Statistical Package for the Social Sciences) version 25.0 computer software. Values obtained from the study expressed as mean ± standard deviation was compared using Chi square and T-test and significance was measured at $P<0.05$ and level of significance was taken at 95% confidence.

3. Results

Table.1 shows the socio-demographic characteristics and distribution of the study participants. Pregnant women serve as the test group in this study while the control group were apparently healthy non-pregnant women within the same age range. Majority of the study participants were between 25 to 34 years of age.

Table-1. Sociodemographic characteristics of study participants

	Pregnant women	Non-pregnant women
	Frequency (%)	Frequency (%)
Age		
18-24	33 (44)	33 (44)
25-34	34 (45.3)	34 (45.3)
35-44	8 (10.7)	8 (10.7)
Gestational age		
1st trimester	7 (9.3)	-
2nd trimester	22 (29.3)	-
3rd trimester	46 (61.3)	-
Occupation		
House wife	34 (45.3)	21(28)
Artisan	24 (32)	31 (41.3)
Civil servants	17 (22.7)	23 (30.7)
TOTAL	75 (100)	75 (100)

3.1. Parity

The parity of the respondents is presented in figure 1. Out of 75 pregnant women subjects, 38 were nulliparous, 10 were primiparous and 27 were multiparous.

3.2. Distribution of PT, APTT and Platelets (PLT)

Table 2 showed the distribution of PT, APTT and platelet count among the study participants. Out of the 75 pregnant women enrolled in the study, only 30 (40%) had normal PT values. On the contrary, 22 (29.3%) of them had low APTT values. Regarding platelet (PLT) count estimation, 23 (30.7%) of the pregnant women had low platelet count while the rest 52 (69.3) had normal platelet count.

Compared to the non-pregnant women control, 9 (12%) of the women had low Prothrombin Time (PT), 60 (80%) had normal PT while 6 (8%) had high PT values. Six (8%) had high Activated Partial Thromboplastin Time (APTT) results while the rest 69 (92%) had normal APTT values. Regarding platelet count estimation, 6 (8%) had low platelet count while the rest 69 (92%) had normal platelet count.

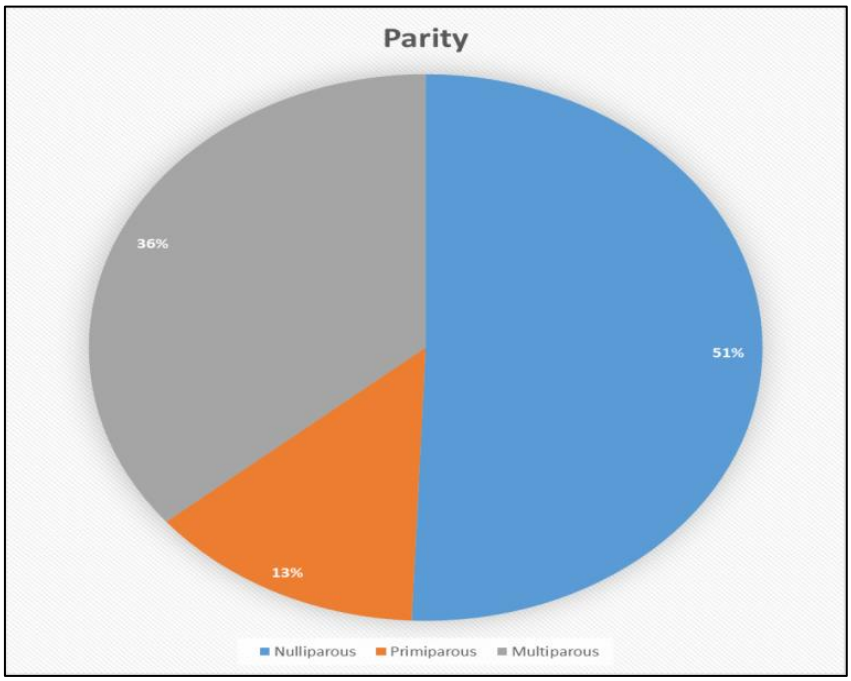

Fig-1. The Parity of respondents

Table-2. Distribution of PT, APTT and platelet count among the study participants

	Pregnant women (Frequency in %)	Non – pregnant women (Frequency in %)
Normal PT (10-15 secs)	30 (40.0)	60 (80.0)
High PT (>15 secs)	45(60.0)	6 (8.0)
Low PT (< 10 secs)	0 (0)	9 (12.0)
Normal APTT (21-38 secs)	53 (70.7)	69 (92.0)
High APTT (> 38 secs)	0 (0.0)	6 (8.0)

Low APTT (< 21 secs)	22 (29.3)	0 (0.0)
Normal PLT (10^9/L)	52 (69.3)	69 (92.0)
High PLT (10^9/L)	0 (0.0)	0 (0.0)
Low PLT (10^9/L)	23 (30.7)	6 (8.0)
Total	75(100)	75(100)

Legend
secs- seconds
PT- Prothrombin Time
APTT- Activated Partial Thromboplastin Time
PLT- Platelet count

3.3. Independent Samples t-test to Compare the PT, APTT and Platelets Values of the Pregnant Women Compared to the Non-Pregnant Women

Table 3 compared the mean ± SD of the PT, APTT and platelet count in the pregnant women with non-pregnant women using student t-test. Pregnant women demonstrated significantly prolonged PT which is relatively longer than that observed among non-pregnant women p <0.01. It also showed shortened APTT among pregnant women when compared non-pregnant individuals though within the normal reference interval p <0.01. On the contrary, there was no significant difference between the platelets count of the pregnant women and non-pregnant women p >0.05.

Table-3. Independent samples t-test to compare the PT, APTT and platelets values of the pregnant women compared to the non-pregnant women

Parameters	Pregnant Mean ± S.D	Non- Pregnant Mean ± S.D	t	p
PT (seconds)	15.76 ± 2.91	13.03 ± 2.01	6.70 <0.01	APTT (seconds)
23.71 ± 5.23	34.86 ± 2.86	-16.2	<0.01	
PLT (10^9/L)	195.55 ± 66.48	174.23 ± 18.34	1.70	0.09

P < 0.05 is statistically significant
Legend
S.D = Standard Deviation
PT = Prothrombin Time
APTT = Activated Partial Thromboplastin Time
PLT = Platelet count

3.4. Chi Square Analysis for the PT Results of the Pregnant Women with Different Parities of Respondents

Table 4 showed Chi Square test was done to determine the significant difference in the PT among pregnant women with different parities. Only 39.5% of nulliparous women had high PT which appears to increase with increased parity as majority of multiparous women (81.5%) showed higher PT. There was significant difference ($\chi 2$= 13.529, P value <0.05) in the PT results of the pregnant women with different parities.

Table-4. Chi Square Contingency Table for significant difference in the PT results of the pregnant women with different parities

Parity		Prothrombin (PT) Normal PT	High PT	Total
Nulliparous	Count	23	15	38
	Expected count	15.2	22.8	38
Primiparous	Count	2	8	10
	Expected count	4	6	10
Multiparous	Count	5	22	27
	Expected count	10.2	16.2	27
Total	Count	30	45	75
	Expected count	30	45	75

($\chi 2$= 13.529, P value <0.01)
NOTE: PT= Prothrombin Time

3.5. Chi Square for APTT Results of the Pregnant Women with Different Parities

Table 5 shows the result of the Chi Square test done to determine the significant difference in the APTT among pregnant women with different parities. Only 13.2% of nulliparous women had low APTT which appears to increase with increased parity as majority of primiparous women (80%) showed lower APTT. There was a significant difference ($\chi 2$= 17.389, P value <0.05) found in the APTT results of the pregnant women with different parities.

Table-5. Chi Square Contingency Table for significant difference in the APTT results of the pregnant women with different parities

Parity		APTT		
		Low APTT	Normal APTT	Total
Nulliparous	Count	5	33	38
	Expected count	11.1	26.9	38
Primiparous	Count	8	2	10
	Expected count	2.9	7.1	10
Multiparous	Count	9	18	27
	Expected count	7.9	19.1	27
Total	Count	22	53	75
	Expected count	22	53	75

($\chi 2$= 17.389, *P* value <0.01)
NOTE: APTT = Activated Partial Thromboplastin Time

3.6. Chi Square Contingency Table for Significant Difference in the Platelets Count Results of the Pregnant Women with Different Parities

Chi Square test was done to determine the significant difference in the platelet count among pregnant women with different parities. Among nulliparous women, 39.5% had low platelet count, which appears to decrease with increased parity, as only 14.8% of multiparous women showed lower platelet count. There was no significant difference ($\chi 2$= 4.987, *P* value= >0.05) found in the platelets count results of the pregnant women with different parities (Table 6).

Table-6. Chi Square Contingency Table for significant difference in the platelets count results of the pregnant women with different parities

Parity		Platelets (PLT) count		
		Low PLT	Normal PLT	Total
Nulliparous	Count	15	23	38
	Expected count	11.7	26.3	38
Primiparous	Count	4	6	10
	Expected count	3.2	6.9	10
Multiparous	Count	4	23	27
	Expected count	8.3	18.7	27
Total	Count	23	52	75
	Expected count	23	52	75

4. Discussion

Pregnancy is a physiological condition described as a hypercoagulable state often associated with deranged clotting profile. Many alterations, including hormonal changes, occur in the coagulation system during pregnancy. These alterations increase the risk of thromboembolism but also aid in preserving placental function during pregnancy and guard against fetal hemorrhage during delivery [8]. A woman who has thrombophilia is more likely to experience early and late pregnancy problems. This encompasses late placental vascular-mediated problems (fetal loss, intrauterine growth restriction, placental abruption, and preeclampsia) as well as recurrent miscarriages [9].

In this study, majority of the participants fell within the observed age range of 18 to 35years. This corresponds to the usual distribution of pregnancy, research by Olufemi-Aworinde, *et al.* [10] reported that majority of pregnant women in Southwest Nigeria were between the age of 20 to 34. The age range seen in this study is also similar to that reported by Oladosu-olayiwola, *et al.* [11].

Prolonged prothrombin time (sec) observed in the majority of pregnant women in this study compared with the control group is suggestive of the effect of pregnancy on the extrinsic clotting factors. The finding is in concordance with the study done in selected community hospitals in Southwest Nigeria by Oluwaseyi, *et al.* [3] which reported that 14.8% of the study population had increased PT. Pregnancy is associated with increased circulatory plasma volume which tends to have dilution effects on the coagulation factors Soma-Pillay, *et al.* [12]. However, these findings were in negation to some other studies like Oluchi [8]; Rishi, *et al.* [6], which reported that shortened PT among majority of pregnancy in their studies. The disparity may be due to sensitivity of the reagents, sample selection and methods used. Plasma PT results obtained by various investigators have been linked to the varying sensitivities of the thromboplastin reagents utilized, the concentration of citrate anticoagulation, and the analytical technique [8]. Prothrombin Time (PT) is useful screening tests for extrinsic coagulation pathway, thus this suggests that pregnancy may impact the extrinsic coagulation pathway.

Significantly shortened APTT seen in this study among pregnant women compared with the non-pregnant female controls showed modulatory effects of pregnancy on the intrisic coagulation pathway. This is in agreement with other studies by Oluchi [8], Hellgren [13], Hammerova, *et al.* [14], which showed that APTT is shortened in pregnancy than in the non-pregnant controls. This demonstrates that in normal pregnancy, levels of the intrinsic pathway's factors (FV, FViii, Fix, and Fxii) are elevated [8]. This may be helpful in pregnancy particularly at the tail end to prevent excessive loss of blood during child birth.

On the other hand, statistically insignificant difference observed among pregnant and non-pregnant women may indicate normal physiological response to need in pregnancy. This is variance to report of a study conducted by [15] who showed decreased platelet count during Pregnancy. The divergent reports may be connected to sampling method and possibly dietary effects as diet is shown to significantly impact platelet count [16]. This is however in consonance with study by Fenton, *et al.* [17]

Also worthy of note in this study is significant association of parity with PT and APTT, increased parity appears to prolong PT among women. On the contrary, it enhances APTT suggesting that women may benefit from increased parity with reduced blood loss from cuts. This study is in compliance with the research carried out by Dai, *et al.* [18] who reported similar findings among Chinese pregnant women with diverse demographics and obstetric history. Repeated pregnancies induce changes in the vascular system, including endothelial function and blood vessel elasticity. These changes can affect coagulation pathways differently, potentially elongating PT and shortening APTT. Multiparous women might experience less endothelial activation or damage compared to first-time mothers, altering the release and activity of coagulation factors. The association of longer PT and shorter APTT with increasing parity can be attributed to physiological adaptations, changes in specific coagulation factors, vascular and endothelial modifications, hormonal influences, and alterations in the inflammatory response. However, parity did not show significant relationship with platelet count indicating that platelet count may not necessarily be affected by parity. This finding is in compliance with the study done by Ajibola, *et al.* [19]

5. Conclusion

The study concluded that pregnancy has a considerable impact on haemostatic parameters, with noticeable changes in PT and APTT, indicating a hypercoagulable state. These changes also varied with the number of previous pregnancies (parity), suggesting that parity influences hemostatic balance during pregnancy. This study provides valuable insights into the hemostatic changes during pregnancy and emphasizes the need for careful monitoring of these parameters to manage potential pregnancy-related complications.

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