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Investigation of Some Haemostatic Parameters in Pregnant Women in Jos South LGA, Plateau State

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Abstract

The aim of this study was to determine the difference in some haemostatic parameters between pregnant women and controls. The haemostatic parameters were assessed using prothrombin time test (PT), activated partial thomboplastin time test (APTT) and platelet count. One hundred and twenty one pregnant and forty four non-pregnant women were used for this research as the test and control populations respectively. The study showed that the pregnant women had longer PT and APTT and higher platelet counts. Nulliparous patients had the highest mean platelet count (199.72×10^9/L) and the longest mean PT (20.01s). The women of parity of 4 through 6 had the longest APTT (54.01s). This research showed no significant effect of pregnancy on the haemostatic parameters studied. The results seen in this study could be attributed to environmental influences like the diet of the subjects or the drugs the pregnant women are taking.

Introduction

Pregnancy is the state of a female after conception until the birth of the child, denoting a female bearing within her the product of conception and normal pregnancy is associated with major changes in the haemostatic system that involve both the coagulation and fibrinolytic systems. These changes are thought to occur in order to prepare the mother for the haemostatic challenge of delivery (1, 2, 3). The physiology of haemostasis involves a delicate balance between coagulation and fibrinolytic activity to maintain the integrity of the vasculature (2, 3) and an inhibition or exaggeration of either may lead to either thrombosis or haemorrhage (4). The complex haemostatic changes of normal pregnancy appear to ensure a balance between coagulation and fibrinolysis and show a potential tilt towards a hypercoagulable state (3). This balance is maintained by an increase in fibrinolytic activity, decreases in the concentrations of factor IX, monocyte tissue factor and other substances that counterbalance the procoagulant changes (3).

There has been a reported link between the concentrations of haemostatic factors and protein C resistance and increased risk for spontaneous abortion during pregnancy (5, 6). Pregnancy and the puerperium are associated with an increased risk of venous thrombosis (7, 3). The relative risk of thromboembolic complications, including pulmonary embolism, that occur during pregnancy and the puerperium are a major cause of maternal morbidity and mortality (8). About 1 to 5 percent of pregnant women have been reported to have serious complications of pregnancy and the most serious of these complications i.e. pre-eclampsia and abruptio placentae (premature separation of the placenta), are leading causes of disseminated intravascular coagulation (9). These conditions are associated with abnormal placental vasculature and disturbances of haemostasis leading to inadequate maternal-foetal circulation (10). Bleeding and blood loss associated with pregnancy and delivery remains one of the major causes of maternal morbidity and mortality (1). Obstetric haemorrhage may be associated with specific complications of pregnancy or labour or it may be due to an inherited or acquired bleeding disorder (1, 10). The severity of these conditions becomes apparent when one considers that obstetric haemorrhage and embolism are the second most common cause of obstetric death in Turkey (11) and that the average obstetric unit in the United Kingdom sees between 6 and 12 cases of thromboembolic complications and deep vein thrombosis each year (12). In developing countries, about 500'000 women die each year due to pregnancy related complications where maternal mortality accounts for 99% of the world's maternal deaths (12). Disturbances in haemostatic balance increase the risk of pregnancy associated venous thromboembolism and may lead to inadequate maternal–foetal circulation and hence increase the risk of pregnancy complications such as placental abruption, foetal growth restriction and pre-eclampsia (3). However, despite the haemostatic changes in pregnancy, 28% of cases of venous thromboembolism are not associated with a clinical risk factor for thrombosis or a thrombophilic defect (3). This highlights the necessity for further research into the mechanisms that are involved in maintaining the haemostatic balance that appears to be central to normal healthy pregnancy.

Materials and Methods

This study was undertaken in Jos South Local Government Area with a total of 165 women that provided information on the changes that occur in a selected range of haemostatic variables during pregnancy. One hundred and twenty one pregnant women attending the Ante Natal Clinics of Vom Christian Hospital, Vom, Mandela Kinik, Vom and Plateau Specialist Hospital, Jos all in Plateau State were studied. Forty four apparently healthy non-pregnant women were sourced from the staff and non pregnant patients of the clinics and from staff and students the Federal College of Veterinary and Medical Laboratory Technology, Vom as the control subjects. Blood samples were collected from both the study and control populations by venepuncture following informed consent and pre-test counselling of the subjects. Five millilitres (5mL) of blood was collected and the first 2mL of blood was collected in tubes containing 0.04mL EDTA (0.47 mol/L), used for determination of haematocrit and platelet count and was analysed that day. The final 3ml of blood was collected in tubes containing 0.33mL of trisodiumcitrate (0.13 mol/L) for the prothrombin time and activated partial thrombin time tests. Sample preparation and test performance for haematocrit, platelet count, prothrombin time and

activated partial thrombin time tests and reporting were by standard methods (4). All women answered a questionnaire aimed at collecting information about each patient.

The data were summarized as means ± standard deviation, and means compared by students t-tests.

Results

The results of this study as presented in table 1 showed that the test group had a mean platelet count of 191.25 × 10^9/L (S.D. = 58.09, S.E.M. = 5.28) while the control group had a mean platelet count of 188.00 × 10^9/L (S.D. = 40.64, S.E.M. = 6.13). The values observed are in the lower reference range described by Lewis (14). The increase the test group showed was not significant when compared to the control group amongst all age groups. This implies that the difference is due to sampling error. This is contrary to the work of McCrae *et al* (15) that reported that pregnant women develop thrombocytopenia especially in the third trimester and Hoffbrand *et al* (16) described a 10% fall in platelet count during pregnancy as a result of the haemodilution effect of pregnancy. In addition, Lewis (14) described dietary or ethnic differences in platelet count and Richardson et al (1996; cited in Lewis, 2001) described 5% diurnal variations in normal individuals. Table 1 also showed that the mean platelet count of both pregnant and non pregnant groups decreased with age. However, Lewis (14) reported no obvious age difference in platelet count so this may represent an attempt at maintaining haemostasis that is less efficient with age. The average value is within the normal range for platelet count during pregnancy and the difference is not reliable ($z = -0.40$, $p \leq .05$), hence is unlikely to produce any significant ill effect amongst the pregnant group. Table 2 shows the test group had a mean prothombin time of 18.66s (S.D. = 7.81, S.E.M. = 0.71) while the control group had a mean prothombin time of 15.94s (S.D. = 2.68, S.E.M. = 0.40). The pregnant women and non pregnant women aged between 35 and 39 had the longest mean prothrombin time. The pregnant women had a longer prothrombin time than their non-pregnant counterparts. This difference is not significant ($z = -5.36$, $P \leq .05$). This is not in agreement with the findings of Holmes & Wallace (3) who described a decrease in PT times during pregnancy. The results as presented in table 3 showed that the test group had a mean activated prothombin time of 51.53s (S.D. = 23.04, S.E.M. = 2.10) while the control group had a mean activated prothombin time of 39.62s (S.D. =17.06, S.E.M. = 2.57). The pregnant women aged between 30 and 35 had the longest mean activated prothombin time. The pregnant women also had a longer activated partial thromboplastin time than their non-pregnant counterparts, but the difference is not significant. This is contrary with the findings of McCrae *et al* (15), who described a reduction in activated partial thromboplastin time over the non-pregnant state, however, they also described both upward and downward deviations in the levels of coagulation inhibitors and in fibrinolytic activity during pregnancy that counter the hypercoagulable changes of pregnancy and this may be responsible for this result.

Furthermore, the research showed that among the test group, subjects who were blood group A and B showed a higher platelet count than their non pregnant counterparts, while group B subjects showing the greatest increase. However, group O subjects showed lower values than their non pregnant counterparts. Group AB individuals were unavailable in the test group. This suggests that a relationship between blood group and platelet count is unlikely. The research also showed that while among the test group, blood group A, B and O subjects had longer APTTs than their non pregnant counterparts with group A having the largest difference. The patients who were blood group A, B and O in the test group showed a longer prothromin time than their non pregnant counterparts. However, group A subjects showed a greater difference than the other groups. The results as indicated in table 5 showed that nulliparous patients had the highest platelet count (199.72 × 10^9/L) and the longest prothromin time (20.01s). The women of parity of 4 through 6 had the longest activated prothromin time (54.01s) (table 5). Since nulliparous women are usually younger than multiparous women and since the platelet count decreased with age (table 1), this result is more likely to be due to age.

Discussion

This study was conducted in Jos South Local Government Area of Plateau State, Nigeria. A total of 121 pregnant and 44 non-pregnant women were used for this research as the test and control populations respectively. The results of this study as presented in table 1 showed that the test group had a mean platelet count of 191.25 × 10^9/L (S.D. = 58.09, S.E.M. = 5.28) while the control group had a mean platelet count of 188.00 × 10^9/L (S.D. = 40.64, S.E.M. = 6.13). The values observed are in the lower reference range described by Lewis (14). The increase the test group showed was not significant when compared to the control group amongst all age groups. This implies that the difference is due to sampling error. This is contrary to the work of McCrae *et al* (1992) that reported that pregnant women develop thrombocytopenia especially in the third trimester and Hoffbrand *et al* (2001) described a 10% fall in platelet count during pregnancy as a result of the haemodilution effect of pregnancy. In addition, Lewis (14) described dietary or ethnic differences in platelet count and Richardson *et al* (1996; cited in Lewis, 2001) described 5% diurnal variations in normal individuals. Table 1 also showed that the mean platelet count of both pregnant and non pregnant groups decreased with age. However, Lewis (2001) reported no obvious age difference in platelet count so this may represent an attempt at maintaining haemostasis that is less efficient with age. The average value is within the normal range for platelet count during pregnancy and the difference is not reliable ($z = -0.40$, $p \leq .05$), hence is unlikely to produce any significant ill effect amongst the pregnant group. Table 2 shows the test group had a mean prothombin time of 18.66 s (S.D. = 7.81, S.E.M. = 0.71) while the control group had a mean prothombin time of 15.94 s (S.D. = 2.68, S.E.M. = 0.40). The pregnant women and non pregnant women aged between 35 and 39 had the longest mean prothrombin time. The pregnant women had a longer prothrombin time than their non-pregnant counterparts. This difference is not significant ($z= -5.36$, $P \leq .05$). This is not in agreement with the findings of Holmes & Wallace (2005) who described a decrease in PT times during pregnancy. The results as presented in table 3 showed that the test group had a mean activated prothombin time of 51.5 s (S.D. = 23.04, S.E.M. = 2.10) while the control group had a mean activated prothombin time of 39.62s (S.D. =17.06, S.E.M. = 2.57). The pregnant women aged between 30 and 35 had the longest mean activated prothombin time. The pregnant women also had a longer activated partial thromboplastin time than their non-pregnant counterparts, but the difference is not significant. This is contrary with the findings of McCrae *et al* (15), who described a reduction in activated partial thromboplastin time over the non-pregnant state, however, they also described both upward

and downward deviations in the levels of coagulation inhibitors and in fibrinolytic activity during pregnancy that counter the hypercoagulable changes of pregnancy may be responsible for this result. Furthermore, the research showed that among the test group, subjects who were blood group A and B showed a higher platelet count than their non pregnant counterparts, while group B subjects showing the greatest increase. However, group O subjects showed lower values than their non pregnant counterparts. Group AB individuals were unavailable in the test group. This suggests that a relationship between blood group and platelet count is unlikely. The research also showed that while among the test group, blood group A, B and O subjects had longer APTTs than their non pregnant counterparts with group A having the largest difference. The patients who were blood group A, B and O in the test group showed a longer prothromin time than their non pregnant counterparts. However, blood group A subjects showed a greater difference than the other groups. The results as indicated in table 5 showed that nulliparous patients had the highest platelet count (199.72×10^9/L) and the longest prothromin time (20.01s). The women of parity of 4 through 6 had the longest activated prothromin time (54.01s) (table 5). Since nulliparous women are usually younger than multiparous women and since the platelet count decreased with age (table 1), this result is more likely to be due to age.

Conclusion

The haemostatic changes of pregnancy are associated with the development of a tendency toward hyper coagulation and these changes are influenced by the genetic makeup of the patient and environmental factors. The effects of these factors could alter the delicate balance between the activities of the coagulation and fibrinolytic systems and their inhibitors that are responsible for maintaining normal haemostasis. This shift in balance can predispose a patient towards either thrombosis or haemorrhaging, depending on which tendency is favoured. The results obtained in this research suggest that during pregnancy there is a shift in haemostasis that favours hypocoagulation.

From the research carried out, it was noted that although the pregnant women had an average platelet count within the normal range, it was slightly higher than that observed in their non-pregnant counterparts. This is contrary to the work of McCrae *et al* (15), who reported the development of thrombocytopenia during pregnancy, especially in the third trimester. Since mean platelet count of the pregnant women was within the normal range for platelet count during pregnancy, this increase is unlikely to produce any significant ill effect in the pregnant group unless they are ingesting food or drugs that interfere with platelet function. Some items that have been found to interfere with platelet function include amongst other things, aspirin, garlic, antibiotics (like penicillin and cephalosporins), corticosteroids, non-steroidal inflammatory drugs, antihistamines and ethanol (4, 18).

This investigation also showed that the test group showed prolonged PT and APTT and this combination has been reported to be caused mainly by a lack of vitamin K, administration of oral anticoagulants, liver disease and rare congenital or acquired defects of factors V, X, prothrombin and combined V and VIII deficiency (4). The information collected from the questionnaire and the patients' medical files did not indicate liver disease, vitamin K nor anticoagulant use and factor defects can only be determined by factor assays. If vitamin K deficiency is to be implicated, a failure of vitamin K absorption has to be determined. A probable cause could be alcohol; it is known to inhibit liver function.

In conclusion, the findings of this study do not indicate a significant effect of pregnancy on the haemostatic parameters studied. The variation in the results of the two groups seen in this study could be attributed to environmental influences like the diet of the subjects or the drugs the pregnant women are taking.

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Table 1: Mean Platelet Count By Age Distribution

Age Group	Platelet Count ($\times 10^9$/l) Pregnant			Non Pregnant			Comment
	Number	Mean	S.D	Number	Mean	S.D	
15-19	4	238.50	86.03	2	203.00	14.14	Not Significant
20-24	43	203.93	70.73	12	188.17	37.23	Not Significant
25-29	52	184.08	41.41	18	194.44	45.50	Not Significant
30-34	12	187.00	62.26	10	178.80	43.41	Not Significant
35-39	8	166.55	42.27	2	160.00	2.83	Not Significant
40+	2	125.00	14.14	-	-	-	-
Total	121	191.25	58.09	44	188.00	40.64	Not Significant

Table 2: Mean Prothrombin Time by Age Distribution

Age Group	Prothrombin Time (in seconds) Pregnant			Non Pregnant			Comment
	Number	Mean	S.D	Number	Mean	S.D	
15-19	4	16.00	0.58	2	13.06	0.06	Not Significant
20-24	43	17.52	5.75	12	17.26	3.67	Not Significant
25-29	52	18.16	7.97	18	16.07	1.95	Not Significant
30-34	12	23.68	8.42	10	14.42	1.32	Not Significant
35-39	8	23.06	2.83	2	18.42	0.12	Not Significant
40+	2	14.01	1.14	-	-	-	-
Total	121	18.66	7.81	44	15.94	2.68	Not Significant

Table 3: Mean Activated Partial Thromboplastin Time By Age Distribution

Age Group	Activated Partial Thromboplastin Time (in seconds)						Comment
	Pregnant			Non Pregnant			
	Number	Mean	S.D	Number	Mean	S.D	
15-19	4	38.35	8.49	2	30.50	1.41	Not Significant
20-24	43	44.15	21.33	12	42.80	17.06	Not Significant
25-29	52	59.10	23.06	18	43.63	16.50	Not Significant
30-34	12	43.63	16.50	10	33.42	3.81	Not Significant
35-39	8	65.78	26.62	2	32.59	18.14	Not Significant
40+	2	30.00	2.83	-	-	-	-
Total	121	51.53	23.04	44	39.62	17.06	Not Significant

Table 4: Mean Haemostatic Levels Amongst Pregnant Women With Respect To Parity

Parity	Number	Platelet Count ($\times 10^9$/l)		PT (in s)		APTT (in s)	
		Mean	SD	Mean	SD	Mean	SD
0	47	199.72	59.87	20.83	9.69	50.92	21.82
1-3	50	193.40	58.40	17.16	6.26	50.91	22.59
4-6	24	170.17	50.48	17.57	5.56	54.01	26.89
Total	121						