

Prothrombin Time, Clothing Time, Platelet Concentration and Haematocrit During Labour and Postpartum of Women in Zaria, Northern Nigeria

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Abstract: This study was aimed at studying the influence of labour and parturition on the clotting profiles, platelet concentration and haematocrit and causes of variations of women in Zaria, Northern Nigeria. Pregnancy is a physiologic state frequently complicated by thrombo-embolism and haemorrhage. Prothrombin Time (PT), Whole blood Clothing Time (CT) Platelet Concentration and haematocrit (PCV) were measured in 50 women in labour and within one (1) hour postpartum and compared with values in aged matched non pregnant controls. The clothing time of 3.32 ± 0.16 min. during labour was significantly lower than values of 5.30 ± 0.19 and 4.56 ± 0.15 min obtained in control and at post partum respectively ($p < 0.05$). Postpartum haematocrit of 26.10 ± 0.77 and $30.14 \pm 0.60\%$ obtained during labour were significantly lower than the PCV of $36.66 \pm 0.36\%$ obtained in the control non pregnant subject ($p < 0.001$, $p < 0.05$). Prothrombin Time (PT) of 8.30 ± 0.15 sec obtained during labour was significantly lower than values of 9.20 ± 0.29 and 9.40 ± 0.34 sec obtained in controls and postpartum respectively ($p < 0.05$). Platelet concentration of $214.38 \pm 21.0 \times 10^9$ and $217.50 \pm 12.0 \times 10^9$ /L within 1hr postpartum and during labour, respectively were significantly lower than the concentration of $376.47 \pm 26.21 \times 10^9$ /L in the control subjects. We conclude that the subjects had features of hyper-coagulation state during labour which reversed within 1hr postpartum and the subjects were anemic postpartum. The CT and PCV were significantly altered postpartum by parity and mode of delivery.

Key words: Clotting time, haematocrit, labour, parturition, platelet count and prothrombin time, pregnancy

INTRODUCTION

Normal pregnancy is accompanied by major changes in the homeostatic mechanisms particularly an increase in the levels of coagulation factors (Fibrinogen, V, VIII and X) and a noticeable decrease in fibrinolytic activity. (Saidi *et al.*, 1979; EL-Mowafi, 2008; Kleiner *et al.*, 2008; Pretorius *et al.*, 2009; Heuwieser *et al.*, 2010). Such changes have been interpreted as a physiological development to provide for effective haemostasis and preservation of the maternal blood during parturition (Alexander *et al.*, 1956; Bonnar *et al.*, 1970 and Urasoko *et al.*, 2009). Increase in the blood level of these coagulation factors is maximal in the 3rd trimester of pregnancy (Saidi *et al.*, 1979; Mizoguchi *et al.*, 2010). Twin delivery, caesarian section, abruptio Placentae, Intrauterine Fetal Death (IUFD) and elevated serum estrogen and progesterone levels are factors associated with altered clotting and fibrinolysis homeostasis in pregnancy (El-Mowafi, 2008; Kleiner *et al.*, 2008; El-Belely *et al.*, 2000; Mizoguchi *et al.*, 2010; Heuwieser

et al., 2010). Many haemological complications are associated with pregnancy and parturition and unfortunately, often lead to significant morbidity and mortality for both mother and child (Bick *et al.*, 2006). Recurrent miscarriage syndrome and infertility are reported to be associated with blood coagulation protein or platelets deficit (Bick, 2000).

In developing countries like Nigeria, high maternal mortality and fetal wastage is associated with high incidence of anaemia in pregnancy, antepartum and postpartum haemorrhage, high parity, home deliveries not supervised by trained personnel, inadequate and inaccessible health facilities and late presentation of cases to health facilities (Harrison and Ibeslako, 1973; Harrison, 1975; Isah *et al.*, 1985; Fleming, 1989; Malteli *et al.*, 1994; Ogbeide *et al.*, 1994; Lamina, 2003; Idowu *et al.*, 2005). Disorders of clotting, fibrinolysis and platelet will further worsen the outcome of pregnancy in such environment. The aims of this study were to determine the clotting time, prothrombin time, platelet concentration and haematocrit during labour and

immediate postpartum and determine possible causes of variations in selected women in Zaria, Northern Nigeria.

METHODOLOGY

Study site: The study was conducted between the month of February and March 2011 in Zaria (latitude 11°3'N, longitude 7°42'E), Kaduna state in the Guinea Savannah belt of Northern Nigeria, with a mean annual temperature of 27°C. The monthly temperature varies between 15.6° and 32.1° with three distinct seasons (Igono and Aliu, 1982; Ati, 2004).

Subjects: Fifty (50) parturients aged 15-42 years admitted into the delivery suites of Ahmadu Bello University Teaching Hospital, Shika, Zaria and Salama Infirmary, Kwangila, Zaria between February and March 2011 were screened with questionnaires after obtaining informed consent from them. Information obtained using the questionnaires included age, tribe, parity, past history of hypertension, diabetes mellitus, presence of infections, history of thrombo-embolic phenomenon, ant coagulants therapy and bleeding tendencies. Mode of delivery and outcome of delivery were also noted. Blood pressure was also recorded. Fifty (50) aged matched non pregnant women were also screened and served as controls.

Exclusion criteria: Parturients and control subjects with hypertension, diabetes mellitus, haemoglobinopathies, known bleeding disorders, evidence of sepsis and antibiotics therapy, anticoagulants drugs and Non-steroidal Anti-inflammatory agent (NSAI) and patients that refused to give consent were excluded. Subjects who had transfusion of blood or blood products within previous 3 months were also excluded.

Ethical committee approval: Approval of the Ethical Committee on Human Research of the Faculty of Medicine, Ahmadu Bello University, Zaria was obtained before the commencement of the study.

Blood collection: For each subject, a tourniquet was applied around the arm; the antecubital fossa was cleaned and disinfected with a methylated spirit soaked swab. 8 mL of venous blood was collected with a 10 mL syringe and 21G needle, 2 mL of the blood was emptied into a 5 mL sterile test tube containing Ethylenediamine Tetraacetic Acid (EDTA) as an anticoagulant for determination of PCV, platelet count and prothrombin count. The remaining 6 mL of blood was used to determine the whole blood clotting time.

Determination of whole blood Clotting Time (CT): 6mL of the blood sample was dispensed into four

prewarmed test tubes (1.5 mL each) fixed in a rack previously placed in a water bath maintained at 37°C. Each bottle was tilted to check for the sign of blood clot every 30 sec. Using a stop watch, the time interval between blood collection and the time the clot appeared in each test tube was recorded in min. The average of the four reading was taken as the clotting time for each subject.

Determination of Haematocrit (PCV): Whole Blood Packed Cell Volume (PCV) for all subjects were determined directly after sampling using a micro-haematocrit centrifuge and reader (Hawksley, West Sussex, UK). Results were recorded in percentages (%).

Determination of Prothrombin Time (PT): PT was determined by the Quick method as followed. 1.5 mL of the citrated blood sample was centrifuged with a bench centrifuge at 3000 rpm for 15 min. 0.1 mL of the supernatant plasma was removed and dispensed in a clean glass tube and then placed in a water bath kept at a 37°C. 0.1 mL of thromboplastin was added and after one min., 0.1 mL of calcium chloride (CaCl₂) was added and the contents mixed thoroughly. The lower end of the tube was submerged in the warm water in the water bath. The stopwatch was started and the tube was continuously tilted to observe for signs of clot. The time taken for fibrin clot to develop was recorded in seconds. One normal control plasma sample was setup for each batch of tests.

Determination of platelet count: Platelet concentration was determined using Abacus Junior Haematology Analyser (Diatran, Messtechnik, GmbH, Vienna, Austria and result recorded as number of cells/uL of blood.

RESULTS

Clotting time: Clotting time of 3.32±0.16 min obtained during labour was significantly lower than the values of 5.30±0.19 and 4.56±0.15 min obtained in the control non-pregnant subjects and during the immediate postpartum period, respectively. Postpartum clotting time of 3.60±0.27 min. in subjects delivered by caesarian section was significantly lower than the clotting time obtained following vaginal deliveries with or without episiotomy and forceps (p<0.05). Similarly, post-partum clotting time of 2.50±0.22 min. in subjects with parity of 3 was significantly lower than clotting time recorded in subjects with parity of 1,2,4 and 5 (p<0.05), (Table 1, 2 and 3).

Prothrombin time: Prothrombin time of 8.30±0.15 sec during labour was significantly lower than values obtained in the control subjects and during the immediate postpartum period (p<0.05) (Table 1).

Table 1: Effect of labour and parturition on CT, PCV, PT & platelet count

	Control (n = 50)	Labour (n = 50)	Postpartum (n = 50)
Clotting time (min)	5.30±0.19	3.32±0.16*	4.56±0.15
Prothrombin time (sec)	9.20±0.29	8.30±0.15*	9.40±0.34
PCV (%)	36.66±0.36	30.14±0.60*	26.10±0.77**
Platelets count, (000 cells/μL)	376.47±26.21	217.50±12.05*	214.38±21.0*

*: p<0.05; **: p<0.001

Table 2: Effect of mode of delivery on postpartum clotting time and PCV

Mode of delivery	Clotting time (min.) Mean±SEM	PCV (%) Mean±SEM
SVD (n = 31)	4.60±0.21	29.41±0.96
SVD + Episiotomy (n = 6)	4.17±0.31	26.00±1.63
Vaginal + Forceps Delivery (n = 6)	5.67±0.33	27.44±2.38
C/S (n = 9)	3.60±0.27*	22.25±1.33*

SVD: safe vaginal delivery; C/S: caesarian section; *: p<0.05

Table 3: Effect of parity on postpartum clotting time and packed cell volume

Parity	Clotting time (min) Mean±SEM	PCV (%) Mean±SEM
1. (n = 20)	4.19±0.22	30.20±0.89
2. (n = 7)	5.00±0.52	29.83±1.96
3. (n = 6)	2.50±0.22*	26.00±1.29*
4. (n = 8)	4.75±0.41	25.38±1.57*
5+ (n = 9)	3.89±0.45	22.52±1.72**

*: p< 0.05; **: p<0.001

Haematocrit: The haematocrit concentration of 36.66±0.36% of the non pregnant control subjects was significantly higher than values of 30.14±0.60% during labour (p<0.05) and 26.10±0.77% during the postpartum period (p<0.001). Postpartum PCV of 22.25±1.33% in subjects delivered by caesarian section was significantly lower than values obtained following other methods of delivery (p<0.001) and significantly decreased with increasing parity(p<0.05), (Table 2 and 3).

Platelet concentration: The mean platelet concentration of 376.47±26.21×10⁹/L in the non pregnant controls was significantly higher than the concentration of 217.50±12.05×10⁹ and 214.38±21.0×10⁹/L obtained during labour and postpartum period respectively (p<0.05), (Table 1).

DISCUSSION

Pregnancy is frequently complicated by thromboembolism and haemorrhage attributable to abnormal blood coagulation. In the northern part of Nigeria, peripartum haemorrhage, anaemia in pregnancy occasioned by malaria, poor diet, low socio- economic status of women and poor and inadequate health facilities are frequently reported as contributory factors to increased maternal and perinatal mortalities (Fleming, 1989; Ogbeide *et al.*, 1994; Lamina, 2003). There is paucity of report on the coagulation profile of pregnant women and the interrelationship between coagulation profile and the indices of high maternal and perinatal mortality in the northern part of Nigeria.

From our study, the clotting time of the women during labour (3.32±0.16 min.) was significantly lower than values obtained in pregnant control (5.30±0.19 min.) and during the postpartum period (4.56±0.15 min.). The normal range is 5 to 15 min. and measures the integrity of the intrinsic pathway of coagulation.

Dietary factors such as low magnesium and high homocysteine levels, deficiency of vitamin B6 and B12 and folic acid are reported to alter clotting time. Garlic, ginger and purple grape juices are also reported to have anticoagulation activity and therefore can prolong clotting time (Rosenberg, 2000).

From the result of this study, clotting time during the first 1 h postpartum (3.60±0.27 min.) was significantly lowered in patients delivered by caesarian section than values obtained for subjects that had vaginal delivery with or without episiotomy (4.60±0.21, 4-17±0.31 and 5.67±0.33 min. for vaginal, vaginal with episiotomy and vaginal with episiotomy and forceps deliveries, respectively). The surgical wound of caesarian section probably led to release large amount of coagulation factors from the liver leading to the shortened postoperative (postpartum) clotting time.

Prothrombin (factor II) is synthesised in the liver in the presence of Vitamin K. Prothrombin time (Thromboplastin time) described by A. J. Quick in 1961 is a screening test used in the diagnosis of coagulation defects due to deficiency of factors I, II, V, VII and X when it is prolonged. It measures the integrity of the extrinsic pathway of coagulation and normal values ranges from 11-16 sec. (Rao *et al.*, 2000). In addition to congenital deficiencies of the clotting factors in the

extrinsic pathway of coagulation, PT is prolonged in liver diseases (in cirrhosis), Vitamin K deficiency and during warfarin administration while decreased in acute alcoholism. In our study, PT of 8.30 ± 0.15 sec obtained during labour was significantly lower than values obtained in control subjects (9.20 ± 0.29) and (9.40 ± 0.34 sec) during the postpartum period (). The PT values in this population is generally lower than what is reported in other population (Rao *et al.*, 2000). Kleiner *et al.* (2008) reported a fall in level of factor V, VIII with marked decrease in fibrinolytic activity during parturition. They reported that the changes *observed* were more marked with twin delivery, in abruptio placentae or prolonged Intrauterine Fetal Death (IUFD). They suggested the high levels of Fibrin Degredation Products (FDPs) in their subjects indicated physiological defibrination. Heuwieser *et al.* (2010) found prothrombin time to be shorter in early pregnancy but increased significantly towards term in association with increased in fibrinogen level just before parturition in dairy cattle. Retained placenta was significantly associated with increased fibrinogen concentration (Heuwieser *et al.*, 2010). Our findings is consistent with the reports of Badraoui *et al.* (1973), Saidi *et al.* (1979) and El-Mowafi (2008) who reported a decrease prothrombin time and platelet concentration in association with sharp increase in levels of factor I, VII, VIII, IX, X and moderate increase in factor II & XI during pregnancy and labour.

It was further reported that though the concentration of plasminogen increases by about 100% during pregnancy, there is generally a decrease in fibrinolytic activity because of the high concentration of plasminogen inhibitors in the plasma and placenta. High serum concentration of estrogen and progesterone are also known to reduce fibrinolysis (El-Mowafi, 2008; Bonnar *et al.*, 1969, 1970). Escapes of tissue thromboplastin substances from placental separation are also a factor reported for the decrease prothrombin time during delivery.

Platelet play important role in haemostasis by forming primary (temporary) haemostatic plug when blood vessels are injured, where exposure of the vascular collagen fibers causes platelets activation, aggregation and degranulation and consequent release of Adenosine Diphosphate (ADP), serotonin and von Willebrand factor which is an important coagulation factor (Rodgers, 1999). From our study, the platelet count of $217.50 \pm 12.05 \times 10^9/L$ and $214.38 \pm 21.0 \times 10^9/L$ obtained during labour and within 1 h postpartum were significantly lower than platelet count of $376.47 \pm 26.21 \times 10^9/L$ obtained in the control subject ($p < 0.05$). Normal platelet count in normal non pregnant subject ranges from 150,000-450,000/ μL and ranges from 213,000-250,000/ μL in normal pregnancies

(Sejeny *et al.*, 1975; Karim and Sacher, 2004; Enrique, 2009).

Thrombocytopenia has been reported in pregnancy by several authors (Sejeny *et al.*, 1975; Burrows and Keltron, 1990; Lew and Murphy, 2002; Mc-Crae, 2003; Karim and Sacher, 2004; Kam *et al.*, 2004; Enrique, 2009). Thrombocytopenia in pregnancy is diagnosed when platelet count is consistently less than 116,000/ μL . Gestational thrombocytopenia (213-250,000/ μL) is explained by haemodilution, increased consumption with reduced life span and increased aggregation by increased levels of thromboxane A2 at placental circulation (Burrows and Keltron, 1990; Kam *et al.*, 2004 and Karim and Sacher, 2004). Gestational thrombocytopenia is more apparent during the 3rd trimester of pregnancy and normalizes within 2 to 12 days after delivery (Burrows and Keltron, 1990; Lescale *et al.*, 1996). Thrombocytopenia in pregnant women can be associated with substantial maternal and neonatal morbidity (Karim and Sacher, 2004). For example, Preeclampsia Toxaemia (PET)/eclampsia accounts for 21% of maternal thrombocytopenia and thrombocytopenia correlates with severity of PET and is an indication for early delivery (Mc-Crae, 2003). Severe PET is frequently complicated by syndrome of HELLP (haemolysis, elevated liver enzymes and low platelets) where perinatal mortality is about 11% from placental abruptio, asphyxia, extreme prematurity, intrauterine growth restriction and neonatal thrombocytopenia (Burrows and Keltron, 1993; Samuels *et al.*, 1990; Karim and Sacher, 2004). The platelet count in our subject during labour and within 1 h postpartum, though significantly lower than values obtained from the controls were higher than values reported in the literatures (Burrows and Keltron, 1990; Kam *et al.*, 2004; Karim and Sacher, 2004). Parity and mode of delivery did not affect postpartum platelet count in our subjects.

Haematocrit of $30.14 \pm 0.60\%$ obtained during labour was significantly lower than $36.66 \pm 0.36\%$ obtained in the controls. Dilutional anaemia is a feature of normal pregnancy arising from disproportionate increase in red blood cell mass and plasma volume. Haematocrit of $26.10 \pm 0.77\%$ within 1 h postpartum period indicated postpartum anaemia which could result from blood loss during parturition in a population with borderline haematocrit during pregnancy.

CONCLUSION

We conclude that clotting time, prothrombin time, platelet concentration and haematocrit were significantly reduced during labour and that mode of delivery and parity significantly affected the packed cell volume and clotting time during the immediate postpartum period in our subjects.

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