

INVESTIGATION OF SOME HAEMOSTATIC PARAMETERS IN PREGNANT WOMEN  
IN DERNA CITYDr. Amal S. Elhassade\*<sup>1</sup>, Dr. Adham Saad<sup>2</sup> and Ebtisam Barakat<sup>3</sup><sup>1</sup>College of Medical Technology, Derna, Libya.<sup>2</sup>College of Medical Technology, Department of Laboratory Medicine, Derna Libya.<sup>3</sup>College of Medical Technology, Department of Laboratory Medicine, Derna Libya.

\*Corresponding Author: Dr. Amal S. Elhassade

College of Medical Technology, Derna, Libya.

Article Received on 26/07/2019

Article Revised on 16/08/2019

Article Accepted on 05/09/2019

## ABSTRACT

**Background:** 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 hemorrhaging, depending on which tendency is favored. **Objective:** The aim of this study was to determine the effect of pregnancy on some of haemostatic parameters. The haemostatic parameters were assessed using prothrombin time test (PT), activated partial thromboplastin time test (APTT) and platelet count. **Material and method:** A total of (30) healthy pregnant women aged between 21-38 years in the third trimester of pregnancy, and 30 non pregnant women aged between 24-42 years. Platelet count, PT and APTT were measured for pregnant women and non pregnant women. **Result:** In pregnant women mean of platelets count was  $(223.2 \times 10^9/l \pm 57.8)$  whereas in non pregnant was  $(195.2 \times 10^9/l \pm 27.9)$ , there was no significant difference between platelets in control (non pregnant) and pregnant women in third trimester  $P = 0.08$  Mean level of PT in pregnant women was  $14.7\text{sec} \pm 5.2$  whereas in non pregnant was  $12.4 \text{ sec} \pm 0.9$ , there was no significant difference between pregnant and non pregnant  $P = 0.107$ . Mean level of APTT among pregnant women in the third trimester was  $33.3 \text{ sec} \pm 5.9$  whereas in non pregnant was  $28.5 \pm 2.3$ , APTT was significantly higher in pregnant women than non pregnant. **Conclusion:** This study showed no significant effect of pregnancy on platelets count, prothrombin time whereas APTT increase in pregnant women this may result from decrease activity of intrinsic coagulation factors or due to environmental influences like the diet.

**KEYWORDS:** Activated Partial Thromboplastin, Prothrombin Time, Thrombocytopenia, Pregnancy.

## INTRODUCTION

The process of haemostasis is a dynamic and delicate equilibrium between coagulation and fibrinolysis. Coagulation results from an interaction among vessel walls, platelets and coagulation factors.<sup>[1]</sup> Following endothelial damage, platelets adhere to the sub endothelium forming a platelet plug which then becomes permanent with fibrin deposition<sup>1</sup>. Clot formation is limited by antithrombin (AT) and proteins C and S. The fibrinolytic system functions to maintain the fluid state through the breakdown of fibrin by plasmin. Plasmin is generated from plasminogen by the action of tissue plasminogen activator (t-PA).<sup>[2-3-4]</sup>

Normal pregnancy poses significant challenges to hemostasis. Overall, it is a state of hypercoagulability with hypofibrinolysis mitigating the risk of bleeding at the time of delivery.<sup>[4]</sup> These physiological variations place a woman at risk of thrombosis during pregnancy

and puerperium.<sup>[5]</sup> This risk is four to six fold high in comparison to a non pregnant women.<sup>[6]</sup>

Changes in hemostasis, including an increase in the majority of clotting factors, a decrease in the quantity of natural anticoagulants, and a reduction in fibrinolytic activity.<sup>[2]</sup> The platelet count decreases in normal pregnancy, possibly due to increased destruction and hemodilution, with a maximal decrease in the third trimester.<sup>[4-7]</sup>

As most coagulation factors increase in normal pregnancy, the prothrombin time (PT) and the activated partial thromboplastin time (APTT) may be shortened. The PT and its derived measure, the international normalized ratio (INR), test for factors such as coagulation factors II, V, VII, X, and fibrinogen.<sup>[8]</sup> Some nutritional deficiencies and/or liver disease will decrease these factors prolonging the PT. Furthermore, PT and

APTT may be artificially prolonged due to the presence of an antiphospholipid antibody (APLA), such as lupus anticoagulant. In fact, patients with APLA are prothrombotic. The APTT is considered a good screening test for deficiencies of coagulation factors VIII, IX, XI and XII.<sup>[8]</sup> 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.<sup>[9]</sup>

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.<sup>[10]</sup> 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.<sup>[10]</sup>

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 thromboplastin time test (APTT) and platelet count.

## MATERIAL AND METHOD

**Study design:** A case control study was designed evaluate some type of hemostatic parameters in pregnant women who never suffering any disease and compare their finding with healthy non pregnant women.

**Ethical approval:** Approval was granted from the Research and Ethics Committee of the college. Consent was gotten from all participated patients.

The study was conducted in department of obstetrics and gynecology at alwahda hospital and different clinic (out patients), after taking written informed consent from pregnant women prior. A total of (30) healthy pregnant women aged between 21-38 years in the third trimester of pregnancy, and 15 non pregnant women aged between 24-42 years. All of them included this study for coagulation parameters.

### Sample assay

About 5 mL of venous blood divided in two vacuoner tubes, 2.5 mL of whole blood in K2 ethylenediaminetetraacetic acid for platelets counts and other (2.5 mL) of whole blood with 1:9 ratio of trisodium citrate, were collected and then centrifuged in order to obtain platelets poor plasma for performing PT and APTT. All blood samples were collected between 9 am and 12 noon each day and analyzed within 2hr of collection. Hematological and coagulation analysis were done at room temperature ( $27.5 \pm 0.5^{\circ}\text{C}$ ).

## METHODS

Sysmex KX-21 (hematology analyzer) was used for complete blood counts. PLTs were considered to be measured directly, three hydraulic subsystems were used to determine the hemogram; the WBC channel, the RBC channel, the plats channel, and a separate Hb channel. All automated analysis was done after proper bar coding to easy identification.

PT and APTT were determined by manual method that based on fibrin clot formation in glass tube. The test measures the plasma clotting time in addition of tissue extract thromboplastin (PT) and activation of contact factors (partial thromboplastin time [PTT]) depend on normal values of PT (10–13 s) and APTT (24–34 s).

### Statistical analysis

Statistical analyses were conducted using SPSS. Data were expressed as mean  $\pm$  standard deviation. Comparisons between pregnant subjects and non pregnant controls were made using the Student's *t*-test for parametric data. A without denoted a statistically significant difference in all statistical comparisons. Correlation was compared using a version of linear regression analysis.

## RESULT

Thirty sample were collected from pregnant women as case and fifteen sample as control (non pregnant). The mean age of pregnant women was  $30.8 \pm 5.3$  years and the mean age of non-pregnant women was  $30.1 \pm 5.9$  years (table 1).

Most of pregnant women were multi pregnant and 80 % of them had no history of abortion.

The study included measurement of some coagulation parameters included platelets count, prothrombin time and activated partial thromboplastin time in healthy pregnant women and non pregnant women the mean of platelets count was ( $213.8 \times 10^9 / \text{l}$  range: 141-357), mean of APTT was ( $31.7 \text{ sec} \pm 5.5$ ) range : 25-49 sec), and PT was  $13.9 \pm 5.5 \text{ sec}$  range (11-32 sec).

In pregnant women mean of platelets count was ( $223.2 \times 10^9 / \text{l} \pm 57.8$ ) whereas in non pregnant was ( $195.2 \times 10^9 \pm 27.9$ ), there was no significant difference between platelets in control (non pregnant) and pregnant women in third trimester  $P = 0.107$  as in table 2.

Mean level of APTT among pregnant women in the third trimester was  $33.3 \text{ sec} \pm 5.9$  whereas in non pregnant was  $28.5 \pm 2.3$ , APTT was significantly higher in pregnant women than non pregnant  $P=0.085$  as in table 3.

Mean level of PT in pregnant women was  $14.7 \pm 5.2$  whereas in non pregnant was  $12.4 \pm 0.9$ , there was no

significant difference between pregnant and non pregnant  $P=0.107$  as in table 4.

In our study there was no significant difference in coagulation parameters when compared to age with  $P$  value 0.318 for APTT, PT 0.640.

Tables 4 show comparison of mean  $\pm$  standard deviation of prothrombin and activated partial thromboplastin time and control group of pregnant women in different trimesters Prothrombin time (PT) in the first, second and third trimesters did not rise above the control. There was a significant reduction in the PT value during the second trimester.

**Table 4.1:** Comparison of Mean  $\pm$  SD of prothrombin time (PT) value.

In pregnant women mean of platelets count was ( $223.2 \times 10^9/l \pm 57.8$ ) whereas in non pregnant was ( $195.2 \times 10^9 \pm 27.9$ ), there was no significant difference between platelets in control (non pregnant) and pregnant women in third trimester  $P=0.107$  as in table 1.

**Table 1:** Comparison mean  $\pm$  SD of platelets count in pregnant and non pregnant.

Platelets count x $10^9/l$	num ber	mean	SD	P_value
Pregnant women	30	223.2	57.9	0.085
Control	15	195.2	27.9	

$P=0.085$  non sig by using t test

**Table 4:** variation of some coagulation parameters (platelet count, APTT, PT) in pregnant women according to Age group.

Parameters	Age group/years	No of cases	Mean	SD	p.value
Platelets count x $10^9/l$	Less than 25 years	5	185.8	7.6	0.347
	26-30	10	226.7	16.9	
	More than 30	15	233.2	17.1	
APTT /sec	Less than 25 years	5	37.1	3.4	0.318
	26-30	10	33.2	2.0	
	More than 30	15	31.9	1.6	
PT	Less than 25 years	5	18.8	3.6	0.640
	26-30	10	15.1	1.9	
	More than 30	15	13.1	0.5	

## DISCUSSION

A total of 30 pregnant and 15 non-pregnant women were used for this study as the test and control. The results of this study as presented in table 1 showed that the test group had a mean platelet count of  $223 \times 10^9/L$

Mean level of APTT among pregnant women in the third trimester was  $33.3 \text{ sec} \pm 5.9$  whereas in non pregnant was  $28.5 \pm 2.3$ , APTT was significantly higher in pregnant women than non pregnant but still within normal range  $P=0.005$  as in table 2.

**Table 2:** comparison of mean  $\pm$  SD of APTT in pregnant women and non pregnant (control).

APTT	Number of case	mean	SD	P_value
Pregnant women	30	33.3	5.9	0.005
Control	15	28.5	2.3	

$P=0.05$  sig level by using t test.

Mean level of PT in pregnant women was  $14.7 \pm 5.2$  whereas in non pregnant was  $12.4 \pm 0.9$ , there was no significant difference between pregnant and non pregnant  $P=0.107$  as in table 3.

**Table 3:** comparison of mean  $\pm$  SD of PT in pregnant women and non pregnant.

PT	Number of case	mean	SD	P_value
Pregnant women	30	14.7	5.2	0.107
Control	15	12.4	0.9	

$P=0.107$  non sig level by using t test

In our study high value of APTT, PT present in pregnant women less than 25 years but this difference was not significant when compare to age group with  $P$  value 0.318 for APTT, PT 0.640 and platelets count (0.347) as in table 4.

(S.D. =5.2) while the control group had a mean platelet count of  $195.00 \times 10^9/L$  (S.D. = 27.9). The values observed are in the lower reference range described by Lewis<sup>[14]</sup> the test group showed was not significant when compared to the control group amongst all age groups. This is contrary to the work of McCrae *et al* that

reported that pregnant women develop thrombocytopenia especially in the third trimester<sup>[12]</sup> and Hoffbrand *et al* (2001) described a 10% fall in platelet count during pregnancy as a result of the haemo dilution effect of pregnancy.<sup>[13]</sup> In addition, Lewis described dietary or ethnic differences in platelet count<sup>[14]</sup> and Richardson *et al*<sup>[15]</sup> (described 5% diurnal variations in normal individuals. Table 4 also showed that the mean platelet count of 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 ( $p \leq .05$ ), hence is unlikely to produce any significant ill effect amongst the pregnant group.

The pregnant women also had a longer activated partial thromboplastin time than their non-pregnant counterparts, the difference was significant. This is contrary with the findings of McCrae *et al* who described a reduction in activated partial thromboplastin time over the non-pregnant state, however, they also described both upward.<sup>[12]</sup> A decrease in coagulation factors of the intrinsic pathway could be responsible for the prolonged APTT in all the trimesters

Table 4 shows the test group had a mean prothrombin time of  $14.7 \pm 5.2$ s while the control group had a mean prothrombin time of  $12.4 \pm 0.9$ . The pregnant women aged less than 25 years had the longest mean prothrombin time. The pregnant women had a longer prothrombin time than their non-pregnant counter parts. This difference is not significant ( $P \leq .05$ ).

## CONCLUSION

The haemostatic changes of pregnancy are associated with the development of a tendency toward hyper coagulation 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 study suggest that during pregnancy there is a shift in haemostasis that favours hypocoagulation.

From the study 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.

## ACKNOWLEDGMENT

The authors express sincere thanks to the medical technologists and medical lab technicians in the hematology section and the medical staff of the gynecology and obstetrics department in alwahda hospital.

## REFERENCES

- Norris LA. Blood coagulation. *Best Pract Res Clin Obstet Gynaecol*, 2003; 17: 369–383.
- Bremme KA. Haemostatic changes in pregnancy. *Best Pract Res Clin Haematol*, 2003; 16:153–168.
- Dahlman T, Hellgren M & Blomba M. Changes in blood coagulation and fibrinolysis in the normal puerperium. *Gynecol Obstet Invest*, 1985; 20: 37–44.
- O’Riordan MN & Higgins JR. Haemostasis in normal and abnormal pregnancy. *Best Pract Res Clin Obstet Gynaecol*, 2003; 17: 385–396.
- Heit JA, Kobbervig CE, James AH, Petterson TM, Bailey KR, Melton LJ 3rd. Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. *Ann. Intern. Med.*, 2005; 143(10): 697-706. DOI: 10.7326/0003-4819-143-10-200511150-00006.
- Valera MC, Parant O, Vayssiere C, Arnal JF, Payrastre B. Physiologic and pathologic changes of platelets in pregnancy. *Platelets*, 2010; 21(8): 587-95.
- Boehlen F, Hohlfeld P, Extermann P, Perneger TV, de Moerloose P. Platelet count at term pregnancy: are appraisal of the threshold. *Obstet Gynecol*, 2000; 95(1): 29–33.
- Thornton P, Douglas J. Coagulation in pregnancy. *Best Practice & Research Clinical Obstetrics and Gynaecology*, 2010; 24: 339-352.
- Akar, EM, Eyi EGY, Yilmaz, ES, Yuksel, B, & Yilmaz, Z (2004), Maternal Deaths and Their Causes in Ankara, Turkey, 1982-2001, *J Health Popul Nutr*, 22(4):420-428.
- Holmes, VA and Wallace, JMW (2005), Haemostasis in Normal Pregnancy: A Balancing Act?, *Biochemical Society Transactions*, 33(2): 428.
- Lewis, SM (2001), ‘Reference Ranges and Normal Values’ in Lewis, SM, Bain, BJ and Bates, I (eds), Dacie and Lewis Practical Haematology, 9th edn, Churchill Livingstone, Edinburgh, 12: 16.
- McCrae KR, Samuels P and Schreiber AD (1992), Pregnancy-Associated Thrombocytopenia: Pathogenesis and Management, *Blood*, December 1; 80(11): 2697-2714.
- Hoffbrand, AV, Pettit, JE & Moss, PAH (2001), *Essential Haematology* 4th edn. Blackwell Science, Oxford, 319: 321.
- Lewis, SM (2001), ‘Reference Ranges and Normal Values’ in Lewis, SM, Bain, BJ and Bates, I (eds), Dacie and Lewis Practical Haematology, 9th edn, Churchill Livingstone, Edinburgh, 12: 16.