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Determination of prothrombin time, INR and platelet count in Some pregnant women in kosti Teaching hospital (Sudan)

Rehab Omer Adam Mohammed Gibla, Abdelrizak Sharef Ali, Eiman Gaily Ali, Muhanad Khalaf Allah Ebrahim

University of El-Imam Al-Mahdi, Faculty of medicine and health sciences, Sudan

Abstract
This study was performed at kosti teaching hospital (Sudan). The aim of the study was to investigate the changes that occur in the coagulation parameters in pregnant women, which include estimation of prothrombin time, platelet count and international normalization ratio (INR). Hundred pregnant and hundred non pregnant women were randomly chosen and individually filled informed consent. The ages of the test group were ranging from 21-30 years, whereas the ages of the control group were ranging from16 to 35 years. Blood samples were taken from each woman. The prothrombin time, international normalization ratio (INR), and platelet count were determined using fully automated hematology analyzer and coatron M2. The obtained results were statistically analyzed using SPSS program. For the pregnants group, the analysis showed a mean prothrombin time of 17 sec, international normalized ratio of 1.4sec, mean international normalized ratio of 1.4sec, mean Platelet count of $165x10^3$cmm, mean platelet volume (MPV) mean of 8.7fl, and platelet distribution width 15.7.
In control group the analysis showed mean prothrombin time of 15.1sec, mean international normalized ratio of 1.3sec, mean Platelet count 286cmm, mean (MPV) 10.3fl, and mean platelet distribution width of 19.6fl. It was found that, prothrombin time is prolonged especially in the third trimester and the Platelet count was significantly reduced in the pregnant group. The mean platelet volume and platelet distribution width were found to be normal in the two groups.

Keywords: prothrombin time, international normalize ratio, pregnancy, coagulation, third trimester, platelet count

1. Introduction
Hemostasis in normal pregnancy involves a complex network of interactions with positive and negative feedback loops, integrating blood vessels; platelets, coagulation Factors, coagulation inhibitors and fibrinolysis; all these has evolved the likely to protect women from hemorrhage during miscarriage or childbirth. Normal pregnancy is associated with substantial changes in the tissue factor pathway and in the wider hemostatic system [1]. Normal pregnancy is a characterized by impressive changes in the activating and inhibitory pathways of coagulation and fibrinolysis resulting in an accelerated, but well balanced, process of thrombin formation and resolution. These changes serve to protect the mother from the hazard of bleeding imposed by placentation and delivery, but they also carry the risk of an exaggerated response, localized or generalized, to coagulant stimuli [2].
Hemorrhage occupies an important position in the etiology of maternal mortality and therefore, remains a major problem [3]. There is activation of blood coagulation and a simultaneous increase in fibrinolysis without signs of organ dysfunction during normal pregnancy. These changes increase as pregnancy progresses. During delivery there is consumption of platelets and blood coagulation factors [4].
Pregnancy is a risk factor for venous thrombosis and the incidence of venous thromboembolism during normal pregnancy is 6-fold higher than in the general female population of child bearing age. Venous thromboembolism is an important cause of maternal morbidity and mortality [5]. The coagulation cascade is in an activated state in pregnancy. Activation includes increased concentrations of all clotting factors, except factors XI, XIII, with increased levels of High molecular weight fibrinogen complexes. Changes in the hemostatic mechanism also involve decreased levels of anticoagulant proteins such as protein C and Protein S as well as enhanced thrombin generation and decreased fibrinolytic activity [6]. Thrombocytopenia is second to anemia as the most common hematologic abnormality encountered during pregnancy. Thrombocytopenia affects 6–10% of all pregnancies [7]. A decrease in platelet count is normal of β-thromboglobulin [10] and of thromboxane A2 derivatives. (11)
In pregnancy although most platelet counts remain within normal limits (150x109 l1) [6, 8] a lower than physiological platelet count may occur in pregnancy for many reasons, ranging from the relatively benign, gestational thrombocytopenia to more sinister conditions, such as HELLP syndrome. In many healthy women (around 10%) late pregnancy (third trimester) is associated with thrombocytopenia. At least in part this is due to hemodilution but the increase in mean platelet volume [9] suggests that a compensated state of progressive platelet destruction occurs. Additional evidence of in vivo platelet activation in late Pregnancy is the increased concentration Haemostasis, defined as the arrest of bleeding,/ comes from the Greek roots, haeme meaning blood and stasis meaning causing to stop. 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 [12]. Following endothelial damage, platelets adhere to the subendothelium forming a platelet plug which then becomes permanent with fibrin deposition. 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) [12]. Platelets are produced in the bone marrow by fragmentation of the cytoplasm of megakaryocytes, one of the largest cells in the body. The precursor of themegakaryocyte-the megakaryoblast-arises by a process of differentiation from the haemopoietic stem cell. The megakaryocyte matures by endomitotic synchronous replication (i.e. DNA replication in the absence of nuclear or cytoplasmic division) enlarging the cytoplasmic volume as the number of nuclear lobs increase in multiples of two. Platelets form by fragmentation of megakaryocyte cytoplasm, approximately each megakaryocyte giving rise to 1000-5000 platelets [13]. The time interval from differentiation of the human stem cell to the production of platelets averages approximately 10 days [13].

Platelets are extremely small and discoid, (3.0x0.5 micro meter) in diameter, with a mean volume 7-11 fL. The glycoproteins of the surface coat are particularly important in the platelet reactions of adhesion and aggregation which are the initial events leading to platelet plug formation during haemostasis. Adhesion to collagen is facilitated by glycoprotein Ia (GpIa). Glycoproteins Ib (defective in Bernard-Soulier syndrome) and IIb/IIIa (defective in thrombasthenia) are important in the attachment of platelets to von Willebrand factor (VWF) and hence to vascular subendothelium where metabolic interactions occur. The binding site for IIb /IIIa is also the receptor for fibrinogen which is important in platelet-platelet aggregation. The plasma membrane invaginates into the platelet interior to form an open membrane (canalicular) system which provides a large reactive surface to which the plasma coagulation proteins may be selectively absorbed. The membrane phospholipids (previously known as platelet factor 3) are of particular importance in the conversion of coagulation factor X to Xa and prothrombin (factor II) to thrombin (factor IIa) [13].

The study area

The study was conducted at Kosti town Teaching Hospital, in White Nile state (Sudan). Kosti is 317Km far from Khartoum to the south. The state area is 39701Km^2.

So many people from kosti locality and surroundings, daily, visit Kosti teaching hospital as outpatients and inpatients.

2. Materials and Methods

5ml of blood sample was taken from each participant; 2.5ml was transferred to EDTA container, and 2ml to tri sodium citrate container. Prothrombin time was estimated using the highly sensitive 2-channel-photometer, coagulation analyzer Coatron M2. Platelets count was determined by automated haematological analyzer µSysmex K21. All reagents and chemicals used were of analytical grade.

3. Results and discussion

3.1 Prothrombin time

Prothrombin time in the pregnant group showed minimum value as 11.7sec and maximum value as 21sec, with a mean of 16.9sec. In the control group the minimum prothrombin time was 12.3sec and the maximum was 17.1 sec with a mean value of 15.1sec. The normal range is from 11 to 16sec. figures (No.1 and 2) may clearly explain the effect of pregnancy in prothrombin time. Lloyd R *et al.*, (1983) reported that prothrombin time was decreased in pregnancy and it was associated with a significant increase in activity factors VII, VIII, IX, X and in the concentrations of fibrinogen, -1-globulin, and -1- antitrypsin [6]. According to Cerneca. F. *et al* (1997) the parameters, which, showed greatest variation during pregnancy were PT, FBG, PS, and Prothrombin fragments F1+2. The existence of a hyper coagulable state in pregnancy was suggested by the increased levels of F1+2. [17]

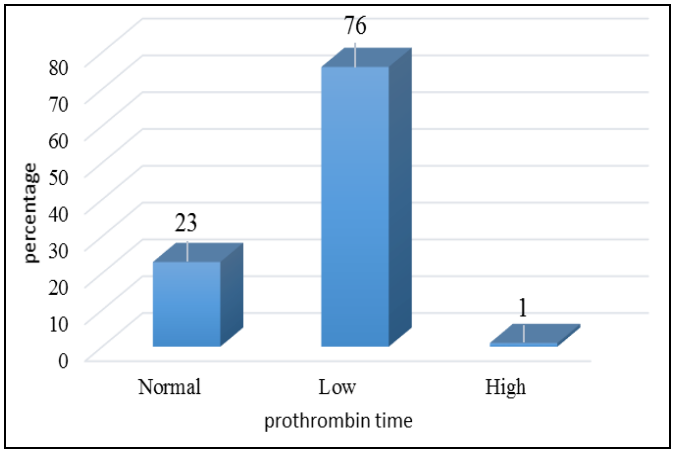

Fig 1: prothrombin time in pregnant women

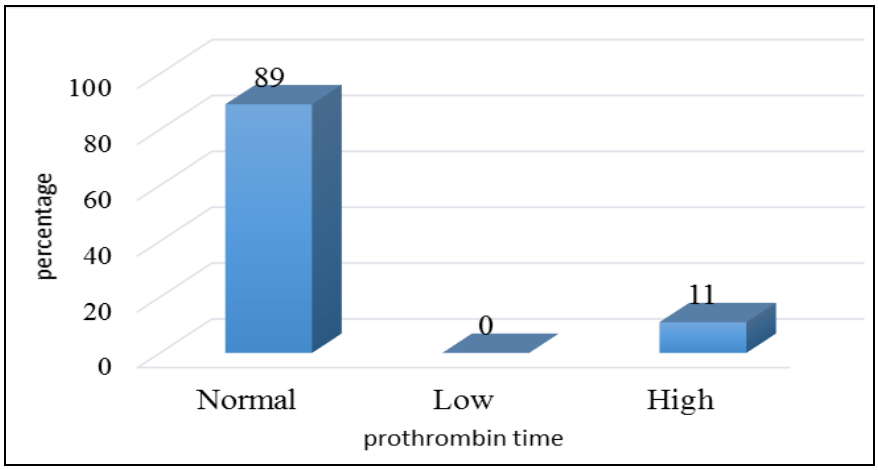

Fig 2: prothrombin time in non-pregnant women

3.2 International normalized ratio

In pregnant women group the lower INR value was 0.8Sec, the higher value was 15.1sec and the mean value was 1.42sec, the p value is p=0.0000 by independent sample test is significant.

In the non-pregnant group the minimum INR value was 0.82sec, the higher value 1.9sec, and the mean was 1.3sec. Figures (No.3 and 4) may explain the changes in INR between pregnant and non-pregnant cases.

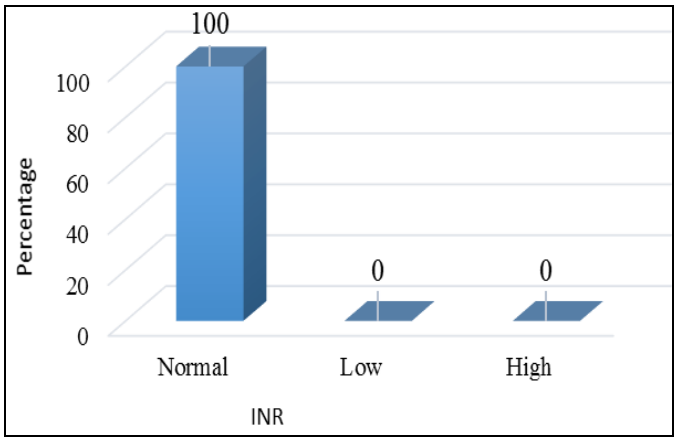

Fig 3: international normalization ratio in pregnant women

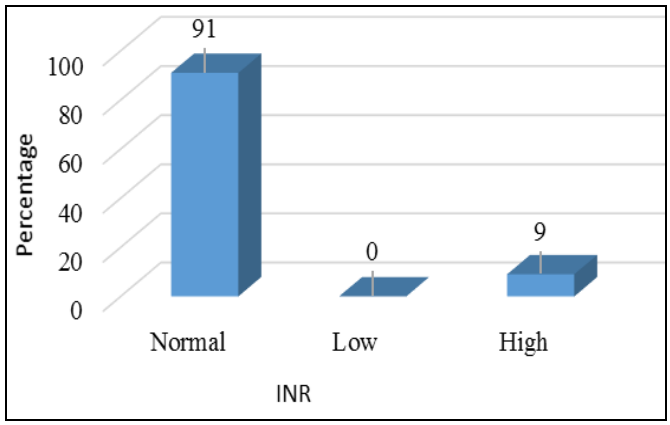

Fig 4: International Normalization Ratio in control women

3.3 The platelet count

From the obtained results the minimum platelet count in pregnant group was (127 x10^3cmm), the maximum count was 300x10^3/cmm and the mean was (165 x10^3cmm). The mean is significantly low, compared with the normal range (150 x10^3cmm- 450 x10^3cmm cmm)

The control group was also showed low mean platelet count but here it is not significant. The minimum count was 139 x10^3cmm, the maximum count 426 x10^3cmm cmm, and the mean value was 286 x10^3cmm.

Along platelet count prothrombin time was also prolonged in case group but normal in control group. This may agree with Helgren M. study which proposed that during pregnancy there were increased endogenous thrombin generation, acquired activated protein C resistance and increased prothrombin level [15].

Figures (No. 5 and 6) may show the variations in platelet count between the pregnant and non-pregnant women, where it was found to be low in vast majority of the pregnant group. These findings did not agree with the results reported by Huda. I. Babiker *et al.*, (2014) [73] and Pannala Srimala *et al.*, (2013) [74].

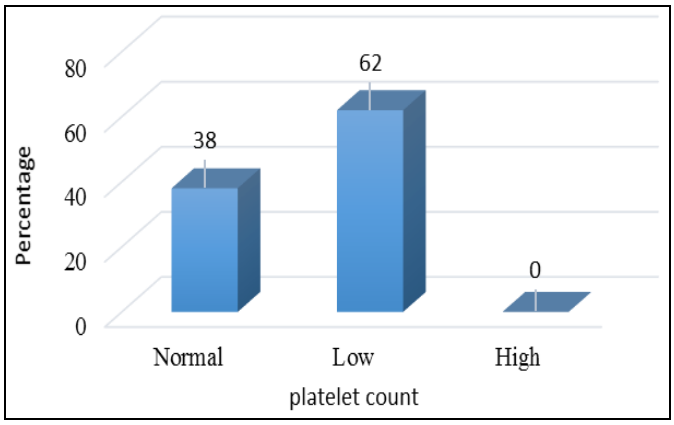

Fig 5: Platelets count in pregnant women

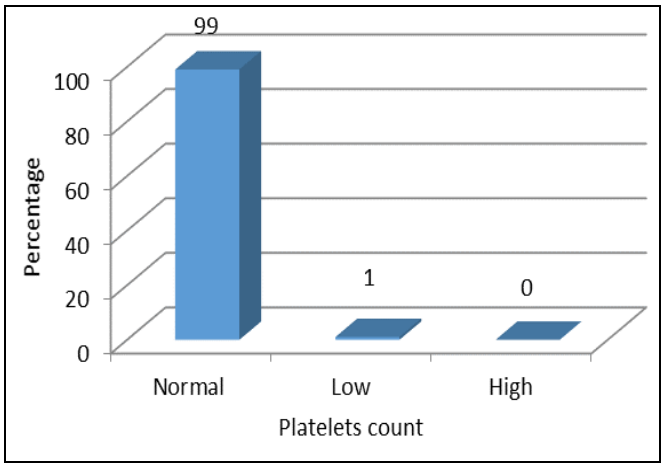

Fig 6: Platelets count in control

3.4 Mean platelet volume

Mean platelet volume had a minimum value of 6.7fl, maximum value of 11.30fl and mean value as 8.7fl in pregnant group, compared with 7.5fl as minimum value, 14.5fl maximum value, and 10.3fl as a mean value in the non-pregnant group. These values may be considered in the normal range for the two cases (Fig no. 7 and 8).

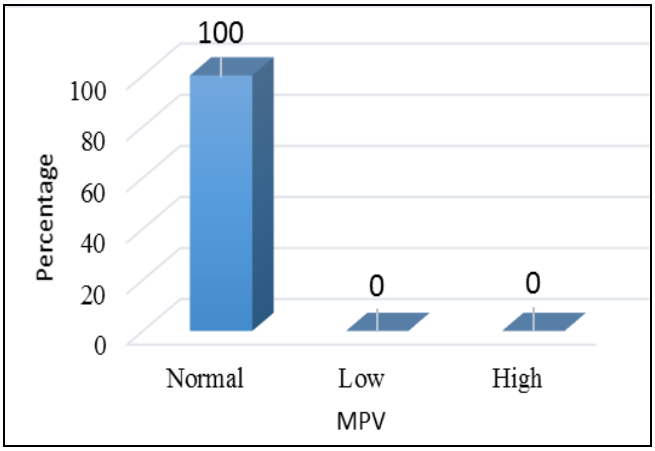

Fig 7: Mean platelet volume in pregnant women

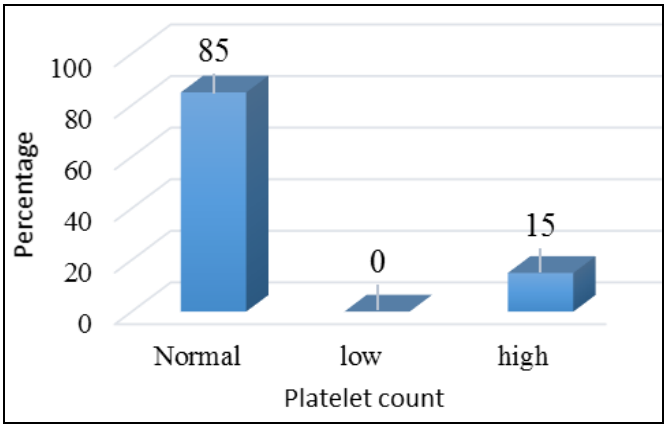

Fig 8: Platelet count in control

3.5 Platelet distribution width

Platelet distribution width showed minimum value of 10.0, maximum value of 17.1 and mean value as 15.7 in the pregnant group, whereas the control group showed 8.31 as minimum value, 19.6 maximum value and 12.8 mean value. Although these values showed a clear variations between the two groups, but they are still within the normal range in the two cases (fig No. 9 and 10)

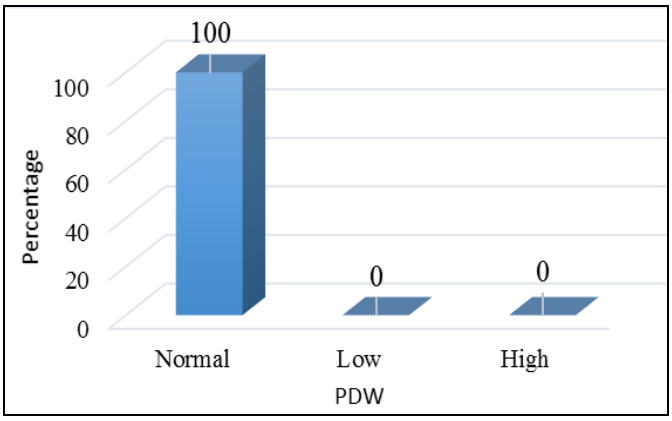

Fig 9: platelet distribution width in pregnant women

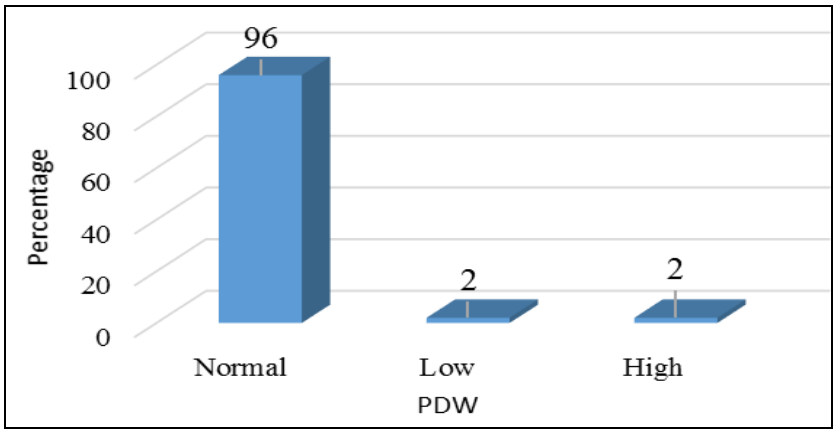

Fig 10: Show the platelets distribution width in control

Table 1: the effect of pregnancy on coagulation parameter

The measured parameters (mean)	Pregnant group	Control group	Normal range
PLT/cmm	165	286	150000 -450000
MPV/fl	8.7	10.3	19-13
PDW	15.7	12.9	9-14
PT/sec	16.9	15.1	11-16
INR	1.42	1.3	1.2 -2

4. Conclusion

Depending on the findings of this study we may conclude that, prothrombin time was prolonged in normal pregnancy especially in the third trimester. The international normalization ratio was found to be normal. The platelet count was significantly reduced in pregnant group. The mean platelet volume was slightly decreased and the platelet distribution width was slightly increased pregnant group so according to the findings of this study pregnancy may cause considerable changes in the main coagulation parameters as shown by table (no. 1).

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