

Thrombocytopenia in Iraqi Pregnant Women

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Summary:

Background: Thrombocytopenia is the second most common hematological abnormality in pregnancy following anemia. However, its incidence causes and outcomes received scarce attention, particularly in developing countries like Iraq.

Objective: This study was conducted to determine the incidence, causes and consequences of thrombocytopenia on both the mother and fetus.

Material and Methods: Platelet counts were performed on 600 pregnant women in their third trimester and on 200 age matched non pregnant healthy women, as well as 150 of the newborns of the former groups.

Results: The overall incidence of thrombocytopenia in pregnancy was 8.6%, with the gestational thrombocytopenia implicated in 76.9%. Hypertensive disorders (pregnancy induced hypertension, preeclampsia) were the second most common causes of thrombocytopenia in the studied group. Other diagnoses such as HELLP syndrome and Disseminated Intravascular Coagulation (DIC) were infrequent. The 2.5th percentile significantly differed in pregnant women ($117 \times 10^9/L$) than the control group ($162 \times 10^9/L$) with the histogram of platelets counts shifted to the left during pregnancy. Among pregnant women with mild thrombocytopenia (platelets count $100-149 \times 10^9/L$), 94% were gestational in origin with a decreasing proportion of the latter with increased severity of the thrombocytopenia. Except for one lady with DIC, all other pregnant ladies completed their pregnancy with no reported complications and none of the followed up neonates had thrombocytopenia.

Conclusion: Similar to worldwide studies gestational thrombocytopenia is the commonest cause for thrombocytopenia in pregnancy in Iraqi ladies and for healthy pregnant women, platelets count $> 117 \times 10^9/L$ late in pregnancy does not require further investigations and could be considered as a safe threshold.

Keywords: Thrombocytopenia, Platelets, Pregnancy.

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Introduction:

Thrombocytopenia in pregnant women is a relatively common finding. The causes and mechanisms of such thrombocytopenia are still a matter of controversy. There are several well established causes of thrombocytopenia such as pregnancy induced hypertension, preeclampsia, HELLP syndrome, and immune thrombocytopenic purpura (1-3). However, the majority of thrombocytopenic women are healthy, have no history of thrombocytopenia and are not hypertensive and their platelets count returns to normal within 12 weeks of delivery (4) and it usually has no influence neither on the evolution of pregnancy, and delivery nor on the newborns, including the risk of neonatal thrombocytopenia (3-5). The underlying mechanism is unclear, although it might be secondary to accelerated platelets consumption, increased plasma volume associated with pregnancy and chronic compensated coagulopathy. Pregnancy induced hypertension (PIH), Preeclampsia (PE) and HELLP (hemolysis, elevated liver enzymes and low platelet count) syndrome are considered to be the cause of thrombocytopenia in pregnancy in about 21% of cases were maternal platelet count returns to normal within 3–5 days of delivery (5,6,7).

There are additional, rarer causes of thrombocytopenia during pregnancy, including thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), disseminated intravascular coagulation (DIC), systemic lupus erythematosus (SLE), and anti-phospholipid antibodies syndrome, or it may be induced by drugs (such as heparin) (6,7,8). Obstetricians in our locality have no comprehensible guide for managing pregnant women with thrombocytopenia due to a lack of data about the frequency, severity and causes of this condition. Moreover, little data is available from the other parts of Iraq. Therefore, we thought it was necessary to carry out this study in order to provide a guide for approaching women with thrombocytopenia. This study is aimed at determining the incidence of thrombocytopenia among pregnant women and to assess its consequences on both the mother and fetus.

Material and Methods:

This prospective study was carried out from Jan 2007 – Sept 2007. A total of 600 pregnant women at their third trimester of pregnancy attending the outpatient's clinics of obstetric and gynaecology of Azadi general hospital in Kirkuk /Iraq were screened for the presence of thrombocytopenia. Exclusion criteria included any history of immune disorders (Systemic Lupus Erythematosus, antiphospholipid syndrome, and Immune Thrombocytopenic

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Purpura). A control group of 200 healthy non-pregnant women aged 18-47 years from the medical staff and volunteers was also included. Pregnant women were interviewed and examined after obtaining their informed consent, and the study was approved by the research council of College of Medicine, University of Sulaimani.

About 2 ml blood was taken from each pregnant lady and control in an EDTA tube to perform full blood count using automated Hematology analyzer machine (Sysmex- Japan) which was daily calibrated by the manufactures controls. The laboratory evaluation included to start with a complete blood count and peripheral smears to exclude pseudo-thrombocytopenia and to detect features of microangiopathy. In hypertensive women (sustained BP > 140 /90 mmHg) (8,9) extra 5ml of blood was taken in a plain tube for the measurement of total serum Bilirubin (TSB), serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), alkaline phosphatase (ALP), blood urea and serum creatinine according to the standard methods. Coagulation tests represented by Prothrombin time (PT), Partial thromboplastin Time (PTT), Thrombin time (TT) and D-dimer were done for any pregnant women presenting with bleeding manifestation unrelated to the severity of thrombocytopenia and in the absence of evident gynaecological causes, using the fully automated coagulation STA COMPACT (Diagnostica Stago / France). The study also included follow up and reassessment of the thrombocytopenic pregnant women as recommended by previous investigators (10-13) throughout the third trimester and post partum. The frequency of follow up depended on the underlying aetiology of thrombocytopenia. In hypertensive women, an extra screening for the possible complications of hypertension, preeclampsia, HELLP and DIC was performed in addition to performing daily post delivery platelet counts. In addition, 150 neonates were checked for platelets count within 24 hours postpartum using either cord blood if (feasible) or venous blood. They included 51 neonates born from the thrombocytopenic pregnant ladies; also included were 99 neonates born from the non thrombocytopenic pregnant women. All statistical analysis (mean, medium, standard deviation, coefficient interval (CI) percentiles, t-test, f-test and graphical presentation) were performed on STAGRAFICS. $P < 0.05$ was considered as statistically significant.

Results:

A total of 600 pregnant women were included in this study, their ages ranged between 16-44 years (mean 28.8 yrs \pm 6). The control group included 200 apparently healthy non-pregnant women with ages ranged between 18 and 45 years (mean of 29.5 yrs \pm 7.1). The overall mean platelets count of pregnant women was significantly lower compared to mean platelets count of the control women ($241 \times 10^9/L$ versus $288 \times 10^9/L$) (Table 1) ($p=0.001$) and the 2.5th

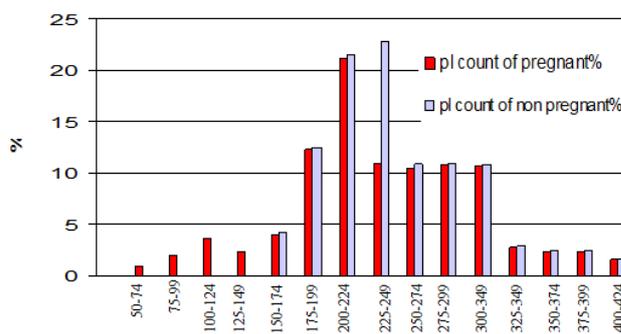
percentile significantly differed in pregnant women ($117 \times 10^9/L$) than the control group ($162 \times 10^9/L$) ($p= 0.0001$) with the histogram of platelets count shifted to the left during pregnancy (Figure 1). Out of the 600 pregnant women 52(8.6%) had platelets count less than $150 \times 10^9/L$. Of the latter: 33(63.5%) had mild thrombocytopenia ($100-149 \times 10^9/L$) and 19(36.5%) had moderate thrombocytopenia ($50-99 \times 10^9/L$), while none had severe thrombocytopenia ($<50 \times 10^9/L$) (Table 2). Furthermore, in 40 of the 52 thrombocytopenic ladies (76.9%) there was no identifiable cause for the thrombocytopenia (i.e. it was gestational). In this category of patients, the platelets count ranged from $80-146 \times 10^9/L$, with a mean of ($115 \times 10^9/L \pm 16.4$). Among the remaining 12 women, the most common causes were: preeclampsia (6 cases 11.5%), followed by pregnancy induced hypertension (4 cases 7.7%), a case of HELLP syndrome and another of disseminated intravascular coagulation (1.9% each) (Figure 2), their platelet counts ranged between $54-130 \times 10^9/L$ with an overall mean of $93 \times 10^9/L \pm 23.34$ which significantly differed from the mean platelets count in the gestational group ($p=0.001$). It was noted that the proportion of thrombocytopenia of unknown origin decreased with the severity of thrombocytopenia (Table 2) and if we considered the 33 pregnant women with mild thrombocytopenia, 31(94%) had gestational thrombocytopenia while hypertension related disorders accounted for the two remaining cases. No thrombocytopenia related complications reported in pregnant ladies apart from the pregnant woman with disseminated intravascular coagulation who presented with severe vaginal bleeding followed by shock and fetal death. Regarding the follow up of thrombocytopenic pregnant women through pregnancy, the platelets count values showed little changes and were nearly similar to the first time evaluation. In post partum follow up, all those with thrombocytopenia of known etiology showed fast recovery, which was encountered within 48 hours for the pregnancy related hypertension and DIC and 72 hours for HELLP syndrome. On the other hand, it was found that 28% of women with gestational thrombocytopenia remained thrombocytopenic at 2 weeks and one woman even showed more delayed platelets recovery (after 8 wks post partum). No neonatal thrombocytopenia was reported in this study in any of the 150 neonates screened for it, with no significant difference in mean platelets count noticed between neonates born from thrombocytopenic pregnant women ($267 \times 10^9/L + 50.8$) and non thrombocytopenic mothers ($271 \times 10^9/L + 49.3$) ($p= 0.09$)

(Table 1) Mean Platelets Count of Control Group and pregnant Women

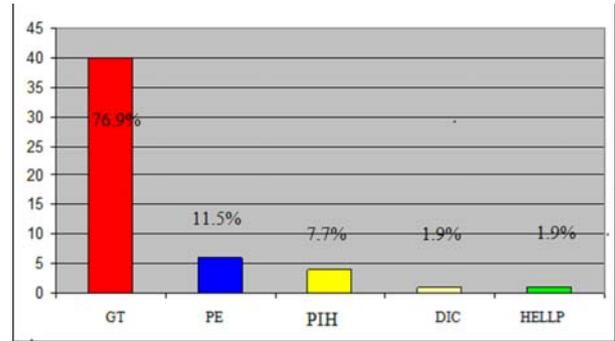
Characteristics	Control (n=200)	Pregnant women (n=600)	P value
Range (yr)	18-45	16-44	
Mean age (yrs)	29.5+7.1	28.8+6	
Platelets count(x 10 ⁹ /L)			
Range	180-415	50-450	
Mean (+ SD)	288 +44.3	241+73.4	0.001
Median	252	236	0.001
2.5 th percentile	162	117	0.0001
97.5 th percentile	410	398	0.08
Thrombocytopenia (<150 x 10 ⁹ /L)	0	52	

(Table 2) Diagnosis and Incidence of Maternal Thrombocytopenia According To Platelets Count

Characteristics	Maternal Platelets Count			
	Normal Platelets Count (>150x10 ⁹ /L)	Mild Thrombocytopenia (100-149 x10 ⁹ /L)	Moderate Thrombocytopenia (50-99 x10 ⁹ /L)	Sever Thrombocytopenia (< 50 x10 ⁹ /L)
No. of Pregnant Women = 600 No. of thrombocytopenic Women=52	548	33 (63.5%)	19 (35.5%)	0
Thrombocytopenia of Unknown Origin (n=40)		31(94%)	9 (47.4%)	
Thrombocytopenia of known Origin (n=12)		2 (6%)	10 (52.6%)	
Preeclampsia/Hypertension (n=10)		2	8	0
HELLP Syndrome (n=1)		0	1	0
DIC (n=1)		0	1	0



(Fig 1)Histogram of platelets count in pregnant women compared with non pregnant women



(Fig 2) Etiological classification of thrombocytopenic women ,GT gestational thrombocytopenia, PE preeclampsia, PIH pregnancy induced hypertension, DIC disseminated intravascular coagulation, HELLP hemolysis with elevated liver enzyme and low platelets

Discussion:

The increased recognition of maternal and fetal thrombocytopenia has resulted in controversies regarding management. Such controversies stem from the fact thrombocytopenia tends to be a common problem in pregnancy and in majority of cases it is quite a benign finding requiring no active management. Therefore, the value of screening for it specifically has been questioned by many (13). The overall incidence of thrombocytopenia in our study was 8.6%, with gestational thrombocytopenia accounting for more than three fourths of all cases, while hypertensive disorders represented collectively 19.2%, in accordance with previous figures reported by Boehlen et al(1,15) and Burrows and Kelton(16,17) and a local study from Erbil(18) showing nearly similar incidence of thrombocytopenia. In our study, the control group of non-pregnant women of child bearing age had a 2.5th percentile at 164 x 10⁹/L, while it was 117 x10⁹/L for the pregnant. The latter is very close to the figure reported by Boehlen et al study in Switzerland in 2000 (116 x 10⁹/L). The mean platelets count (241x10⁹/L) of pregnant women also significantly differed from that of the control group mean (288 x10⁹/L) in accordance with that previous study which is most likely due to thrombocytopenia in the group of pregnant women (14). In our study, we observed no maternal or neonatal bleeding complications or death in the group of 33 (63.5%) pregnant women with mild thrombocytopenia. Indeed, it does not seem reasonable to perform detailed investigations in all cases of mild thrombocytopenia during the third trimester, as a specific diagnosis is rarely found and mild maternal thrombocytopenia is usually not associated with maternal or neonatal morbidity. For these reasons in the absence of an underlying disease, we propose to follow the clinical course of these pregnant women and to refrain from detailed investigations in the presence of platelets count above the 2.5th percentile (117 x 10⁹/L). The clinical history (prior autoimmune disease, prior history of maternal or neonatal thrombocytopenia, bleeding disorder, drug

ingestion, infection, etc) and clinical examination (bruises, hypertension, icterus, hepatosplenomegaly, etc) must be taken into account (7, 11, and 14). Nineteen women had platelets count between $50-100 \times 10^9/L$ (Table 1), 10 (53%) of them had an underlying mechanism that were detected by either examination (including blood pressure measurement) or blood test (full blood count and liver function tests). Based on the above findings and previous reports (19-21) it seems reasonable to consider limited investigations in this group of pregnant women. Serology tests for human immune deficiency virus and hepatitis C virus might be considered (14). Other investigations may be indicated in specific cases (e.g. screening coagulation tests). Furthermore, detailed investigation was recommended by previous investigators when platelets count dropped below $50 \times 10^9/L$, a threshold below which the diagnosis of gestational thrombocytopenia is generally not considered. (11, 12, 14) This attitude does not imply that thrombocytopenia late in pregnancy should be neglected. Indeed, this shows the importance of the postpartum platelets count that can assist in determine the cause of pregnancy- associated thrombocytopenia and differentiate this from other potential causes (7,14).

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