THE INCIDENCE OF THROMBOCYTOPENIA AMONG 600 PREGNANT LADIES IN SULAIMANI-IRAQ

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ABSTRACT

Background

Thrombocytopenia in pregnancy is quite common; it's the second most common hematological abnormality, after anemia, during pregnancy. Thrombocytopenia results from a wide range of conditions, several of them being pregnancy related. While some of these are not associated with adverse pregnancy outcomes, others are associated with substantial maternal and /or neonatal morbidity and mortality.

Objective

To determine the incidence and various underlying causes of thrombocytopenia in pregnant women in Sulaimani-Iraq.

Methods

In this study a total of 600 pregnant women at different gestational ages, and 150 non- pregnant apparently healthy women, as control, were included. They were randomly selected from different primary health care centers and outpatient clinics of Maternity Teaching Hospital in Sulaimani city. Full history, physical examination and laboratory investigations were performed.

Results

The incidence of thrombocytopenia in the pregnant group was 7.7 % with gestational thrombocytopenia accounting for 76.1% of cases, followed by pregnancy induced hypertensive disorders in 19.6% of cases. The platelets count in pregnant women included in the study ranged from 60-450 x 10^9 /L with a mean of (250.2 x 10^9 /L ± 68.39), a value that is significantly lower than the value in control group with a range of platelets from 162-392 x 10^9 /L, and a mean of (285 x 10^9 /L± 48.2) (P value= 0.001).

Conclusion

Gestational thrombocytopenia is the commonest cause (76.1% of cases) for thrombocytopenia occurring later in pregnancy in this study, and a platelets count ≥ 121 x 10^9/L detected late in pregnancy does not require sophisticated investigations and should be regarded as safe threshold.

Keywords: *Thrombocytopenia, Pregnancy, Gestational thrombocytopenia, Sulaimani*

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INTRODUCTION

Thrombocytopenia (TCP) in pregnant women is a relatively common finding. The causes and mechanisms are still a matter of controversy. TCP is defined as a platelets count of less than 150 x 10^9 /L [1]. It's classified as mild with platelets count of 100- 150 x 10^9 /L, moderate as 50- 100 x 10^9 /L and marked when counts are less than 50 x 10^9 /L [2].

It is well known that pregnancy is associated with physiological fall in platelets count which is of multifactorial origin, including hemodilution, increased platelets consumption and increased platelets aggregation caused by increased Thromboxane A2 level [3]. It is estimated that TCP affects 7-10% of all pregnant women [4-6], and gestational TCP amount for most of cases , occurring in approximately 75% of all [7]. Although the exact pathophysiology is unknown, it is thought to be related to increased activation and peripheral consumption. Further more most experts consider the diagnosis of gestational TCP to be less likely when the platelets count falls below 70 x 10^9 /L [8, 9]. This is a benign condition that occurs in later half of pregnancy (from mid-second to third trimester), women are typically asymptomatic, with no past history of TCP.

Gestational TCP is usually self limited and resolves within 1 to 2 months after delivery. Usually it's not associated with adverse outcomes for the baby. The most difficult differential diagnosis is immune thrombocytopenia (ITP) which accounts for 3% of all thrombocytopenic gravidas [10]. ITP is the most common cause of TCP in first and second trimesters. IgG antibodies can cross the placenta and have the potential to cause TCP in the infant [6]. ITP may be indistinguishable from gestational TCP, however, patients with ITP usually have prior history of ITP or other immune mediated disorders, and they are more likely to present with severe TCP earlier in pregnancy compared with gestational TCP. Detection of TCP in infants of ITP mothers is uncommon [11].

Preeclampsia on the other hand is the second most common cause of TCP developing in late second or third trimester, accounting for 21% of cases of TCP at the time of delivery. It develops in approximately 50% of patients with preeclampsia and may be the only initial manifestation, with the severity being proportional to that of the underlying disease [12]. Other less frequent causes of TCP in pregnancy include: HELLP, Thrombotic Thrombocytopenic Purpura, Disseminated Intravascular Coagulation (DIC), Systemic Lupus Erythematosis, secondary to viruses (HIV, EPV, CMV) or a common adverse reaction from many drugs (heparin, antibiotics, nonsteroidal anti-inflammatory drugs) [13]. This study aimed at determining the incidence and causes of TCP among pregnant women in Sulaimani-Iraq for the first time

MATERIALS AND METHODS

This is a case control study that was carried out from July 1st 2010 – December 30th 2010. A total of 600 pregnant women were enrolled, from 4-38 weeks gestation. Furthermore, 150 non- pregnant apparently healthy women, as control, were included too. They were randomly selected from different primary health centers and outpatient clinics of Maternity Teaching Hospital in Sulaimani city. After obtaining their informed consent, full history, physical examination and complete blood count were performed. Blood specimens were collected with minimum stasis with clean venipunctures. About 3 ml of blood was dispensed into EDTA anticoagulant tubes; complete blood count was done by automated hematology analyzer (Beckman coulter analyzer USA) with daily calibration according to manufacturer's direction. A peripheral smear was done to exclude pseudothrombocytopenia and to check for microangiopathic features. An extra 5ml of blood was taken from hypertensive ladies to check the liver function tests (total serum bilirubin (TSB), serum aspartate aminotransferase (AST), serum alanin aminotransferase (ALT), alkaline phosphatase (ALP) and renal function tests (urea and creatinine) according to standard methods. Coagulation screening (Prothrombine Time (PT), Partial Thromboplastine Time (PTT) by manual method using Bio lab kits, and D-dimer test by Latex agglutination method were done for pregnant ladies presenting with bleeding manifestations. Statistical analysis was performed on STATGRAFICS plus software using t-test and f-test. $P \leq 0.05$ was considered statistically significant value.

RESULTS

The age range of the enrolled pregnant ladies was 15-45 years with a mean of (28.5 ±5.7 yrs). Out of these, 29 (4.8%) were in the first trimester, 117 (19.5%) in the second trimester and 454 (75.7%) were in the third trimester. The control group included 150 healthy looking non-pregnant women, their age ranged from 18-45 years with a mean of (29.5±7.2 yrs).

The platelets count in control group ranged from 162-392 x 10^9 /L with a mean of (285 x 10^9 /L ± 48.2), none of

them was thrombocytopenic. While the platelets count in the pregnant group ranged from 60-450 x 10^9 /L with a mean of (250 x 10^9 /L ±68.39) which was significantly lower than the control group (P <0.01)

Among the pregnant women, 46 (7.7%) had TCP (Figure 1), their platelets count ranged from 60-148 x 10^9 /L with a mean of (120 x 10^9 /L ±18.9). Most of them were in the third trimester 32 (69.6%), while 10(21.7%) were in second trimester and only 4 (8.7%) were in first trimester (Figure 2). Of the 46 pregnant cases with TCP, 89.1% showed mild TCP, while 10.9% showed moderate TCP. No marked TCP reported (Table 2).

Gestational thrombocytopenia was found in 35 pregnant women constituting 76.1% of the thrombocytopenic pregnant ladies and 5.8% of the whole pregnant ladies. The platelets count ranged from119-148 x 10^9 /L with a mean of (125 x 10^9 /L ± 8.1).

In the rest eleven pregnant ladies (23.9%), the following diagnoses were found: preeclampsia (6 cases), pregnancy induced hypertension PIH (3 cases), representing collectively 19.6%, while the diagnosis of DIC and ITP was made in one case each (2.2%). (Figure 3)

Table 1. The age and platelets characteristics in control and pregnant groups.

Characteristics	Control (n=150)	Pregnant (n=600)	P value
Age Range(years)	18-45	15-45	
Mean age ±SD	29.5±7.2	28.5±5.7	
Range of platelets count (x10^9 /L)	162-392	60-450	
Mean Platelets count ± SD (x 10^9 /L)	285±48.2	250.2±68.39	0.001
TCP (<150 x 10^9 /L)	0	46	0.0001
2.5th percentile	162	121	0.001
97.5th percentile	432	399	0.5

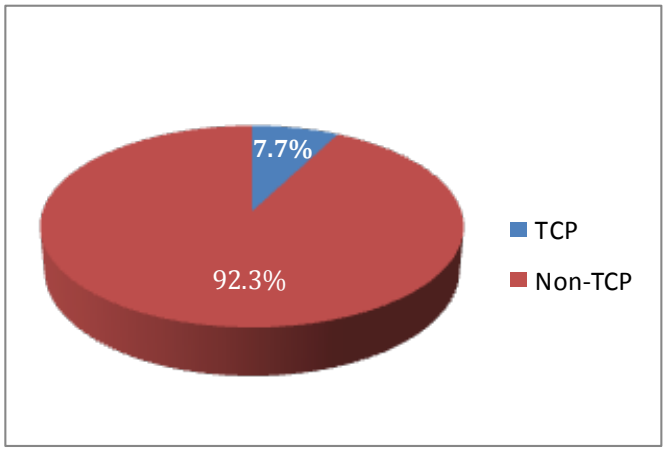

Figure 1. The incidence of TCP among the 600 pregnant ladies in Sulaimani.

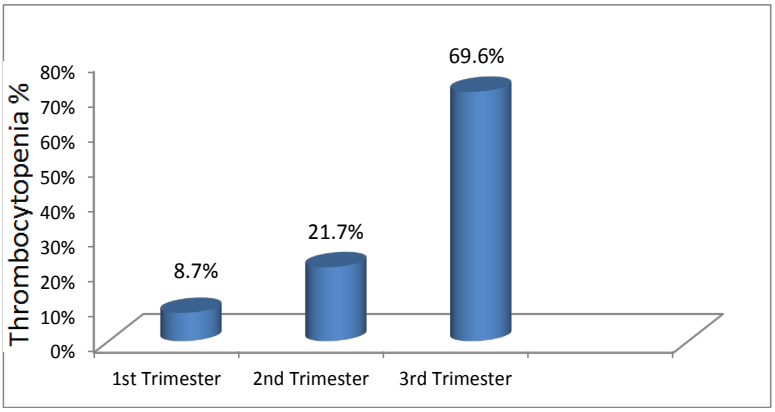

Figure 2. Thrombocytopenia according to gestational age.

Table 2. Maternal platelet count according to severity and diagnosis.

Characteristics	Maternal Platelets count			
	Normal	Mild TCP	Moderate TCP	Marked TCP
	150 x 10^9 /L	100-150 x 10^9 /L	50-100 x 10^9 /L	50 x 10^9 /L>
No. of pregnant ladies [n=600]	554 (92.3%)	41 (89.1%)	5 (10.9%)	0
No. of pregnant ladies with TCP [n=46 (7.7%)]				
TCP of unknown origin [n=35(76.1%)]		35 (100%)	0	0
TCP of known origin [n=11(23.9%)]		6 (54%)	5 (46%)	0
Preeclampsia/hypertension		6 (67%)	3 (33%)	0
[n=9/11(81.8%)]				
DIC [n=1/11(9.1%)]		0	1	0
ITP [n=1/11(9.1%)]		0	1	0

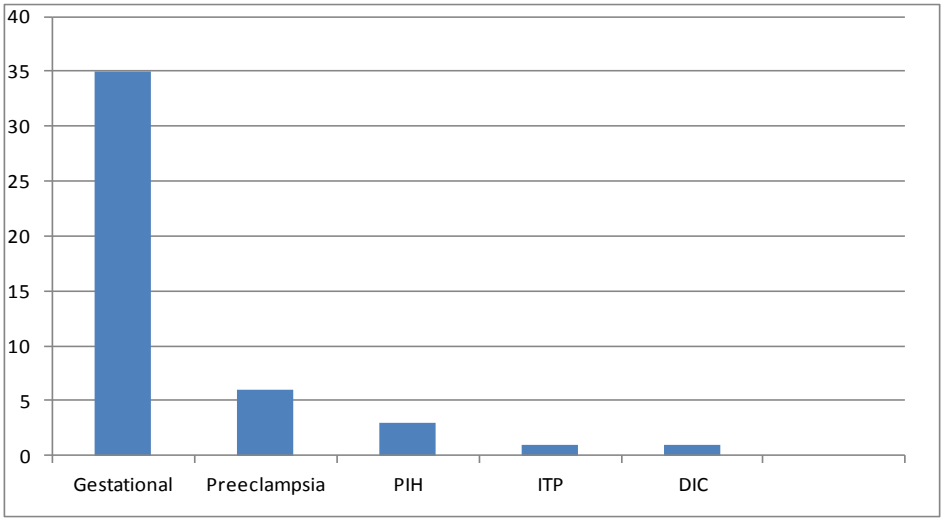

Figure 3. Etiological classification of TCP.

DISCUSSION

TCP in pregnancy is a common reason for hematology consultation, and the screening for is done as part of the initial laboratory evaluation with automated blood counters. Hence, women are more commonly diagnosed with platelets disorders during pregnancy nowadays. However, in the majority of cases, it is a quite benign finding, requiring no active intervention; therefore the value of further testing might be questionable [14].

The overall incidence of TCP among pregnant ladies in our study (7.7%) was close to the figures in studies from other parts in Iraq; like Kirkuk (8.6%) and Erbil (8%) [15, 16], and a previous two population based survey studies that showed a close figures as well (ranging from 6%-7.3%) [17, 18]. It's noteworthy to mention that the incidence rate of TCP would have risen to > 8% if the pregnant women of < 20 wks of gestation were excluded from the study.

Gestational TCP accounted for 76.1% of cases, in agreement with previous reports [11, 19]. Such diagnosis is difficult to distinguish from ITP when TCP is identified for the first time during pregnancy and no previous counts have been documented, even with different platelets associated antibodies which showed elevated results in majority of gestational TCP cases [20].

Pregnancy induced hypertensive disorders was the second common cause of TCP in pregnancy in our study, constituting 19.6% of cases , a result that was similar to previous studies [21, 22], but slightly higher than some studies that reported an incidence of 16 % [18]. This could be explained by the sample size difference. In this study, one pregnant woman had history of ITP preconception, her platelets count at the time of presentation (14 weeks of gestation) was 60 x 10^9/L, therefore ITP in the current study amounted to only 2.2% of cases which approximated the figures reported in other studies [18, 22].

Moreover, another pregnant woman presented with uncontrolled vaginal bleeding at 30 week gestation, after clinical examination and investigations she was diagnosed with abruptio placenta and intrauterine death. Her platelets count at presentation was 72 x10^9/L, with prolonged PT, PTT and positive D-dimer test. DIC incidence (2.2%) was not a frequent cause for TCP in this study in accordance with other studies [18, 23]

Among the pregnant ladies with TCP, 89.1% showed mild TCP, with no maternal complains or complications. Of the mild TCP group (41 ladies), 35 (85.4%) ladies didn't show any underlying cause for the TCP, and were regarded as gestational TCP. For this group, follow up without enrolling them in detailed investigations when the platelets count is > 2.5th percentile (121 x10^9/L) would be most appropriate. The clinical history of prior autoimmune diseases, previous maternal or neonatal thrombocytopenia, bleeding disorders, infections and drug ingestion together with clinical examination (bruises, hypertension, jaundice, hepatosplenomegaly, etc) must be taken into consideration [24, 25]. On the other hand, only 5 (10.9%) cases had moderate TCP, among those, 3 (60 %) had preeclampsia, 1 (20%) had DIC and 1 (20%) had ITP. Therefore, it seems reasonable to

perform limited investigations in this group including serology tests for HIV and HCV [23]. Furthermore, detailed investigations were recommended by previous investigators when platelets count dropped below 50 x 10^9 /L, a threshold below which the diagnosis of gestational thrombocytopenia is generally not considered [23, 24].

In accordance with worldwide studies, this study confirmed that gestational TCP is the commonest cause for TCP in pregnant ladies from Sulaimani-Iraq and platelets count $\geq$ 121 x 10^9/L late in pregnancy does not require sophisticated investigations and can be regarded as safe threshold.

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