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Effects of Maternal Thrombocytopenia on Pregnancy Outcome: A Prospective Observational Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Introduction: Platelets are non -nucleated cellular fragments of megakaryocytes, they play a critical role in haemostasis. Thrombocytopenia is a common medical disorder and is defined as platelet count less than 150,000/µl.
Objective: To study the aetiology of maternal thrombocytopenia and its effect on pregnancy outcomes.
Subjects and Methods: This prospective study was carried over a period of two years from July 2015-May2017 in SKIMS Medical College Bemina. Pregnant women with low platelet counts (count less than 150,000 /µl) in third trimester were taken as cases and rest served as controlled. All the thrombocytopenic cases were followed up throughout the antenatal period till delivery to record any complications that may develop due to low platelet counts. Platelet counts were repeated in the postpartum period at 1 & 6 weeks. Babies of all cases were tested for thrombocytopenia.
Results: The prevalence of thrombocytopenia in pregnant Kashmiri females was found to be 9.38%. Most cases were due to the condition labelled as gestational thrombocytopenia, the exact cause of which is unknown. It accounted for 60.2% of cases. Obstetric causes accounted for

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23.2% of cases and medical causes accounted for 16% of cases. The incidence of postpartum haemorrhage in cases was 6.8% and in controls 2.4%, though the incidence is higher but statistically insignificant.

Conclusion: No significant increase in maternal complications and pregnancy seen with regards to thrombocytopenia.

Keywords: Antenatal period; HELLP; gestational thrombocytopenia; Postpartum haemorrhage.

1. INTRODUCTION

Platelets are non -nucleated cellular fragments of megakaryocytes, they play a critical role in hemostasis [1]. Thrombocytopeniat is a common medical disorder and is defined as platelet count less than 150,000/µl [2,3]. It is second only to anaemia as the most common haematological abnormality in pregnancy [4]. Due to haem dilution secondary to expansion of plasma volume, platelet count in normal pregnancies may decrease by approximately 10%, most of this decrease occurs during the third trimester; [5-8] though the absolute platelet count remains within normal reference range in most patients [6,9]. Thrombocytopenia in pregnant women may result from the effects of several diverse processes, which may be either physiological or pathological. Thrombocytopenia can be classified as mild (platelet count of 100,000-150,000 X 10^9/L), moderate (platelet count of 50,000-100,000 X 10^9 /L) or severe (platelet count less than 50,000 X 10^9 /L) [10]. The majority of thrombocytopenic pregnant women healthy, has no history of thrombocytopenia, and is incidentally diagnosed by blood testing. This condition, called incidental or gestational thrombocytopenia (GT), usually has no influence on pregnancy, & delivery or the newborn [2,5,11,12]. However, in a significant proportion of cases it may have great clinical impact. There may not be a risk of severe haemorrhage in gestational thrombocytopenia, but preeclampsia, HELLP (Haemolysis, Elevated Liver enzymes, Low Platelets) syndrome and ITP (Immune Thrombocytopenic Purpura) expose mother and child to potentially life threatening complications. Other rare causes of thrombocytopenia like Thrombotic thrombocytopenic purpura (TTP), Haemolytic uremic syndrome (HUS), disseminated intravascular coagulopathy (DIC) and disease IIB (vWD IIB) are also associated with severe complications. An accurate etiological diagnosis is essential to ensure optimal therapeutic management. Thrombo-cytopenia is divided according to aetiology into gestational, medical (ITP, hypersplenism, hepatic disorders, etc.) and obstetric (hypertensive disorders, DIC, multifetal gestation etc.) thrombocytopenia [3].

Gestational thrombocytopenia is a diagnosis of exclusion, use of automated blood counters in routine pre-natal screening has resulted in an increased diagnosis and the following five characteristics make it more likely: (a) The degree of thrombocytopenia is usually mild to moderate; (b) The patients are asymptomatic with no history of bleeding; (c) There is no preconception history of thrombocytopenia; (d) An early gestation or preconception platelet count is normal; (e) The platelet count returns to normal within 2-12 weeks postpartum. The cause of gestational thrombocytopenia is unclear, although it might be secondary to accelerated platelet consumption and the increased plasma volume associated with pregnancy [13,14].

In this study we tried to elucidate the aetiology of maternal thrombocytopenia and its effect on pregnancy outcomes.

2. MATERIALS AND METHODS

2.1 Study Design

This prospective study was carried over a period of two years from July 2015-May 2017 in SKIMS Medical College Bemina after taking due clearance from the institutional ethical clearance committee. In this study, 778 pregnant women attending Department of Obstetrics and Gynaecology, SKIMS Medical College & Hospital, Srinagar from July 2015 to May 2017 were included, among them those with low platelet counts (count less than 150,000 /µl) in third trimester were taken as cases and rest served as controlled. The detailed work up of all cases of thrombocytopenia was done to ascertain the cause of thrombocytopenia. Cases with no apparent cause and whose platelet count normalized within 6 weeks after delivery were labelled as gestational thrombocytopenia.

All the thrombocytopenic cases were followed up throughout the antenatal period till delivery to

record any complications that may develop due to low platelet counts. Platelet counts were repeated in the postpartum period at 1 & 6 weeks. Babies of all cases were tested for thrombocytopenia. Depending upon the history, clinical examination and laboratory investigation, the cases were classified into gestational, obstetric or medical cause of thrombocytopenia.

2.2 Sample Collection

Blood specimen was withdrawn with minimal stasis from the antecubital vein using a dry sterile disposable syringe and needle. Three milliliters of blood were dispensed into ethylenediamine tetraacetic acid EDTA anticoagulant tubes. The specimens were properly. The EDTA samples were kept at room temperature until processed within 4 hours of collection.

2.3 Laboratory Analysis

Platelet count were performed using the Sysmex KX-21N Automated haematology Analyzer. Standardization, calibration of instrument and processing of samples done according to manufacturer's instructions. Patients with low platelet counts (count less than 150,000 /µl) also had their manual platelet counts done in order to substantiate the results. Pseudo thrombocytopenia was diagnosed if the CBC was done by using EDTA vial and patients peripheral blood film demonstrated platelet clumps. The platelet count was repeated using a citrate vial and if the platelet count improved the patient was labelled as pseudo thrombocytopenia.

2.4 Statistical Analysis

Statistical data analysis was done utilizing SPSS 23. Normality of test was done by Shapiro-Wilk test. Median with Interquartile range (IQR) was calculated for age, gestational age at delivery, systolic and diastolic BP, hemoglobin, platelet count, sugar fasting, SGOT and SGPT as they were not normally distributed. Nonparametric data analyzed utilizing Mann-Whitney U test. Nominal categorical data between the groups were compared using Chi-square test or Fisher's exact test as appropriate. Continuous categorical data between the groups were compared using sample t-test.

3. OBSERVATION AND RESULTS

A total of 778 patients were enrolled in the third trimester. Out of them 73 were found to have thrombocytopenia (platelet count < 1,50,000) giving a prevalence of 9.38%. 705 age, and race matched pregnant females with platelet counts more than 1,50,000 served as controls. Baseline characteristics of cases and controls is shown in Table 1.

Table 1. Baseline characteristics of cases and controls

	Cases 73	Controls 705	P value
Age [years] (median (IQR))	27 (5)	27 (5)	0.83
SBP [mm Hg] (median(IQR))	120 (20)	120 (20)	0.02
DBP [mm Hg] (median(IQR))	80 (10)	80 (10)	0.10
Hb [g/dL] (median(IQR))	11.7 (1.7)	11.4 (2)	0.10
Platelet [10^9 cells/L] (median(IQR))	100 (30)	178 (50)	0.00
Sugar F [mg/dL] (median (IQR))	87 (13)	84 (12)	0.08
SGOT [mg/dL] (median (IQR))	39 (55)	29 (20)	0.00
SGPT [mg/dL] (median (IQR))	35 (46)	27 (23)	0.00
Gestational age at del [weeks] (median (IQR))	38 (1)	38 (2)	0.99

Table 2. Liver function abnormalities among cases & controls

	LFT normal	LFT abnormal	P Value
Cases	42 (57.5 %)	31 (42.5 %)	0.00
Controls	540 (76.6 %)	165 (23.4 %)	

Table 3. Preterm deliveries in cases and controls

	Preterm	Term	P Value
Cases	8 (11 %)	65 (89 %)	0.59
Controls	64 (9.1 %)	641 (90.9 %)	
Total	72	706	778

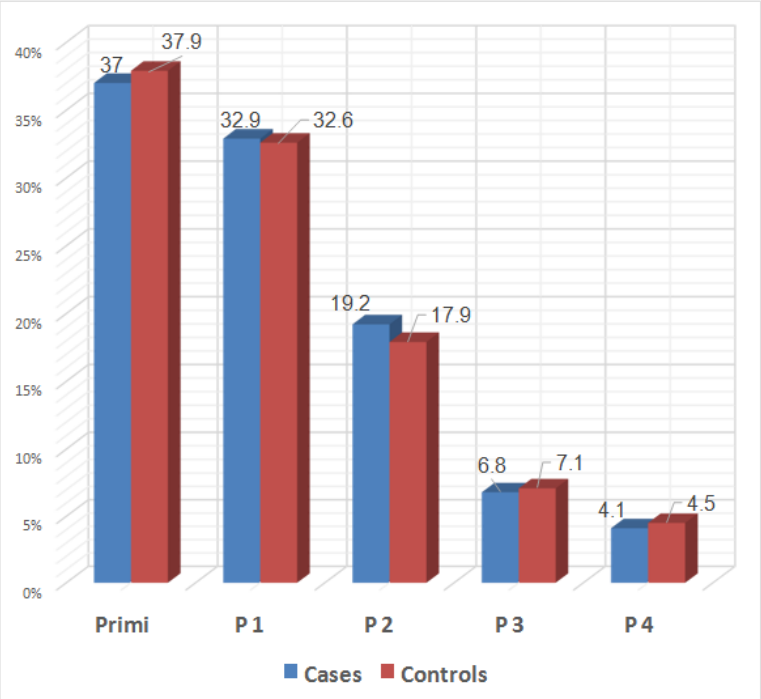

Fig. 1. Bar chart showing percent distribution of parity among cases and controls

Table 4. Severity of thrombocytopenia among cases

	Mild thrombocytopenia	Moderate thrombocytopenia	Severe thrombocytopenia
Number	24 (32.87%)	47 (64.38 %)	2 (2.73 %)
Median (IQR) Platelet count	120000 (9)	96000 (19)	35000 (18)

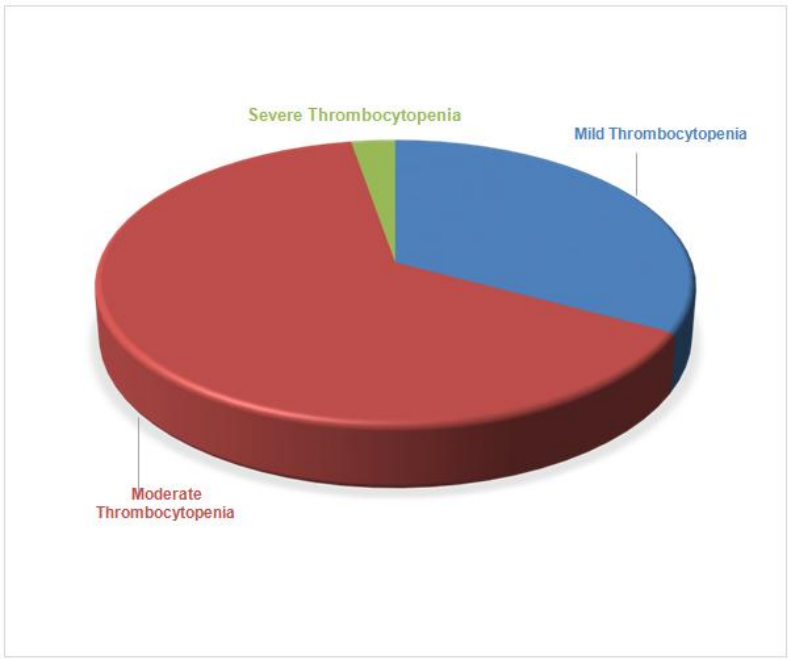

Fig. 2. Pie chart showing severity of thrombocytopenia among cases

Table 5. Characterization of thrombocytopenia

	Gestational thrombocytopenia	Obstetric thrombocytopenia	Medical thrombocytopenia
Number	44 (60.27%)	17 (23.28%)	12 (16.43%)
Median (IQR) Platelet count	109500 (20)	100000 (13)	73000 (19)

Table 6. Severity of thrombocytopenia in various classes of thrombocytopenia

	Mild thrombocytopenia	Moderate thrombocytopenia	Severe thrombocytopenia	Total
Gestational thrombocytopenia	21 (47.7%)	23 (52.3%)	0 (0%)	44
Obstetric thrombocytopenia	3 (17.6%)	13 (76.5%)	1 (5.9%)	17
Medical thrombocytopenia	0 (0%)	11 (91.7%)	1 (8.3%)	12
Total	24	47	2	73

Table 7. Distribution of thrombocytopenia cases

S no	Etiology	No of cases	Percent in TCP cases
1 Gestational thrombocytopenia		44	60.27%
2 Obstetric thrombocytopenia		17	23.28%
	Gestational HTN	4 (23.5%)	5.47%
	Mild PET	4 (23.5%)	5.47%
	Severe PET	7 (41.17%)	9.58%
	Partial HELLP	2 (11.76%)	2.73%
	HELLP	0	
	Eclampsia	0	
	Pre-Ecl+HTN	0	
	Ch HTN	0	
3 Medical		12	16.43%
	ITP	5 (41.66%)	6.84%
	Drugs	1 (8.33%)	1.36%
	AVH	1 (8.33%)	1.36%
	Undetermined	5 (41.66%)	6.84%

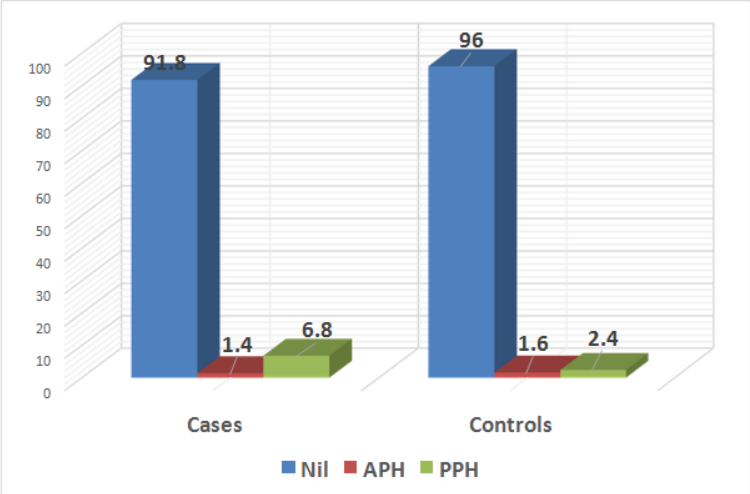

Fig. 3. Bar chart depicting complications in cases and controls

Table 8. Complications in cases and controls

	Nil	APH	PPH	Total	P value
Cases	67 (91.8%)	1 (1.4%)	5 (6.8%)	73	
Controls	677 (96%)	11 (1.6%)	17 (2.4%)	705	
Total	744	12	22	778	0.093

The incidence of complications (APH & PPH) was 8.2% in cases and 3.97% in controls, a difference that was statistically insignificant.

4. DISCUSSION

Thrombocytopenia is a common problem during pregnancy, often under diagnosed and mismanaged. In our study we found the prevalence of thrombocytopenia in pregnancy 9.38%. Boehlen F in their study reported a prevalence of 7-8% of thrombocytopenia in pregnancy, Singh Nisha reported 8.8%, while Burrows reported 7.6% prevalence.

Our study found no influence of age on prevalence of thrombocytopenia in pregnancy similar to Mathews et al and Singh Nisha et al. Further this study found no influence of parity on distribution of cases and controls.

The median platelet count in controls in our study was 178000, and that of cases 100000, these results are consistent with Singh Nisha et al and Boehlen F et al.

In our study there were 60.2% cases of gestational thrombocytopenia, 23.2% cases of obstetric thrombocytopenia and 16% cases of medical thrombocytopenia. Sainio S in his study found 81% cases of gestational, 16% cases of obstetric and 3% cases of medical thrombo-cytopenia. In the study by Myers B there were 75% cases of gestational, 15-20% cases of obstetric and 3-5% cases of medical thrombocytopenia. Federici et al found 74% cases of gestational, 21% cases of obstetric and 4% cases of medical thrombocytopenia. The difference in our study and that in the others is the increased percentage of thrombocytopenia cases due to medical reasons. A possible reason might be a high prevalence of an autosomal dominantly inherited form of IGPD (inherited giant platelet disorder) with mild to severe thrombocytopenia in the Muslim population in Kashmir valley in northern Indian subcontinent as reported by Felipe R, Lorenzo et al in their study.

In our study there were 32.87% cases of mild thrombocytopenia, 64.38% cases of moderate thrombocytopenia and 2.73% cases of severe thrombocytopenia. Karim et al documented severe thrombocytopenia in <0.1%, Singh Nisha et al documented severe thrombocytopenia in 0.64%. Thus our study reports a higher prevalence of severe thrombocytopenia. This difference might be due to the higher incidence of thrombocytopenia due to medical causes in our study and it is the thrombocytopenia due to medical reasons which have been found to be severe in other studies as reported by Singh Nisha et al.

In the study the preterm delivery rate in cases was 11% and in controls was 9.1%, the difference being insignificant. The proportion of vaginal and caesarean delivery among thrombocytopenia cases was similar to overall proportion of hospital statistics.

42.5% of cases in our study had an associated liver function abnormality as compared to 23.4% of controls. This area needs to be studied and investigated further.

The incidence of postpartum haemorrhage was 6.8% in cases, and 2.4% in controls. In the study by Singh Nisha et al the incidence of postpartum haemorrhage among cases was 9.89%.

No maternal and neonatal haemorrhagic complications were seen in new-borns of cases complicated by gestational thrombocytopenia suggesting overall good neonatal outcomes as found in studies by Boehlen F, Mathews J H, Singh Nisha and Burrows R F.

In our study we found favourable for neonates as well as mothers in cases complicated by immune thrombocytopenic purpura. Most other studies have reported a favourable outcome like Ozkan et al, Fujita et al, Gasim. There are few studies report adverse outcomes for mother and baby in cases with immune thrombocytopenic purpura especially when associated with hypertensive disease, diabetes as reported by Belkin et al.

The maternal and neonatal outcomes in cases complicated by obstetric thrombocytopenia which were mostly due to hypertensive causes depended on the severity of preeclampsia, although no haemorrhagic complications in neonates were seen as reported by other studies.

5. CONCLUSION

The prevalence of thrombocytopenia in pregnant Kashmiri females was found to be 9.38%. Most cases were due to the condition labelled as gestational thrombocytopenia, the exact cause of which is unknown. It accounted for 60.2% of cases. Obstetric causes accounted for 23.2% of cases and medical causes accounted for 16% of cases.

No significant increase in maternal complications with regards to thrombocytopenia was found apart from the two cases of severe thrombocytopenia platelet transfusions the delivery. The incidence of postpartum haemorrhage in cases was 6.8% and in controls 2.4%, though the incidence is higher statistically insignificant. One important point concluded from the study was a statistically significant presence of liver function abnormalities in cases (42.5%) than in controls (23.4%). This is an area of further research.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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