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Prospective study of thrombocytopenia in pregnancy

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Abstract

Aim: To study the prevalence, causes, treatment and outcome of thrombocytopenia in pregnancy.

Methods: 15,721 antenatal women were screened for thrombocytopenia using automated blood counter. Women with thrombocytopenia were further evaluated using history, clinical examination & investigations to diagnose the cause of thrombocytopenia. These women were treated appropriately according to the cause and followed up to know the outcome of thrombocytopenia in pregnancy.

Results: Out of 15,721 patients screened, 1,212 patients had thrombocytopenia (7.7%). 949 patients found to have gestational thrombocytopenia accounting for 78.3% of all thrombocytopenic patients. Hypertension complicating pregnancy was the second major cause (15.01%). 1.60% of thrombocytopenic women had ITP. Other causes were fever complicating pregnancy (50 patients), Bone marrow disorders (2 patients), and Jaundice complicating pregnancy (9 cases).

Platelet count normalized within 2 weeks of delivery without treatment in gestational thrombocytopenia patients. All the patients with ITP and Aplastic anaemia responded well to steroids. Patients with fever and liver disease complicating pregnancy were treated supportively. Platelets transfused in all patients with severe thrombocytopenia to avoid hemorrhagic complications during delivery.

Maternal morbidity and mortality was high in hypertension complicating patients. Regarding perinatal outcome only 2 neonates of ITP mothers had platelet count < 50,000/cumm (one delivered by vaginal and other by LSCS) but none of them developed hemorrhagic complications.

Conclusion: Prevalence of thrombocytopenia in pregnancy is 7.7%. Gestational thrombocytopenia is the major cause of thrombocytopenia in pregnancy (78.9%). Platelet count > 1lakh/cumm and without past h/o thrombocytopenia should rise the doubt of Gestational thrombocytopenia. ITP should be considered in patients with past history of low platelets. Caesarean deliveries should be reserved for obstetric indications alone. For gestational thrombocytopenia normalization of platelet count after delivery is necessary.

Keywords: Thrombocytopenia, Pregnancy, Gestational Thrombocytopenia, HELLP, ITP

Introduction

Platelets also called as thrombocytes are formed in the bone marrow by fragmentation of megakaryocytes. The normal concentration of platelet in the blood is 1,50,000 – 4,00,000/ μ L and they usually remain in the peripheral circulation for eight to ten days and eliminated from the circulation by tissue macrophage system.

Platelets play a vital initiating role in the hemostatic system. Hemostasis is usually achieved by several mechanisms ^[1]. Vascular constriction ^[2]. Platelet plug formation ^[3], blood clot formation as a result of blood coagulation, and ^[4] eventual growth of fibrous tissue into the blood clot to close the hole in the vessel permanently.

Primary hemostatic phase begins when platelets attach to the site of endothelial damage and lead to platelet clumping. This is immediately followed by platelet activation and release of granules containing von Willebrand factor, adenosine 5'-diphosphate (ADP), and serotonin. This helps in recruiting other platelets into the growing platelet plug, which acts to stop the bleeding. Simultaneously, the production of thromboxane A₂ and release of serotonin cause vasoconstriction and reduce blood loss at the injured site.

The secondary hemostatic phase starts when the coagulation pathway is activated on the surface of the activated platelets to establish a fibrin meshwork, which helps to reinforce the platelet plug.

Thrombocytopenia is seen in 7-8% of all pregnancies. Thrombocytopenia in pregnancy are easily detected because screening is done as a part of initial clinic evaluation.

Materials and Methods

Study design

Prospective study

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Study setting

Institute of obstetric and gynaecology, Egmore, Chennai.

Period of study

2015-2016 (1 Year)

Study population

All pregnant women admitted in IOG

Sampling technique

Universal sampling, all pregnant women admitted will be included in this study

Methodology

All the antenatal patients who got admitted at institute of obstetrics and gynaecology during the period of 1 year 2015-2016 were included in this study. Platelet count is done to all these pts as a screening procedure. Patients with platelet count less than 1,50,000 were further evaluated in this study to know the causes and to render optimal treatment for better maternal and perinatal outcome.

Results

Total no of antenatal admissions 19462
 Total no of Patients screened 15721
 Total no of patients with thrombocytopenia 1212(7.7%)
 Of the 15721 patients screened 1212 patients found to have thrombocytopenia i.e; platelet count <1,50,000/cumm. They were further categorized into 3 classes depending on the platelet levels
 Mild Cases- 1080(89.1%)
 Moderate Cases- 93(7.6%)
 Severe Cases- 39(3.2%)

Table 1: Causes of thrombocytopenia

Causes	Total	Mild	Moderate	Severe
Gestational Thrombocytopenia	949	949	-	-
HELLP	20	-	7	13
Partial HELLP	162	98	53	11
Fever	50	27	18	5
ITP	20	6	9	5
BM Disorders	2			2
Jaundice Complicating	9		6	3

In my study the commonest cause of thrombocytopenia in pregnancy is gestational thrombocytopenia accounting for 78.3% and the next leading cause is hypertension complicating pregnancy (15.01%)

Table 2: Gestational thrombocytopenia

Total no of cases: 949

Table 2: Gestational age at presentation

	Mild	Moderate	Severe
I Trimester			
II Trimester	41(4.3%)		
III Trimester	908(95.6%)		

All the patients had mild thrombocytopenia at the time of presentation and at the time of delivery.

Gravida

527 patients were primigravida (55.6%) and 422 patients were

multigravida (44.4%)

Treatment

No specific treatment was given. Their platelet count was monitored periodically.

Table 3: Mode of delivery

Vaginal-Spontaneous	395(41.6%)
Vaginal-induced	99(10.4%)
Forceps	11(1.1%)
LSCS	444(46.7%)

Mode of delivery was determined by maternal and obstetric indications alone

Table 4: Perinatal outcome

IUD	3(0.3%)
Term-alive	878(92.5%)
Term-expired	Nil
Preterm-alive	65(6.8%)
Preterm-expired	3(0.3%)
Abortions	Nil

Table 5: Hypertension complicating pregnancy

Total no. of cases: 182

HELLP – 20

Partial HELLP -162

Table 5: Platelet count age

	Mild	Moderate	Severe
<20	4(4.0%)	3(5%)	1(4.1%)
20-24	48(48.0%)	27(45.0%)	11(45.8%)
25-29	32(32.6%)	19(31.6%)	8(33.3%)
30&>	14(14.2%)	11(18.3%)	4(16.6%)

Table 6: Gestational age at presentation

	Mild	Moderate	Severe
I Trimester			
II Trimester	8(8.1%)	7(11.6%)	4(16.6%)
III Trimester	90(91.8%)	53(88.3%)	20(83.3%)

Table 7: Gravida

	Mild	Moderate	Severe
Primi	55(56-1%)	32-3%)	12(50%)
Multi	43(43.8%)	28(46.6%)	12(50%)

Discussion

The purpose of the study is to know the prevalence, causes, treatment and outcome of thrombocytopenia in pregnancy.

This study was conducted in IOG from 2015-2016.

A total of 15,721 antenatal patients were screened of which 1212(7.7%) had thrombocytopenia (i.e; <1,50,000)

They were classified as mild, moderate and severe thrombocytopenia

Mild (1,00,000-1,50,000) - 1080 (89.1%)

Moderate (50,000-1,00,000)- 93 (7.6%)

Severe (<50,000) - 39 (3.2%)

Incidence

Burrow *et al* - 7.6% [5]

Karim R *et al* - 7-10% (27)

Boehlen *et al* - 11.6% (28)

My study - 7.7%

The incidence of my study correlates with the above studies

Causes

The most common cause of thrombocytopenia in my study was gestational thrombocytopenia. Of the 1212 cases with thrombocytopenia 949 patients had thrombocytopenia which was incidentally detected accounting for 78.9% of all thrombocytopenic patients.

Incidence

Burrows *et al* - 78.2% [5]

Susanna *et al* - 81% [8]

My study - 78.3%

My study result is comparable with the above studies

Classification

All the patients with gestational thrombocytopenia came under mild thrombocytopenia According to Jeffrey A. Levy all patients with gestational thrombocytopenia had platelet count above 70,000/cumm.

Age

The peak age incidence was between 20-24 yrs (55.9%)

Treatment

No specific treatment was given for this group of patients. Their platelet count was monitored periodically.

Mode of delivery

Mode of delivery was determined by obstetric/maternal indication.

In my study 505 patients had vaginal delivery (53.2%). Among them 395 patients had spontaneous vaginal delivery (41.6%), 99 patients had induced vaginal delivery (10.4%), 11 patients had forceps delivery (1.1%). Remaining 444 patients had LSCS (46.7%). All were done under spinal anaesthesia.

Marco Ruggeri *et al* 1997;documented in his study that vaginal delivery was carried out in 80% patients and 20% patients underwent caesarean section because of obstetric indication.

The variation in the results between our study and the above study might be due to increased incidence of caesarean section in recent years.

Maternal complications

In our study 8 patients had mild atonic PPH and all were managed medically.

Marco Ruggeri *et al* also reported 2 patients of 41 pregnancies had PPH due to atonicity.

In our study none of the patients had anaesthesia complications which correlates with Rolbin *et al* [10], Beilin *et al* [11] and Rasmus *et al* [12] studies.

Neonatal outcome

In my study out of 949 deliveries there were 946 live births, 3 IUD. Among the 946 live births there were 3 neonatal deaths due to prematurity. All the neonates had platelet count >50.000 and none of the neonates had bleeding complications and my results were comparable with Burrows *et al* [7].

Follow up

All the patients had normal platelet count after delivery (within 2 weeks)

Similarly Burrows *et al* [5] reported that all women with GT had normal or normalizing platelet counts by the seventh postpartum day.

Hypertension complicating pregnancy

The next common cause of thrombocytopenia in pregnancy in my study is hypertension.

Incidence

In my study 182 antenatal patients with thrombocytopenia were complicated with hypertension accounting for 15.01%.

Among them 20 cases had complete HELLP and 162 cases had incomplete HELLP

Susanna *et al* - 16% [6]

Burrows *et al* - 21% [5]

My study - 15.01%

Incidence of my study correlates with Susanna *et al* study between 27-37 weeks which correlates with my study.

Treatment

Inj dexamethasone 10mg 12th hrly was started for all patients with platelet count <1,00,000/cumm. But the efficacy of steroids in improving platelet count could not be assessed because once patients with pre eclampsia found to have low platelets pregnancy was terminated.

Platelet transfusion was given to all patients with severe thrombocytopenia patients to avoid hemorrhagic complications during delivery.

Mode of delivery

LSCS was done in 89 patients (48.9%), 59 cases had spontaneous vaginal delivery (32.4%), 26 cases had induced vaginal delivery (14.2%), 6 had forceps delivery (3.2%) and 2 had hysterotomy (1.0%).

According to Sibai 1999 rate of caesarean section is high with HELLP syndrome especially when pregnancy is less than 34 weeks of gestation (68%). In pregnancies <30 wks caesarean section rate is 87%.

Maternal outcome

Atonic PPH occurred in 13 patients (7.1%), abruption in 5 patients (2.7%), eclampsia in 4 patients (2.1%), DIC in 4 patients (2.1%), ARDS in 1 patient (0.5%) and incisional site oozing in 1 patient (0.5%).

All the 4 cases of DIC occurred in complete HELLP group accounting for 20%.

In a retrospective cohort study by Sibai *et al* 38% of pregnant women with HELLP developed DIC (13%).

Audibert *et al* reported cerebral bleeding in 1.5% (15%).

But in my study and in Sibai *et al* study there were no cerebral bleeding.

In my study there were 7 maternal deaths in hypertension complicating pregnancy giving rise to maternal mortality rate of 3.8%. In Sibai *et al* study maternal mortality was 1.1% (14%).

Perinatal outcome

In my study there were 161 live births (88.4%) and 7 IUDs (3.8%)

There were 11 neonatal deaths of which 10 were preterm babies and 1 term baby (died due to birth asphyxia). None of the neonates had bleeding complications or platelet count <50,000/cumm.

Follow up

Except for 7 patients who died, all the other patients had normalizing platelet count postpartumly (within 2 weeks)

Idiopathic thrombocytopenic purpura

Incidence

In my study a total of 20 cases had ITP (1.6%). All of them were diagnosed before pregnancy.

Susanna salnlo <i>et al</i> ; 2000 -	3% [8]
Gill KK <i>et al</i> ; 2000 -	3% [34]
Burrows <i>et al</i> -	5% [5]
My study -	1.6%

Mode of delivery

According to British committee for standards in haematology the mode of delivery in women with ITP should be decided primarily by obstetric indications. There is no evidence to support the routine use of caesarean section.

In my study 12 patients (60%) delivered vaginally and 7 patients delivered by LSCS (35%) and suction evacuation was done for 1 patient for missed abortion. All caesarean sections were done for obstetric indications and the patients who were taken for caesarean section had platelet count of >80,000/cumm as advised by BCSH.

None of the neonates delivered by vaginal route had intracranial haemorrhage.

Maternal outcome

In my study none of the patients had GDM/bone loss due to corticosteroid therapy and none had anaesthesia related complications. 1 patient had ecchymoses who recovered with platelet transfusion. None had major hemorrhagic complications. Our goal to maintain maternal platelets >50,000 has resulted in minimal bleeding complications.

Perinatal outcome

Kelton JG [7] found that 5% of infants of ITP patients have severe thrombocytopenia and 1% have significant bleeding complications.

In my study out of 19 deliveries 17 neonates had platelet count >50,000/cumm and 2 had platelet count <50,000 (10.5%) but none developed hemorrhagic complications.

Follow up

2 weeks after delivery 17 patients found to have platelet count <1,50,000/cumm. Of which 12 patients had mild, 5 patients had moderate thrombocytopenia and none had severe thrombocytopenia

Other Causes

Fever Complicating Pregnancy

In my study 50 patients had fever with thrombocytopenia accounting for 4.1%. Of which 13 patients had malaria (26%), 10 patients had dengue (20%), 2 patients had swine flu (4.0%), 5 patients had typhoid (10%), 6 patients had leptospirosis (12%), 2 patients had intra uterine sepsis (4.0%), 2 patients had urinary tract infection (4.0%) and 10 patients had fever of unknown origin (20%).

All these patients were treated with appropriate antibiotics and supportive therapy. Steroids withheld in these patients in view of exacerbation of infections.

Panpanich R *et al* in his study also stated that corticosteroids are no more effective than placebo for reducing no of deaths/need for blood transfusion (46).

Maternal outcome

Among the 50 patients 1 patient died of dengue hemorrhagic shock, 2 patients had atonic PPH and they were treated with

uterotonics and blood transfusion.

Perinatal outcome

There were 2 IUDs and 2 neonatal deaths

Follow up

All patients had normalizing platelet count with specific treatment except for 1 patient who died of dengue.

Liver Disease Complicating Pregnancy

A total of 9 patients with thrombocytopenia had liver disease (0.7%). Of which 3 patients had chronic liver disease with portal hypertension and splenomegaly and 6 patients had viral Hepatitis (4 patients had Hepatitis B, 1 had Hepatitis C and 1 had Hepatitis A).

In this group 1 patient developed oozing from surgical site which was treated by platelet transfusion and 1 patient had atonic PPH managed medically. A total of 3 patients received platelet transfusion at the time of delivery to avoid hemorrhagic complications. Steroids were avoided in these patients.

Rajan S *et al* also stated that use of steroids can exacerbate the viral infection and also stated that use of interferon alpha in treatment of HCV associated thrombocytopenia is controversial (48).

During follow up patients with viral hepatitis had normalizing platelet count with recovery of hepatitis but those patients with splenomegaly had persistent thrombocytopenia and they were referred to MGE for further management.

Bone Marrow Disorders

2 Patients had bone marrow disorders of which 1 had aplastic anaemia and 1 had Myelofibrosis.

Aplastic anaemia patient was treated with steroids and platelet transfusion and she responded well to steroids.

IMF patient was treated with blood and platelet transfusion. No specific treatment strategy exist for Idiopathic myelofibrosis. Anaemia can be corrected with recombinant erythropoietin and packed cell transfusion. Erythropoietin may worsen splenomegaly and will be ineffective if the serum erythropoietin level is >125mU/L. Erythropoietin was not given to this patient as it may worsen splenomegaly. After delivery both the patients were referred to hematology department

The prevalence of thrombocytopenia in pregnancy was studied in all antenatal patients admitted in Institute of Obstetrics and Gynaecology from 2015-2016. This study was intended to analyse the cause, treatment and outcome of thrombocytopenia in pregnancy.

The prevalence of thrombocytopenia in pregnancy was 7.7%. Major cause of thrombocytopenia was Gestational thrombocytopenia accounting for 78.9% of all thrombocytopenic patients. Other causes were hypertension complicating (15.01%), ITP (1.6%), others (5.0%).

No specific treatment was given to gestational thrombocytopenia patients. Periodic monitoring of platelet count was done and platelet count normalized within 2 weeks of delivery. Steroids were given to moderate and severe group of hypertension complicating pregnancy, in all patients with ITP and aplastic anaemia. All the patients with ITP and Aplastic anaemia responded well to steroids. Patients with fever were treated with antipyretics and anti-infective therapy. Jaundice complicating patients were treated supportively. Steroids were withheld in patients with fever and hepatitis in view of exacerbation of infection. Platelets transfused in all patients with severe thrombocytopenia to avoid hemorrhagic complications during

delivery.

Maternal morbidity and mortality was high in hypertension complicating patients. Regarding perinatal outcome only 2 neonates of ITP mothers had platelet count < 50,000/cumm (one delivered by vaginal and other by LSCS) but none of them developed hemorrhagic complications.

Conclusion

Prevalence of thrombocytopenia in pregnancy is 7.7%

Gestational thrombocytopenia is a major cause of thrombocytopenia in pregnancy (78.9%) but other underlying causes must be considered as well.

A detailed history and physical examination is mandatory to rule out most other causes.

A thorough study of CBC and smear should be done to r/o pancytopenia and platelet clumping associated with pseudo thrombocytopenia.

Platelet count > 1lakh/cumm and no past h/o thrombocytopenia the condition is likely to be Gestational thrombocytopenia.

Previous h/o thrombocytopenia should rise the doubt of ITP

Caesarean deliveries should be reserved for obstetric indications alone because vaginal delivery itself has not been demonstrated to be a cause of ICH.

For gestational thrombocytopenia normalization of platelet count after delivery is necessary.

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