"PROSPECTIVE STUDY OF THROMBOCYTOPENIA IN PREGNANCY AND ITS MATERNAL AND NEONATAL OUTCOME"

By

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DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA IN PARTIAL

FULFILLMENT OF THE REQUIREMENTS FOR THE

DEGREE OF

MASTER OF SURGERY

IN

OBSTETRICS AND GYNAECOLOGY

Under the Guidance of

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SRI DEVARAJ URS MEDICAL COLLEGE

TAMAKA, KOLAR 563101

MAY 2022

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ACKNOWLEDGEMENT

First and foremost I thank my **"Almighty God"** for giving me his endless blessings and giving me the strength both mentally and physically during my post graduation and to make this dissertation book possible.

I would like to acknowledge all those who have supported me, not only to complete my dissertation, but helped throughout my post graduation course.

I wish to express my heart full indebtedness and owe a deep sense of gratitude to my mentor and guide, **Dr. MUNIKRISHNA.M** Professor, Department of Obstetrics and Gynecology, for being very helpful throughout the study and offered her invaluable guidance and support to fully understand and complete this study. Through her vast professional knowledge and expertise, he ensured that I understand everything before I apply the information in my study. Without him constant supervision and advice, completion of this dissertation would have been impossible.

I am sincerely thankful to **Dr. RATHANAMMA .P** Associate Professor & HOD, Dept. of OBG, SDUMC, Kolar. Without her constant encouragement this study would not have been possible. Her precious advice on both the dissertation as well as the path of my career has been priceless.

I am thankful to **Dr.SHEELA S.R**, Professor of Obstetrics and Gynecology, for encouraging me to the highest peak, paying close and continuous attention towards me to finish all tasks and also providing her kind support, valuable suggestions, immense patience and great care.

I wholeheartedly acknowledge **Dr. VASANTHA KUMAR** professors in the department of Obstetrics and Gynecology, for their valuable teachings of perseverance, professional ethics moral support and commitment.

I sincerely thank all the associate professors, assistant professors & senior residents, Department of OBG, SDUMC, Kolar, for their constant guidance and encouragement

I express my sincere thanks to my colleague and friend**, Dr .Deeksha Rao , juniors Dr. Pratyusha, Dr Nandhini, Dr. Komal** for their co- operation and help in carrying out this study.

I express my profound gratitude to my beloved PARENTS **Sri. KANIKI REDDY .M** and **Smt. VIJAYA LAKSHMI** for giving me continuous encouragement, unfailing support and unconditional love throughout my life. Also, my gratitude goes to my sisters **PRABHA , GOURI** and my special thanks to my husband **Dr. VANKATA RAMA REDDY** for his unconditional patience and support.

Last but not the least, I extend my gratitude towards all the patients who agreed to participate in this study, without their precious support it would not be possible to conduct this research.

Dr.SUDHA MALLIDI

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LIST OF ABBREVIATIONS

GLOSSARY	ABBREVIATIONS
ADAMTS13	A disintegrin and metalloproteinase with thrombospondin motifs 13
AFLP	Acute Fatty Liver of Pregnancy
aHUS	Atypical HUS
APS	Antiphospholipid antibody syndrome
APTT	Activated partial thromboplastin time
CAMT	Congenital amegakaryocytic thrombocytopenia
CBC	Complete blood count
COVID 19	Coronavirus 19
DF	Dengue fever
DIC	Disseminated intravascular coagulation
DITP	Drug-induced immune thrombocytopenia
EDTA	Ethylenediaminetetraacetic acid
FDP	Fibrin degradation products
FTLS	Familial thrombocytopenia-leukemia syndrome
GT	Gestational thrombocytopenia
HBsAg	Hepatitis B surface antigen
HELLP	Hemolysis, elevated liver enzymes and low platelet count
HIT	Heparin-induced thrombocytopenia
HIV	Human immunodeficiency virus
HUS	Haemolytic uremic syndrome
ICH	Intra cerebral haemorrhage

ICU	Intensive care unit
ITP	Idiopathic thrombocytopenic purpura
IUFD	Intrauterine fetal demise
IUGR	Intrauterine growth restriction
LDH	Lactate dehydrogenase
LFT	Liver function tests
NICU	Neonatal intensive care unit
PNH	Paroxysmal nocturnal haemoglobinuria
PT	Prothrombin time
RBC	Red blood cells
RFT	Renal function tests
SGOT	Serum glutamic-oxaloacetic transaminase
SGPT	Serum glutamic-pyruvic transaminase
TAR	Thrombocytopenia-absent radii syndrome
TMA	Thrombotic microangiopathy
TTP	Thrombotic thrombocytopenic purpura
VCF	Velocardiofacial syndrome
VDRL	Venereal disease research laboratory test
WAS	Wiskott-Aldrich syndrome
WBC	White blood cells

ABSTRACT

Introduction: Thrombocytopenia is the most frequent hematological condition observed during pregnancy. Evidence has shown foetus and maternal outcomes of thrombocytopenia during pregnancy that aren't good. This study aimed to find the causes and maternal, neonatal outcomes in pregnant with thrombocytopenia.

Materials and methods: The present study is a prospective observational study that included antenatal cases with gestational age more than or equal to 28 weeks with low platelet count. Pregnant women with ages between completed 18-40 are included. Patients included in the study followed up by estimation of platelet count till 5th postpartum day. Outcomes including mode of delivery, gestational age at the time of delivery, the need of blood and blood components transfusion, ICU admissions, neonatal thrombocytopenia were documented. P-value < 0.05 will be considered statistically significant.

Results: A total of 95 subjects were analyzed. The majority of the subjects were in the age group of 21-25 years, followed by 26-30years. In the present study shows the majority of them had mild thrombocytopenia. Among the study participants, the most common aeitology was gestational thrombocytopenia followed pre-eclampsia – eclampsia. 27.37% required blood and blood products transfusion. The majority of the neonates had a healthy birth weight of 2.50 to 3.49kg in 54.74%. The maternal complication recorded in the present study is Postpartum Hemorrhage in 9.47%, abruption in 5.2%, ICU Admission for 2.11%, and DIC in 2.11% of participants. 2.11% of the neonates found to have neonatal thrombocytopenia. There was a statistically significant difference was observed in maternal thrombocytopenia between transfusion (P-Value >0.05).

Conclusion: In the present study the most common cause of thrombocytopenia in pregnancy is gestational thrombocytopenia followed by less common causes were preeclampsia, HELLP Syndrome ,anemia, COVID -19, dengue fever and megaloblastic anemia .

Pre eclampsia and HELLP syndrome were associated with post partum hemorrhage with abruptio placenta, DIC, need of transfusion of blood and blood products, ICU admission and intrauterine death in this study .

It is crucial to evaluate thrombocytopenia in pregnancy to distinguish between gestational thrombocytopenia and other serious conditions like pre eclampsia, HELLP syndrome, ITP, infections which have the potential for serious morbidity and mortality.

Management of pregnant women with thrombocytopenia requires a multidisciplinary approach and with close collaboration between obstetrician and hematologist required to reduce the maternal and fetal mortality and morbidity.

Key words: thrombocytopenia, neonate, maternal, pregnancy

INTRODUCTION

INTRODUCTION:

Thrombocytopenia refers to abnormally low levels of circulating platelets.[1] Thrombocytopenia is a frequent haematological ailment after anaemia that occurs during pregnancy. Thrombocytopenia can be classified as mild with a platelet count of 100–150x 10^9/l, moderate at 50–100 x 10^9/l, and severe < 50 x 10^9/l.[2] It can account for about 7to 10% of gestation. During the normal gestation, there is a functional decline of platelets because of dilution of blood, a greater requirement in the peripheral tissues, and greater accretion ("increased thromboxane A2 levels"). Functional and biological thrombocytopenia in gestation is usually mild and is found to have no serious complications to the fetus and mother. The underlying medical complication with thrombocytopenia have feto-maternal complications and thus needs monitoring and timely management.[3]

The majority of the pregnant females with thrombocytopenia are well-to-do and have no symptoms with no prior history of thrombocytopenia and are usually diagnosed while routine screening. This type of thrombocytopenia is known as gestational thrombocytopenia (GT), with no least impact on delivery, perinatal, and pregnancy.[4] There are many causes for low platelet count in pregnancy, but gestational thrombocytopenia (GT) is the most frequent cause.[5] Other related aetiology includes preeclampsia, HELLP syndrome, acute fatty liver of gestation, and hemolysis.[6] Additionally, immune etiology such as primary immune thrombocytopenia lupus erythematosus, and antiphospholipid syndrome in 3-4%, malignancies and infections accounts only for 1 to 2%.[7]

The main contending diagnosis to GT idiopathic thrombocytopenic purpura (ITP). Favouring diagnosis for ITP includes pre-pregnancy thrombocytopenia and response to immunomodulators and steroids. However, there has not been laboratory evaluation to

discriminate among the 2 conditions. ITP accounts for about 2% of subjects with thrombocytopenic pregnancy. ITP found in 5% of thrombocytopenic pregnancy is categorized by a moderate to severe decline in the platelet count because of autoantibodies to the platelet.[8,9]

ITP subjects with severe thrombocytopenia often need immediate attention due to the high risk of haemorrhage in mothers and new-borns. Preeclampsia and HELLP syndrome are the 2nd most common aetiology of thrombocytopenia in the late 2^{nd} and 3^{rd} trimester accounts for 21%.[10] This is defined by a hypertension blood pressure greater than 140/90mmHg, proteinuria greater than 0.3g in one day(24hrs).[11] Further coagulation abnormalities in pregnancy are uncommon, and it is represented with a platelet count greater than100×10^9 / L. It is can cause placental abruption leading to maternal and neonatal death.[12] Acute Fatty Liver of Pregnancy (AFLP) is a condition present with serious complications during the 3^{rd} trimester of gestation affecting one in 20,000 pregnant women. The diagnosis of this condition includes the rise of liver enzymes, coagulopathy, and greater than 5mg/dl of conjugated bilirubin.[13]

NEED OF THE STUDY:

As thrombocytopenia is the condition observed during pregnancy after anaemia, its prevalence in India is least studied. Few Indian studies,[3,7] have shown maternal thrombocytopenia to have an adverse effect on the feto-maternal outcome and have explained that complications depend on the disease-causing it. However, few studies,[10,14] found favourable feto-maternal outcomes among thrombocytopenic pregnant subjects. As a result, the current research attempted to access the etiology and feto-maternal outcome among thrombocytopenia pregnant women.

AIMS & OBJECTIVES

AIM AND OBJECTIVES:

OBJECTIVES:

1. To evaluate the causes of thrombocytopenia in pregnant women.
2. To assess the maternal and neonatal outcome in pregnant women with thrombocytopenia.

REVIEW OF LITERATURE

REVIEW OF LITERATURE:

"Thrombocytopenia is a condition of low platelet count less than 150000/microliter in adults". Platelets are one of the blood components that aid in the assistance of blood thickening and wound repair complications related to thrombocytopenia can be with no peril for bleeding or thrombosis. The relationship of the seriousness of thrombocytopenia and the possibility of bleeding is unpredictable. Spontaneous bleeding can occur if platelet count under 10000/microliter and bleeding of surgical sites with counts under 50000/microlitre.

Thrombocytopenia is related with the peril of thrombosis in conditions like antiphospholipid antibody syndrome (APS), heparin-induced thrombocytopenia (HIT), thrombotic microangiopathy (TMA), "Disseminated intravascular coagulation (DIC)" and paroxysmal nocturnal haemoglobinuria (PNH).[15]

Special attention should be given to a condition known as "Pseudo thrombocytopenia." Thrombocytopenia can occur as acquired and hereditary. However, acquired is most common as the population ages. Based on the platelet count thrombocytopenia is considered with 3 types: "Mild: 100,000 - 150,000/microliter, Moderate: 50,000 - 100,000/microlitre. Severe: <50,000/microlitre". Bleeding intraabdominally and intracranially are the severe complications of severe thrombocytopenia. Hence, early diagnosis can reduce fatality. Need transfusion of platelets depends on the severity of thrombocytopenia. The reasons for the prevalence of thrombocytopenia vary due to geographic region, ethnicity, and underlying causes.[16]

Epidemiology:

The systematic meta-analysis by Mohseni, M et al.[17] showing thrombocytopenia among pregnant women, was 8.4%, and the common etiology for thrombocytopenia was gestational thrombocytopenia. The lowest and highest incidence rate of thrombocytopenia noted was 4.3%, 15.3%, respectively. Pregnant women having hypertensive disorders observed a prevalence of 23.5% of thrombocytopenia.[18] In addition, pregnant women on drug abuse(cocaine) observed a prevalence of 6.7% of thrombocytopenia.[19]

The most common cause of Thrombocytopenia in the meta-analysis was GT reported in 95% of the study population.[20] The pathophysiology of GT is unknown; nevertheless, it is expected that its cause may be the high consumption of platelets during pregnancy or increased plasma volume due to pregnancy.[21] GT is usually benign, asymptomatic, and mild with no prior history of thrombocytopenia apart from in previous pregnancies. The onset of thrombocytopenia is normally at the last trimester of pregnancy and is not linked with neonatal thrombocytopenia.[22]

Pathophysiology:

There is 3 major pathophysiological process involved in thrombocytopenia:

1. Rapid demolishing,
2. Reduced producing, and
3. Sequestration.

Secondary thrombocytopenia can be noticed as a consequence of catching platelets that are growing in the spleen and identifying aberrant platelets. In various scenarios, such as sepsis, preeclampsia, and immune thrombocytopenia, there is a particularly high rate of platelet

deterioration, the average number of platelet is high, and diseases such as aplastic anaemia, in which platelet production decreases.[16]

Classification of Thrombocytopenia:[16]

1. Artificial thrombocytopenia

- pseudo thrombocytopenia
- Platelet satellism
- Giant platelets

2. Decreased production of thrombocytes

- Megakaryocyte hypoplasia or suppression
- Ineffective thrombopoiesis
- Defeat in the mechanism which is controlling thrombopoiesis
- Hereditary thrombocytopenia

3. Increased platelet destruction

- Immunological
- Autoimmune -Primary (Immune thrombocytopenia) - Secondary (pregnancy, infections, drugs)
- Alloimmune-Post-transfusion purpura -Neonatal thrombocytopenia Nonimmunologic -Thrombotic micro angiopathies -DIC -TTP – HUS

4. Abnormal platelet distribution."

a. The disease that captures spleen (congestive, neoplasia, infiltration)

b. Hypothermia

DIAGNOSTIC ASSESSMENT OF THROMBOCYTOPENIA IN PREGNANCY:

1) History

A complete history can lead to clues for causes for thrombocytopenia and aid in diagnosis. Important points to be noted are:

Positive family history of thrombocytopenia (history of recent vaccinations, infections viral or bacterial history of the disease[23], cancer the likelihood of pregnancy; new travels (e.g., contact to rickettsiosis, malaria, or dengue fever); current transfusions; alcohol consumption; eating habits; and risk factors for viral hepatitis and HIV.[24,25]

Note on the medications consumed by subjects, particularly in those who started one to two previously to the onset of thrombocytopenia.

Physical examination:

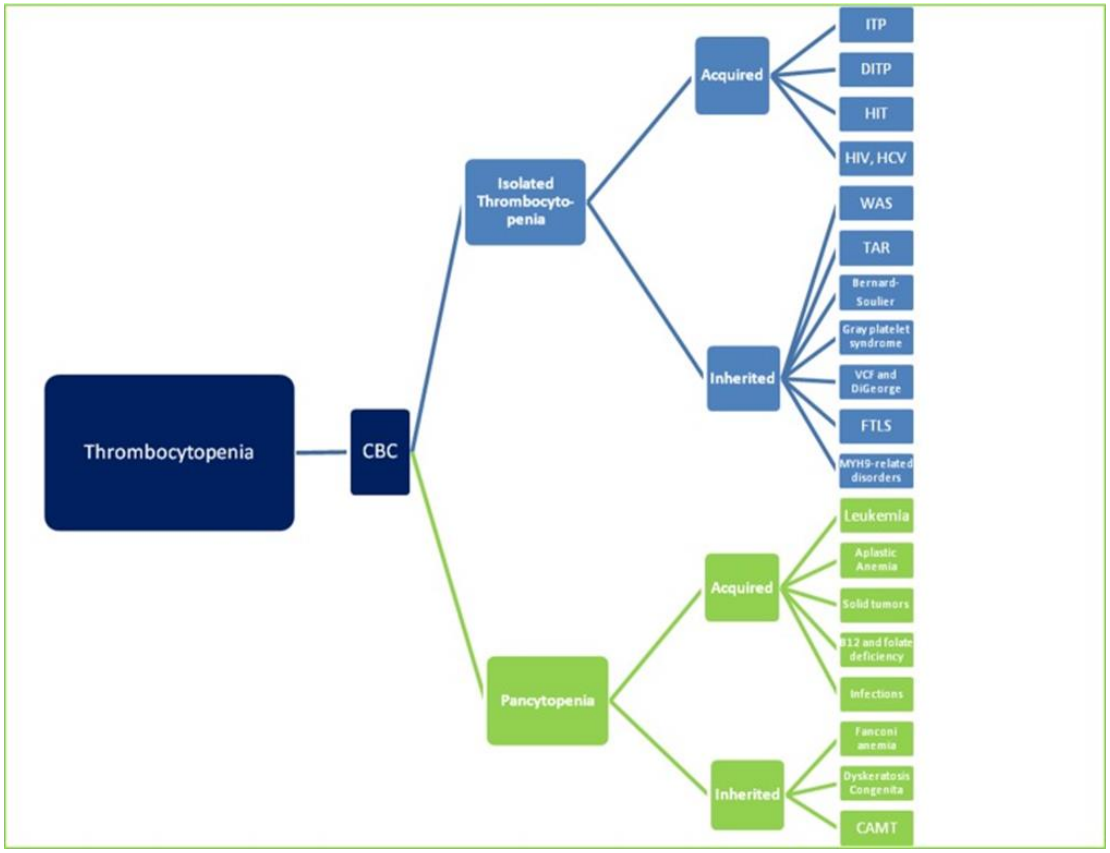
First, a general physical examination involving inspection, palpation, and auscultation could provide details regarding the patient's overall health, such as the presence of comorbidities.[26]

Bleeding: Some patients, regardless of origin, have a tendency to bleed. Petechiae, purpura, and ecchymoses are common in people with platelet counts are lower than 20 $x10^9$/L. Platelet-related bleeding is marked by Petechiae.[26] Check for blood pressure (preeclampsia) and for abdominal tenderness (HELLP syndrome).

Complete blood count (CBC):

Isolated thrombocytopenia is commonly associated with immune-mediated disorders (e.g., ITP, DITP) and hereditary disorders (e.g., Bernard-Soulier syndrome, TAR syndrome); however, it is uncommon in bone marrow cancers.

Figure 1: "Thrombocytopenia": "diagnostic algorithm starting with the complete blood count (CBC)" Abbreviations: "CAMT, congenital amegakaryocytic thrombocytopenia; CBC, complete blood count; DITP, drug-induced immune thrombocytopenia; FTLS, familial thrombocytopenia-leukemia syndrome; HIT, heparin-induced thrombocytopenia; HIV, human immunodeficiency virus; HCV, hepatitis C virus; ITP, immune thrombocytopenia; TAR, thrombocytopenia-absent radii syndrome; VCF, velocardiofacial syndrome; WAS, Wiskott-Aldrich syndrome." "Blood smear"



Blood smear

The blood smear can be used to know the type of thrombocytopenia that cannot be overstated. First and foremost, pseudo thrombocytopenia should be ruled out. Second, blood cell morphology should be thoroughly studied in situations of genuine thrombocytopenia.[27]

Table 1: "Morphologic aspects of the peripheral blood smear in diagnosis of thrombocytopenia."[28]

Platelets
Platelet clumping
Platelet clumping caused by EDTA-dependent platelet autoantibodies is a common cause of artifactual thrombocytopenia. It occurs in about 1 in 1000 normal adults and is not associated with bleeding or thrombosis.
Platelet size and granularity
Consistently large platelets suggest hereditary macrothrombocytopenia. Large platelets with a gray color on Wright-Giemsa stain define the gray platelet syndrome, an autosomal-dominant macrothrombocytopenia associated with bleeding tendency due to absent or greatly reduced α-granules.
In thrombocytopenia due to peripheral destruction, large platelets or giant platelets are often seen in addition to platelets of normal size.
When thrombocytopenia is due to reduced platelet production (eg, after chemotherapy), platelets are of normal size. In myelodysplastic syndromes, platelets have variable size (giant platelets may be seen) and are frequently hypogranular. In Wiskott-Aldrich syndrome, and X-linked thrombocytopenia, both caused by mutations of the WAS gene, platelets are small.
WBCs
Leukemic cells
Malignant hematological disorders (leukemias and lymphomas) are often associated with thrombocytopenia, which is almost never an isolated finding.
Other abnormalities of WBCs, including leukocyte inclusions
A constellation of nonspecific abnormalities of WBCs are common to many conditions (eg, neutrophilia, lymphocytosis, leukopenia, etc) and may be associated with thrombocytopenia. The presence of hypolobulated neutrophils (Pelger-Huët anomaly) suggests a myelodysplastic syndrome. Dark coarse granules (toxic granulations) found in neutrophils suggest sepsis. Atypical lymphocytes suggest viral infection. The presence of WBC inclusions ((Döhle-like bodies)) should be investigated carefully when platelets are mostly large (MYH9-related congenital macrothrombocytopenia).
RBCs
Schistocytes
The presence of RBC fragments known as schistocytes is indicative of a thrombotic microangiopathy (TTP/HUS) or DIC.
Size and other morphological features
Microspherocytes may suggest Evans syndrome, but may also be present along with shistocytes in thrombotic microangiopathies. Macrocytosis (and hypersegmentation of neutrophils) suggest vitamin B12 or folate deficiency. Dacryocytes (teardrop-shaped cells) suggest myelofibrosis. Nucleated RBCs suggest hemolytic anemia, myelofibrosis, or an infiltrative process of the BM.
Parasites
The presence of intracellular parasites (eg, in malaria) is diagnostic of infection.

A review of WBC and RBC morphology may suggest a specific condition.[15]

- Schistocytes are a feature in thrombotic microangiopathic conditions.
- Teardrop cells, nucleated RBCs, leucoerythroblastic findings suggest the bone marrow infiltrative process.
- Immature WBCs suggest leukemia.
- Megaloblastic process characterized by hyper segmented neutrophils seen in nutritional deficiencies. [29,30]

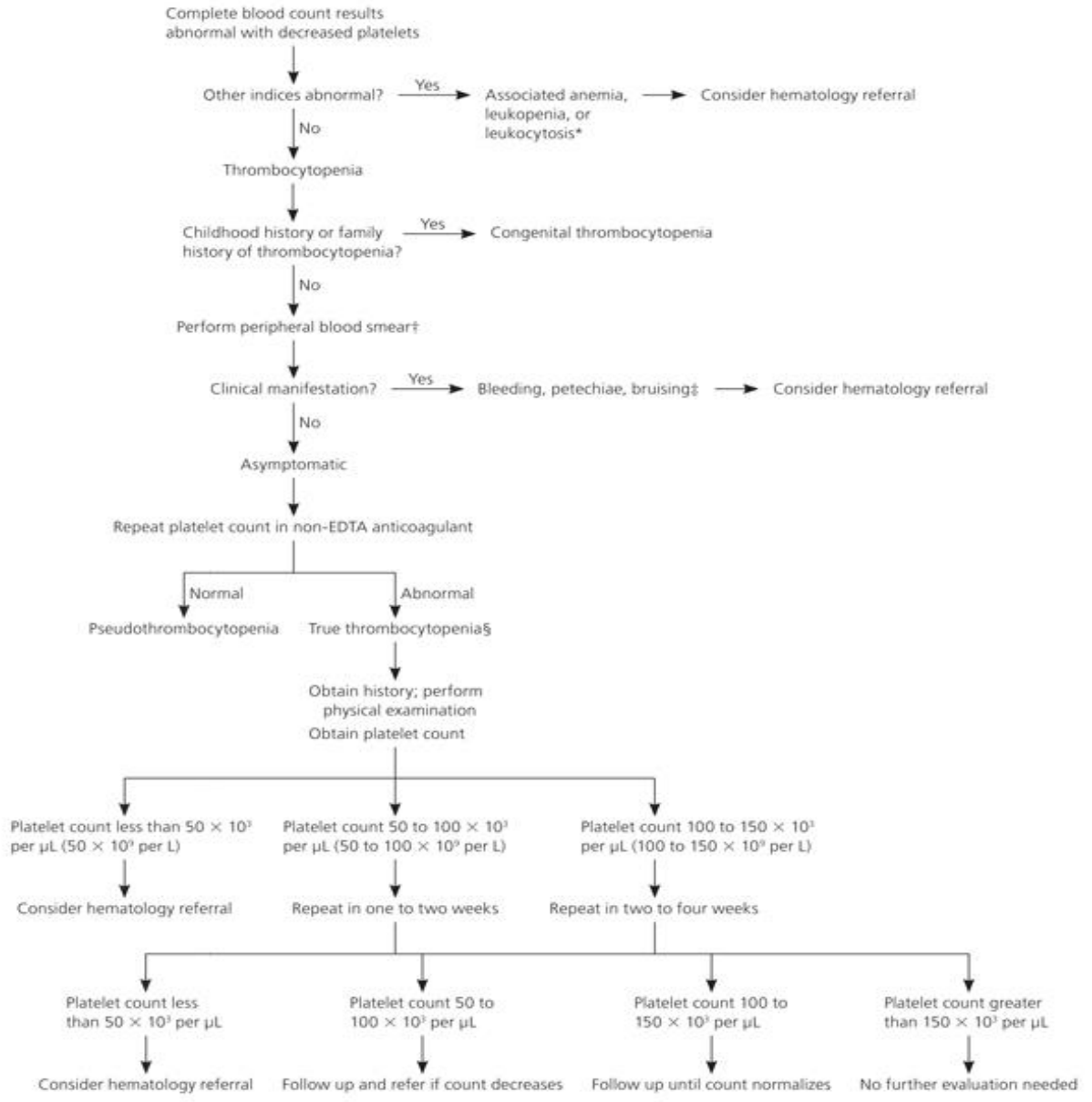
Supplementary investigations:

DIC is characterized by a prolonged prothrombin time (PT), reduced fibrinogen, and high D-dimers in blood coagulation assays.

LDH, and alkaline phosphatase, liver function tests (HELLP syndrome).

Serological testing for viruses, blood cultures, anti-platelet antibodies, bone marrow biopsy, and a variety of other diagnostic tests can all be done at the doctor's discretion based on the symptoms and history of the disease.

Figure 2: "Algorithm of treatment of thrombocytopenia. (DIC = disseminated intravascular coagulation; EDTA = ethylenediaminetetraacetic acid; HELLP and low platelet count; HUS = haemolytic uremic syndrome; ITP = immune thrombocytopenic purpura; TTP = thrombotic thrombocytopenic purpura."[31]



*—Bone marrow suppression, hematologic or infiltrative malignancy, TTP/HUS, liver disease, DIC, viral/rickettsial infection, nutritional deficiency, preeclampsia/HELLP syndrome (in pregnancy).

†—Giant platelets suggest congenital thrombocytopenia. Clumping is seen in pseudothrombocytopenia. Fragmented red blood cells suggest microangiopathic hemolytic anemia (TTP/HUS, DIC).

‡—ITP, TTP/HUS, heparin-induced thrombocytopenia if exposed, hypersplenism, viral/rickettsial infection, DIC, mechanical destruction, preeclampsia/HELLP syndrome (in pregnancy).

§—ITP, heparin-induced thrombocytopenia if exposed, drug-induced thrombocytopenia, hypersplenism, viral/rickettsial infection, mechanical destruction, gestational thrombocytopenia (in pregnancy).

Psuedo thrombocytopenia:

Invitro platelet clumping results from ethylenediaminetetracetic acid (EDTA) dependent agglutinins, inadequately anticoagulated specimen, glycoprotein IIb/IIIa inhibitors. Giant platelets are counted as white blood cells rather than platelets by an automated counter.[15]

Thrombocytopenia in pregnancy:

Gestational thrombocytopenia (GT) affects 4.4 percent to 11.6 percent of pregnancies, accounting for around 75 percent of all instances of thrombocytopenia in pregnancy. Platelet clearance as a function of mean platelet volumes platelet.[32,33] There is no absolute platelet value below gestational thrombocytopenia may be excluded. Most experts consider other diagnosis if the value of platelets dips below 70 X 10^9 /L. The main differential diagnosis at this level or lower is ITP. However, there have been reports of more severe thrombocytopenia that is non-responsive to steroids and which resolved postnatally, consistent with gestational thrombocytopenia. It is not possible to differentiate between gestational thrombocytopenia and ITP, as both are diagnoses of exclusion. Gestational thrombocytopenia is otherwise asymptomatic, with no history of ITP or other autoimmune disorders. The degree of thrombocytopenia is not severe enough to increase the risk of bleeding at delivery but may compromise the ability to receive epidural anaesthesia. General physical examination does not reveal hypertension or findings associated with other causes of pregnancy-associated thrombocytopenia. Serological tests like antinuclear antibodies and antiphospholipid antibodies are usually negative.

Practical points to underline from the standpoint of the haematology consultant include:

1. Mild to moderate thrombocytopenia (>70 x 109/L).
2. Asymptomatic with no history of abnormal bleeding.

3. No history of thrombocytopenia outside pregnancies.
4. Occurs in mid-trimester or third trimester.
5. No fetal or neonatal thrombocytopenia.
6. Complete postpartum resolution.
7. Recur in subsequent pregnancies.
8. Detected on routine prenatal screening with no specific diagnostic tests.

Table 2: "Displaying the clinical presentation of gestational thrombocytopenia."[34,35]

Table 2. Characteristics of gestational thrombocytopenia (GE) [18,19,20,21,22]

Characteristics of GE
No specific diagnostic test - the diagnosis is made by excluding other causes;
Usually mild thrombocytopenia, platelet counts above 70 G/l;
Usually no bleeding in the mother;
No thrombocytopenia in history taken before pregnancy;
Usually occurs in the middle of the second trimester or in the third trimester of pregnancy;
Is not associated with a reduced platelets count in the newborn;
Relieves spontaneously after birth (in 1-2 months);
May recur in subsequent pregnancies.

"IMMUNE THROMBOCYTOPENIC PURPURA"

After gestational thrombocytopenia, another important cause of thrombocytopenia is ITP. It is hard to distinguish this type of thrombocytopenia from gestational thrombocytopenia.[36]

ITP affects one in every 1000 to 10,000 pregnancies. ITP is not a contraindication to pregnancy in and of itself. Specific investigations are not there to differentiate between ITP and GT, thrombocytopenia s. ITP is a diagnosis of exclusion based on history. When a woman is otherwise healthy (save for bleeding), ITP should be investigated.[8]

If ITP is suspected, regular follow-up (every 1-3 weeks) is necessary, depending on the count and the expected delivery date. Treatment for ITP is only required in the first and second trimesters if the patient is symptomatic; if a procedure is required, such as an amniocentesis, platelet count dips below 20 $X10^9$/L. The patient is asymptomatic therapy may be needed only for epidural anaesthesia or Caesarean delivery. Low-dose prednisone (10-20 mg/day) or intravenous immunoglobulin (or both) are viable choices. In symptomatic pregnant ITP patients (e.g., if there is bleeding), other therapy options are available. Steroids at high doses, especially in combination with other drugs, can be utilized.[37] Many other ITP treatments are not safe to use during pregnancy because they have the potential to cause teratogenic effects.

Management:

When it comes to platelet counts below 20 $x10^9$/L to 30 $x10^9$/L, treatment is started for bleeding, procedures, delivery; risk of haemorrhage with platelet count is below 20 $x10^9$/L to 30x 10^9/L for a vaginal delivery or below 50 $x10^9$/L for a caesarean section.[38] Hematomas during neuraxial anaesthesia are extremely uncommon in individuals with stable ITP. who do not have coagulopathy or have been exposed to an antithrombotic drug such as low-molecular-weight heparin.[39] In unstable patients, platelet counts should be tested regularly at 32-34 weeks repeated weekly.[40,41]

Obstetrical concerns should guide the mode of delivery. Instrumental deliveries are avoided despite the low risk of severe haemorrhagic complications. The rate of intra cerebral haemorrhage (ICH) in neonates is less than one percent.[33,39]

Preeclampsia /Eclampsia:

Preeclampsia with concomitant thrombocytopenia less commonly seen during the first week after delivery, while even later appearances have been observed. Thrombocytopenia affects around half of all women with Preeclampsia, with platelet counts often exceeding 100x 10^9/L and seldom falling below 50 X10^9/L unless there are additional problems.[42] Thrombocytopenia is a rare complication that occurs before other symptoms.

Diagnosis:

Preeclampsia is hypertension that appears after 20 weeks of pregnancy. Preeclampsia can also occur in women who already have high blood pressure. HELLP is a Preeclampsia subtype. Although overt clinical disseminated intravascular coagulation (DIC) is uncommon, biochemical alterations consistent with DIC can be found in up to 10% of women and serve as a predictor of disease development.[43]

Criteria:

Preeclampsia is defined as increased blood pressure after the 20th week of pregnancy, with one or more severe characteristics:

1) "Thrombocytopenia" (less than 100 × 10^9/L).
2) Deranged liver function tests.
3) Deranged renal function test.
4) Newly developed visual or cerebral disturbances.
5) Consistent systolic /diastolic BP of 160 mm Hg or 110 mm Hg.

Management:

The distinction between Preeclampsia, HELLP syndrome, TTP and HUS, is crucial because delivery is the only therapeutic option. Some studies showing that corticosteroids can prevent maternal haemorrhage or other morbidity.[44] Depending on the mother's clinical status, expectant management may be appropriate for certain women who are 34 weeks pregnant. Women who are managed expectantly, probability of rapid and severe disease progression, including DIC with associated haemorrhage. Clinically, most women improve quickly after delivery, while laboratory parameters may take longer. Patients not improving is necessary to assess for TTP or HUS.

Attentions for successive pregnancies:

Based on multiple factors, including the number of past afflicted pregnancies, the prevalence of chronic hypertension, predicted recurrence chances in a subsequent pregnancy range from 5% to 94 percent.[43] In low-dose aspirin (60-150 mg per day) is started at 12 to 16 weeks gestation.

"Thrombotic thrombocytopenic purpura."

The incidence of the anti-body induced TTP is about 1 in 20,000, according to serological evidence.[45,46] Most of them appear during pregnancy, generally the first pregnancy[46], or postpartum.[45] This propensity could be due to the natural decrease in ADAMTS13 and increase in von Willebrand factor during pregnancy.

Diagnosis:

Because early detection and treatment can minimize maternal mortality by 80 percent to 90 percent, prompt diagnosis is critical. It is most commonly seen in the second trimester.[47] With

no previous history appearing in the first trimester with thrombocytopenia, neurological problems, with renal dysfunction, and few more pointing towards TTP after ruling out of preeclampsia.[48]

A decrease in the platelets less than $20x\ 10^9/L$, with renal dysfunction (creatinine > 2.2 mg/dL), with neurological impairment will help in the diagnosis of TTP from atypical HUS (aHUS).[49]

Management:

Plasmapheresis is the treatment of choice for TTP, and corticosteroids can be used. Evidence is showing no improvement even after termination of pregnancy. Some studies showing patients not responding to plasmapheresis can be started on rituximab, azathioprine. Use of factor VIII preparation, recombinant ADAMTS13, low-dose aspirin, and low-molecular-weight heparin could be used.

DENGUE IN PREGNANCY:

Dengue fever (DF) is a febrile disease found in the tropics and is endemic in more than 100 countries. Dengue is the fastest-spreading infection and remains a major health concern with cyclic epidemics. Management of dengue infection in pregnancy should be taken seriously to reduce morbidity, mortality in the mother as well as the foetus.[50]

Symptoms of dengue in pregnant women are the same as non-pregnant; some important symptoms include:[50]

- Pyrexia with body pains.
- Pain abdomen.

- Nausea and vomiting.
- Bleeding from the gums.
- Rashes on body.
- Fluid in the pleural cavity and.
- Fetal death.
- Liver dysfunction (high SGOT/SGPT)- to be distinguished from HELLP Syndrome.

Fetomaternal Complications:

- Maternal complications include Miscarriages, Premature labor, still birth, Hemorrhage during labor, Retroplacental hematoma
- Fetal complications, Prematurity, Low birth weight/intrauterine growth retardation, Fetal death in utero, Acute fetal distress during labor, Maternal-fetal transmission.

Management:

In most cases, dengue fever in pregnancy is managed conservatively. The platelet count may drop rapidly, but unless the patient is in labor or has a bleeding condition, no active intervention is required. Fresh blood or packed cells should be supplied to compensate for losses in the case of postpartum hemorrhage. Intramuscular injections should be avoided if at all possible. Close monitoring is need for pregnant women with dengue fever. A repeat CBC can be done after 24 hours if the platelets continue to fall or the hematocrit continues to rise, indicating that the patient's condition is deteriorating.[51]

COVID 19 in pregnancy:

Pregnant women are more suspectable to COVID 19 infection compared to the general population.[52]

COVID infection aggravated when associated with conditions like:

- Increased blood pressure
- Gestational diabetes
- Bronchial asthma
- HIV infection
- Cardiac diseases
- Patients on drugs causing immunosuppression

Presentation in pregnant women remain same as general population like:[52]

- Pyrexia
- Cough
- Breathlessness
- Diarrhea.
- Body pains.

COVID 19 infection mimic preeclampsia-like symptoms and can lead to mild to severe thrombocytopenia.

Mild infections in the first and second trimesters are treated by symptomatic management by antipyretic hydration. The third trimester with mild infection is managed by decision for delivery individualized on the obstetric indication.

Intrapartum management depends upon the maternal gestational age, fetal condition, and severity of the condition, multi-disciplinary approach by obstetrician, neonatologist, the physician is required in the treatment of COVID 19 infection.

A study by Maraskolhe, D et al 2021 aimed to find the various causes related and the outcome of thrombocytopenia in pregnancy. They involved 130 subjects, of which 107(17.69%) reported severe thrombocytopenia and 23 subjects (82.3%) with moderate thrombocytopenia. About 2.8% p regnant people are effected. The most frequent cause for thrombocytopenia was GT was in 42%, followed by eclampsia in 25.5% and infections. The majority of the cases reported (63.7%) were in the gestation period ≥36 weeks. The neonatal mortality was 7.69%. The findings of this study hence suggested that thrombocytopenia incidence in pregnancy was low[14].

An observational prospective study by Singh, J et al 2020 involved 263 subjects, of which 90 females recorded thrombocytopenia, remaining recorded normal platelet count. The prevalence of thrombocytopenia among the study subjects was 34%. GT is the most common cause (50%), followed by eclampsia in 22.4% and ITP in 11.11%, and infection in 5.5%[53].

A prospective study by Misra, D et al 2020 aimed to assess pregnant subjects with low platelet count on clinical, etiology, and outcome of thrombocytopenic subjects. This study included 280 pregnant subjects, and they were all checked for thrombocytopenia post 28 weeks. This study included a control group with a platelet count under normal limits and cases with a platelet count below 150×109/L. Nearly 70.71% of women with GT had mild thrombocytopenia, and haemorrhagic complications were found in 30.72%. 27.14% found to have PPH followed by placental abruption in 5%, perineural sepsis in 9.28%, need for transfusion in 20%, neonatal thrombocytopenia in 12.14%, neonatal jaundice in 20%, NICU

admission in 12.14%, birth asphyxia in 12.86%, low Apgar score in 37.14% and nee for revival was in 30%. The study results found more maternal and perinatal complications such as C section, NICU admission, low Apgar score, neonatal mortality, and ICH in cases than the controls[54].

A prospective study by Godara, D et al 2020 included a total of 2750 subjects, of which 100 were discovered to have thrombocytopenia. The frequent cause was GT in 66%. The complications seen in maternal were PPH in 9%, placental abruption in 5%, wound hematoma in 1%, whole blood transfusion in 26%, transfusion of FFP in 10%, transfusion of platelet in 23%, ICU admission in 7%, and episiotomy hematoma in 5%. Complications in fetal recorded NICU admission in 21%, Apgar score at 5min with <7 scores were 43%, Apgar score at 1 min score less than 7 were 59%, IUFD in 2%, IUGR in 4% and neonatal thrombocytopenia in 1%[3].

A prospective study by Zutshi, Vet al 2019 found an incidence of gestational thrombocytopenia to be 12.82%. They found a favourable feto-maternal outcome. Only 2.5% found to have abruption and haemorrhage in 3.5%, blood transfusion was required in 6.5%, with no mortality recorded among mothers Nearly 3% of the neonates found to have thrombocytopenia irrespective of the severity of thrombocytopenia. The perinatal complications included NICU admission in 13% and needed a mechanical ventilator for 5.5% with mortality recorded. [2]

A retrospective study by Kapadia S et al 2018 involved 120 expecting women regardless of their gestational age. The most prevalent reason is for thrombocytopenia was gestational thrombocytopenia. This condition had shown to resolve over time. [55]

A study by Anita H et al 2018 aimed in order to determine the prevalence and etiology of thrombocytopenia among normal pregnant females. This study included 76 expecting women regardless of gestational age. The study findings found GT (70%) to be the most frequent cause. They had found no prior history of thrombocytopenia, and the previous history of thrombocytopenia would be a case of ITP. These cases should be followed by for one to two months. GT has shown to revive after a few days of delivery. [6]

A cross-sectional study by Bai, P et al 2018 aimed to assess the causes of low platelet count during pregnancy. They involved a total of 87 subjects with an average age of 26.91±5.28 years. The main reason of thrombocytopenia was GT in 57.5%, pre-eclampsia, and eclampsia in 16.1%each, DIC in 3.4%, ITP in 3.3%, and HELLP syndrome in 12%. Postpartum bleeding was observed in the majority at 41.3% as a maternal outcome, followed by antepartum bleeding at 16%, and mortality was found in 8%. The majority of the neonates were delivered in term 77%, and preterm was seen in 22.9%. The proportion of alive neonates were 77.1%, IUGR was 6.9%, and IUD in 16%.[21]

A study by Vishwekar P et al 2017 aimed to assess the etiology of maternal thrombocytopenia along with outcomes on maternal and neonates in an uncomplicated pregnancy. This study included 1460 expecting females. They found the most common cause is GT (68.46%), followed by severe preeclampsia in 18.46% and HELLP syndrome in 7.69%. This study found placental abruption and haemorrhage at postpartum. The fetal outcome was most severe in the thrombocytopenic group. This study results found minimal feto and maternal complications among the study population. [10]

A prospective study by Arora, M et al. 2017 aimed to determine the frequency of thrombocytopenia in expecting mothers. This study included 1450 pregnant women and found 137 females to have thrombocytopenia in their 3rd trimester.GT was the most common cause for the prevalence, followed by severe eclampsia and HELLP syndrome among the prevalent population. The fetal outcomes included still birth, low Apgar score, low birth weight, and neonatal thrombocytopenia. [7]

A prospective study by Suresh U et al 2016 included 160 subjects with moderate to severe thrombocytopenia from 2 years. They found the greatest proportion of thrombocytopenia in the 21 to 25 years of age group. This study found GT as the most frequent cause, followed by severe eclampsia and infections. The neonatal outcomes include stillborn IUGR, especially in eclampsia subjects. This study found a significant association of neonatal outcomes in subjects with severe thrombocytopenia. [56]

An observational study by Dwivedi, P et al 2012 aimed to find the maternal and fetal outcomes among pregnant with severe thrombocytopenia. This study included 1150 women and found the prevalence of thrombocytopenia to be 8.17%. The maternal complications included prolonged bleeding from the wound site and menorrhagia. This study found low feto-maternal complications in thrombocytopenia subjects; however, severe cases need to be surveyed carefully. [57]

LACUNAE OF LITERATURE:

As already known, thrombocytopenia is the second most prevalent condition during pregnancy. There have been numerous Indian and global studies which have estimated the prevalence of thrombocytopenia among pregnant women. These studies are observational hospital-based studies with a small sample size limiting the results to be generalized. Hence there is a need for more large studies including different parts of the globe, assessing the etiology and feto-maternal outcomes among thrombocytopenic pregnant women. Identifying thrombocytopenia in medically compromised conditions present during pregnancy should be researched as there are increased complications among them. There is also a scarcity of studies into the effects of different health conditions on Thrombocytopenia.

MATERIALS & METHODS

MATERIALS AND METHODS

SOURCES OF DATA: The main source of data for the study are pregnant women visiting admitted in the Obstetrics and Gynecology department of R.L Jalappa Hospital during the period of study

Study design: A prospective observational study.

Sample size: 95

The sample size is estimated based on the prevalence of thrombocytopenia (6.6%-11.6%) of pregnant women according to a study by Zutshi V, Gupta N, Arora R, Dhanker S.[2] Prevalence of gestational thrombocytopenia and its effects on maternal and fetal outcome. Iraqi J Hematol2019:8:21-4.

The sample size came to be around 95 by utilizing the above formula at prevalence 6.6%, q is (100 - p), 5% absolute precision.

$$n = \frac{Z_{\alpha}^{2} * p * q}{d^{2}}$$

P is the estimate of expected proportion with the valuable of interest in the population (literature review or pilot study)

D is the margin of error (Absolute precision)

Z α is the standard normal variable at the desired level of confidence (usually 95% confidence level)

Study period: JAN 2020- JUNE 2021

Inclusion Criteria:

1. Antenatal cases with gestational age more than or equal to 28 weeks with thrombocytopenia.
2. Antenatal women with age between completed 18-40 years.

Exclusion Criteria:

1. Patients on medications such as quinine, furosemide, aspirin, captopril, digoxin, phenytoin which are to known to cause thrombocytopenia.

METHOD OF COLLECTION OF DATA:

Patient attending antenatal clinic and admitted in the department, Blood from the patient collected under aseptic condition using vacutainer system from ante cubital vein in EDTA tube.

Platelet count assessed by using automated blood count analyzer; Platelet count less than 150 $x10^9$/l will be taken as cut off.

Detailed history, presenting complaints if any, findings of general, systemic, and obstetrical examination including pelvic examination recorded in the proforma after taking consent.

Baseline investigations like complete hemogram, urine analysis, HIV, HBsAg, VDRL serology, special investigation like PT, APTT, FDP, Fibrinogen) RFT and LFT were done if clinically indicated.

All the cases were followed till delivery to record any maternal complications like postpartum hemorrhage, abruption, puerperal infection, and any other morbidity.

Duration of pregnancy at the time of delivery, mode of delivery, including indication for cesarean section, were recorded. Progress of labor was monitored by using a partograph, and fetal condition was monitored using a cardiotocograph.

Blood sample from all neonates is collected and seen for thrombocytopenia.

Estimation of platelet count done on 5th postpartum day in all study subjects.

Appropriate statistical methods were used to analyze the data.

STATISTICAL METHODS:

Alive/IUD, Birth weight(kg), APGAR at 1'min& 5'min, Foetal outcome, NICU admission, neonatal thrombocytopenia, and maternal complications were considered as primary outcome variables. Thrombocytopenia was considered a secondary outcome variable.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Non-normally distributed quantitative variables were summarized by the median and interquartile range (IQR). Data was also represented using appropriate diagrams like bar diagrams, pie diagrams.

All Quantitative variables were checked for normal distribution within each category of an explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro- Wilk test was also conducted to assess normal distribution. Shapiro Wilk test p-value of >0.05 was considered as a normal distribution.

For normally distributed Quantitative parameters, the mean values were compared between study groups using an independent sample t-test (2 groups). Categorical outcomes were compared between study groups using the Chi-square test.

P-value < 0.05 was considered statistically significant. SPSS was used for statistical analysis

OBSERVATIONS AND RESULTS

RESULTS

A total of 95 subjects were included in the final analysis.

Table 3: Descriptive analysis of Age group in the study population (N=95)

Age group (years)	Frequency	Percentage
19-20	11	11.58%
21 to 25	51	53.68%
26 to 30	24	25.26%
>30	9	9.47%

Out of total 95 study population, the age group was 19-20 years for 11 (11.58%) participants, 21 to 25 years for 51 (53.68%) participants, 26 to 30 years for 24 (25.26%) participants and >30 years for 9 (9.47%) participants. (Table 3 & Figure 3)

Figure 3: Bar chart of age group in the study population (N=95)

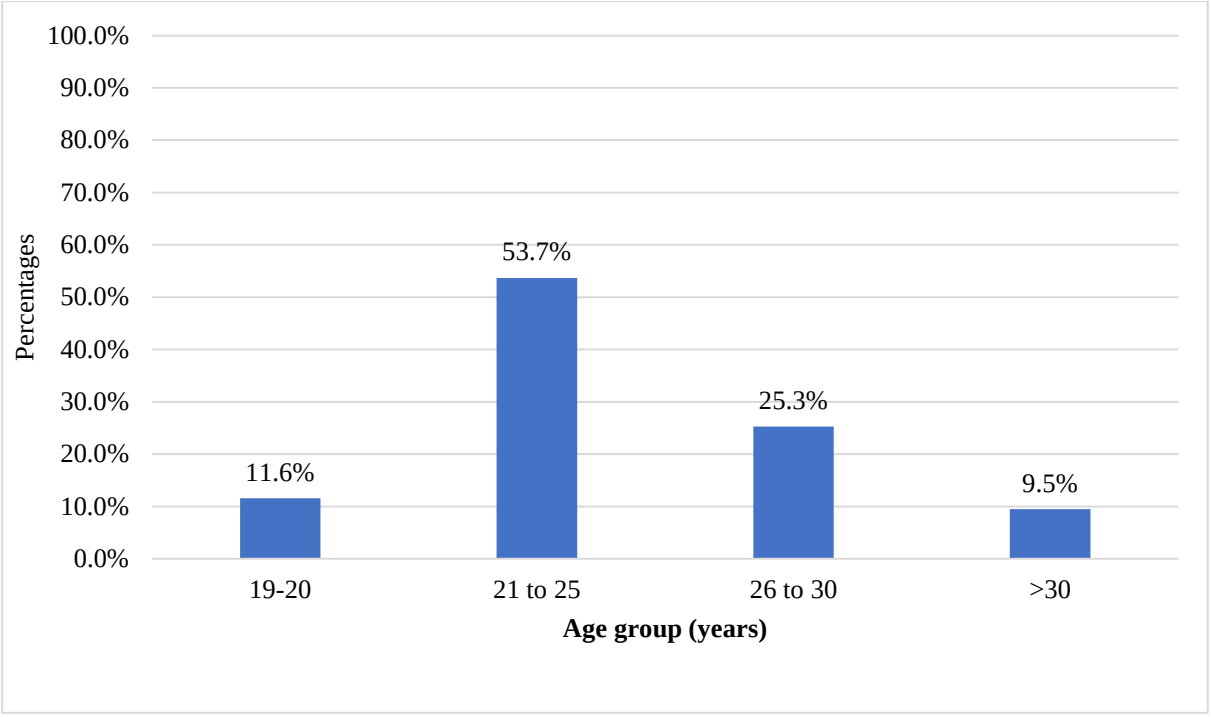


Table 4: Descriptive analysis of Parity status in the study population (N=95)

Parity status	Frequency	Percentage
Primi gravida	41	43.16%
Gravida 2	33	34.74%
Gravida 3	15	15.79%
Gravida 4	6	6.32%

Out of the total 95 study population, Primi gravida were 41 (43.16%) participants and women with Gravida 2 are 33 (34.74%) participants, Gravida 3 were 15 (15.79%) participants and Gravida 4 were 6 (6.32%) participants. (Table 4 & Figure 4)

Figure 4: Pie chart of Parity status in the study population (N=95)

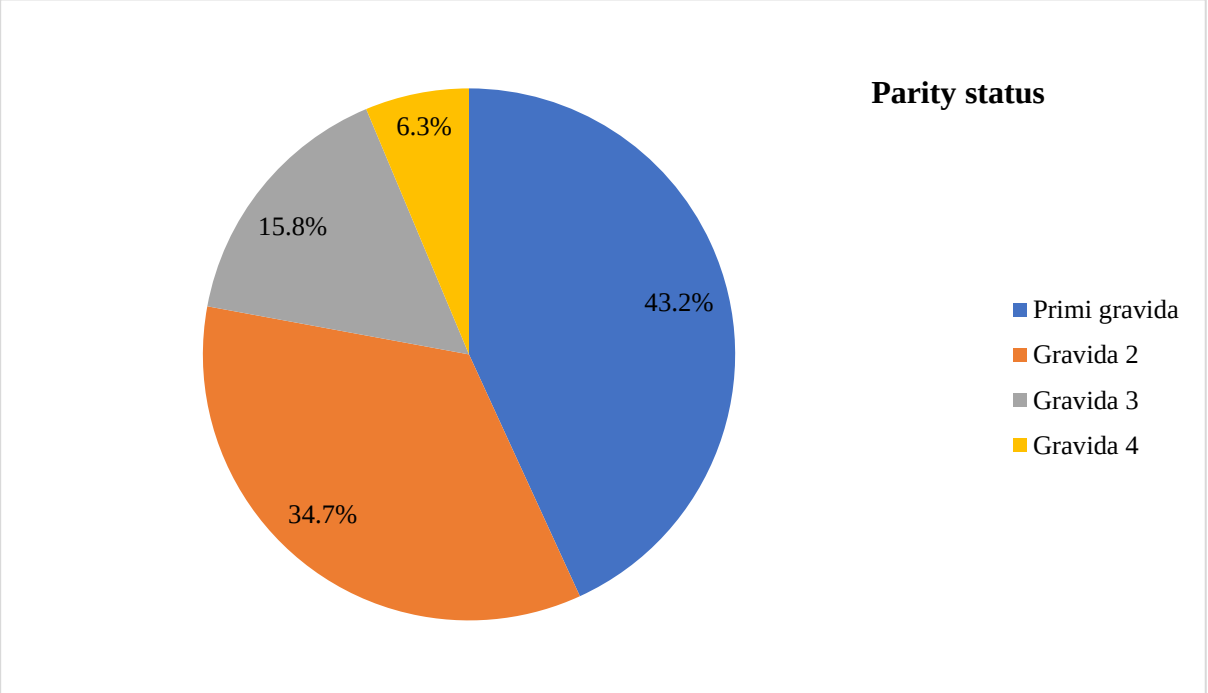


Table 5: Descriptive analysis of Gestational age in the study population (N=95)

Gestational age (weeks)	Frequency	Percentage
28 to 31 $^{+6}$ weeks	4	4.21%
32 to 36^{+6} weeks	16	16.84%
37 weeks to 40 weeks	75	78.95%

Out of the total 95 study population, the gestational age was 28 to 31 $^{+6}$ weeks for 4 (4.21%) participants, 32 to 36^{+6} weeks for 16 (16.84%) participants and 37 weeks to 40 weeks for 75 (78.95%) participants. (Table 5 & Figure 5)

Figure 5: Pie chart of Gestational age in the study population (N=95)

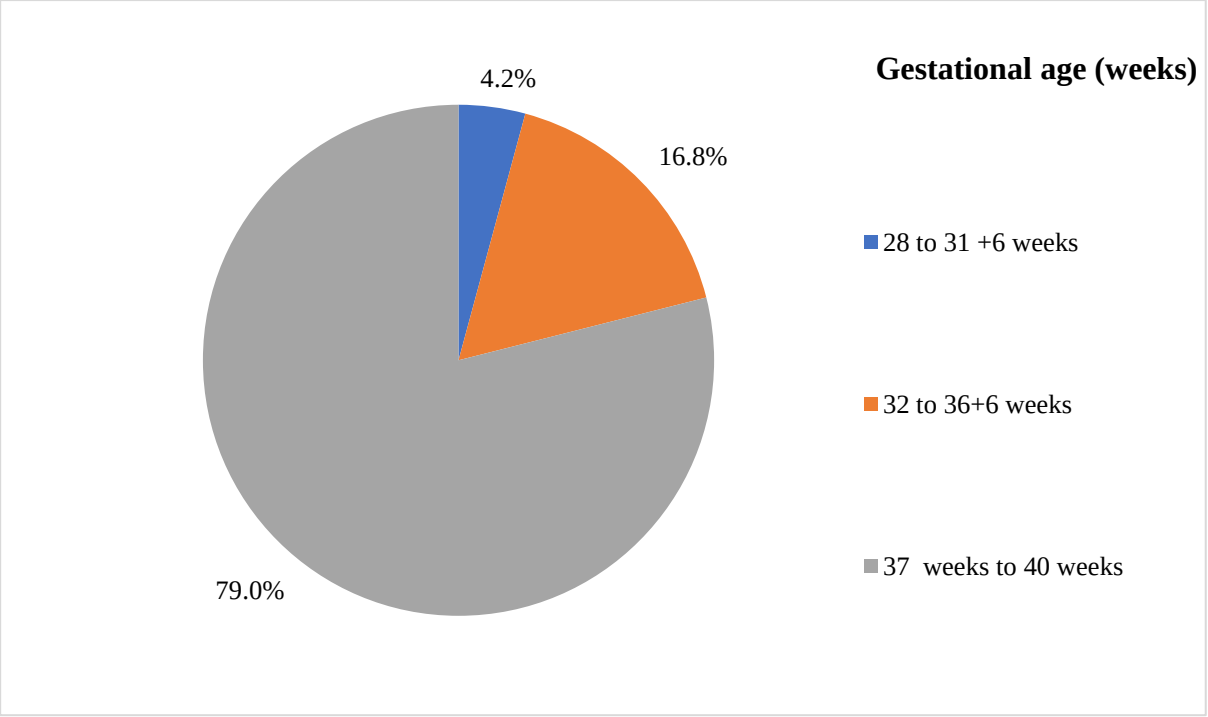


Table 6: Descriptive analysis of Thrombocytopenia in the study population (N=95)

Thrombocytopenia	Frequency	Percentage
Mild	51	53.68%
Moderate	37	38.95%
Severe	7	7.37%

Out of the total 95 study population, the thrombocytopenia was mild for 51 (53.68%) participants, moderate for 37 (38.95%) participants and severe for 7 (7.37%) participants. (Table 6 & Figure 6)

Figure 6: Pie chart of Thrombocytopenia in the study population (N=95)

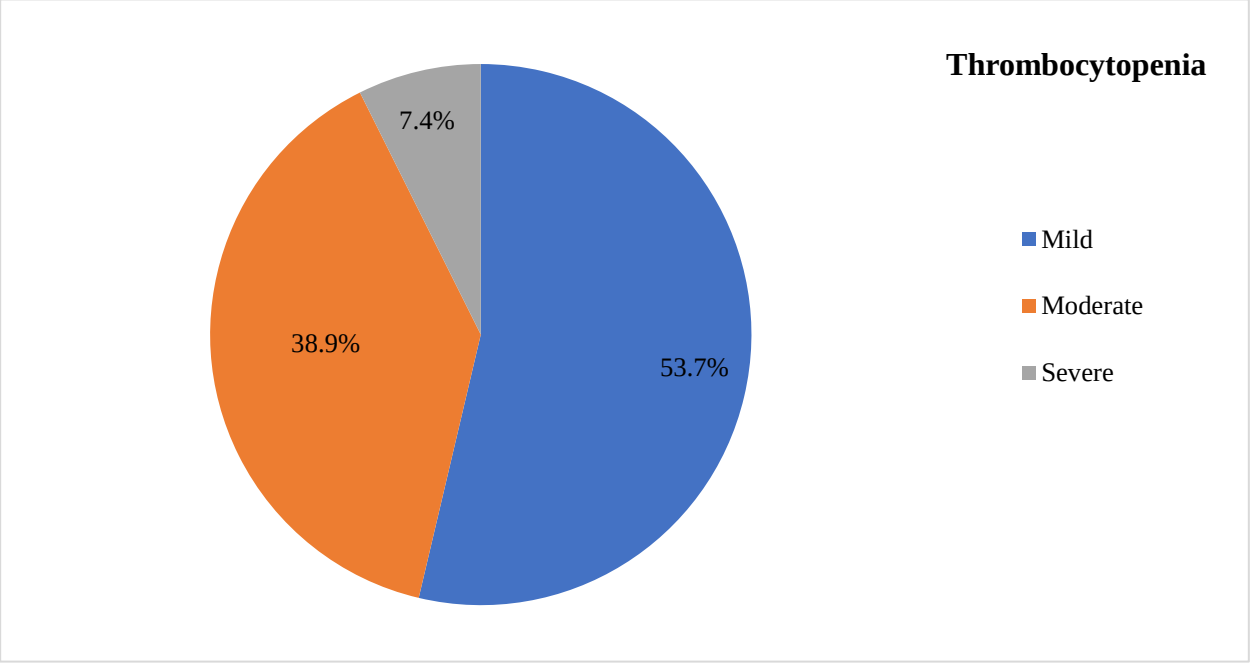


Table 7: Descriptive analysis of Aetiology of Thrombocytopenia in the study population (N=95)

Aetiology of Thrombocytopenia	Frequency	Percentage
Gestational thrombocytopenia	49	51.5%
Pre-eclampsia – eclampsia	36	37.8%
Anaemia	5	5.26%
COVID -19	2	2.11%
Dengue fever	2	2.11%
Megaloblastic anaemia	1	1.05%

Out of the total 95 study population, the aetiology was Gestational thrombocytopenia for 49 (51.5%) participants, pre-eclampsia- eclampsia for 36(37.8%) participants, anaemia for 5(5.26%) ,COVID-19 for 2 (2.11%) participants , Dengue fever for 2 (2.11%) participants, Megaloblastic anaemia for 1(1.05%) (Table 7 & Figure 7)

Figure 7: Bar chart of Aetiology of thrombocytopenia in the study population (N=95)

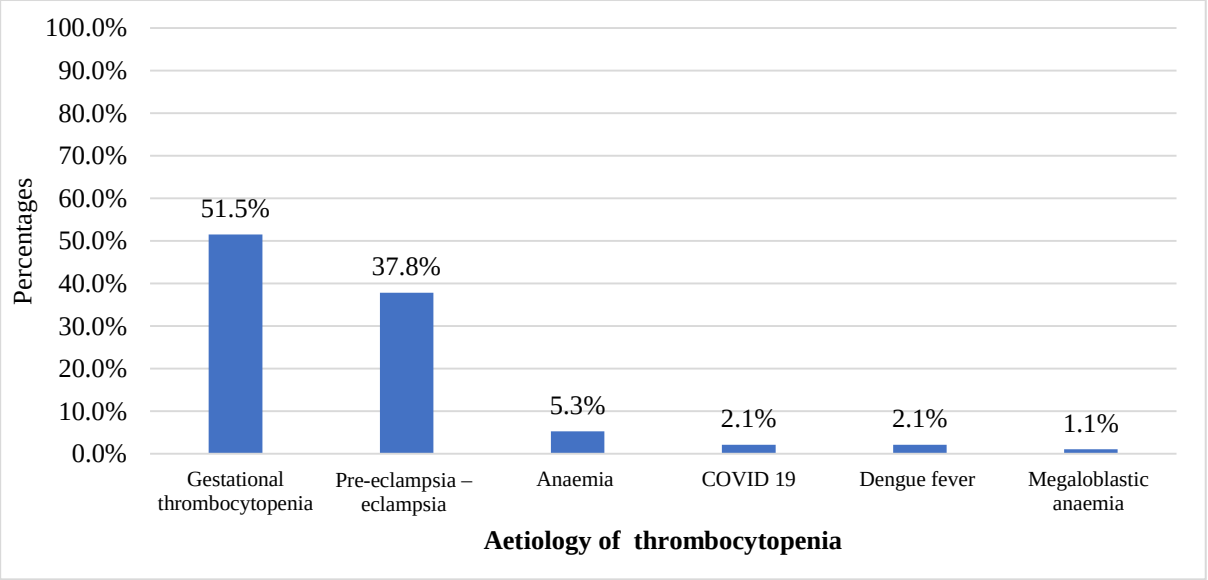


Table 8: Distribution of study of subjects-based on severity of Preeclampsia-eclampsia (N=36)

Severity of Preeclampsia - eclampsia	Frequency	Percentage
HELLP syndrome	14	38.3%
Eclampsia	12	33.3%
Severe preeclampsia	5	13.8%
Non severe preeclampsia	5	13.8%

Out of 36 participants with preeclampsia – eclampsia with thrombocytopenia, the majority of 14 (38.3%) participants had HELLP syndrome, followed by Eclampsia 12(33.3%), severe preeclampsia was 5(13.8%) and non-severe preeclampsia 5(13 .8 %) in the study population. (Table 8 & Figure 8)

Figure 8 : Bar chart of subject based severity of preeclampsia- eclampsia(N = 36)

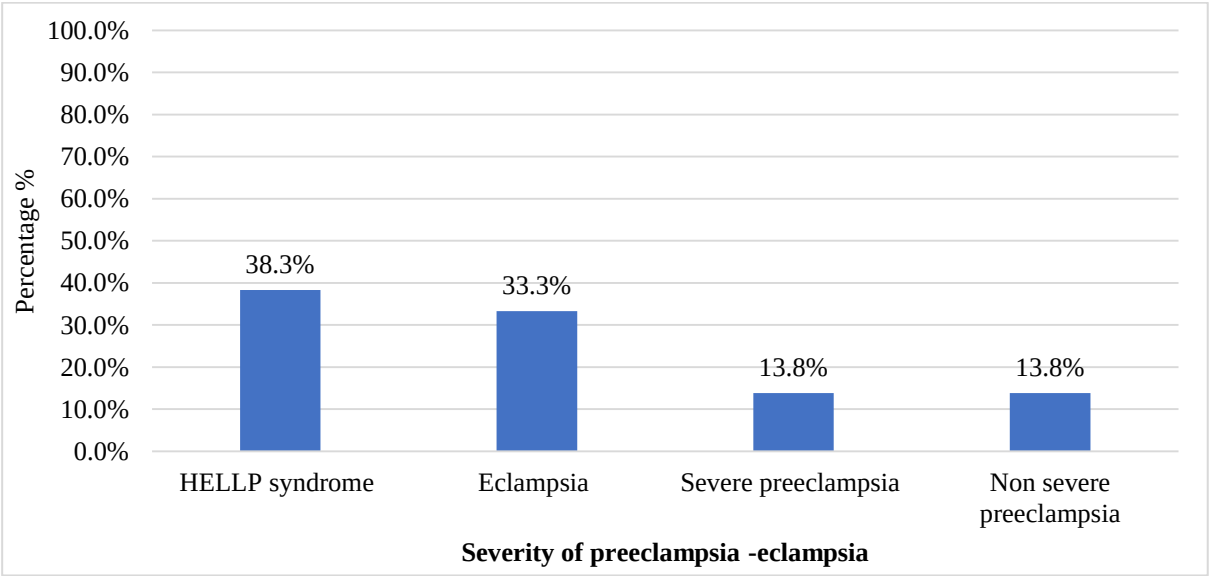


Table 9: Descriptive analysis of Transfusion of Blood and blood products in the study population (N=95)

Transfusion of blood and blood products	Frequency	Percentage
Yes	26	27.37%
No	69	72.63%

Out of the total 95 study population, blood and blood products transfusion observed in 26 (27.37%) (Table 9 & Figure 9)

Figure 9: Pie chart of Transfusion of Blood and blood products in the study population (N=95)

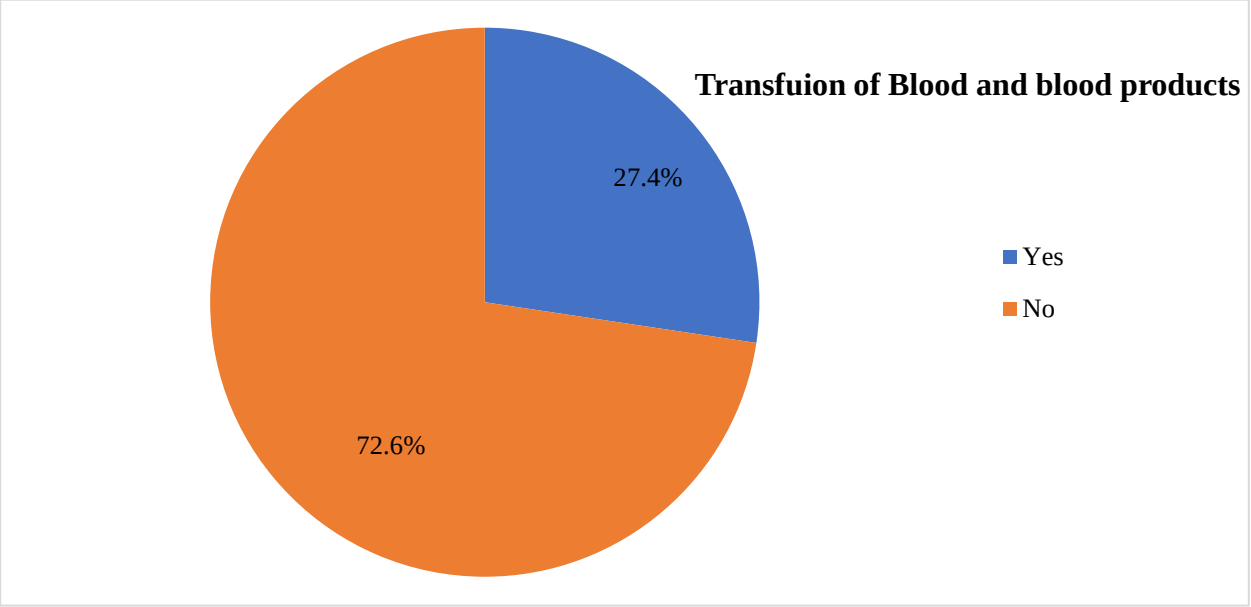


Table 10 : Descriptive analysis Blood and blood products transfusion in the study population (N=26)

Blood and blood products transfusion	Frequency	Percentage
Packed RBC	9	34.62%
Packed RBC+Fresh frozen plasma	5	19.23%
Packed RBC +Fresh Froze Plasma+ Platelets	5	19.23%
Platelets	7	26.92%

Out of the total 26 participants, 9(34.62%) participants received packed RBC, 5 (19.23%) participants received packed RBC + Fresh frozen plasma, 5 (19.23%) received Packed RBC+ Fresh frozen plasma + platelets and 7 (26.92%) received platelets. (Table 10&figure 10)

Figure 10: Bar chart of transfusion of Blood and blood products transfusion in the study population (N=95)

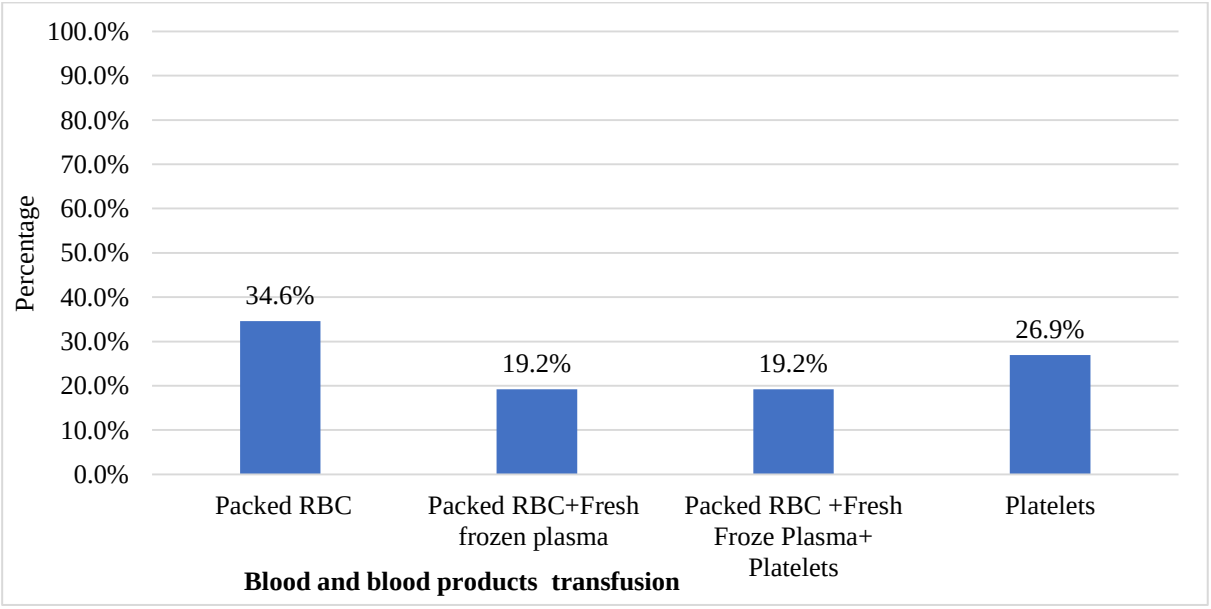


Table 11: Descriptive analysis of mode of delivery in the study population (N=95)

Mode of Delivery	Frequency	Percentage
Caesarean delivery	54	56.8%
Full term vaginal delivery	16	16.8%
Pre term vaginal delivery	20	21.0%
Vacuum delivery	5	5.2%

Out of the total 95 study population, the mode of delivery was Full term vaginal in 16 (16.8%%) participants, preterm vaginal delivery in 20(21.0%), vacuum delivery in 5(5.2%) and 54 (56.84%) participants underwent Caesarean delivery . (Table 11 & Figure 11)

Figure 11: Bar chart of mode of delivery in the study population (N=95)

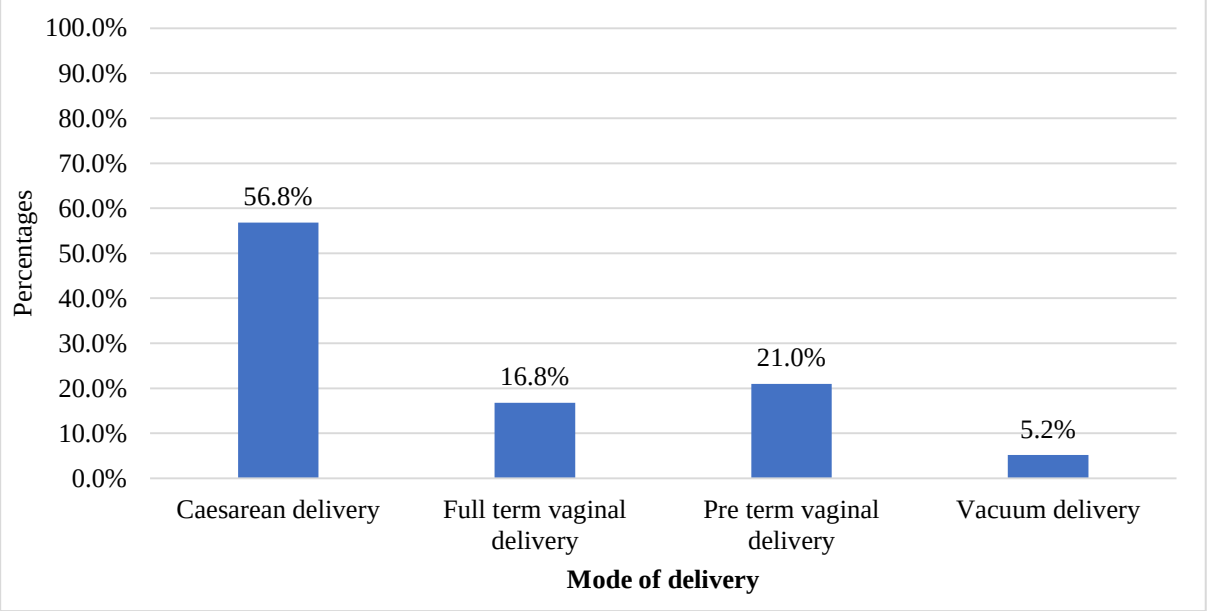


Table 12: Descriptive analysis of indication for Caesarean section in the study population (N=54)

Indication for Caesarean section	Frequency	Percentage
Fetal distress	24	44.44%
Previous caesarean section	22	40.74%
Breech presentation	3	5.56%
Cephalo pelvic disproportion	3	5.56%
Non-progression of labour	2	3.70%

Among the caesarean section cases 54, the indication was Fetal distress for 24 (44.44%) participants, Previous caesarean section for 22 (40.74%) participants, Breech presentation for 3 (5.56%) participants, Cephalopelvic disproportion for 3 (5.56%) participants and Non-progression of labour for 2 (3.70%) participants. (Table 12 & Figure 12)

Figure 12: Pie chart of Indication for Caesarean section in the study population (N=95)

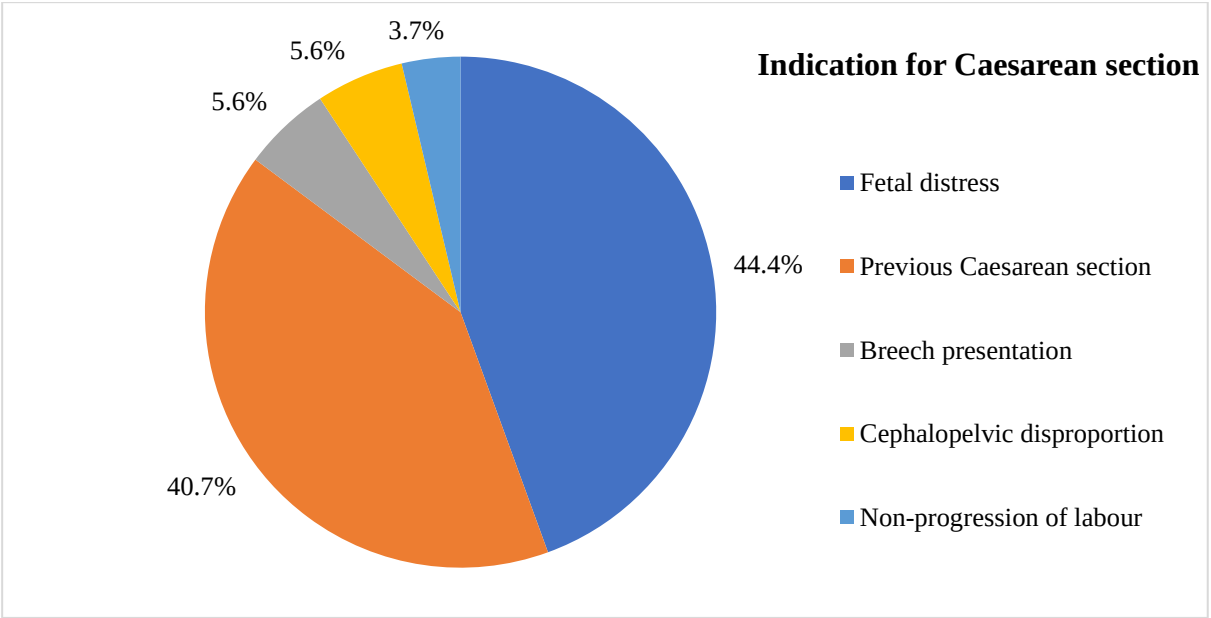


Table 13: Descriptive analysis of Maternal complications in the study population (N=95)

Maternal Complications	Frequency	Percentage
Postpartum haemorrhage	9	9.47%
Abruptio placenta	5	5.26%
DIC	2	2.11%
ICU admission	2	2.11%
No complication	77	81.05%

Out of the total 95 study population, about 18.95% reported to have maternal complications including Postpartum haemorrhage in 9 (9.47%) participants, abruptio placenta in 5 (5.26%) participants, ICU Admission in 2 (2.11%) participants and DIC in 2 (11.11%) participants. (Table 13 & Figure 13)

Figure 13: Bar Chart for Maternal complications in the study population (N=95)

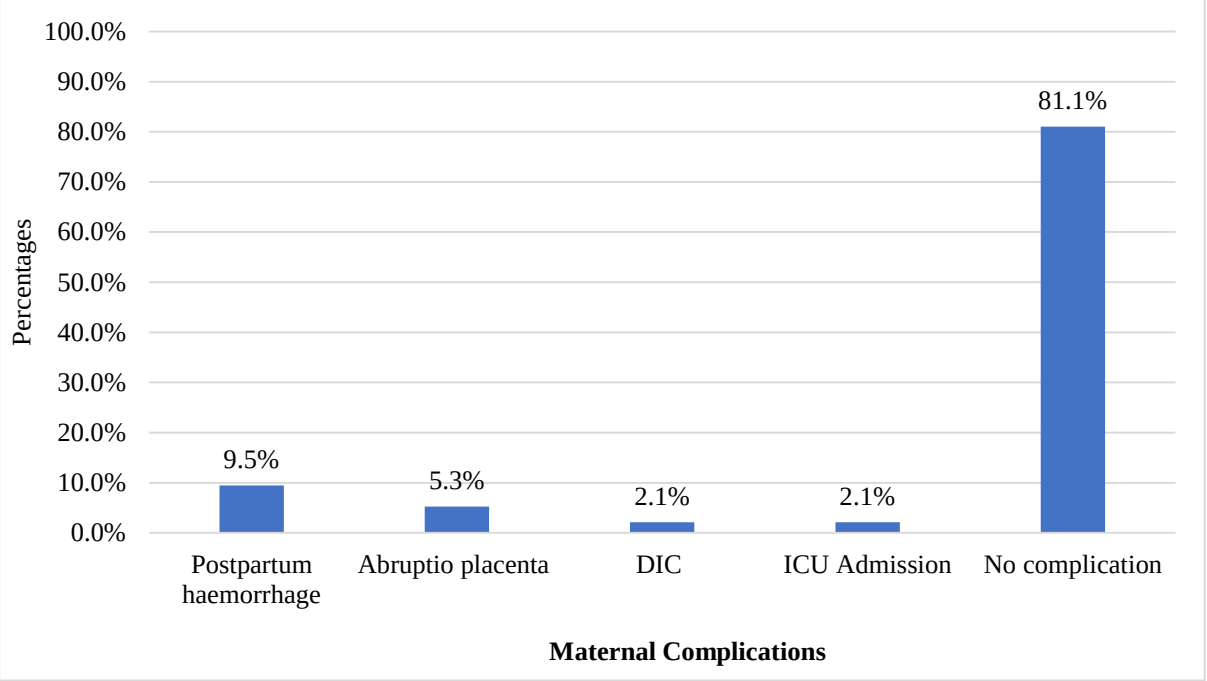


Table 14: Descriptive analysis of Maternal platelet count on day 5 in the study population (N=95)

Maternal platelet count on day 5	Frequency	Percentage
Mild (100–150x 10^9/L)	52	54.74%
Moderate (50–100 x10^9/L)	42	44.21%
Severe (< 50 x 10^9/L)	1	1.05%

Out of the total 95 study population, the maternal platelet count on day 5 was mild for 52 (54.74%) participants, moderate for 42 (44.21%) participants and severe in 1 (1.05%) participants. (Table 14 & figure 14)

Figure 14: Bar chart of Platelet count on day 5 in the study population (N=95)

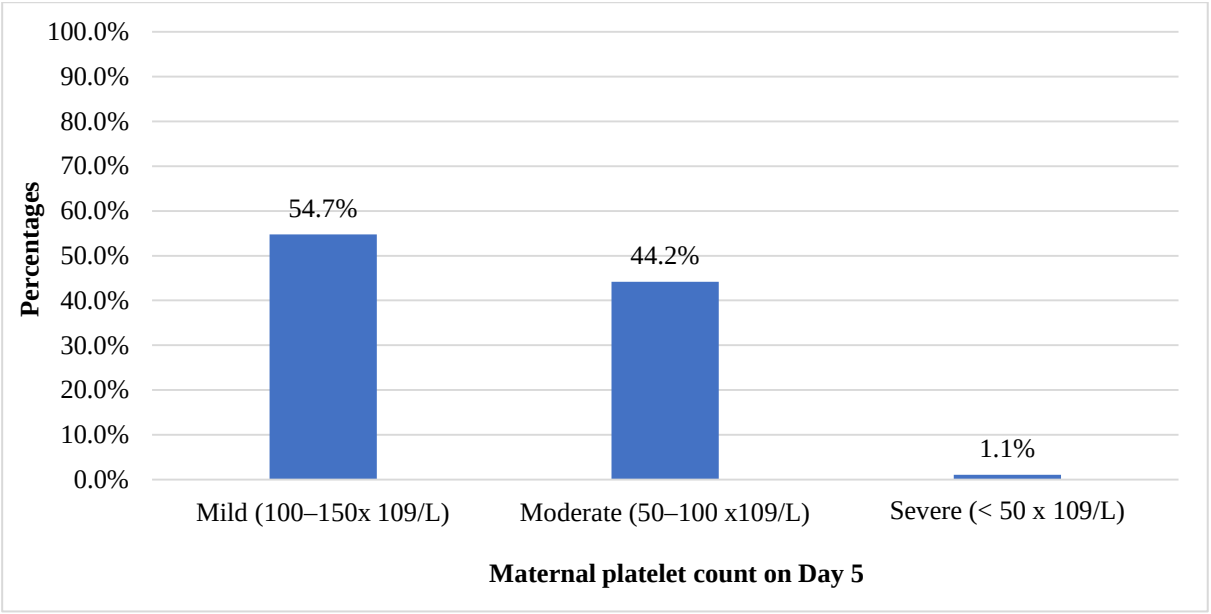


Table 15 : Descriptive analysis of Birth status in the study population (N=95)

Birth status	Frequency	Percentage
Preterm	20	21.05%
Term	75	78.95%

Out of the total 95 babies born preterm were 20 (21.05%) and term were 75 (78.95%) babies . (Table 15)

Table 16: Descriptive analysis of Fetal outcome in the study population (N=95)

Fetal outcome	Frequency	Percentage
Alive	93	97.89%
Still birth	2	2.11%

Out of the total 95 babies born 93 (97.89%) babies were alive and 2 (2.11%)babies were still born . (Table 16&figure 15)

Figure 15: Pie chart for Fetal outcome (N=95)

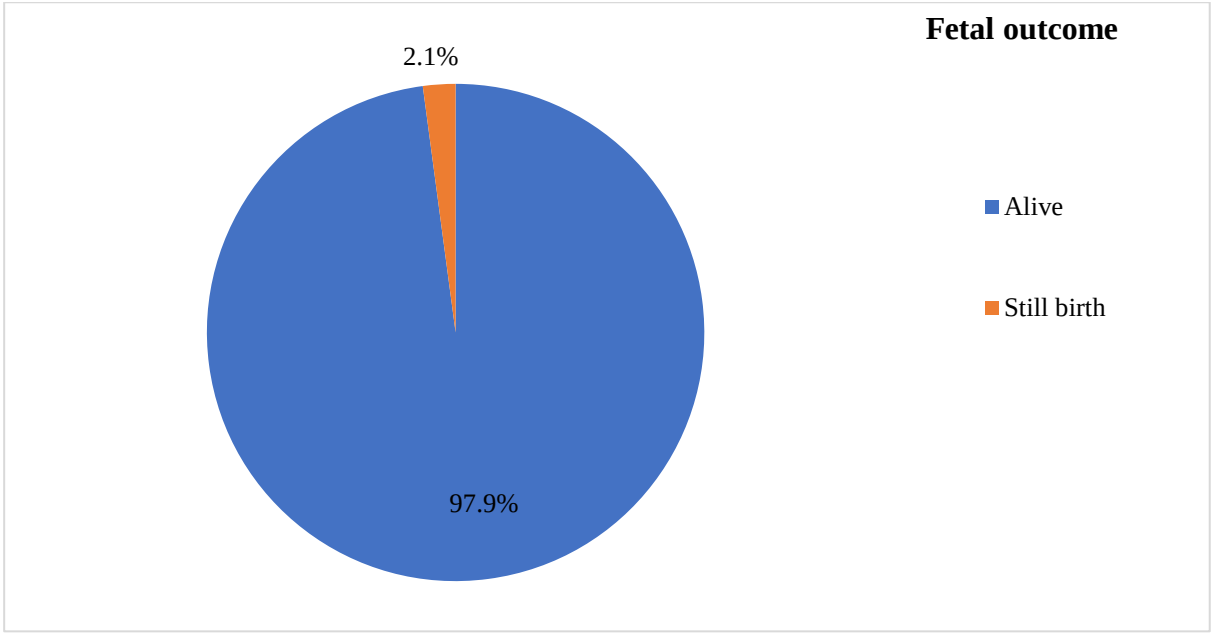


Table 17: Descriptive analysis of Birth weight of neonates in the study (N=95)

Birth Weight (Kg)	Frequency	Percentage
1 to 1.49	6	6.32%
1.50 to 2.49	30	31.58%
2.50 to 3.49	52	54.74%
≥ 3.5	7	7.37%

Among the total 95 babies , the birth weight was 1 to 1.49 kg for 6 (6.32%) babies , 1.50 to 2.49 kg for 30 (31.58%) babies , 2.50 to 3.49 kg for 52 (54.74%) babies and >3.5 kg for 7 (7.37%) babies . (Table 17)

Table 18: Descriptive analysis of Apgar score at 1min and 5 min in the study population (N=93)

Apgar score	1min		5min	
	Frequency	Percentage	Frequency	Percentage
1-3	**0**	0%	**0**	**0%**
4-6	**23**	24.73%	**17**	**18.2%**
7-10	**70**	75.27%	**76**	**81.7%**

Out of the 93 babies Apgar score at 1 min for 23 (24.73%) had 4-6 and for 70 (75.27%) babies had 7-10. Apgar score at 5 min for 17 (18.2%) had 4-6 and for 76(81.7%) babies had 7-10. (Table 18)

Table 19: Descriptive analysis of NICU admission in the study (N=93)

NICU Admission	Frequency	Percentage
Yes	37	39.78%
No	56	60.22%

Out of the 93 babies 37 (39.78%) babies were admitted to NICU (Table 19&figure 16)

Figure 16: Bar chart of NICU admission in the study (N=93)

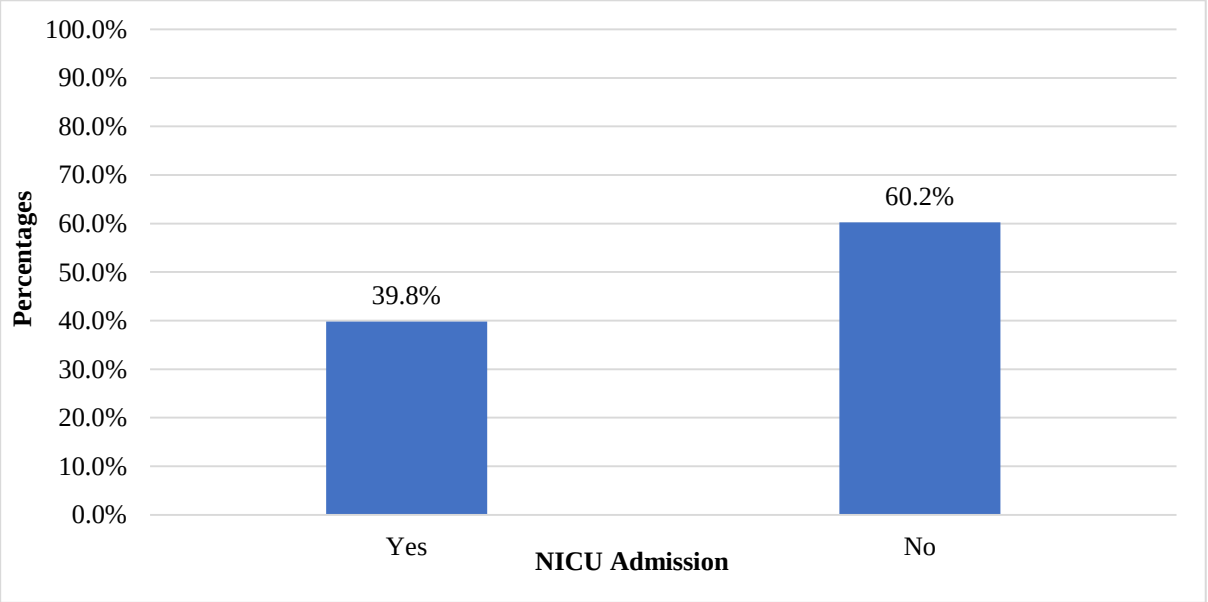


Table 20: Descriptive analysis of cause for NICU admission in the study (N=37)

Cause of NICU admission	Frequency	Percentage
Respiratory distress syndrome	17	45.95%
Preterm care	16	43.24%
Meconium aspiration syndrome	4	10.81%

Out of the 37 NICU admitted babies, the cause of NICU admission was respiratory distress syndrome for 17 (45.95%) babies, preterm care for 16 (43.24%) babies and meconium aspiration syndrome for 4 (10.81%) babies. (Table 20&figure 17)

Figure 17: Bar chart cause of NICU admission in the study (N=37)

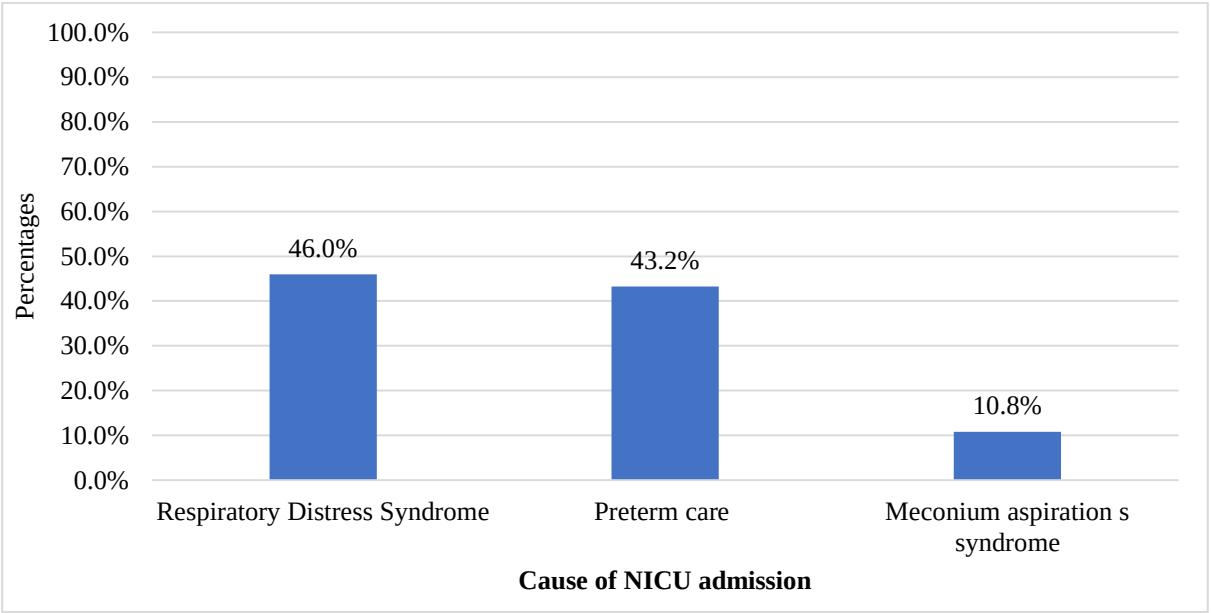


Table 21 : Descriptive analysis of Neonatal thrombocytopenia in the study (N=95)

Neonatal thrombocytopenia	Frequency	Percentage
Yes	2	2.11%
No	93	97.89%

Out of the total 95 babies, 2 (2.11%) babies had neonatal thrombocytopenia. (Table 21& Figure 18

Figure 18: Bar chart of Neonatal thrombocytopenia in the study (N=95)

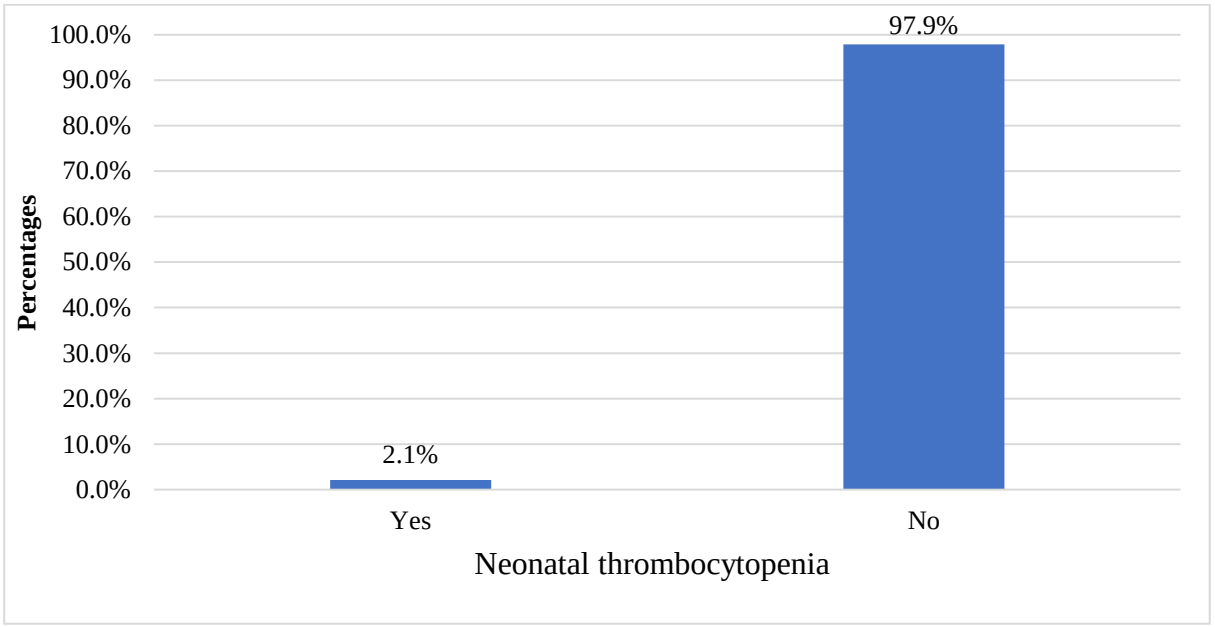


Table 22: Comparison of severity of Pre eclampsia – eclampsia and maternal thrombocytopenia (N=95)

Severity of preeclampsia – eclampsia	Maternal thrombocytopenia			Chi square	P value
	Mild (N=51)	Moderate (N=37)	Severe (N=7)		
Yes	17	15	4	1.663	0.435
No	34	22	3		

Out of 51 participants with mild maternal thrombocytopenia, 17 had pre-eclampsia. Out of 37 participants with moderate maternal thrombocytopenia, 15 had pre-eclampsia. Out of 7 participants with severe maternal thrombocytopenia, 4 had pre-eclampsia.

No statistically significant difference was observed in maternal thrombocytopenia between pre-eclampsia (P Value 0.435). (Table 22 & figure 19)

Figure 19: Clustered bar chart Comparison of severity of Pre-eclampsia-eclampsia and maternal thrombocytopenia (N=95)

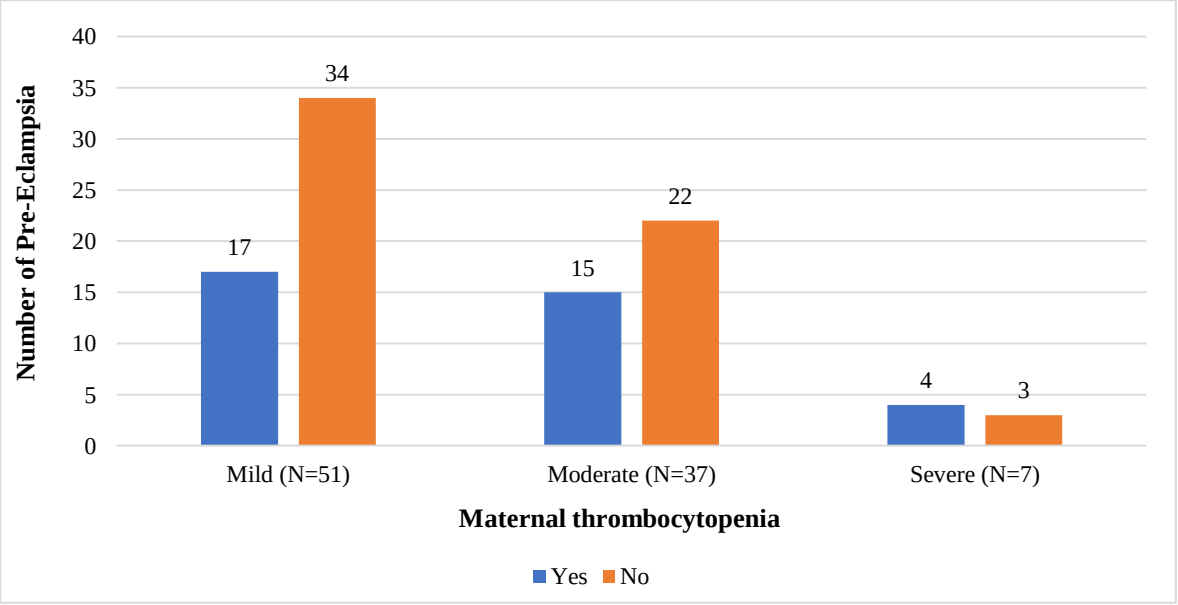


Table 23: Comparison of Blood and Blood products transfusion with severity of maternal thrombocytopenia (N=95)

Blood and Blood products transfusion	Maternal thrombocytopenia			Chi square	P value
	Mild (N=51)	Moderate (N=37)	Severe (N=7)		
Yes	9	13	4	6.669	0.036
No	42	24	3		

Out of 51 participants with mild maternal thrombocytopenia, blood transfusion observed in 9. Out of 37 participants with moderate maternal thrombocytopenia blood transfusion observed in 13. Out of 7 participants with severe maternal thrombocytopenia blood transfusion observed in 4.

There was a statistically significane was observed between severity of maternal thrombocytopenia and transfusion (P Value >0.05). (Table 23 & figure 20)

Figure 20: Cluster bar chart of comparison of Blood and blood products transfusion with severity of maternal thrombocytopenia (N=95)

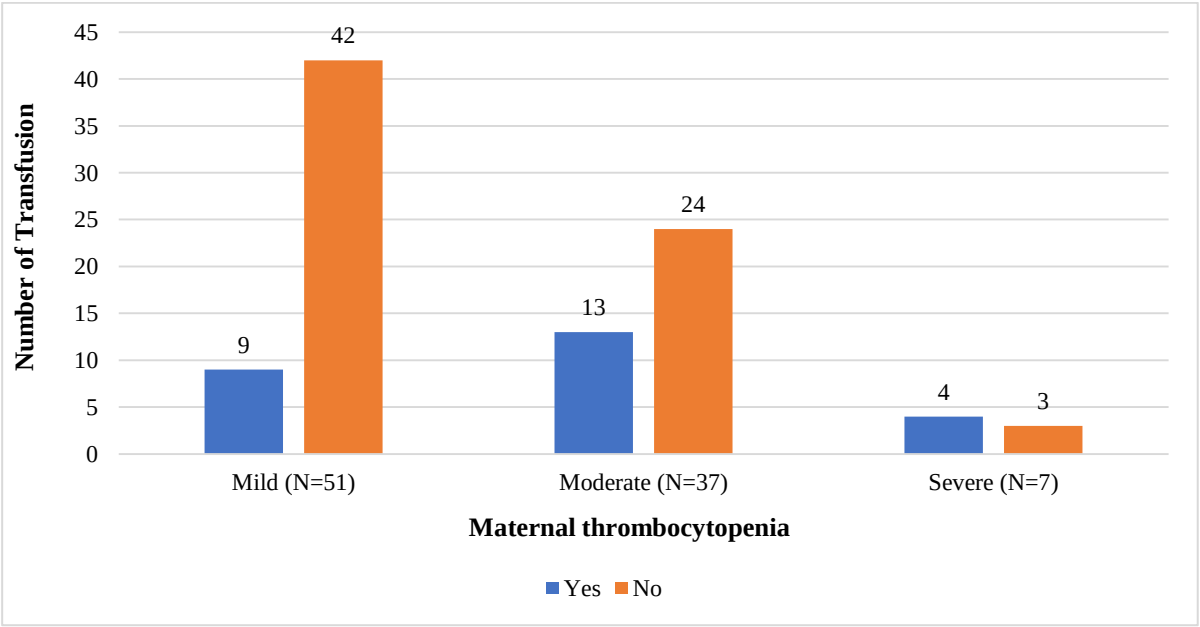


Table 24: Comparison of Maternal complications across thrombocytopenia (N=18)

Maternal Complications	Maternal thrombocytopenia		
	Mild	Moderate	Severe
Postpartum Haemorrhage (N=9)	3	5	1
Abruption placenta (N=5)	0	2	3
ICU Admission (N=2)	0	0	2
DIC (N=2)	0	0	2

No statistical test was applied- due to 0 subjects in the cells

Out of 9 participants with Postpartum Haemorrhage, the thrombocytopenia was mild for 3 participants, moderate for 5 participants and severe for 1 (11.11%) participant. Out of 5 participants with abruption, the thrombocytopenia was mild for no participants, moderate for 2 participants and severe for 3. Out of 2 participants with ICU admission, the thrombocytopenia was mild, moderate for no participants, and severe for 2 participants. Out of 2 participants with DIC, the thrombocytopenia was mild for no participant, moderate for no participant and severe for 2 participants. (Table 24)

Table 25: Comparison of NICU admission with severity of maternal thrombocytopenia (N=93)

NICU admission	Maternal thrombocytopenia			Chi square	P value
	Mild (N=50)	Moderate (N=36)	Severe (N=7)		
Yes	18	14	5	3.237	0.198
No	32	22	2		

Severe thrombocytopenia reported high NICU admission with 5 followed by moderate with 14 and mild with 18.

There was no statistically significant difference was observed in thrombocytopenia between NICU admission (P Value >0.05).. (Table 25)

DISCUSSION

DISCUSSION:

Thrombocytopenia in pregnancy may occur secondary to a variety of causes ranging from benign disorders such as gestational thrombocytopenia to syndromes associated with significant morbidity such as eclampsia, HELLP syndrome , ITP, TTP-HUS and rare causes such as Type II von Wiillebrand Disease (vWD), and disseminated intravascular coagulation. Among the all causes most common cause is Gestational Thrombocytopenia. Gestational Thrombocytopenia which is 75 % occur mostly in third trimester and is through to be predominantly due to hemodilution.. To reduce the platelet disorder related complications during pregnancy, there should be stratification done regarding the predictors, frequency and their effects on the mother and foetus. Hence the present study aimed to find the prevalence of maternal and fetal complications among pregnant women with thrombocytopenia.

This study involved 95 subjects for the final analysis.

Age and parity

The age group was 19-20 years was 11.58%, 21 to 25 years was 53.68%, 26 to 30 years was 25.26% and >30 years was 9.47% participants. The parity among the present study population, was primigravida for 43.16% and multigravida for 56.84% participants and the multi gravida among present study population, the gravida was 2 in 34.74%, 3 in 15.79% and it was 4 in 6.32 % participants. In a study by Sumarthy, D et al, found primigravida in 55.6% and multi in 44.4%.[58] A similar study by Maraskolhe, D et al 130 study population, found primigravida in 42.3%, multigravida in 58% similar to present study .[14]

Among the study population, the gestational age, 28 to 31^{+6}weeks was found in 4.21% participants, 32 to 36^{+6} weeks in 16.84% and >37 weeks in 78.95% participants. . A similar

study by Maraskolhe, D et al, 130 study population, found 10.7% cases were of 26-30 weeks of gestation, 26.1% cases were of 31-35 weeks of gestation, 63.7% cases were of ≥36 weeks of gestation. However, present study we found greater frequency of study population belonging to >37 weeks of gestation. [14]

Severity of thrombocytopenia

The severity of thrombocytopenia in the present study population was mild in 53.68%, moderate in 38.95% and severe in 7.37% participants. Study done by Vishwekar, P et al, out of 1480 antenatal cases, 130 were found to have thrombocytopenia with platelet count <150 x 10 /L having a prevalence of 8.78%. Of these 78.4% were mild, 15.2 % were moderate and 6.4% were severe thrombocytopenia cases. [10]A prospective study by Misra, D et al, found greater proportion of mild thrombocytopenia cases compared to moderate and severe .Similarly, we found mild thrombocytopenia cases greater in proportion thrombocytopenia compared to present study. [54] In another study by Harde, M et al, observed increased moderate cases of thrombocytopenia . [59]

Table:26 Comparing the distribution of severity of thrombocytopenia of present study population across different studies

Studies	Mild	Moderate	Severe
Vishwekar, P et al,[10]	78.4%	15.2%	6.4%
Harde, M et al,[59]	29.3%	66%	4.7%
Misra, D et al,[54]	70.71%	27.15%	2.14%
Present study	53.68%	38.95%	7.37%

Aetiology of thrombocytopenia

In the present study gestational thrombocytopenia was a major cause of 51.5% followed by pre-eclampsia- eclampsia in 37.8%, Anaemia in 5.26%,COVID-19 in 2.11% Dengue fever in 2.11% and megaloblastic anemia in 1.05% participants.In the present study out of 36 subjects with preeclampsia – eclampsia with thrombocytopenia majority were found (38.3%) had HELLP syndrome , followed by Eclampsia in 33.3% ,Non severe preeclampsia in 13.8% and severe preeclampsia in 13.8 % . A study by Godara, D et al, involved 2750 study population where 100 women were found to have thrombocytopenia. They found the aetiology for thrombocytopenia among study population was found to be gestational thrombocytopenia (66 %) as leading cause followed by hypertensive disorder of pregnancy (preeclampsia, eclampsia) is second most common cause (23 %), 1 % due to ITP, 6 % due to malaria and 4% due to dengue. [3] In the present study we also found gestational thrombocytopenia as major cause in 57.89% participants . A similar study by Harde, M et al,[59] with a study population of 135, found preeclampsia to be leading cause for thrombocytopenia (54%) followed by gestation thrombocytopenia in 28%,infectious cause in 12.7%, immune thrombocytopenic purpura(ITP) in 3.3% and heparin induced thrombocytopenic purpura in 1.3% and aplastic anaemia in 0.7%.

Table 27 Comparing aetiology for thrombocytopenia in present study and with other studies

Etiology	Godara, D et al,[3]	Harde, M et al,[59]	Maraskolhe, D et al,[14]	Present study
Preeclampsia	23%	54%	1.5%	37.89%
Gestational thrombocytopenia	66%	28%	42%	57.89%
Infections	10%	12.7%	9.1%	4.22%
ITP	1%	3.3%		-
HTP	-	1.3%	0.7%	-
Aplastic anemia	-	0.7%	-	-
HEELP syndrome	-	-	25.5%	38.3%
Idiopathic	-	-	3.8%	-

Mode of delivery

In the current study the mode of delivery was Full term vaginal in 16 (16.8%%) participants , preterm vaginal delivery in 20(21.0%) , vaccum delivery in 5(5.2%) and 54 (56.84%) participants underwent Caesarean delivery . In 54 cases of caesarean section the indication for the same was Fetal distress in 44.44%, previous Caesarean section for 40.74%, Breech presentation in 5.56%, Cephalopelvic disproportion in 5.56% and non-progression of labour in 3.70% participants.A prospective study by Sumathy, Det al, found vaginal spontaneous labour in 41.6%, vaginal induced in 10.4%,forcep delivery in 1.1% and LSCS in 46.7% similar to present study .[58] In another study by Maraskolhe, D et al, found vaginal delivery to be more frequent (87%) than LSCS in 13.07%.[14]

The blood transfusion in our study was observed in 27.37%. In 26 participants,34.62% participants received packed RBC, 19.23% participants received packed RBC + Fresh frozen plasma, 19.23% received Packed RBC+ Fresh frozen plasma + platelets and 26.92% received platelets. A study by Vishwekar,P et al, reported 33% of subjects needed transfusion of platelets prior to delivery.[10]

Maternal outcome

The maternal complications reported in present study were Postpartum haemorrhage in 9.47%, Abruptio placenta in 5.26% , ICU Admission in 2.11% and DIC in 11.11% participants. A study by Sumarthy, D et al, found maternal complications as follows: Atonic PPH occurred in 7.1 %, abruption in 2.7%, eclampsia in 2.1%, DIC in 2.1%, ARDS in 0.5% and incisional site oozing in 0.5% similar to present study .[58] . Findings from Singh, J et al, study found maternal complications as follows:massive haemorrhage in 6.66%, puerperal sepsis in 5.55% , DIC in 7.78%, 10% developed pulmonary edema. [53]Aprospective study by Misra, D et al, found Maternal complications among the cases with thrombocytopenia like postpartum haemorrhage (27.14%), puerperal sepsis (9.28%), need for transfusion (20.0%), placental abruption (5.0%).[54] A study by Vishwekar, P et al, observed maternal complications occurred in 12% patients, in the form of HELLP, ICU admission, PPH and sepsis. They also found that women with severe thrombocytopenia, experienced more maternal complications (44.44%).[10]

Table 28 comparing the maternal outcome present study with different studies

Maternal complication	Sumarthy, D et al[58]	Singh, J et al [53]	Misra, D et al [54]	Present study
Postpartumhaemorrhage	7.1.%	8.8%	27.14%	9.47%,
Abruptio placenta	2.7%		5.0%	5.26%
ICU Admission	-		-	2.11%
DIC	2.1%	7.78%	-	11.11%
ARDS	0.5%	10%	-	-

Perinatal outcome:

Neonatal outcome of the present study population was as follows: birth status alive in 97.89%, still birth in 2.11%. Majority of the neonates had healthy birth weight of 2.50 to 3.49kg in 54.74%, followed by 1.50 to 2.49kg in 31.58%, 1to 1.49kg in 6.32% and >3.5 kg in 7.37% participants. In the present study nearly 21.05% neonates were born preterm and majority 78.95% of the neonates were born at term. NICU admission were reported in 39.78% of neonates. The cause for NICU admission was respiratory distress syndrome in 45.95%, preterm in 43.24% and meconium aspiration Syndrome in 10.81% participants. Only 2.11% of the neonates found to have neonatal thrombocytopenia. In a study by Sumathy, D et al, found live births in 88.4% and IUDs (intrauterine deaths) in 0.3%. [58]According to the findings of Godara, D et al, study the prevalence of thrombocytopenia in neonates was just 1%.[3] In another recent study by Singh, J et al, found no morbidity perinatally in 54.4%. . The cases which reported morbidity were due to fetal growth restriction in 11.11%, Birth asphyxia in 10%, severe thrombocytopenia in 10%, intracranial haemorrhage in 4.4%, and death were due to still birth in 5.5% and IUD in 4.4%. [53] In another prospective study by Misra, D et al,

included cases(thrombocytopenia cases) and controls (normal platelet count), found perinatal complications more in cases compared to control group. These included jaundice (20.0%), birth asphyxia (13.57%) and neonatal thrombocytopenia (12.14%).[54] A prospective study by Singh, J et al, found no perinatal morbidity in 54.4%. The various perinatal morbidities which they reported were fetal growth restriction in 11.11%, Birth asphyxia in 10%, severe thrombocytopenia in 10%, intracranial haemorrhage 4.4%, stillbirth in 5.5% and IUD in 4.4%.[53]

Table 29 comparing the perinatal outcome present study with different studies

Neonatal outcome	IUD	Live-term births	Preterm alive	Preterm dead	NICU admission	Perinatal mortality	Neonatal thrombocytopenia
Sumathy, D et al,[58]	0.3%	92.5%	6.8%	0.3%	-	-	none
Maraskolhe, D et al,[14]	3.86% still birth	76.15%	38.46%	-	20%	8.5%	-
Godara, D et al, [3]	2%	-	-	-	21%	-	1%
Singh, J et al,[53]	4.4%	54.44%	-	-	-	9.99%	10%
Misra, D et al,[54]	3.57%	-	-	-	12.14%	1.4%	12.14%
Present study		78.95%	21.05%	-	39.8%	-	2.11%

SUMMARY

SUMMARY:

- This study was a prospective observational study of 95 pregnant women with thrombocytopenia to evaluate causes of thrombocytopenia in pregnant women and assess the maternal and fetal out come .
- Majority of the age group are 21 to 25 years (53.68%) followed by 26-30years(25.26%).
- Distribution of partity shows majority multi gravida (56.85%) compared to Primi gravida(43.16%)
- Distribution of gestational age showed more are term gestation(78.95%)
- In the present study shows majority of them had mild thrombocytopenia (53.68%)t
- Among the study participants most common aeitology was gestational thrombocytopenia(51.5%) followed pre eclampsia – eclampsia (37.8%).
- In 95 study population, the mode of delivery was Full term vaginal in 16 (16.8%%) participants , preterm vaginal delivery in 20(21.0%) , vaccum delivery in 5(5.2%) and 54 (56.84%) participants underwent Caesarean delivery. Hence, the mode of delivery was normal in 43% and low segment CS in 56.84%.
- Caesarean section was indicated due to Fetal distress in 44.44%, previous Caesarean section for 40.74%, Breech presentation in 5.56%, Cephalopelvic disproportion in 5.56% and non-progression of labour in 3.70% participants.
- The blood and blood products transfusion in our study observed in 27.37%
- The maternal complications reported in present study reported were Postpartum haemorrhage in 9.47%, Abruptio placenta in 5.26% , ICU admission in 2.11% and DIC in 2.11% participants.
- Neonatal outcome of the present study population was as follows: birth status alive in 97.89%, still birth in 2.11%.

- Nearly 21.05% neonates were born preterm and majority 78.95% of the neonates were born at term.
- NICU admission were reported in 39.78% of neonates. The cause for NICU admission was respiratory distress syndrome in 45.95%, preterm in 43.24% and meconium aspiration Syndrome in 10.81% participants.
- Only 2.11% of the neonates found to have neonatal thrombocytopenia.
- There was a statistically significant difference was observed between blood and blood products transfusion and severity of maternal thrombocytopenia (P Value >0.05).

CONCLUSION

CONCLUSION

In the present study the most common cause of thrombocytopenia in pregnancy is gestational thrombocytopenia followed by less common causes were preeclampsia, HELLP Syndrome ,anemia, COVID -19, dengue fever and megaloblastic anemia .

Pre eclampsia and HELLP syndrome were associated with post partum hemorrhage with abruptio placenta , DIC , need of transfusion of blood and blood products ,ICU admission and intrauterine death in this study .

It is crucial to evaluate thrombocytopenia in pregnancy to distinguish between gestational thrombocytopenia and other serious conditions like pre eclampsia, HELLP syndrome, ITP, infections which have the potential for serious morbidity and mortality.

Management of pregnant women with thrombocytopenia requires a multidisciplinary approach and with close collaboration between obstetrician and hematologist required to reduce the maternal and fetal mortality and morbidity

LIMITAIONS AND RECOMMENDATIONS:

- Inclusion of normal count of platelets should have been included to compare the fetal and maternal complications.
- Large multi-center studies should be conducted with prospective study design to understand the fetal and maternal outcomes and hence treatment management.

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ANNEXURES

INFORMED CONSENT FORM

I Mr./Mrs. _____ have been explained in my own understandable language, that I will be included in a study which is **PROSPECTIVE STUDY OF THROMBOCYTOPENIA IN PREGNANCY, AND ITS MATERNAL AND NEONATAL OUTCOME**

I have been explained that my clinical findings, investigations, intraoperative findings, will be assessed and documented for study purpose.

I have been explained my participation in this study is entirely voluntary, and I can withdraw from the study any time and this will not affect my relation with my doctor or the treatment for my ailment.

I have understood that all my details found during the study are kept confidential and while publishing or sharing of the findings, my details will be masked.

I have principal investigator mobile number for enquiries.

I in my sound mind give full consent to be added in the part of this study.

Signature of the patient:

Name:

Signature of the witness:

Name:

Relation to patient:

Date:

place:

PATIENT INFORMATION SHEET

STUDY TITLE: "A PROSPECTIVE STUDY OF THROMBOCYTOPENIA IN PREGNANCY AND ITS MATERNAL AND NEONATAL OUTCOME".

STUDY SITE: R.L Jalappa Hospital and Research Centre, Tamaka, Kolar.

This is to inform you that you require routine antenatal investigations. The investigations are required for making the diagnosis of the disease

We are conducting this study to predict the onset and severity of this condition.

If you are willing, you will be enrolled in this study, and we will do routine antenatal investigations other relevant investigations which are required

You will receive the standard care pre and post operatively

This will facilitate identifying THROMBOCYTOPENIA AND ITS COMPLICATIONS (if any) in the early stage and treating it. It will also benefit other patients with thrombocytopenia in the future. You are free to opt out of the study at any time if you are not satisfied or apprehensive to be a part of the study. Your treatment and care will not be compromised if you refuse to be a part of the study. The study will not add any risk or financial burden to you if you are part of the study.

Your identity and clinical details will be confidential. You will not receive any financial benefit for being part of the study. You are free to contact DR SUDHA MALLIDI or any other member of the above research team for any doubt or clarification you have.

Dr. SUDHA MALLIDI

Mobile no: 9177901494

E-mail id: sudhamallidi@gmail.com

CASE PROFORMA

NAME: IP NO:

AGE: DOA:

OCCUPATION: DOD:

ADDRESS:

EDUCATION:

HUSBANDS OCCUPATION:

SOCIOECONOMIC STATUS:

CHIEF COMPLAINTS:

HISTORY OF PRESENT ILLNESS:

OBSTETRIC HISTORY:

Marital life: Consanguinity:

Gravida: Para: living: Abortion: Dead:

Details of previous pregnancy: Details of present pregnancy:

MENSTRUAL HISTORY:

Last menstrual period: Age of menarche: Expected delivery date:

Period of gestation:

Period of gestation according to early scan:

Past menstrual cycle:

PAST HISTORY

Hypertension /Diabetes Mellitus/Bronchial Asthma/Tuberculosis /Blood Dyscrasias/ Epilepsy/ Thyroid Disorder/ Cardiac Disease/Allergy

H/O blood transfusions:

H/O Surgeries or hospitalization:

PERSONAL HISTORY:

Sleep and appetite:

Diet:

Bowel and bladder:

FAMILY HISTORY:

DRUG HISTORY:

GENERAL EXAMINATION:

General condition:

Fair/ moderate/ Poor Built: Nourishment:

Ht: cms Wt: kgs BMI: Pallor: Icterus: Cyanosis:

Clubbing: Lymphadenopathy:

Edema:

VITALS:

Pulse rate: Respiratory rate:

Blood pressure: Temperature: Breast: Spine: Thyroid:

SYSTEMIC EXAMINATION:

Cardiovascular system: Respiratory system:

Central nervous system:

Per abdomen: Uterus size:

Relaxed / Irritable / Acting Presentation: cephalic/ Breech/ other FHS:

LOCAL EXAMINATION:

Per Speculum:

Per Vaginum: Effacement:

Dilatation:

Station:

Membranes:

Pelvis:

Modified Bishop Score:

DIAGNOSIS:

Mode of delivery:

Indication for cesarean section:

Maternal adverse effects:

postpartum haemorrhage:

Need for blood or blood components transfusion: yes/no

Puerperal complication: yes/no

ICU ADMISSION:

Maternal morbidity: yes/no

Fetal heart rate tracing (non-stress test and cardiotocograph findings):

DETAILS OF THE NEONATE:

Sex: Date:Time: Birth weight: APGAR score: 1'- 5'-

Admission to NICU:

Neonatal resuscitation Perinatal morbidity/mortality:

INVESTIGATIONS:

CBC: -

Hb: TC: DC: N-, L-, E-, M-, B- PLATELET:

BLOOD GROUP: RBS:

HIV: HBsAg: VDRL:

URINE ROUTINE & MICROSCOPY:

LFT

TOTAL BILIRUBIN: DIRECT BILIRUBIN:

ALKALINE PHOSPHATASE: TOTAL PROTEIN:

TOTAL ALBUMIN:

A/G Ratio:

SGOT:

SGPT:

BLEEDING TIME: CLOTTING TIME:

PT: INR: APTT:

OBS SCAN:

KEY TO MASTER CHART

IP.No: In-patient hospital number

A) AGE (yrs)

1: 19-20

2: 21-25

3: 26-30

B) **Parity**

1: Primigravida

2: Gravida 2

3: Gravida 3

4: Gravida 4

c) **Gestational age**

1: 28-31+6 Weeks

2: 33-36+6 Weeks

3: 37 weeks to 40weeks

D) Severity of thrombocytopenia

1: MILD

2: MODERATE

3: SEVERE

E) Aetiology

1: Gestational thrombocytopenia

2: Pre-eclampsia – eclampsia

3: Anaemia

4: COVID -19

5: Dengue fever

6: Megaloblastic anaemia

F) Blood and blood products transfusion

YES

NO

G) Mode of delivery

1: Full term vaginal delivery

2: Pre term vaginal delivery

3: Caesarean delivery

4: Vaccum delivery

H) Indication for caesarean section

1: Fetal distress

2: Previous Caesarean section

3: Breech presentation

4: Cephalopelvic disproportion

5: non-progression of labour

i) **BIRTH STATUS**

1: Alive

2: Still birth

J) BIRTH WEIGHT

1: 1 to 1.49

2: 1.50 to 2.49

3: 2.50 to 3.49

4: > 3.5

K)APGAR AT 1 MIN

1: 1-3

2: 4-6

3: 7-10

L)APGAR AT 5 MIN

1: 1-3

2: 4-6

3: 7-10

M) BIRTH STATUS

1: TERM

2: PRETERM

N)NICU ADMISSION

1: YES

2: NO

O) REASON FOR NICU ADMISSION

1: RESPIRATORY DISTRESS SYNDROME

2: PRETERM CARE

3: MECONIUM ASPIRATION SYNDROME

P)NEONATAL THROMBOCYTOPENIA

1: YES

2: NO

Q)MATERANAL COMPLICATIONS

1: No complication

2:Postpartum hemorrhage

3: Abruptio placenta

4:DIC

5: ICU Admission

R) PLATELET COUNT ON DAY 5 OF POST PARTUM

1: 100–150x 109/L

2: 50–100 x109/L

3: < 50 x 109/L

S.NO	IP NO	A	B	c	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
1	838875	1	1	3	2	2	1	3	1	1	3	3	3	1	2		2	1	2
2	837207	3	3	3	2	2	2	3	2	1	3	3	3	1	2		2	1	2
3	835036	1	1	3	2	2	2	3	1	1	3	3	3	1	2		1	1	1
4	838034	2	2	3	2	2	2	3	2	1	3	3	3	1	2		2	1	2
5	818520	4	4	3	3	2	2	3	1	1	3	3	3	1	2		2	1	2
6	839613	1	1	3	3	2	2	3	1	1	2	3	3	1	2		2	1	2
7	841582	2	2	3	2	1	2	3	6	1	3	3	3	1	2		2	1	2
8	842638	3	3	3	1	1	2	3	2	1	3	3	3	1	2		2	1	2
9	843115	1	1	3	1	1	2	3	2	1	3	3	3	1	2		2		1
10	842688	2	2	3	1	1	1	3	2	1	4	3	3	1	2		2	1	2
11	843087	2	2	3	2	2	2	3	2	1	3	3	3	1	2		2	1	1
12	849034	4	4	3	1	1	2	3	1	1	3	3	3	1	2		2	1	2
13	844720	2	2	3	1	3	1	3	2	1	2	2	2	1	1	1	1	1	1
14	847861	3	3	3	2	2	1	3	1	1	3	2	2	1	2		2	1	1
15	848927	1	1	3	2	2	1	3	1	1	2	3	3	1	1	3	2	1	2
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17	849773	4	4	3	2	1	2	3	3	1	2	3	3	1	2		2	1	2
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19	853696	3	3	3	1	1	2	3	2	1	4	3	3	1	2		2	1	2
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21	855561	1	1	1	1	1	2	2		1	1	2	2	2	1	4	2	1	2
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23	856470	4	4	3	2	2	1	3	1	1	3	3	3	1	2		2	2	2
24	856505	1	1	3	2	2	1	3	1	1	2	3	3	1	1	1	2	1	2
25	859192	3	3	3	2	2	1	1		1	3	3	3	1	2		2	1	2
26	861487	2	2	3	2	3	1	1		1	3	3	3	1	2		2	1	2
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29	862156	2	2	2	1	1	2	2		1	3	3	3	2	1	4	2	1	1
30	862119	3	3	2	1	1	1	2		1	2	3	3	2	2		2	1	1
31	862166	1	1	1	1	6	2	2		1	2	3	3	2	1	1	2	1	1
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34	865916	1	1	2	1	1	2	2		1	1	2	2	2	1	4	2	1	1
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36	867987	2	2	2	2	1	2	3	1	1	3	3	3	1	2		2	2	1
37	868204	3	3	3	1	1	2	1		1	2	3	3	1	2		2	1	1
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40	868681	2	2	3	1	1	2	1		1	3	2	2	1	1		2	2	1
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44	869587	3	1	3	1	1	2	1		2	1			1			2	3	1
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S.NO	IP NO	A	B	c	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
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56	874235	3	1	2	1	1	1	3	7	1	3	3	3	1	2		2	1	2
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58	875046	3	3	3	2	2	2	3	5	1	3	3	3	1	2		2	4	1
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74	879894	2	1	3	1	1	2	3	2	1	3	3	3	1	2		2	1	1
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76	879965	2	1	3	1	1	2	4		1	3	3	3	1	2		2	1	1
77	880814	2	1	3	1	1	2	3	1	1	3	3	3	1	2		2	3	1
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81	882529	2	1	3	1	1	2	3	1	1	3	3	3	1	2		2	5	2
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83	883473	3	1	3	2	2	2	4		1	3	2	3	1	1	1	2	1	2
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86	884650	3	1	3	1	1	1	3	7	1	3	3	3	1	2		2	1	1
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88	885251	2	1	3	1	1	2	3	1	1	3	3	3	1	2		2	1	1
89	884421	2	1	2	3	2	1	2		1	3	3	3	2	2	4	2	1	2
90	885112	2	1	3	2	1	2	3	3	1	2	3	3	1	2		2	1	2
91	885299	2	1	3	1	1	2	3	2	1	3	3	3	1	1	1	2	3	2
92	886926	2	1	3	1	1	2	3	3	1	3	3	3	1	2		2	1	1

S.NO	IP NO	A	B	c	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
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94	888138	2	1	3	1	1	2	3	5	1	4	3	3	1	2		2	1	1
95	888140	2	1	3	1	1	2	3	2	1	3	3	3	1	2		2	1	1