# "PREVALENCE OF THROMBOCYTOPENIA IN PREGNANCY – A HOSPITAL BASED STUDY"


**Submitted by**

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# Dissertation

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## IN
## PATHOLOGY


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**KARNATAKA**


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KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH

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# ABSTRACT

**Introduction:**

An understudied and frequently underdiagnosed disease in Indian women is thrombocytopenia during pregnancy. Seven to eight percent of all pregnant women experience thrombocytopenia, which is the second most common hematological disorder to occur during pregnancy.

For the purpose of creating detailed plans for any antenatal interventions as well as for the management of labour, the postpartum period, and the neonate, an accurate diagnosis and risk assessment in the antenatal period are crucial.

The estimation of platelet count is easy, accurate, quick, and inexpensive. The severity of the illness and the early identification of the underlying disorder that causes thrombocytopenia can both be determined using this method.

**Aim:** To study the relationship between thrombocytopenia in pregnancy due to various causes and its effects on maternal and fetal outcomes.

**Material and Method:**

The current research was a 1-year prospective study that took place in our pathology department's hematology unit of a tertiary care institution. Pregnant patients who were inpatients and outpatients and whose platelets were < 1.5 lakhs/$mm^3$ in the $3^{rd}$ trimester were screened and recruited in the study.

**Results:**

Six-point nine percent of pregnant women in this study had thrombocytopenia. The study found that the most frequent reason for maternal thrombocytopenia was

gestational thrombocytopenia i.e., 65.05% (67/103 cases) followed by pregnancy induced thrombocytopenia (pre-eclampsia and eclampsia) i.e., 22.33% (23/103 cases). Four-point eight five percent cases (5/103) were diagnosed with HELLP syndrome. One case each i.e., 0.97% (1/103 cases) was also seen of megaloblastic anemia and acute fatty liver of pregnancy.

**Conclusions:**

The most common reason for maternal thrombocytopenia was gestational thrombocytopenia. It appears in the 3rd trimester of pregnancy and typically causes no complications for the mother or the foetus. Disorders associated with pregnancy-induced hypertension, or HELLP syndrome, were the second most frequent cause of maternal thrombocytopenia and was attributed to maternal morbidity and potentially fatal maternal complications such post-partum hemorrhage. Platelet count estimation and peripheral blood smear testing can minimize both maternal and foetal issues if the condition causing maternal thrombocytopenia is identified and treated at the earliest of the illness. Serial quantitative platelet estimation in thrombocytopenic pregnant ladies thus significantly reduces foetal and maternal morbidity and death.

# LIST OF ABBREVIATIONS USED

HSC- Hematopoietic stem cells

TPO- Thrombopoietin

CFU- Colony forming unit

PAS- Periodic Acid -Schiff

NSE- Non-specific esterase

SBP- Systolic blood pressure

DBP- Diastolic blood pressure

AFLP- Acute fatty liver of pregnancy

HIT- Heparin induced thrombocytopenia

ITP- Immune thrombocytopenic purpura

TTP- Thrombotic thrombocytopenic purpura

HUS- Hemolytic uremic syndrome

SLE- Systemic lupus erythematosus

DIC- Disseminated intravascular coagulation

ACOG- American College of Obstetrician and Gynecology

IUD- Intra-uterine death

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# INTRODUCTION

An understudied and frequently underdiagnosed disease in Indian women is thrombocytopenia during pregnancy. Seven to eight percent of all pregnant women experience thrombocytopenia, which is the second most common hematological disorder to occur during pregnancy.[1]

The second and third trimesters of pregnancy are when platelet counts are significantly reduced. A reduction in platelet production or rapid platelet destruction can lead to thrombocytopenia. This is explained by increased platelet activation during pregnancy, increased plasma levels of platelet factor 4 and beta thromboglobulin, decreased platelet survival time, and third trimester hemodilution. As a result, there is an enhanced platelet turnover as a normal pregnancy progresses.[2,3,4]

Gestational thrombocytopenia, followed by pregnancy-induced hypertension (PIH), is the most frequent cause of thrombocytopenia in pregnancy.

Between 2-10% of all pregnancies are affected by pre-eclampsia, the most common hypertensive condition of pregnancy, which considerably raises the rates of maternal morbidity and mortality.[5]

Platelets play a critical role in the development of pre-eclampsia because platelet activation occurs when they come into contact with damaged endothelium. Thrombocytopenia results from increased platelet consumption as a consequence. With disease severity, an increase in degree of thrombocytopenia is seen. Greater maternal and fetal morbidity and mortality are associated with lower platelet counts.

For the purpose of creating detailed plans for any antenatal interventions as well as for the management of labour, the postpartum period, and the neonate, an accurate diagnosis and risk assessment in the antenatal period are crucial.[6,7]

The estimation of platelet count is a crucial procedure carried out on pregnant women since it is easy, accurate, quick, and inexpensive. The severity of the illness and the early identification of the underlying disorder that causes thrombocytopenia can both be determined using this method.

Thus, any pregnant woman with platelet counts less than 1,50,000/$mm^3$ requires to undergo additional clinical and laboratory assessment. Strict monitoring of platelet counts in these individuals is necessary to prevent unfavorable outcome in serious conditions that may require specific and urgent management like HELLP syndrome, DIC, etc. and to lower the risks for the mother and fetus.

Patients from nearby areas come to our hospital as it is a tertiary care facility and referral source. For an accurate diagnosis and continued management, many complex cases are sent here. The current study was therefore started.

# AIM AND OBJECTIVES

## AIM

- To study the relationship between thrombocytopenia in pregnancy due to various causes and its effects on maternal and fetal outcomes.

## OBJECTIVES

- To study the prevalence of thrombocytopenia in pregnancy.
- To study various etiological factors of thrombocytopenia in pregnancy.
- To study the maternal and neonatal outcome.

# REVIEW OF LITERATURE

## HISTORICAL ASPECTS OF DISCOVERY OF PLATELETS

Platelets are one of the constituents of blood along with red blood cells and white blood cells.

**Hewson (1780)**, was the first to fully define platelets as very small undefined particles in blood.[8]

French histologist **Alfred Donne (1842)** described them as tiny globules made of plasma. The same were later described as "tiny corpuscles" by **Zimmermann** in **1860**.[9]

Platelets' significance was initially demonstrated by **Giulio Bizzozzero (1882).** He was adamant that these corpuscles, which were completely unrelated to the white and red blood cells, constituted the third morphological component of blood. He made it abundantly obvious that since they lacked hemoglobin and nuclear components, they could not be regarded as erythrocyte precursors.

These items are referred to as little plates by Bizzozzero (later platelets). The biggest strength of Bizzozzero was his insight of platelet function in hemostasis and thrombosis, and he asserted that platelets, not white blood cells, play the primary role in blood clotting.[10]

**Wright** first recognized bone marrow megakaryocytes as the progenitors of blood platelets only between 1906 and 1910.[11]

Ex vivo and in vitro research of platelet function and agonist receptivity were made possible by **Born's** invention of the aggregometer in 1962, and **David Ferreira**

published the first work on platelet ultrastructure examined by electron microscopy two years later.[12]

## HEMATOPOIESIS[13,14,15]

Production of the blood cell is extremely intricate process in which multiplication and differentiation of hematopoietic stem cells take place at a rate of $10^{11}$ cells/day. **Peault** has coined the term "hematon" to describe how HSCs (hematopoietic stem cells) grow into distinct offspring. From this structure, all lineages of committed colony forming cells can be created, including high proliferative potential colony forming cell assays as well as BFU-E (Burst Forming Unit-Erythroid) and CFU-GM (Colony Forming Unit-Granulocyte and Monocyte).

In order to generate more stem cells for differentiation and self-renewal in to the early and late progenitor cells, the hierarchy of hematopoietic stem cells has a broad potential for proliferation. Late progenitors those can differentiate into any type of cell and have receptors for various cytokines (IL-1, IL-6).

The lymphoid progenitor cells produce late progenitor cells, which differentiate into the mature T-cells, B-cells, and NK cells.

Myeloid progenitor cells generate late progenitor cells, which include G-CSF receptors and mature into neutrophils, monocytes, basophils, and eosinophils.

Megakaryocyte progenitors contain thrombopoietin receptors, whereas erythrocyte precursors have erythropoietin receptors.

Within region of red marrow hematopoiesis is highly compartmentalized with erythropoiesis taking place is linked to stromal cells. Megakaryocytopoiesis

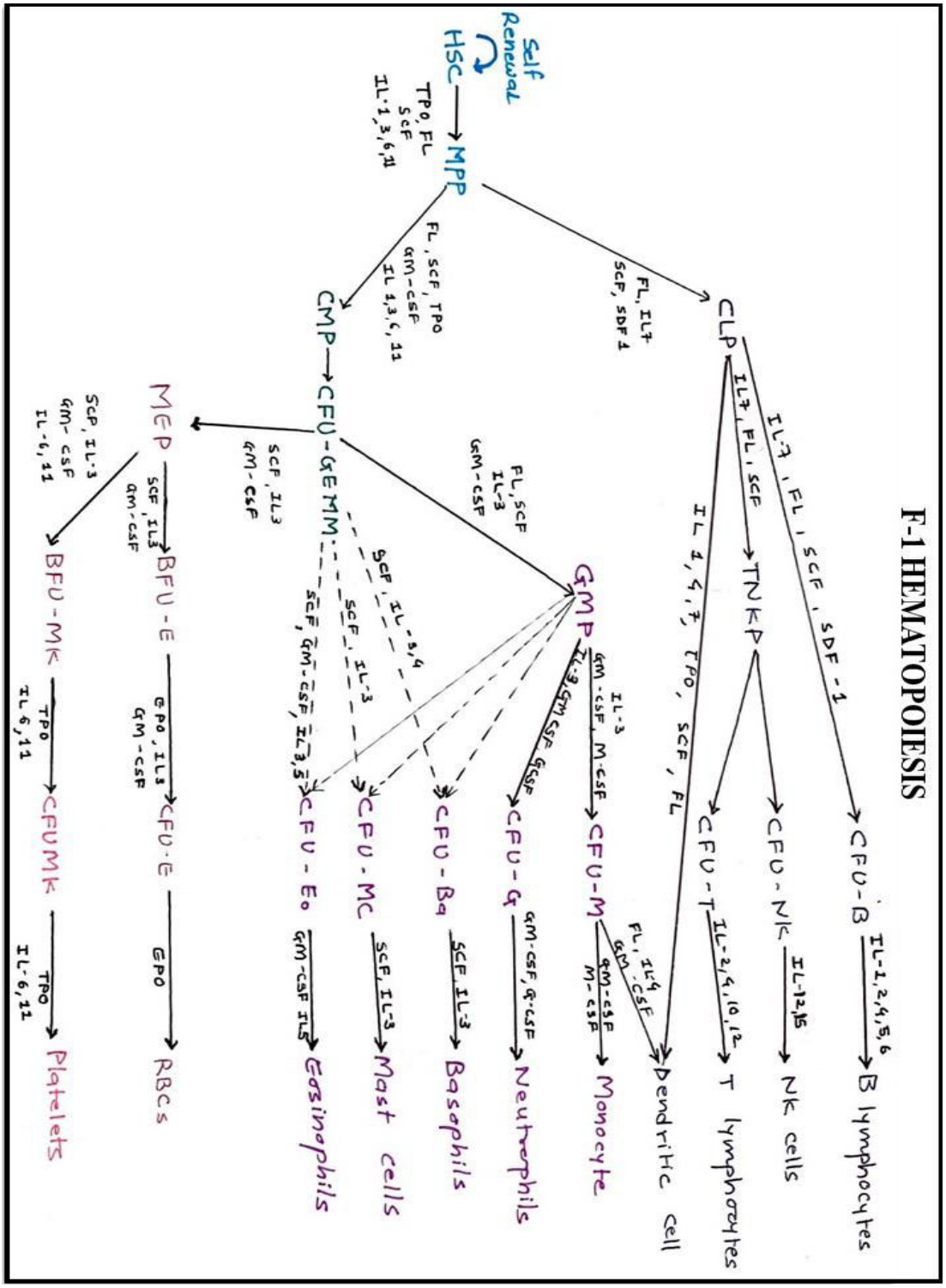
happening next to the endothelial sinusoidal cells.

## SITES OF HEMATOPOIESIS[16]

In first three weeks of gestation, the yolk sac is the main site of hematopoiesis. However, definitive hematopoiesis arises from a population of stem cells first observed on the dorsal aorta termed the AGM (Aorta-Gonads-Mesonephros) region. These common precursors of endothelial and hematopoietic cells called hemangioblasts are alleged to seed the liver, spleen and bone marrow. The liver and spleen are the major hematopoietic organs and continue to produce blood cells until about 4th month of fetal life after which it is taken over by the bone marrow.

` The bone marrow is the most important site of hematopoiesis from 6 to 7 months of fetal life till birth. During normal childhood and adult life, the marrow is the only source of new blood cells.

**FIGURE:1 HEMATOPOIESIS (The differentiation of blood cells from a pluripotential stem cell)**



Hematopoietic stem cell (HSC)

Multipotential progenitor cell (MPP)

Common myeloid progenitor (CMP)

Colony-forming unit granulocyte, erythrocyte, macrophage, and megakaryocyte (CFU-GEMM)

Granulocyte, monocyte progenitor (GMP)

Megakaryocyte erythroid progenitor (MEP)

T-lymphocyte, natural killer cell progenitor (TNKP)

CFU-G (Colony-Forming Unit -Granulocyte)

CFU-M (Colony-Forming Unit -Monocyte)

CFU-Eo (Colony-Forming Unit -Eosinophil)

CFU-Baso (Colony-Forming Unit -Basophil)

BFU – E (Burst-Forming Unit - Erythrocyte)

CFU-E (Colony-Forming Unit -Erythrocyte)

BFU-Mk (Burst-Forming Unit - Megakaryocyte)

CFU-Mk (Colony-Forming Unit -Megakaryocyte)

## MEGAKARYOCYTOPOIESIS

Megakaryocytes, an unique type of bone marrow cell, produce platelets. The largest and most chromosome-diverse cells in the bone marrow are known as megakaryocytes.

Megakaryocytopoiesis involves the commitment of hematopoietic stem cells, and the proliferation, maturation and terminal differentiation of the megakaryocytic progenitors.

### Role of thrombopoietin

Megakaryocytes and platelets have receptors for thrombopoietin called c-mpl receptors. Circulating levels of thrombopoietin (TPO), the primary growth factor for the megakaryocyte (MK) lineage, bring concentration dependent proliferation and maturation of megakaryocyte progenitors by binding to the c-mpl receptor and signaling induction.[17]

Decreased platelet turnover rates result in increased concentration of free TPO, facilitating the compensatory response of marrow megakaryocytes to increased platelet production. c-mpl activity is coordinated by a complex cascade of signaling molecules that makes the action of specific transcription factors to initiate megakaryocyte proliferation and maturation.[18]

Newly established thrombopoietic agents operating via c-mpl receptor may prove useful in supporting platelet production in thrombocytopenic state.[19]

**Developmental pathway of megakaryopoiesis**[20,21,22]

Common myeloid progenitors develop into megakaryocyte progenitors thanks to the GATA-1 (transcription gene product), which is coordinated by FOG1 (cofactor). MYB, a distinct transcription gene product, prevents the development of megakaryocytes. GATA-1 and MYB operate antagonistically to maintain a balance between megakaryocytopoiesis in one arm and erythropoiesis in another arm.

Three megakaryocyte lineage-committed progenitor stages are produced by the common myeloid progenitor in response to the growth factor thrombopoietin (TPO). These are the least mature burst forming unit (BFU-Meg), the intermediate colony forming unit (CFU-Meg), and the more developed progenitor, the light density CFU (LD-CFU-Meg), in that order of differentiation. The third stage, known as LD-CFU-Meg, is a partially defined form of mitosis that is unique to megakaryocytes and fails to divide while maintaining DNA replication and cytoplasmic maturation (nuclear division without cytoplasmic division). DNA replication keeps going until 8N, 16N, or even 32N ploidy with doubled chromosomal sets are produced. Megakaryocytes generate a large amount of cytoplasm, which develops into platelets, using their numerous copies of DNA.

Endomitosis is successful in reaching terminal differentiation through a variety of maturation stages.

**S-1 Megakaryoblast:** Here the cells range in size from 10 to 15 micrometres, have a big, distinct nucleus with three to five nucleoli, and a blue, non-granular scanty cytoplasm.

**S-2 Promegakaryocyte:** These cells range in size from 15 to 25 micrometres, with a reduced nucleo-cytoplasmic ratio and sparse blue cytoplasm with azurophilic granules. These type cells occasionally have non-granular cytoplasmic processes and platelet-like structures at the edge of its cytoplasm.

**S-3 Mature Megakaryocyte:** Here the cells can range in size from 25 to 120 micrometres, it is often quite large. The nucleus is lobulated or highly intended, and the amount of lobulation varies somewhat with ploidy. Megakaryocytes with basophilic, polychromatophilic, and oxyphilic cytoplasm range in hue from blue to pink and contain distinctive azurophilic granules along the perinuclear area.

Megakaryocytes are rarely found in the circulation of healthy people, and because of low concentration, they can only be detected during buffy coat preparation. Megakaryocytes exhibit a positive cytochemical staining response to acid phosphatase, NSE, and PAS.

Megakaryocytes can typically be distinguished at all stages using CD41/CD61. In the bone marrow and the lungs, platelet shedding, or thrombocytopoiesis, takes place after full maturation.

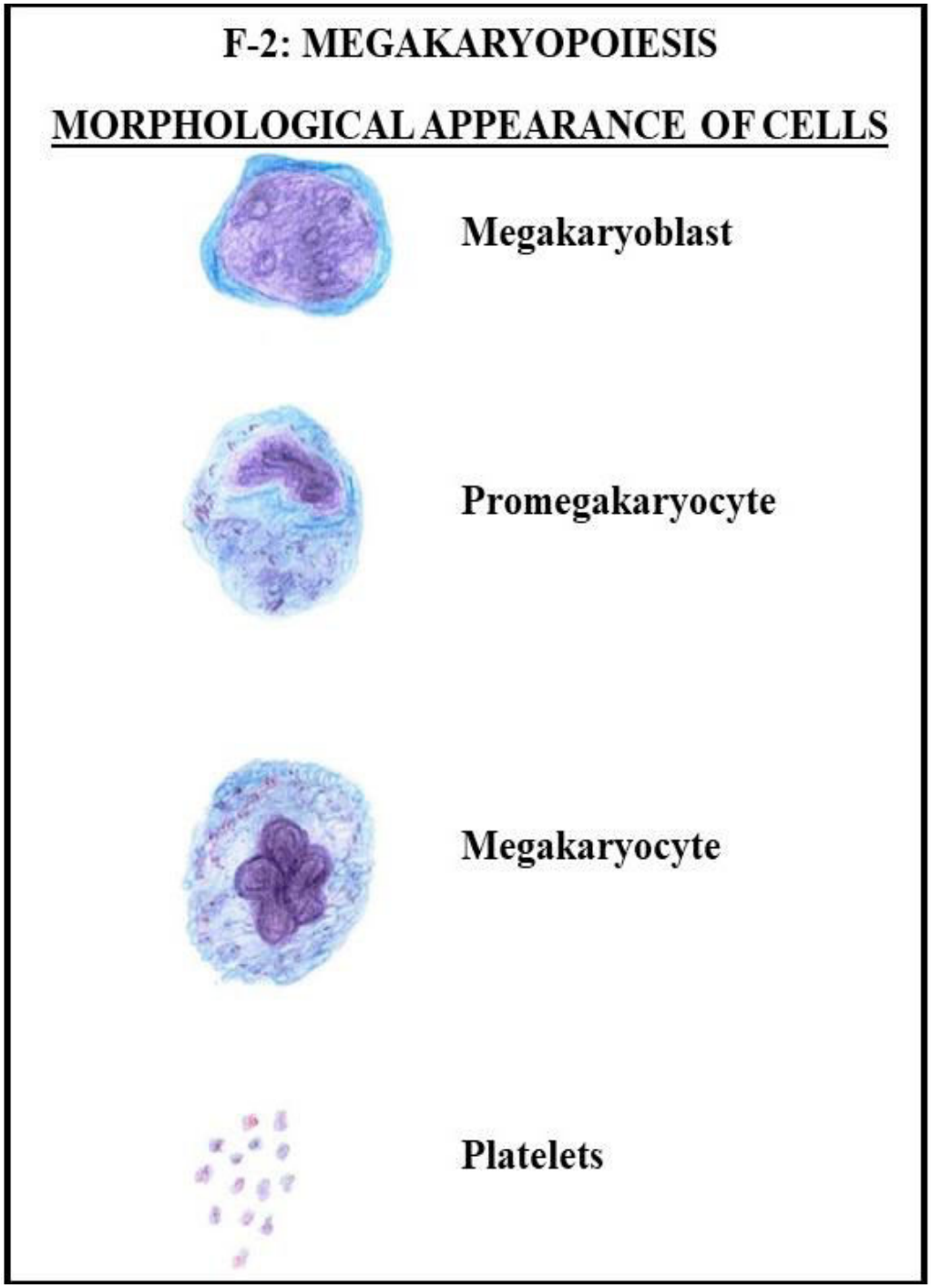
**Megakaryocyte Membrane Receptors Markers[22,23,24]**

Visually indistinguishable megakaryocyte progenitors in hematologic illness are identified via immunostaining of fixed tissue, flow cytometry with immunologic probes, and fluorescent in situ hybridization (FISH) with genetic probes.

There are numerous flow-cytometric megakaryocyte membrane markers, including CD34 (stem cell and common myeloid progenitor marker), as well as Mpl. The site for TPO receptor is seen present at all maturation stages. As differentiation

progresses, the CD34 marker disappears. Along with CD36, CD42, CD61, and CD62 (immunologic markers), the platelet membrane GPIIb/IIIa first arises on megakaryocyte progenitors and persists throughout maturation.

**FIGURE: 2 MEGAKARYOPOIESIS**



## THROMBOPOIESIS

A single megakaryocyte may shed up to 2000 to 4000 platelets, a process called thrombopoiesis. In an average size healthy human there are $10^8$ megakaryocytes producing $10^{11}$ platelets per day, a total turnover rate of 8 to 9 days.[25]

Platelets are released from fragmenting megakaryocytes by two ways:

- Extension of pseudopodia through the wall of the sinuses; pseudopodia contain "strings" of platelets that are pinched off and released into the circulation.
- Passage of mature megakaryocyte into circulation and fragmentation in the pulmonary vascular bed.[26]

Megakaryocyte nuclei left behind from thrombopoiesis are consumed by marrow macrophages. In the circulation, thrombocytes or platelets move as cytoplasmic discs. They are the primary cells that regulate hemostasis by maintaining the integrity of the blood vessels. The surface of injured blood vessels is quickly contacted by platelets, which then group together to block the capillaries and emit proteins and tiny molecules that promote thrombosis and keep the blood channels open.

**Platelet turnover and removal** [25]: A mature platelet has a lifespan of around 9days ± 1day. After that, they are phagocytized by the mononuclear phagocytic system's macrophages, which are found in the liver, spleen, and other tissues.

**Platelet distribution**[25]: Data indicates that two thirds of the platelets are in the bloodstream and that the spleen contains one third of the total platelet mass.

**Light microscopy**[27,28]: There are 7 to 21 platelets per 100x oil immersion field distributed throughout the red cell monolayer. In a normal person there should be 1 platelet for every 10-25 red cells. Their diameter in a monolayer of a peripheral blood film stained with Wright's stain is between two and three micrometres. Platelets on Wright appear as tiny, anucleate, ovoid or spherical cells with pale greyish blue cytoplasm and uniformly dispersed purple-red granules in Giemsa-stained blood smears. Although platelet size varies from person to person, unusually big platelets can be found in some illness states.

**Electron microscopy**[29,30,31]**:** When viewed under an electron microscope, resting platelets resemble flat discs with smooth edges, infrequent spiny filopodia, and sporadic channel system openings. An intricate surface and a cytoplasm crammed with organelles that are essential for maintaining healthy hemostasis are visible under transmission electron microscopy.

Platelets are anucleate and are surrounded by a typical lipid bilayer membrane. Underneath the outer membrane lies the marginal band of microtubules, which maintain the shape of the platelet and depolymerize when aggregation begins.

The central cytoplasm is dominated by three types of platelet granules: The dense granules, alpha granules and lysosomal granules with organelles namely micro peroxisomes, coated vesicles and mitochondria. The platelet membranous system has muscle like qualities and are of 2 types: surface coated canalicular system and dense tubules.

The contractile system of the platelet consists of the dense microtubular system and the circumferential microfilaments, which maintain the disc shape.

## ALTERATION IN HEMATOLOGICAL PARAMETERS IN NORMAL PREGNANCY[32]

Hematologic parameters are altered, among other physiologic changes, that occur during a typical pregnancy.

**Blood volume and RBCs:** During pregnancy, the volume of the mother's blood and plasma increases. From about 2600 ml to 3700 ml, the volume of circulating plasma has increased by 40%, with the majority of the increase occurring in the 2$^{nd}$ trimester (before 32weeks). As the plasma volume rises proportionately more than the red cell mass, there is a dilutional decline in hemoglobin concentration, which causes it to fall.

Erythropoietin levels rise during pregnancy and, at term, are around 150% more than they were before. The increasing red cell mass, growing foetus, and developing placenta all demand more iron, which results in a decrease in blood ferritin levels.

Hemoglobin values of less than 10.5 g/dl in the second trimester and less than 11 g/dl in the first and third trimesters are considered anemia in pregnant women. This is because the need exceeds the average young women's iron reserve, and the diet is unable to match this demand.

As the plasma colloid osmotic pressure decreases during pregnancy, fluid is forced into the extravascular compartment, resulting in oedema in about 80% of pregnant women.

**White blood cell counts:** White blood cells rise during pregnancy with shift to left occasionally. There is rise in the total leucocyte count during labour and the early puerperium.

**Erythrocyte sedimentation rate (ESR):** ESR is a problematic marker of inflammation because it increases during pregnancy due to higher plasma globulin and fibrinogen levels.

**Plasma proteins:** During pregnancy, the levels of various plasma proteins rise as well, with C-reactive protein being particularly high.

Von Willebrand Factor (VWF), fibrinogen, factor VII, factor VIII, and factor X show significant rise in plasma levels, although factor II, V, IX, and XII remain largely stable, and factor XIII decreases. While total protein and free protein S levels decrease with advancing gestational age, protein C and antithrombin levels stay steady throughout pregnancy.

**Hemostasis in pregnancy[32,33]**

Nature has designed pregnancy to be hypercoagulable in order to reduce blood loss during birth. As a result, procoagulants such as fibrinogen, factor VIII, and VWF are present in greater amounts, whereas naturally occurring anticoagulants such as protein S and antithrombin are decreased. There is an enhanced net turnover of coagulation factors as fibrinolysis is also elevated.

Pregnancy increases the risk of venous thromboembolism by up to 10 times compared to non-pregnant women. Up to 6 weeks following delivery, the alterations in coagulation factors and blood flow velocity may continue.[34]

In normal pregnancy, there is proportionate increase in biosynthesis of particular eicosanoids namely prostacyclin PGI2 and thromboxane A2. PGI2 is a vasodilator with platelet inhibitory properties, and thromboxane A2, a vasoconstrictor with a tendency to stimulate platelet aggregation. Hence there is net neutralization and homeostasis is thus maintained.

## PLATELET COUNT IN NORMAL PREGNANCY[35,36,37]

The mean and 2.5$^{th}$ percentile platelet count declines up to 10% in pregnant ladies according to recent research that examined platelet counts in over 4000 pregnant patients. They also showed that the platelet distribution at term is normally distributed but displaced to the left in histogram.[35,36] This physiological reduction in platelets often takes place in the 3$^{rd}$ trimester. These findings imply that pregnancy is linked to a mild, typically undetected drop in the number of platelets in the blood.

Asymptomatic thrombocytopenia affects up to 5% of pregnant ladies, making it a rather prevalent condition. Many of the factors that lead to thrombocytopenia during pregnancy are the same as those that lead to the condition when a woman is not pregnant. However, gestational thrombocytopenia, pre-eclampsia, eclampsia, HELLP syndrome, and AFLP are a few disorders that are specific to pregnancy and cause thrombocytopenia.

## CAUSES OF THROMBOCYTOPENIA IN PREGNANCY

Thrombocytopenia complicates up to 10% of all pregnancies. Thrombocytopenia in pregnancy may result from a variety of causes, ranging from benign disorders such as gestational thrombocytopenia to life threatening syndromes such as the HELLP syndrome (hemolysis, elevated liver enzymes, low platelets syndrome).[36]

It is necessary to estimate the platelet count and carefully examine blood smears in order to rule out platelet clumping, microangiopathic hemolytic anemia, and other hematological disorders. If more testing is required to rule out systemic lupus erythematosus (SLE), it can be done. These tests include renal function tests (RFT), liver function tests (LFT), antiphospholipid antibodies, and anti-DNA antibodies. A detailed history and physical examination are essential, to rule out significant causes of thrombocytopenia during pregnancy.

## CAUSES OF THROMBOCYTOPENIA IN PREGNANCY[37]

**I Isolated thrombocytopenia**

a. Spurious / Artifactual

b. Gestational thrombocytopenia

c. Immune thrombocytopenia

d. Drug induce thrombocytopenia and Heparin induced thrombocytopenia

e. Type IIb Von Willebrand Disease

f. Congenital thrombocytopenia

**II Thrombocytopenia associated with systemic disorders**

A. Pregnancy specific disorders:

a. Pre-eclampsia and Eclampsia

b. HELLP syndrome

c. Acute fatty liver of pregnancy

B. Non pregnancy specific disorders:

a. Thrombotic thrombocytopenic purpura/ Hemolytic uremic syndrome

b. Systemic lupus erythematosus/ Antiphospholipid antibodies

c. Disseminated intravascular coagulation

d. ineffective Thrombopoiesis

e. Nutritional deficiency

f. Thrombocytopenia associated with infections

g. Post transfusion purpura

h. Hypersplenism

**I. Isolated thrombocytopenia**

**a. Artifactual Thrombocytopenia:**

When platelets are incorrectly counted, a condition known as artifactual thrombocytopenia. Patients who have thrombocytopenia but no petechiae or ecchymosis, this mechanism should be taken into account.

The most common cause of artifactual thrombocytopenia or pseudo-thrombocytopenia is platelet clumping. The first step in evaluating a low machine count is to check for the presence of blood clot in the vacutainer and confirm the finding by microscopic examination of the blood film.

Platelet clumping in pseudo-thrombocytopenia seems to be brought on by immunoglobulins of the IgG, IgA, or IgM subtypes those are anticoagulant dependent platelet agglutinins. Ethylene diamine tetra acetic acid anticoagulant collected blood is most commonly associated with platelet clumping**.** The diagnosis is confirmed by demonstrating that platelets are substantially higher when measured in citrated or heparinized blood without an anticoagulant.[38,39]

The amount of platelet clumping is also time-dependent and depends on the automatic counting apparatus being utilized. Presence of giant platelets which are not counted as platelet by electronic cell analyzers also cause spurious thrombocytopenia.

Inaccurate platelet counting may also occur in the presence of platelet satellitism.

Platelet satellitism is an in vitro phenomenon of platelet resetting or adherence of platelets around polymorphonuclear neutrophils and is observed exclusively in blood treated with EDTA as an anticoagulant at room temperature.[40]

**FIGURE: 3 PSEUDOTHROMBOCYTOPENIA (PLATELET CLUMPING)**

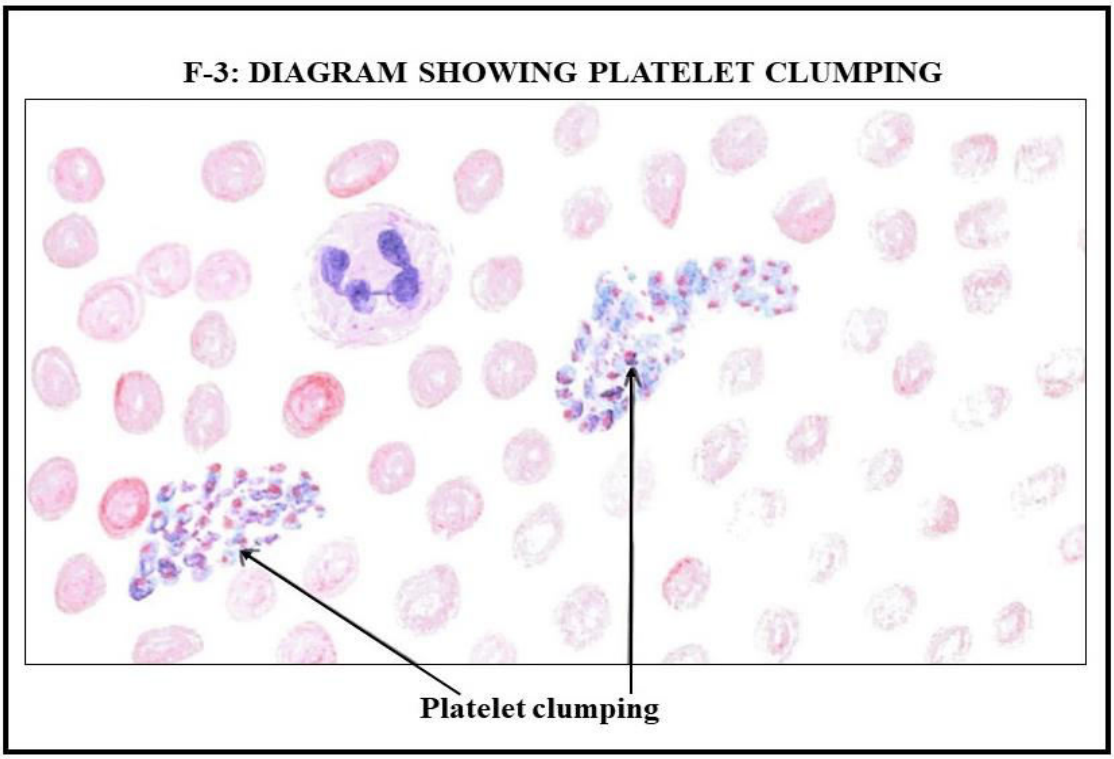
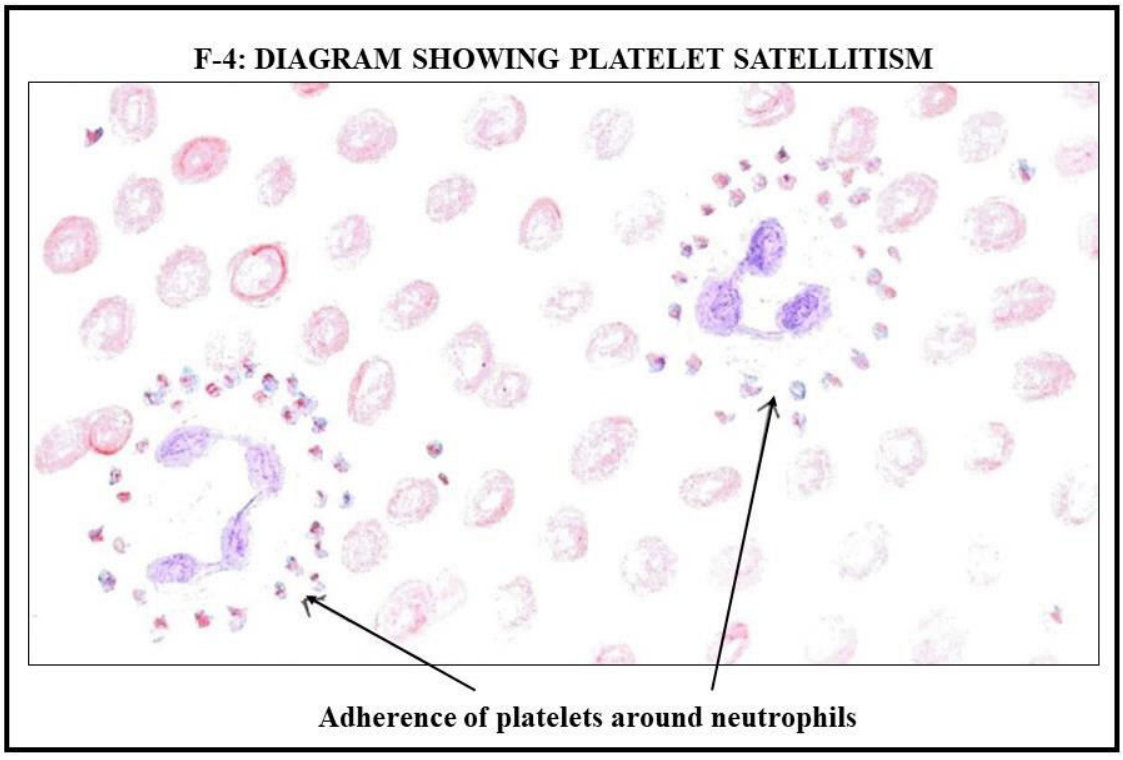



**FIGURE: 4 PSEUDOTHROMBOCYTOPENIA (PLATELET SATELLITISM)**



**b. Gestational Thrombocytopenia:**

The most frequent cause of thrombocytopenia in pregnancy is gestational thrombocytopenia, a form of physiologic thrombocytopenia that occurs along with pregnancy. Approximately 5% of all pregnant women have this condition, which is responsible for >75% of all occurrences of pregnancy-related thrombocytopenia.

Although the pathophysiology of gestational thrombocytopenia is unknown, it is thought to be caused by immunological or nonimmune-mediated hemodilution or rapid platelet clearance.

Despite the fact that most pregnant ladies with gestational thrombocytopenia maintain normal platelet counts between 1,10,000 and 1,50,000/$mm^3$, most experts believe that a platelet count of more than 70,000/$mm^3$ in a pregnant woman who is otherwise healthy and has no history of immune-mediated thrombocytopenia is indicative of this condition. Patients with a platelet count below this threshold have a greatly increased risk of developing thrombocytopenia from other, more serious reasons.[41,42]

Both the incidence and the risk of giving birth to thrombocytopenic offspring are not enhanced in patients with gestational thrombocytopenia. Verdy et al (1997), McCrae et al (1992). An otherwise healthy pregnant lady with platelet counts above 70,000/$mm^3$ with no previous history of thrombocytopenia, therefore may require a routine physical examination, blood pressure monitoring, and careful peripheral blood film examination.[43]

Gestational thrombocytopenia does not require any treatment as not enough data exist on treatment modality of any proven efficacy and the few cases who received either steroid or intravenous immunoglobulins (IVIG) showed no response to treatment.

In a 1997 prospective research, Marco Ruggeri et al. verified that substantial neonatal thrombocytopenia is infrequently seen in pregnant thrombocytopenia, which is a benign disease. Additionally, it has been noted that gestational thrombocytopenia could reoccur during subsequent pregnancies and was not an early sign of autoimmune disorders.[44]

According to ACOG, most cases of gestational thrombocytopenia will show normal platelet counts within days and almost all will do so within 2-12 weeks postpartum.[45] However there is no agreement on the duration of postpartum observation period needed to monitor these patients.

**c. Immune Thrombocytopenia (ITP):**

ITP was first described by Werlhof in 1735 who in his book 'De Variolis et Anthracibus' described in footnote a 16-year-old girl with cutaneous and mucosal bleeding.[46]

ITP is common acquired autoimmune disorder defined by low platelet count secondary to accelerated platelet destruction by antiplatelet antibodies.

Secondary autoimmune thrombocytopenia can occur in pregnancy and SLE in association with drugs and several other miscellaneous diseases.[47]

ITP accounts for about 1 instance of thrombocytopenia per 1000 pregnancies and 5% of all cases of thrombocytopenia related to pregnancy, making it the most frequent cause of severe thrombocytopenia in the first trimester.[48]

ITP, as opposed to gestational thrombocytopenia, can happen at any stage of pregnancy and can cause a substantial drop in platelet count.

The reticuloendothelial system clears IgG-coated platelets that are directed against platelet glycoproteins, especially GPIIb/IIIa and GPIb/IX, in pregnant patients just as it does in non-pregnant ones.

ITP in pregnancy is diagnosed by ruling out other conditions. These individuals typically present with moderate to severe thrombocytopenia and a prior history of thrombocytopenia. In the absence of a pregestational platelet count, the start of severe thrombocytopenia in 1st trimester and declining of platelet counts as pregnancy progresses, is most consistent with ITP, although gestational thrombocytopenia appears to occur more frequently in the second or third trimester.

Platelets appear to be morphologically aberrant in the peripheral blood smear, coming in large, tiny, and unusual forms. Megathrombocytes cause the mean platelet volume to be high (MPV). Additionally, the aberrant degree of platelet anisocytosis is reflected by an increase in platelet distribution width (PDW). Megathrombocytosis of this kind may be caused by accelerated platelet formation in reaction to platelet breakdown, while the precise mechanism underlying it is still unknown.[50]

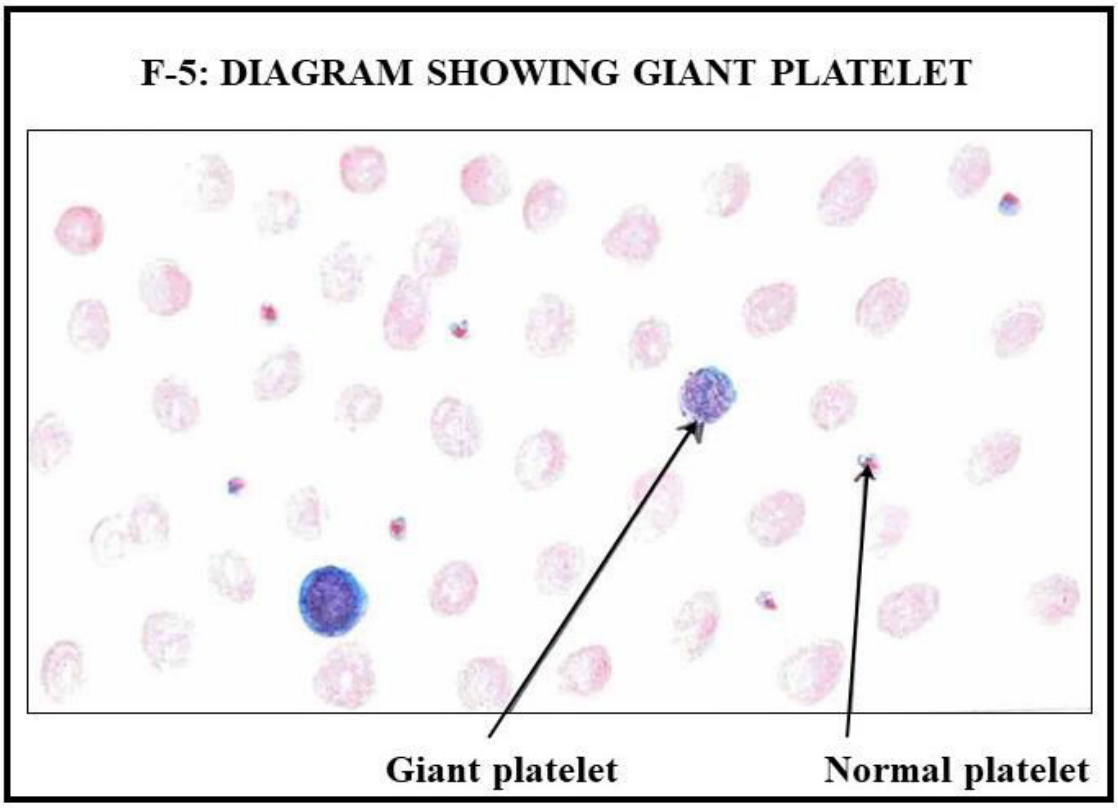
The severity of the thrombocytopenia must be considered while treating ITP in pregnant women, and symptoms must be addressed. In order to achieve an acceptable platelet count for safe delivery, patient and platelet count monitoring is essential. The primary line of treatment is the use of corticosteroids, while IVIG may also be helpful for increasing platelet count before delivery. Due to the low survival duration of transfused platelets, platelet transfusions are not advised.[51,52]

Foetal thrombocytopenia - ITP most frequently manifests as asymptomatic maternal thrombocytopenia, although transplacental antibody transfer can also cause foetal thrombocytopenia in 9–15% of affected infants and intra cerebral hemorrhage in 1.5% of infants. The risks associated with foetal sampling prevent routine recommendations for foetal platelet count estimate.

In fact, a prior sibling's history of thrombocytopenia may be the most accurate predictor of newborn thrombocytopenia. All newborns should have their cord blood

platelet counts assessed, and the following 5-7 days call for close observation. Intravenous IgG administration may prevent the placental transfer of maternal antibodies to the foetus that is Fc dependent.[51]

**FIGURE: 5 IMAGE SHOWING GIANT PLATELET**




d. **Heparin induced thrombocytopenia and Drug induced thrombocytopenia[53,54]**

The most frequent reason for drug induced thrombocytopenia is HIT. The reason being a high chance of possibly fatal venous or arterial thrombosis, this dangerous consequence of heparin therapy is known as "white clot syndrome."

An antibody that binds to platelet factor 4 (PF4) that has been linked to heparin on the platelet surface results in immune HIT. After forming this complex, the antibody can bind to the Fc receptor and cause aggregation (thrombosis). The main clinical signs of HIT are therefore thrombocytopenia and thrombosis.

Within 1 to 3 days after starting heparin, 30% of patients experience HIT type I, a benign and restricted thrombocytopenia. In contrast, thrombotic HIT type II manifests after 5 days and the platelet count reduction may surpass 40%.

Patients with thrombosis have a mortality rate of about 25%. The platelet counts of patients using heparin must be checked often. Five to fifteen days following the administration of heparin, if the platelet count falls below 50% of the baseline, this disease should be investigated.

Both the serotonin release assay and the ELISA assay have sensitivities of over 90% and extremely high specificities for HIT antibodies.

According to north American recommendations, only low molecular weight heparin has little dangers, and these pregnant patients do not need to undergo routine platelet count monitoring. Heparin should be stopped, though, 24 hours prior to a caesarean section or labour induction.

**Other medications causing thrombocytopenia:** Acetaminophen, digoxin, gold, procainamide, carbamazepine, and hydrochlorothiazide. The most typical medications that can cause ITP include quinidine, quinine, rifampin, trimethoprim-sulfamethoxazole, danazol, and methyldopa (Aldomet).

Platelet levels recover to normal within days or by one week after the medicine is stopped.[55]

**e. Von Willebrand Disease:** Erik Von Willebrand, a Finnish professor, initially identified VWD as a prevalent mucocutaneous bleeding condition in 1926. It has an autosomal dominant inheritance pattern and is found in roughly 1% of several populations.[56]

A mutant VWF molecule that binds to its primary platelet receptor, glycoprotein Ib, with greater affinity causes Type IIb Von Willebrand disease, which includes platelet agglutination, rapid platelet clearance, and thrombocytopenia.

Von Willebrand Factor is a glycoprotein made in the endoplasmic reticulum of endothelial cells and is kept in the cytoplasm of these cells' Weibel-Palade structures. Additionally, it is produced in megakaryocytes and kept in the platelet's alpha granules.

At the site of vascular damage, VWF links platelets to the sub-endothelium, whereas factor VIII's association with VWF in the plasma prevents factor VIII from deteriorating.

Reduced platelet adhesion in Von Willebrand disease causes mucocutaneous bleeding of varied severity. APTT, VWF antigen/activity, and factor VIIIc levels should also be checked in suspected cases.[57,58]

Pregnancy and acute phase response are both associated with a customary rise in VWF/factor VIII. Since it reaches its peak concentration in the third trimester, prenatal treatment is typically not indicated. However, Von Willebrand factor levels fall rapidly immediately after birth. Hence, untreated cases have a 13 - 29 % risk of postpartum haemorrhage.[59]

Prenatal diagnosis may be necessary, and all women with Von Willebrand Disease who are considering getting pregnant should be informed of the bleeding risk and offered genetic counselling regarding Von Willebrand Disease inheritance. Plasma-derived factor concentrates that contain both factor VIII and Von Willebrand factor is effective therapy for the most prevalent and mild form of VWD.[60]

**f. Congenital Thrombocytopenia[61,62,63]**

Although rare, congenital diseases including Bernard Soulier, Glanzmann's thrombasthenia, and May Hegglin anomaly can be identified during pregnancy using platelet aggregation investigations and the recognition of aberrant platelet morphology on blood smear evaluation.

Less than 5% of neonatal thrombocytopenia occurs, as the platelet production reduces in newborns, making this type of thrombocytopenia rare.

Hereditary thrombocytopenia can be acquired during pregnancy or it can be inherited as an autosomal dominant trait, autosomal recessive trait, or X-linked recessive trait (e.g., congenital rubella syndrome). These illnesses typically show only moderate clinical symptoms at first. However, because they may not respond to intravenous immunoglobulin therapy or steroid treatment and may be hazardous, it is crucial to detect these moderate variants of familial thrombocytopenic syndrome that resemble ITP.

Various causes of congenital thrombocytopenia are:

i. constitutional aplastic anemia (Fanconi syndrome)

j. congenital amegakaryocytic thrombocytopenia

k. Autosomal recessive thrombocytopenia - Thrombocytopenia with absent radius, Bernard soulier syndrome, Familial thrombocytopenia with micromegakaryocyte.

l. Autosomal dominant thrombocytopenia - Alport's syndrome variants, May hegglin thrombocytopenia.

m. Sex linked thrombocytopenia - Wiskott-Aldrich syndrome.

## II. THROMBOCYTOPENIA ASSOCIATED WITH SYSTEMIC DISORDERS

### A. PREGNANCY SPECIFIC DISORDERS

a. **Pre-eclampsia and eclampsia**

Pregnancy-related thrombocytopenia is linked to hypertensive disorders in about 20% of cases.[64]

Pre-eclampsia is a pregnancy specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation. Fifteen to twenty percent of patients with pre-eclampsia, a disease characterized by hypertension, proteinuria, and seizures experience thrombocytopenia.[65]

Pre-eclampsia normally develops at around 20 weeks of pregnancy and complicates roughly 5% of all pregnancies. The emergence of proteinuria and hypertension are two symptoms of the condition. Systolic blood pressure >140 mmHg or a diastolic blood pressure >90 mmHg on two occasions at least 4 hours apart or SBP >160 mmHg and DBP >110 mmHg, proteinuria >0.3 grams in 24-hour urine specimen in the criteria for diagnosis. Symptoms can include edema in the feet and legs and pain in abdomen, headache, blurred vision, or mental function issues.[66]

The pathogenesis of pre-eclampsia originates in the placenta. Disruption in the vasoactive factors have also largely been responsible for pre-eclampsia, hence, it is known as the 'disease of theories.' Observation in abnormal interfaces between maternal, paternal and fetal tissue have led to the hypothesis that the syndrome is a two-stage disorder.[67,68]

**Phase 1** is associated with abnormal placentation – Abnormal placentation may be result of maternal immune rejection of placental antigens expressed by the fetus. HLA-G is a class IB major histocompatibility antigen that is expressed by extra villous trophoblast and may protect cells from natural killer cell lysis. Pre-eclampsia appear to have extra villous trophoblast that does not express HLA-G.

**Phase 2** is characterized by an exaggerated maternal inflammatory response, endothelial dysfunction and reduced organ perfusion. Disrupted homeostasis in pre-eclampsia is because of a relative deficiency in prostacyclin owing to either a decrease in its synthesis or an increase in production of thromboxane A2. This imbalance leads to vasoconstriction, hypertension, and platelet stimulation.

Proteinuria is an important sign of pre-eclampsia and the diagnosis is questionable in the absence. Similarly, abnormal laboratory findings in tests of renal, hepatic and hematological function increase the certainty of pre-eclampsia.[69,70]

**Eclampsia**

It is the occurrence of grandmal seizures in a woman with pre-eclampsia that cannot be attributed to other causes and may present any time before, during or after labor. Eclampsia is estimated to occur 1 in 200 cases of pre-eclampsia when magnesium prophylaxis is not administered.

Most individuals who develop thrombocytopenia have high fibrinogen, D-dimers, and thrombin-antithrombin complexes in their lab results, which are typical levels of PT, aPTT, and fibrinogen.[71]

The cure for pre-eclampsia and eclampsia is delivery of the fetus. It is associated with more severe intrauterine growth retardation. Antihypertensive therapy does not fundamentally alter the progress of the condition.[72,73]

b. **HELLP syndrome**[74,75]

The name HELLP syndrome is coined by Weinstein in 1982 by regarding the signs and symptoms of the disease and constituted a separate entity from severe pre-eclampsia (Hemolysis, Elevated Liver enzymes, Low platelets syndrome).

HELLP syndrome is currently regarded as a variant of severe pre-eclampsia and affects up to 12% of those with pre-eclampsia or eclampsia.

Thrombocytopenia occurs due to increased consumption of platelets. Platelets are activated, and adhere to damaged vascular endothelial cells, resulting in increased platelet turnover with short lifespan.

Criteria for the diagnosis of HELLP syndrome include-

1. Microangiopathic hemolytic anemia (MAHA)
2. SGOT >70 U/L
3. Thrombocytopenia, with a platelet count below 1,00,000/$mm^3$.

In addition to epigastric pain, nausea, vomiting, and right upper quadrant tenderness, women with HELLP syndrome may also exhibit hypertension and proteinuria.

Diagnosis can be made by peripheral blood film examination which may show schistocytes, burr cells and polychromasia consistent with hemolysis, although frank

anemia is uncommon. Thrombocytopenia is a major manifestation of HELLP syndrome and may be severe, with platelet count <50,000/$mm^3$. These patients typically have elevated bilirubin and aspartate transaminase (AST) and lactate dehydrogenase (LDH) levels.

A poor prognosis for both the mother and the foetus is linked to HELLP syndrome. Acute renal failure and diffuse intravascular coagulation are two maternal complications. Most of the perinatal deaths can be attributed to placental abruption, intrauterine asphyxia and prematurity.

In order to treat HELLP syndrome, a mother must be stabilized while also treating any coagulation issues, evaluating the health of the foetus, and determining whether or not delivery is necessary.

Observation for at least 48 hours postpartum is mandatory as deterioration in the maternal condition may occur. The thrombocytopenia normally goes away a few days after delivery. The risk of recurrence of HELLP syndrome in subsequent pregnancies is approximately 20%.[75,76]

Neonatal thrombocytopenia – Prematurity's consequences, including sepsis and acute respiratory distress, are thought to be the aetiology of thrombocytopenia in the newborn.[77]

c. **Acute fatty liver of pregnancy (AFLP)**[79,80,81]

Sheehan initially referred to acute fatty liver of pregnancy (AFLP) as an "acute yellow atrophy of the liver" in 1940. One in 10,000–15,000 pregnancies are affected by this rare but dangerous illness, which is most prevalent in primigravidae during the third trimester. Foetal mortality in this illness is close to 15%, despite maternal mortality occurring fewer than 5% of the time.

Hepatocytes with micro-vesicular fatty infiltration but no necrosis or inflammation are the hallmark of AFLP.

Recent scientific developments imply that mitochondrial malfunction may be the cause of AFLP. Lack of long-chain 3-hydroxy-acyl CoA dehydrogenase (LCHAD) or mitochondrial fatty acid oxidation-related enzymes was frequently seen. At position 478 of LCHAD, a glutamic acid to glutamine mutation appears to be particularly significant for the onset of disease.

Right upper quadrant pain, nausea, vomiting, and cholestatic liver function are the symptoms of AFLP. Hypoglycemia is frequent and severe, and diabetes insipidus may also develop.

Laboratory findings include low platelet count, prothrombin time, low fibrinogen and low antithrombin level in addition to raised bilirubin levels. This results in a clinical picture similar to DIC due to decreased hepatic synthesis of antithrombin due to decreased production by the damaged liver.

Treatment requires intensive supportive care with blood product support for the coagulopathy. Hemostatic irregularities require up to 10 days to return to normal after delivery.

B. **NON-PREGNANCY SPECIFIC DISORDERS**

**a. <u>Thrombotic thrombocytopenic purpura (TTP) and Hemolytic-Uremic-syndrome (HUS)</u>**

In 1960 Brain et al described the clinical and pathological similarities of HUS and TTP and applied the term microangiopathy of both diseases.

Fever, hemolysis, thrombocytopenia, symptoms of the central nervous system, and renal dysfunction are the characteristic pentad of TTP. The onset of TTP, especially recurrent TTP, typically occurs before to 24 weeks of pregnancy.

TTP is characterized by thrombocytopenia, resulting from the consumption of platelets, erythrocyte fragmentation and defective regulation of von-Willebrand factor activity by a circulating metalloproteinase ADAMTS-13. Platelet aggregation, consumption, and subsequent microvascular thrombosis are caused by the resulting excess of circulating Von Willebrand Factor.

Even though pregnancy is linked to a shift in ADAMTS-13 activity, testing ADAMTS-13 and autoantibodies against ADAMTS-13 may be helpful in confirming the clinical diagnosis of TTP in pregnant ladies.[82,83,84]

In 1955, Gasser et al. published the first description of hemolytic uremic syndrome (HUS). Following an episode of hemorrhagic diarrhea, the triad of renal failure, microangiopathic hemolysis, and thrombocytopenia is known as typical HUS. Shiga toxin-producing E. coli (STEC) of the enterohemorrhagic serotype, commonly serotype O157:H7, is linked to HUS infection.

Pathophysiology of HUS involves injury to the kidney and other organs like brain and myocardium as a consequence of the cytotoxic effect of Shiga toxins on vascular endothelial cells.[85]

The laboratory signs of HUS and TTP are thrombocytopenia and microangiopathic hemolytic anemia. Thrombocytopenia is usually severe with platelet counts below 60,000/$mm^3$ in most cases. Platelet survival time is reduced reflecting enhanced platelet disruption in the circulation. Giant platelets may be seen in the peripheral smear. Serum lactate dehydrogenase levels are increased reflecting not only hemolysis but also diffuse tissue ischemia.

Preventing thrombosis and thrombocytopenia during pregnancy should be a major priority because it increases maternal and foetal morbidity and mortality.

Treatment - Apart from endotoxin-related HUS (supportive care is the primary necessity) and congenital TTP, it is difficult to tell the difference between the two syndromes in the majority of pregnancy-related situations. As a result, while considering therapy, both are frequently viewed as a single syndrome. Plasma exchange (new frozen plasma) should be started as soon as possible when the patient presents. [86,87]

**b. <u>Antiphospholipid syndrome and systemic lupus erythematosus</u>**

APL antibodies are acquired antibodies against phospholipid protein complexes. They include Lupus anticoagulant, Anticardiolipin antibodies and anti$\beta_2$-GPI antibodies.

According to reports, anticardiolipin and lupus anticoagulant prevalence in generally healthy individuals ranges around 1.0% to 5.6% and 1.0% to 3.6%, respectively. With advancing years, the prevalence of increased aPL antibodies may rise as well.[88]

These develop in collagen vascular disorders, and autoimmune aPL antibodies are present in 50% of individuals with systemic lupus erythematous.

Secondary APS is the term used when APS is identified in patients with an underlying autoimmune illness, typically systemic lupus erythematosus. Patients with "triple positivity"- positive lupus anticoagulant, raised anticardiolipin antibodies, and elevated anti-2-GPI antibodies- test positive for all three of the primary assays are at significantly higher risk for thrombosis and pregnancy complications.[89]

Antiphospholipid antibody syndrome – Chronic autoimmune aPL antibodies which are characterized by a worsened pregnancy outcome, a higher risk of thrombosis, recurrent miscarriage, and thrombocytopenia.

Antiphospholipid syndrome (APS) has a prevalence of 15% in women with first-trimester recurrent miscarriage, as well as a single second trimester miscarriage. This is also one of the clinical components for the diagnosis of the syndrome. Even when treated, women with APS have increased risks of IUGR, placental abruption and pre-eclampsia and hence should be monitored for complications in all three trimesters.

Anticardiolipin antibody and lupus anticoagulant tests are two examples of laboratory procedures that confirm the diagnosis. Since temporary positivity can be linked to viral infection, these tests must be positive on two times in a row that are at least six weeks apart. [90,91]

Systemic Lupus Erythematosus – SLE, a prototype of immune complex disease is characterized by circulating autoantibodies directed against nuclear, cytoplasmic, membrane and other antigens. Approximately 15-25% of patients with SLE develop thrombocytopenia and raised anticardiolipin antibody.

In order to reduce negative effects, women should be discouraged from

becoming pregnant while their SLE is active. Pregnancy can cause the condition to worsen. In addition, proteinuria and hypertension are linked to lupus nephritis.

Due to pre-eclampsia and preterm delivery, active SLE nephritis during pregnancy is significantly linked to maternal and perinatal mortality and morbidity.

The presence of anti-RO and anti-La antibodies increases the incidence of prenatal congenital heart block. Rare cases of neonatal lupus are marked by congenital heart block, pericarditis, hemolytic anemia, leucopenia, and thrombocytopenia in addition to discoid skin abnormalities. [90]

Laboratory findings in women with lupus nephritis are similar to those with severe pre-eclampsia. Antiphospholipid antibodies are present in 30-40% of the cases, while thrombocytopenia occurs in 40-50% and hemolytic anemia in 14-23% of the women with SLE.

The schedule for monitoring must include, besides physical examination at the first visit, testing for renal function, complete blood counts, anti-Ro/SSA and anti La/SSB antibodies, Lupus anticoagulant (LA) and anticardiolipin antibody (aCL) assay, anti-double stranded DNA antibodies, complement levels and uric acid level.[87]

c. **Disseminated intravascular coagulation**[92,93,94,95,96]

Mant and King provided the best clinical explanation of classic acute DIC 30 years ago. Usually, it causes hemorrhagic symptoms. DIC may be accompanied with hemorrhagic and thrombotic problems, which frequently present in the same patient. Rapid onset and possible platelet and fibrinogen depletion are the symptoms. Defibrination syndrome and consumptive coagulopathy are other names for it.

The platelet count is depressed and an important finding in DIC. Thrombocytopenia can be caused by factors other than platelet destruction in

thrombotic lesions. It is also caused by aggregation and incorporation of platelets into platelet fibrin microthrombi due to presence of thrombi in circulation.

DIC in pregnancy is brought on by amniotic fluid embolism, retained dead foetus, and placental abruption. Overt DIC is present in about 50% of women who retain a dead foetus for five weeks or longer.

Alterations in the endothelium, direct activation of fibrinogen, erythrocyte or platelet lysis, and release of thromboplastin-like substances are some of the trigger events that may predispose patients to DIC. Extravascular trauma, abruptio placentae, retained foetal syndrome, advanced malignancy, and leukemia are all conditions that exhibit tissue thromboplastin activating coagulation.

Injuries to red blood cells or platelets may release phospholipids that hasten coagulation, contributing to consumptive coagulopathy. Coagulation factors V, VIII, XII, and XIII are also released when platelets are destroyed.

An image of a peripheral blood smear reveals fragmented RBC and a low platelet count. With prolonged thrombin time, aPTT, and PT, fibrin split products (FSPs) are present, and fibrinogen levels fall. Protamine sulphate or ethanol gel testing is positive.

Other tests antithrombin II, coagulation factor assays, and plasminogen levels are abnormal, increased serum levels of lactic acid dehydrogenase, presence of D-dimer, and diminished haptoglobin levels and biochemical evidence of end organ failure.

Numerous experimental and pathological studies have demonstrated how the fibrin buildup in DIC contributes to the failure of multiple organs. The apparent etiology of DIC in neonates born to DIC-affected mothers has been determined to be the transplacental transit of thromboplastins or other procoagulant chemicals.

d. **Ineffective thrombopoiesis**[97,98,99]

Ineffective thrombopoiesis despite a normal precursor, hypoplasia or repression of the precursor megakaryocyte, and in rare cases, a lack of or an aberration of thrombopoietic pathways, can all lead to inadequate platelet generation.

Due to the invasive nature of bone marrow examination, platelet production can be indirectly measured by the estimation of thrombopoietin levels. TPO levels are high when thrombocytopenia is due to increased platelet destruction.

Ineffective thrombopoiesis could be due to congenital or acquired causes. Infiltrative marrow disorders associated with thrombocytopenia include metastatic cancer, leukemia, lymphoma, myelofibrosis, myeloma, Gaucher's disease and histiocytosis.

Leucoerythroblastic blood smear, physical exam, and bone marrow analysis are used to diagnose infiltrative illness. Megakaryocyte numbers are reduced in the bone marrow, yet they may still be greater than usual due to thrombocytopenia's physiological effects.

One of the most common side effects of total body radiotherapy is thrombocytopenia. After chemo for acute myeloid leukemia, isolated thrombocytopenia with reduced megakaryocytes has been documented. In women who are ready to have children, these are improbable. In cases when the diagnosis is

suspected, a bone marrow biopsy may be advised. The specific diagnosis, the stage of pregnancy, and the dangers to the mother from delaying therapy all influence the management strategy.

e. **Nutritional deficiency**[100,101]

For both the health of the foetus and the pregnancy, a pregnant woman's nutrition is crucial. Pregnant women with B12 insufficiency prevail in nations where vegetarian diets are prevalent, like India. Low platelet counts can result from severe folic acid and B12 insufficiency, however these deficiencies are typically accompanied by low red blood cell and leucocyte counts. However, given that women receive folic acid supplements to prevent neural tube abnormalities, these are uncommon during pregnancy. Because people with established vitamin B12 insufficiency are sub fertile, vitamin B12 deficiency is uncommon during pregnancy.

Mary D. Smith examined six instances involving megaloblastic anemia and thrombocytopenia over the course of three years and reported her findings in the British Journal of Hematology in 1962. Megaloblastic anemia is characterized by inadequate thrombopoiesis, a specific aberration of platelet production, which leads to vitamin B12 or folate insufficiency and thrombocytopenia. Despite the existence of normal or increasing megakaryocyte bulk, this anomaly is characterized by decreased platelet formation. Whether measured per megakaryocyte or per nuclear unit, platelet output is reduced. This phenomenon most likely stems from a limitation in nuclear endoreduplication caused by decreased DNA synthesis. The lifespan of platelets is normal or slightly shortened. In cases of B12 deficiency, megakaryocytic thrombocytopenia has been documented.

In addition to thrombocytopenia, the blood may also exhibit macrocytosis and

hyper-segmented neutrophils. The morphology of platelets ranges from normal to excessively big. Erythroid and myeloid lineages frequently exhibit megaloblastic alterations in the bone marrow. The use of the right vitamin can hasten the recovery of the platelet count.

**f. Thrombocytopenia associated with infections[102]**

Almost any virus can cause a reduction in platelet count. This is usually very transient, but there may be more prolonged reduction for a number of weeks. HIV, CMV and EBV infections are particularly associated with thrombocytopenia in pregnancy and should be sought when appropriate.

Viral-induced hemophagocytosis, impaired platelet synthesis as a result of viral invasion of megakaryocytes, toxic effects of viral proteins on progenitor cells, immunological and non-immune destruction of circulating platelets, and many other mechanisms may be used by viruses to cause thrombocytopenia. The former mechanism probably is the most common and has been proposed for infections with a variety of different viruses- parvovirus, mumps, Epstein Bar Virus, Rubella, dengue, Varicella and Cytomegalovirus.

Herpes viruses are a group of viruses that have the ability to remain latent in body and get re-activated later. In pregnancy, reactivation of some of these viruses, such as EBV and CMV can cause significant fetal and neonatal disease.

**HIV causing thrombocytopenia**[103]- Thrombocytopenia is a common feature among HIV positive patients and could present as a first sign of disease in approximately 5-15% of patients. (Francielle et al 2011).

It has been postulated that hormonal changes brought on by higher progesterone levels during pregnancy modify local immune responses and the mucosa of the vaginal canal, increasing the risk of HIV infection.

In Kenya, a prospective study of 1085 sero-discordant couples with female partners who were HIV-susceptible revealed a 2-fold risk of HIV infection during pregnancy. This risk appeared to be partially explained by a higher frequency of unprotected sexual activity among pregnant women.

**Malaria causing thrombocytopenia**[104,105] A classic feature of malaria is marked thrombocytopenia, and it can be used as an indicator of malaria in patients with pyrexia of unknown origin. It is a feature of acute malaria and occurs in both P. falciparum and P. vivax infection.

In research from the Asia-Pacific region, a median fatality rate of 39% was found; pregnant women have a three-fold increased chance of developing severe malaria compared to non-pregnant women. Infection with P. vivax has also been linked to maternal mortality.

The absence of normal quantity of platelets on a peripheral smear in a case of fever is often a clue to the presence of malarias.

Testing for the occurrence of DIC should be done on patients who have thrombocytopenia brought on by an infection. Treatment of infection related thrombocytopenia lies in treating the underlying infection.

**g. Post-transfusion purpura**[106]

It is a rather uncommon condition that normally manifests around a week following the transfusion of platelet-containing blood products, such as packed or cleaned RBCs, whole blood, or fresh or frozen plasma.

The temporal association of thrombocytopenia with blood transfusion was first described by Zuker et al and Van Loghmen et al.

During transfusion, PTP is characterized by fever and chills as well as a sudden onset of acute thrombocytopenia. 10% of patients experience an intracranial hemorrhage that is life-threatening.

How the recipient's own platelets are damaged is unknown. In the recipient's plasma, alloantibodies to antigens on the transfused blood product's platelets or platelet membranes are found that are directed against an antigen the recipient does not have. Shulman et al first suggested a relation between the development of platelet specific iso antibodies and consumption of host platelets.

Untreated patients present with thrombocytopenia typically lasting 3 weeks and even up to 4 months. Treatment of choice for now is IVIG only.

h. **Hypersplenism**[107]

Data suggests that approximately two third of platelets are present in the circulation and one third of total platelet mass pools in the spleen.

One of the important functions of the spleen is to act as a large reservoir for platelets. In contrast human spleen contains <2% of total red blood cell mass. Platelets spend about one third of its life (3 days) within the spleen.

In hypersplenism, the spleen platelet pool may contain up to 90% of platelet mass. A syndrome known as hypersplenism includes splenomegaly as well as any of the cytopenias like anemia, leucopenia, or thrombocytopenia. Therefore, after splenectomy, these cytopenias will be treated. Splenomegaly during pregnancy presents a further testing situation to the obstetrician as it is difficult to diagnose in advanced gestation and due to increased risk of splenic rupture.

**ROLE OF PLATELET INDICES IN MATERANAL THROMBOCYTOPENIA**

Platelet indices are biomarkers of platelet activation. Interpretation of platelet indices by automated cell counters can be useful in differentiating thrombocytopenia according to etiology.

Platelet morphology and proliferation kinetics are related to plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW). The composition, metabolic processes, and volume of platelets in the blood are all different.[108]

MPV is determined in the progenitor cell, the bone marrow megakaryocyte. MPV ranges from 8 to 10 fl.

The development of bigger platelets is shown to be regulated by the cytokines thrombopoietin, IL-6, and IL-3, which control megakaryocyte ploidy and platelet quantity. [109]

Young platelets grow larger and more active when platelet production declines, which raises the level of MPV. A measure of platelet production rate and activity, increasing MPV reveals larger platelet diameter. A pseudopod is formed when platelets undergo platelet activation, which causes them to transform from a biconcave disc shape to a sphere.

PDW is an indicator of volume variability in platelet size and is increased in the presence of platelet anisocytosis and reflects the heterogeneity in platelet morphology. PDW is the distribution curve of platelets measured at the level of 20% relative height in a platelet size distribution curve, with a total curve height of 100%.[110]

PCT is the volume occupied by platelets in the blood as a percentage and calculated according to the formula, PCT = platelet count x MPV/10,000.[111]

Platelet larger cell ratio (P-LCR) is an indicator of circulating larger platelets (>12 fl). It has been used to monitor platelet activity.[112]

MPV, P-LCR and PDW play a significant role in differentiating auto-immune thrombocytopenia from hypo-productive thrombocytopenia.

DA Elsewefry et al (2014)[113] showed in his study that MPV and P-LCR were significantly higher in ITP cases with a cut off value of MPV >9.7fl and P-LCR >33.6%.

Annam et al (2011)[114] and Biva Rani et al (2015)[115] in their study conducted in pregnant women showed that platelet counts were lower, while MPV, PDW, P-LCR were increased in pre-eclampsia and eclampsia as compared to normal healthy pregnant women. They found a relationship between platelet indices and severity of pre-eclampsia. Their studies also concluded that estimation of platelet indices method can be considered as an early, economical and rapid procedure in assessment of severity and prognosis of PIH cases in pregnant women.

## PLATELET COUNT ESTIMATION

A patient's platelet count is an important factor to consider when evaluating them. The peripheral blood smear must be carefully examined for platelet amount and shape because these factors can provide important diagnostic hints.

Counting platelets is far more challenging than counting erythrocytes or leukocytes. Due to their small size, propensity to attach to unnatural surfaces, and ability to aggregate when activated, this challenge exists.

There are two methods of estimation;

1. Manual methods
    a. Direct method by hemocytometer.
    b. Indirect method on peripheral smear.
2. Fully automated electronic methods

### 1. Manual methods

a. **Direct method by hemocytometer**[116]

This approach counts platelets the same way leukocytes or erythrocytes are counted after diluting whole blood.

**Principle:** Red blood cells are lysed when a whole blood sample is diluted with brecher cronkite solution, which contains 1% ammonium oxalate. Platelets are counted under a microscope after the liquid has been placed into an Improved Neubauer counting chamber. The result is expressed as the quantity of platelets per microliter.

**Equipment:** Modified Neubauer counting chamber

**Reagent:** Brecher cronkite fluid (Platelet diluting fluid), is used to estimate platelets since it hemolyzes RBCs and makes counting platelets simple. It has 1% ammonium oxalate in it. This is made by combining 100 ml of distilled water with 100 mg of ammonium oxalate. It needs to be kept in a refrigerator (4ºC). Reagent should be rapidly filtered before use since tiny particles could be misinterpreted for platelets.

In addition, estimates of platelets can be made using Rees-fluid Ecker's and formaldehyde-citrate red cell diluent fluids.

EDTA-anticoagulated venous blood is the specimen. For hematological testing, due to its ability to preserve cellular components and blood cell shape to the greatest extent, EDTA is suggested as the best anticoagulant. Furthermore, EDTA typically prevents platelets from adhering to the glass slide, improving the accuracy of the platelet estimate during peripheral smear assessment. [118]

**Method:** A test tube is filled with 1% ammonium oxalate combined to a 1:100 dilution with the addition of thoroughly mixed anticoagulated venous blood.

Having been charged and set into a wet chamber consisting of a lidded petri dish with damp filter paper at the bottom, the improved Neubauer counting chamber is left for 20 minutes. As a result, fluid doesn't dry out and platelets can settle. A 40X objective is used to count 25 smaller squares in the grid's center square to determine the total number of platelets once the charged counting chamber has been put up on the microscope's stage and the large central square has been brought into focus. This center square has a surface size of 1 $mm^2$.

Platelets are seen as small, brilliantly refractile, bluish, round or oval particles with one or more fine dendritic processes.

**Calculation:**

Platelet count/µL of blood =

$$= \frac{\text{Number of platelets counted x Dilution factor}}{\text{Area counted } (mm^2) \text{ x depth}}$$

$$= \frac{\text{Number of platelets counted x 100}}{1 \text{ x } 0.1}$$

= Number of platelets counted x 1000

OR

= Number of platelets counted x $10^3$/µL

b. **Indirect method on peripheral smear**[118]

Peripheral smears made from venous blood collected in EDTA anticoagulant vacutainers are stained with Leishman stain before being observed via a high power oil immersion lens. By counting 10 consecutive fields in the representative area, taking the mean, and multiplying by 20,000, one can determine the approximate platelet count (the estimated platelet count factor). In lakhs per $mm^3$, the computed platelet count is then presented.

**2. Automated method**[119]

The recommended method today uses automated hematology analyzers because they can count platelets more precisely. It is based on the aperture impedance technology theory.

Light scatter, impedance characteristics, or platelet antigen staining are used to identify platelets. Platelets require a tube with a smaller aperture, while larger red blood cells and tiny debris must be excluded by setting a threshold level.

An optical fluorescence platelet count has been introduced in some Sysmex analyzers in addition to traditional impedance count.

An immunofluorescence method for platelet counting by flow cytometry has also been developed. Suitable antibodies to platelet antigens are CD41, CD42 and CD61. These monoclonal antibodies are employed in myeloproliferative diseases and myeloid leukemias to detect megakaryocytic precursors. This method using CD41 and CD61 has been adopted by International Council for standardization in hematology as the reference method.[120,121]

Thiazole orange dyes that bind to RNA can be used in flow cytometric techniques to identify reticulated platelets, as can automated hematology analyzers. The range of normal readings is 3% to 20%. Reticulated platelet counts provide an estimation of thrombopoiesis and may be helpful in differentiating between hypoplastic platelet production and platelet breakdown disorders. [122,123,124]

Numerous non-technical reasons may result in artificially low platelet counts when automated procedures are applied. False elevation of platelet count by this method can result from the presence of micro-spherocytes, large or giant platelets,

platelet satellitism and elevated cryoglobulins. Ethylenediamine tetra acetic acid (EDTA) – induced platelet clumping, artifactually increases the leucocyte count. Therefore, meticulous hand counting techniques might be necessary to get rid of these artefacts and get precise platelet counts.[125]

# MATERIALS AND METHODS

The current research was a 1-year prospective study that took place from January 1,2021 through December 31, 2021 in the pathology department's hematology unit of a tertiary care institution.

At our hospital's obstetrics and gynecology department, pregnant patients who were inpatients and outpatients and whose platelets were <1.5 lakhs/$mm^3$ in the $3^{rd}$ trimester were screened and recruited in the study.

**Inclusion criteria**: $3^{rd}$ trimester pregnant women with platelet count < 150000/$mm^3$.

**Exclusion criteria**:

1. Pregnant women with history of:

   Diabetes mellitus

   Collagen vascular disorders

   Tuberculosis

   Patients on anti-platelet therapy

   Any major diseases (leukemia, lymphoma and malignancy)

2. Women delivering outside KLE hospital.

**Method:**

- In our pathology division, 2 ml of blood were taken into an EDTA anticoagulant vacutainer, and a 5-part automated hematology analyzer Sysmex XN-350 was used to determine the platelet count.

- The existence of blood clots was routinely verified in all vacutainers with low platelet counts.
- By preparing a peripheral smear stained with Wright stain and seeing it under a microscope, the platelet count was double-checked.
- The smears were further analyzed for the presence of platelet aggregates and platelet satellitism in order to rule out pseudo-thrombocytopenia.
- These were disqualified from the study if they were present because they were thought to indicate normal platelet levels.

**Principle of automated hematology analyzer** [126]

The Sysmex XN-350 automated hematology analyzer uses the hydro dynamic focusing method (DC detection) for analyzing the RBCs and platelet counts. The hydro dynamic focusing method improves the blood count accuracy and reproducibility. As the blood cells pass through the aperture in a line, it also prevents the generation of abnormal blood cell pulses.

**Principle of manual platelet estimation** [118]

Total and differential counts, RBC morphology, platelet count, and parasites, if any, are determined from peripheral smears made from venous blood collected in EDTA anticoagulant vacutainers were studied under high power and oil immersion lens. The representative area's 10 consecutive fields were counted to determine the platelet count, which was then calculated in lakhs per $mm^3$ by taking the mean and multiplying it by 20,000.

- A thorough history that includes any complaints, the proforma was filled out with information about each patient's general systemic and obstetric examination results, history of petechiae, bruising, drug use, viral infection, and thrombocytopenia in prior pregnancies. A through work up of all these cases was done to ascertain the cause of thrombocytopenia and to correlate with the maternal and fetal outcome.

- Special investigations like coagulation profile PT, aPTT, LFT, kidney function tests were done only if indicated.

- All these cases were followed till delivery and one week post-partum period.

- Neonatal birth weight was recorded and checked if appropriate for the period of gestation.

- Outcome of mother like gestational age at the time of delivery, mode of delivery, delivery complications and likewise complications in the neonate were also recorded.

## STATISTICAL ANALYSIS:

- All the data were compiled in MS Excel and analyzed using commercially available statistical software (SPSS version 2.0).

- Data was expressed as mean ± standard deviation.

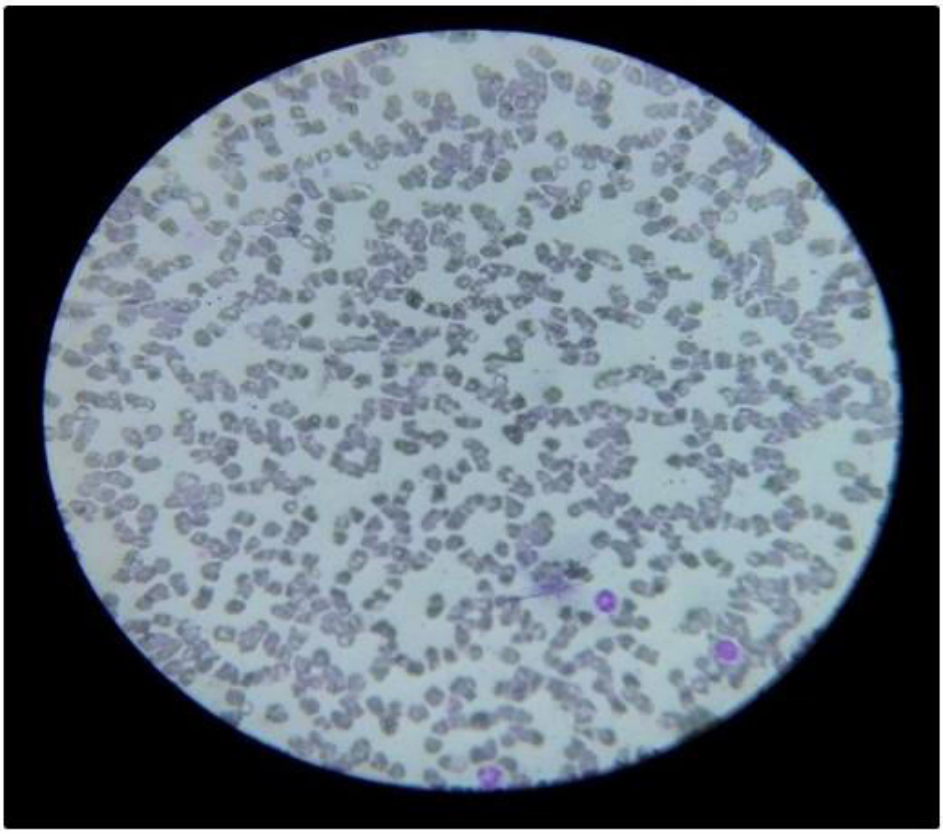
- Categorical variables were evaluated using chi-squared test

- The p-value was calculated for each parameter and $p < 0.005$ is considered statistically significant.

**F-6: STAINING KIT**

**F-7: AUTOMATED HEMATOLOGY ANALYZER (SYSMEX XN-350)**

**F-8: PERIPHERAL SMEAR SHOWING THROMBOCYTOPENIA (40X)**



F-9: PERIPHERAL SMEAR SHOWING THROMBOCYTOPENIA AND MICROANGIOPATHIC HEMOLYTIC ANEMIA IN CASE OF DIC (100X)



F-10: PERIPHERAL SMEAR SHOWING THROMBOCYTOPENIA AND GIANT PLATELET IN CASE OF ITP (100X)

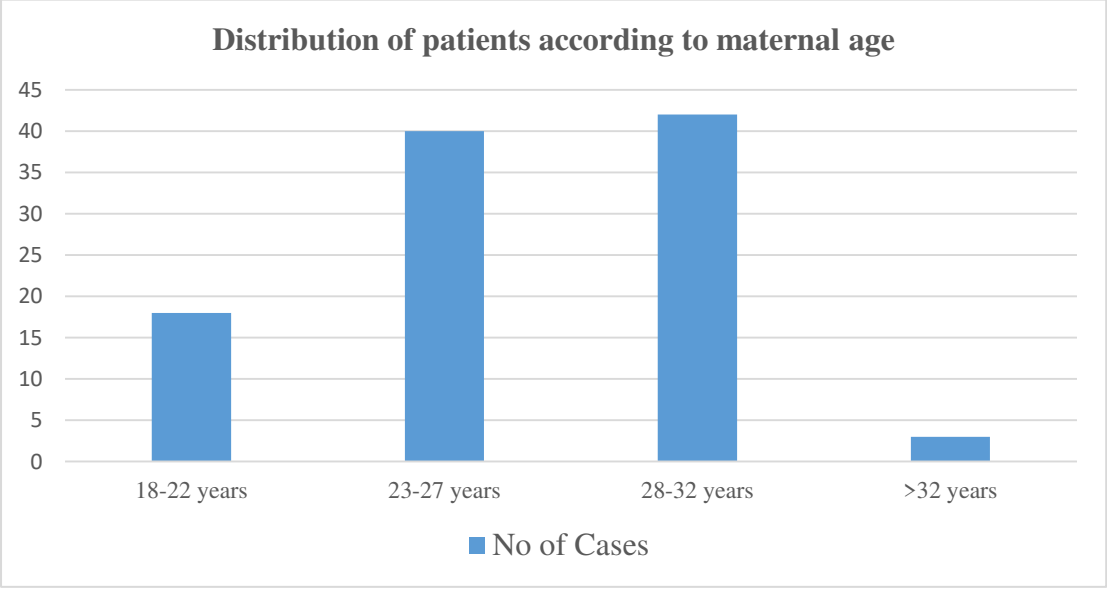
## OBSERVATIONS AND RESULTS

The current investigation was conducted over the course of a year in our institute's pathology department's hematology section. During the study period, 1500 pregnant women were studied who visited the obstetric department, and 103 of those instances had thrombocytopenia identified in the third trimester of pregnancy. Therefore, 6.9% of pregnant women in this study had thrombocytopenia.

### MATERNAL AGE

**T-1: Patient distribution based on maternal age.**

| Age | Cases (n=103) | % |
|---|---|---|
| 18-22 year | 18 | 17.47 |
| 23-27 year | 40 | 38.83 |
| 28-32 year | 42 | 40.78 |
| >32 year | 3 | 2.91 |
| Total | 103 | 100 |

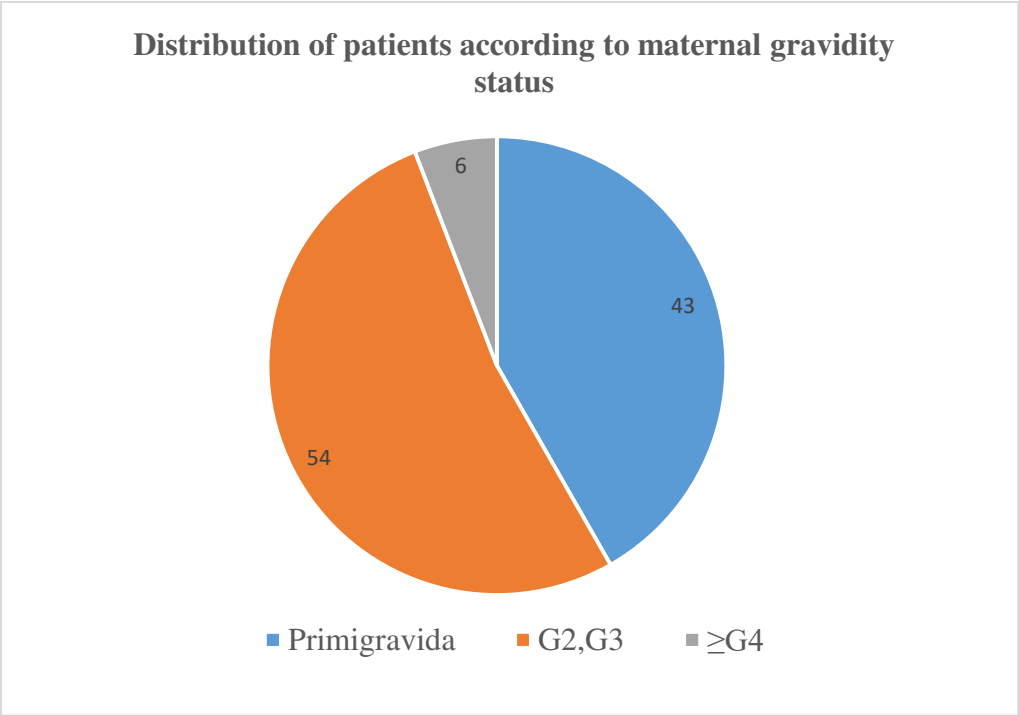



Majority of the cases i.e., 40.78% (42/103 cases) ranged in 28–32 age bracket. In this study, 32 or less was the average age of the cases. The patients in this study had a mean age of 26.25 years.

**MATERNAL GRAVIDITY STATUS**

**T-2: Patient distribution based on gravidity status.**

| Gravidity | Cases (n=103) | % |
|---|---|---|
| Primigravida | 43 | 41.75 |
| G2, G3 | 54 | 52.43 |
| ≥G4 | 06 | 5.82 |
| Total | 103 | 100 |




Gravida 2 and gravida 3 instances made up the majority of the cases in this study i.e., 52.43% (54/103 cases) followed by primigravida i.e., 41.75% (43/103 cases). Only 5.82% (6/103 cases) are of gravida 4 or more. Thrombocytopenia was more common among multigravida in this study.

**MATERNAL GESTATIONAL AGE**

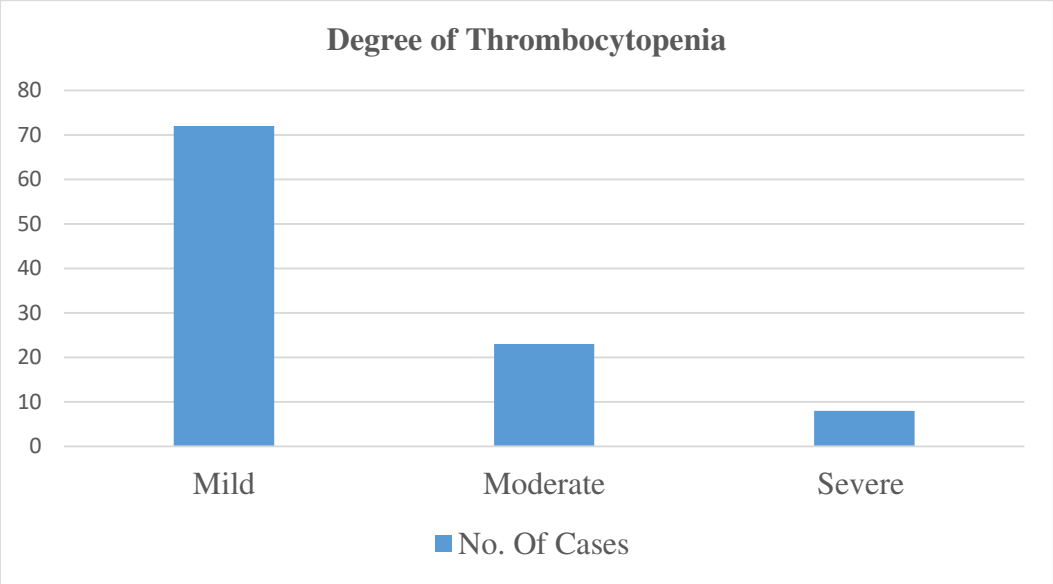
**T-3: Patient distribution based on gestational age at delivery.**

| Gestational age | Cases (n=103) | % |
|---|---|---|
| 29-32 weeks | 10 | 9.71 |
| 33-36 weeks | 22 | 21.36 |
| 37-40 weeks | 70 | 67.96 |
| >40 weeks | 1 | 0.97 |
| Total | 103 | 100 |

Most cases possible in this study, 67.96% (70/103 instances) were between 37 and 40 weeks' gestation, while the lowest number, i.e., 1 case (0.97%), was related with >40 weeks' gestation. Cases delivered to a maximum number at full term.

**T-4: Distribution of patients according to degree of thrombocytopenia.**

| Degree of thrombocytopenia | Cases | % |
|---|---|---|
| Mild thrombocytopenia (100000-150000/$mm^3$) | 72 | 69.90 |
| Moderate thrombocytopenia (50,000-100000/$mm^3$) | 23 | 22.33 |
| Severe thrombocytopenia (<50,000/$mm^3$) | 8 | 7.77 |
| Total | 103 | 100 |




Out of 103 thrombocytopenia cases, 69.90% (72/103) had mild thrombocytopenia, 22.33% (23/103) had moderate thrombocytopenia and 7.77% (8/103) had severe thrombocytopenia. Most cases were of mild thrombocytopenia.

**ETIOLOGY OF THROMBOCYTOPENIA IN PREGNANCY**

**T-5: Distribution of cases of thrombocytopenia in pregnancy according to etiology.**

| Causes of maternal thrombocytopenia | No. of patients | Percentage of cases |
|---|---|---|
| Gestational thrombocytopenia | 67 | 65.05 |
| Pre-eclampsia | 19 | 18.45 |
| Eclampsia | 4 | 3.88 |
| HELLP syndrome | 5 | 4.85 |
| DIC | 2 | 1.94 |
| Dengue fever | 2 | 1.94 |
| ITP | 2 | 1.94 |
| Megaloblastic anemia | 1 | 0.97 |
| Acute fatty liver of pregnancy | 1 | 0.97 |
| Total | 103 | 100 |

The study found that the most frequent reason for maternal thrombocytopenia was gestational thrombocytopenia i.e., 65.05% (67/103 cases) followed by pregnancy induced hypertension (pre-eclampsia and eclampsia) i.e., 22.33% (23/103 cases). Four-point eight five percent cases (5/103) were diagnosed with HELLP syndrome. One case each i.e., 0.97% (1/103 cases) was also seen of megaloblastic anemia and acute fatty liver of pregnancy.

**T-6: Mean platelet count according to the etiology associated with maternal thrombocytopenia.**

| Causes of maternal thrombocytopenia | Mean platelet count | Standard deviation |
|---|---|---|
| Gestational thrombocytopenia | 72,600 | 31822.25 |
| Pre-eclampsia | 73,000 | 32238.68 |
| Eclampsia | 62,500 | 31126.62 |
| HELLP syndrome | 46,000 | 29233.34 |
| Overall | 64,000 | 32475.92 |

**T-7: Correlation of maternal thrombocytopenia with degree of thrombocytopenia.**

| Etiology | Mild | Moderate | Severe | Total |
|---|---|---|---|---|
| Gestational thrombocytopenia | 62 | 5 | 0 | 67 |
| Pre-eclampsia | 9 | 10 | 0 | 19 |
| Eclampsia | 0 | 2 | 2 | 4 |
| HELLP syndrome | 0 | 3 | 2 | 5 |
| DIC | 0 | 0 | 2 | 2 |
| Dengue fever | 0 | 2 | 0 | 2 |
| ITP | 0 | 0 | 2 | 2 |
| Megaloblastic anemia | 1 | 0 | 0 | 1 |
| Acute fatty liver of pregnancy | 0 | 1 | 0 | 1 |
| Total | 72 | 23 | 8 | 103 |

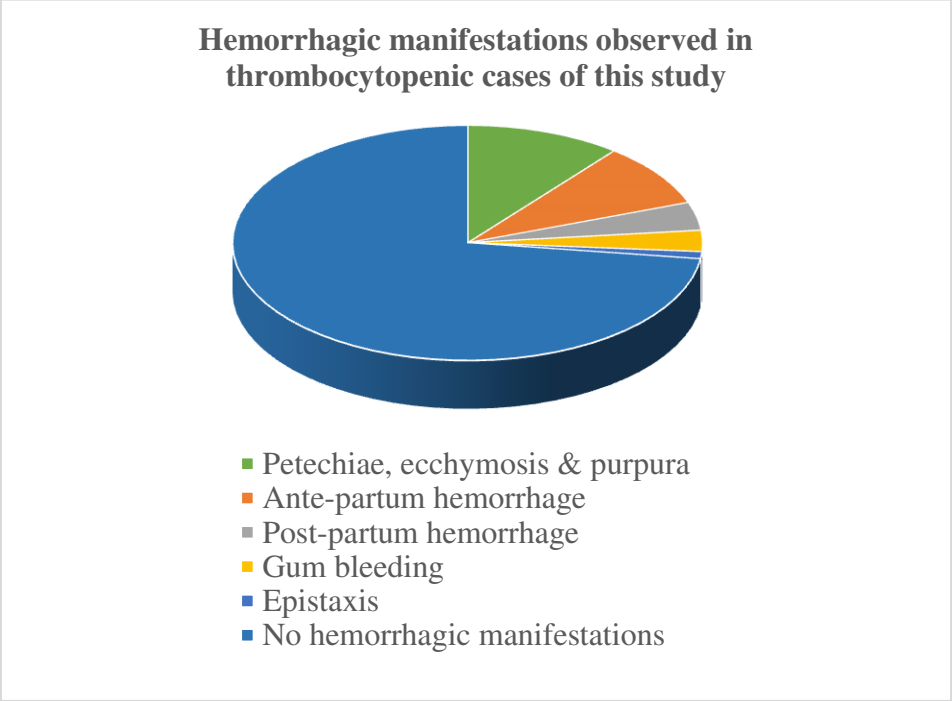
The most common etiological factor causing maternal thrombocytopenia in this study was gestational thrombocytopenia and majority of them i.e., 92.53% (62/67 cases) had mild thrombocytopenia. 52.63% (10/19 cases) of pre-eclampsia, 50% (2/4 cases) of eclampsia and 60% (3/5 cases) of HELLP syndrome were associated with moderate thrombocytopenia. Fifty percent cases (2/4) of eclampsia, 40% cases (2/5) of HELLP syndrome were associated with severe thrombocytopenia. Both the cases of DIC and ITP (100%) were in relation to severe thrombocytopenia. Mild thrombocytopenia was seen in cases with gestational thrombocytopenia. HELLP syndrome and eclampsia have been linked to moderate, and severe thrombocytopenia. Cases of DIC and ITP were linked to severe thrombocytopenia.

## MATERNAL AND FETAL OUTCOME

### MATERNAL COMPLICATIONS

**T-8: Hemorrhagic manifestations observed in thrombocytopenic cases of this study.**

| Site of bleeding | No. of patients | Percentage of cases |
|---|---|---|
| Petechiae, ecchymosis & purpura | 11 | 10.68 |
| Ante-partum hemorrhage | 9 | 8.74 |
| Post-partum hemorrhage | 4 | 3.88 |
| Gum bleeding | 3 | 2.91 |
| Epistaxis | 1 | 0.97 |
| No hemorrhagic manifestations | 75 | 72.82 |



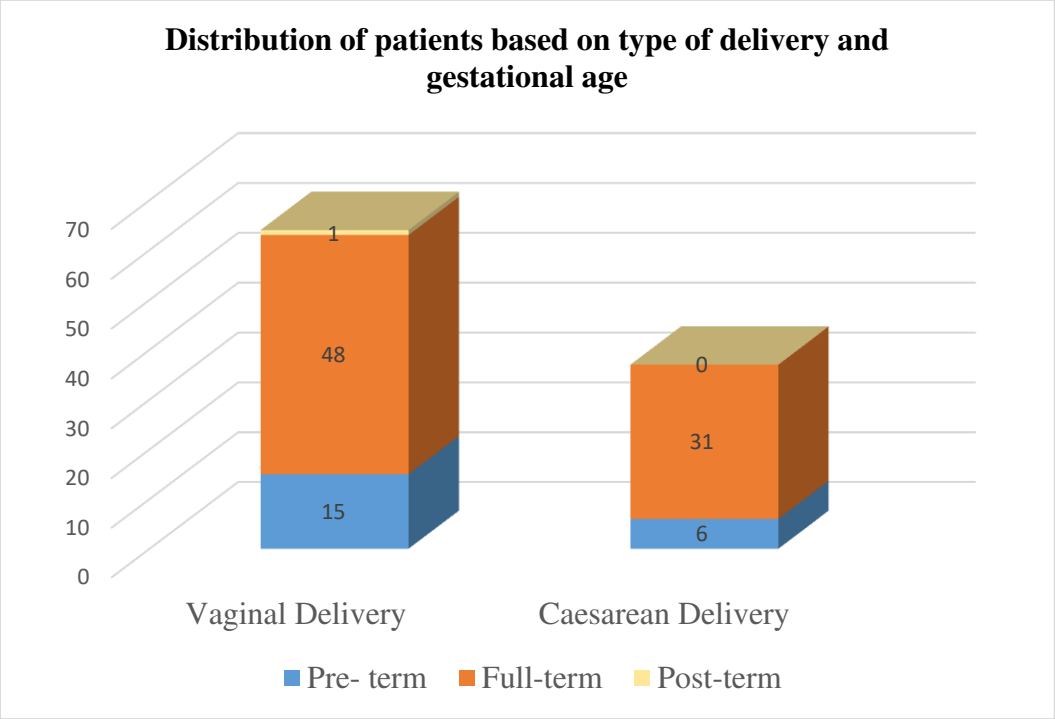
Twenty-seven-point eighteen percent cases (28/103) had hemorrhagic manifestations in this study. Maximum number of cases i.e., 10.68% (11/103) had petechiae, ecchymosis, and purpura after which was the antepartum hemorrhage. i.e., 8.74% (9/103). Post-partum hemorrhage was noted in 3.88%cases (4/103).

In this study, a total of 2/103 (1.94%) incidents of maternal fatalities were documented. One case of DIC, 23-year-old female, died before delivery at 32 weeks of gestation. Second case of 30 years female with acute fatty liver of pregnancy died before delivery at 30 weeks of gestation. She had nausea, vomiting, epigastric pain and deranged LFTs.

Mild thrombocytopenia cases were not associated with hemorrhagic manifestations, whereas moderate and severe thrombocytopenia cases were associated with hemorrhagic manifestations.

**T-9: Distribution of patients based on type of delivery.**

| Age of gestation | Type of delivery | | Total | Percentage |
|---|---|---|---|---|
| | Vaginal delivery | Caesarean delivery | | |
| Pre-term | 15 | 6 | 21 | 20.79% |
| Full-term | 48 | 31 | 79 | 78.22% |
| Post-term | 1 | 0 | 1 | 0.99% |
| Total | 64 | 37 | 101 | 100 |




Excluding two cases of maternal death, thrombocytopenia was commonly seen in vaginal deliveries 64 cases. (63.37%).

**FETAL OUTCOME**

Out of 106 cases, 14.15% (15/106 cases) intra uterine deaths were reported in this study. For a variety of reasons, including respiratory difficulty, birth asphyxia, jaundice, etc., 12.19% (11/91) of neonates were admitted to the NICU. Six neonates presented with neonatal thrombocytopenia.

**T-10: Correlation of gestational maturity with degree of maternal thrombocytopenia.**

| Degree of maternal thrombocytopenia | Pre-term delivery | Full-term delivery | Post-term delivery | Chi square test value (p value) |
|---|---|---|---|---|
| Mild | 4(19.05%) | 67(84.81%) | 1 | 39.583 (<0.0001) |
| Moderate | 11(52.38%) | 11(13.92%) | 0 | |
| Severe | 6(28.57%) | 1(1.26%) | 0 | |
| Total | 21 | 79 | 1 | |

Out of 21 pre term deliveries, 52.38% cases (11/21) neonates had moderate thrombocytopenia in mother and 28.57% (6/21) neonates had severe thrombocytopenia in mother. Rest had mild thrombocytopenia in mother. Chi-square test (p value <0.005) was significant statistically significant. Hence, in this study, preterm births were linked to moderate to severe maternal thrombocytopenia.

Hence, moderate to severe maternal thrombocytopenia was found to be a risk factor for pre term deliveries.

**T-11: Correlation of fetal maturity with etiological factors causing maternal thrombocytopenia.**

| Fetal maturity | Pre-term | Full Term | Post term | Total | Chi square test value (p value) |
|---|---|---|---|---|---|
| Gestational thrombocytopenia | 2 | 64 | 1 | 67 | 55.761(<0.001) |
| Pre-eclampsia | 9 | 10 | 0 | 19 | |
| Eclampsia | 3 | 1 | 0 | 4 | |
| HELLP syndrome | 4 | 1 | 0 | 5 | |
| DIC | 2 | 0 | 0 | 2 | |
| ITP | 2 | 0 | 0 | 2 | |
| Dengue | 0 | 2 | 0 | 2 | |
| Megaloblastic anemia | 0 | 1 | 0 | 1 | |
| Acute fatty liver of pregnancy | 1 | 0 | 0 | 1 | |
| Total | 23 | 79 | 1 | 103 | |

Majority of the Thrombocytopenia cases due to various etiologies gave full term births i.e.,76.70% (79/103) followed by pre term deliveries i.e., 22.33% (23/103). The 2 patients with DIC and AFLP respectively expired during pre-term labor.

Gestational thrombocytopenia in the mother was associated with term deliveries and did not affect the foetal maturity. Eclampsia poses a risk of prematurity in the new-born baby. Among 4.85% cases of HELLP syndrome, (80%) gave birth to premature babies. With chi-square test (p value <0.005) was significant statistically.

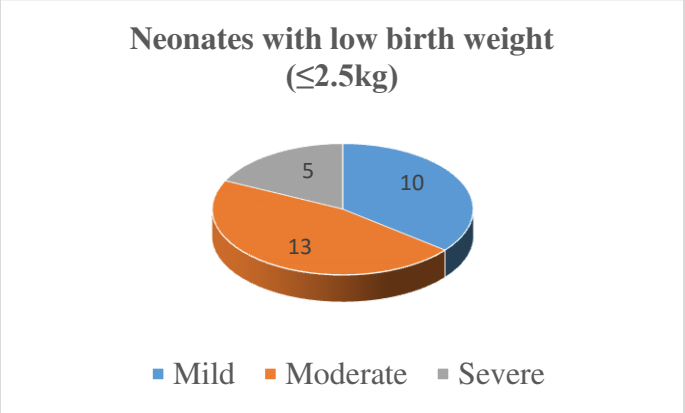
Most of the gestational thrombocytopenia cases were seen associated with full term deliveries.

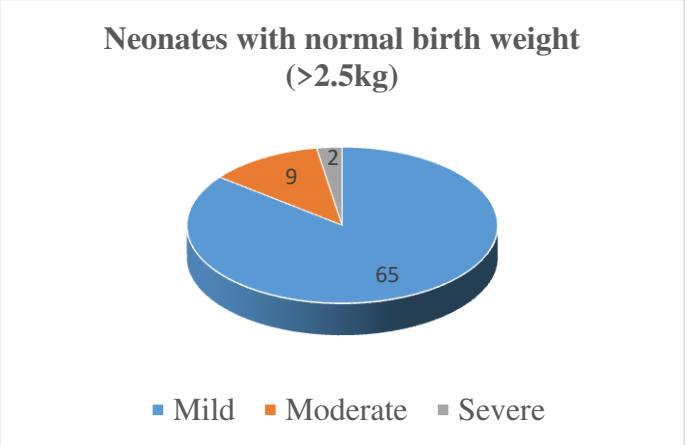
Majority cases of eclampsia, HELLP syndrome, DIC and ITP cases were associated with pre-term deliveries.

**NEONATAL BIRTH WEIGHT**

**T-12: Correlation of neonatal birth weight to degree of maternal thrombocytopenia.**

| Degree of maternal thrombocytopenia | Neonates with low birth weight (≤2.5kg) | Neonates with normal birth weight (>2.5kg) | Total | Chi square test value (p value) |
|---|---|---|---|---|
| Mild | 10(13.33%) | 65(86.67%) | 75 | 25.658(<0.0001) |
| Moderate | 13(59.09%) | 9(40.91%) | 22 | |
| Severe | 5(71.43%) | 2(28.57%) | 7 | |
| Total | 28 | 76 | 104 | |



Majority of the thrombocytopenia cases gave birth to neonates with normal weight 73.08% (76/104) cases. Only 28 /104 (26.92%) cases had low birth weight.

The Chi-square test (p-value <0.005) was significant statistically. Hence, low birth weight was seen associated with the degree of severity of maternal thrombocytopenia.

Mild thrombocytopenia cases were associated with normal birth weight and majority cases of moderate and severe thrombocytopenia were associated with low birth weight.

**T-13: Correlation of neonatal birth weight with etiological factors.**

| Causes of maternal thrombocytopenia | Neonates with Low birth weight | Neonates with normal birth weight | Chi square test value (p value) |
|---|---|---|---|
| Gestational thrombocytopenia | 8 | 62 | 36.031(<0.0001) |
| Pre-eclampsia | 10 | 9 | |
| Eclampsia | 3 | 1 | |
| HELLP syndrome | 4 | 1 | |
| DIC(1 EXPIRED) | 1 | 0 | |
| ITP | 2 | 0 | |
| Dengue | 0 | 2 | |
| Megaloblastic anemia | 0 | 1 | |
| AFLP(EXPIRED) | 0 | 0 | |
| Total | 28 | 76 | |

In cases of gestational thrombocytopenia majority of the neonates were born with normal birth weight i.e., 88.57% (62/70). The twins were of normal weight whereas triplets were of low birth weight.

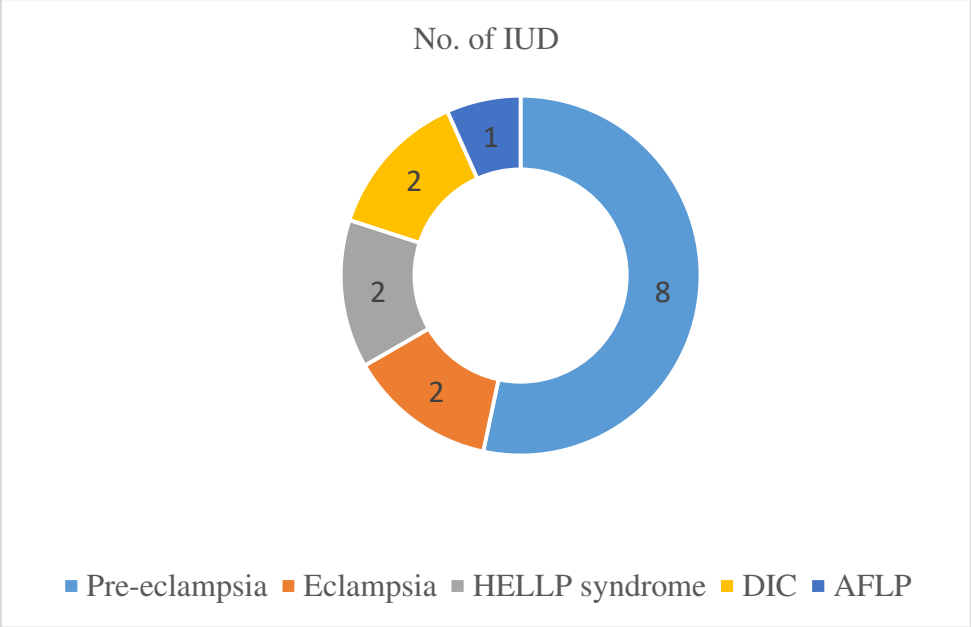
In the remaining etiologies like pre-eclampsia i.e., 52.63% (10/19), eclampsia i.e.,75% (3/4), HELLP syndrome i.e. 80% (4/5), DIC i.e. 100% (1/1), and ITP i.e. 100% (2/2) had neonates with low birth weight.

Chi-square test (p-value < 0.005) was significant statistically. Hence, gestational thrombocytopenia cases were associated with normal birth weight of the new-born and HELLP syndrome cases were associated with low birth weight.

Hence, it was seen that gestational thrombocytopenia mostly gave birth to neonates with normal birth weight and other etiologies gave birth to low birth weight.

**T-14: Causes of IUD in cases of maternal thrombocytopenia.**

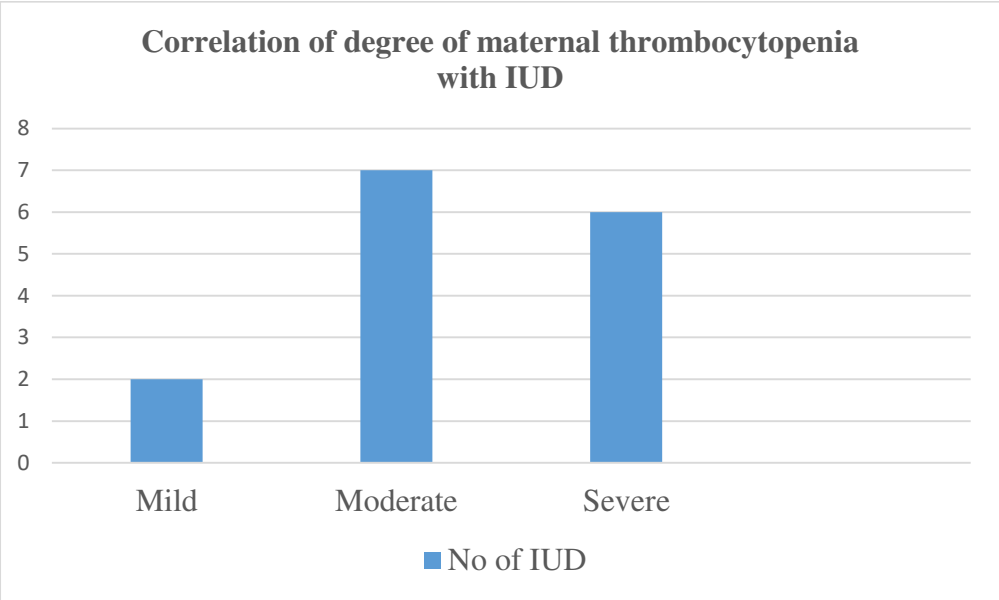
| Etiology of thrombocytopenia | No. of IUD |
|---|---|
| Pre-eclampsia | 8 |
| Eclampsia | 2 |
| HELLP syndrome | 2 |
| DIC | 2 |
| AFLP | 1 |
| Total | 15 |




Gestational thrombocytopenia, dengue and megaloblastic anemia were not associated with intrauterine deaths in cases of maternal thrombocytopenia.

**T-15: Correlation of degree of maternal thrombocytopenia with IUD.**

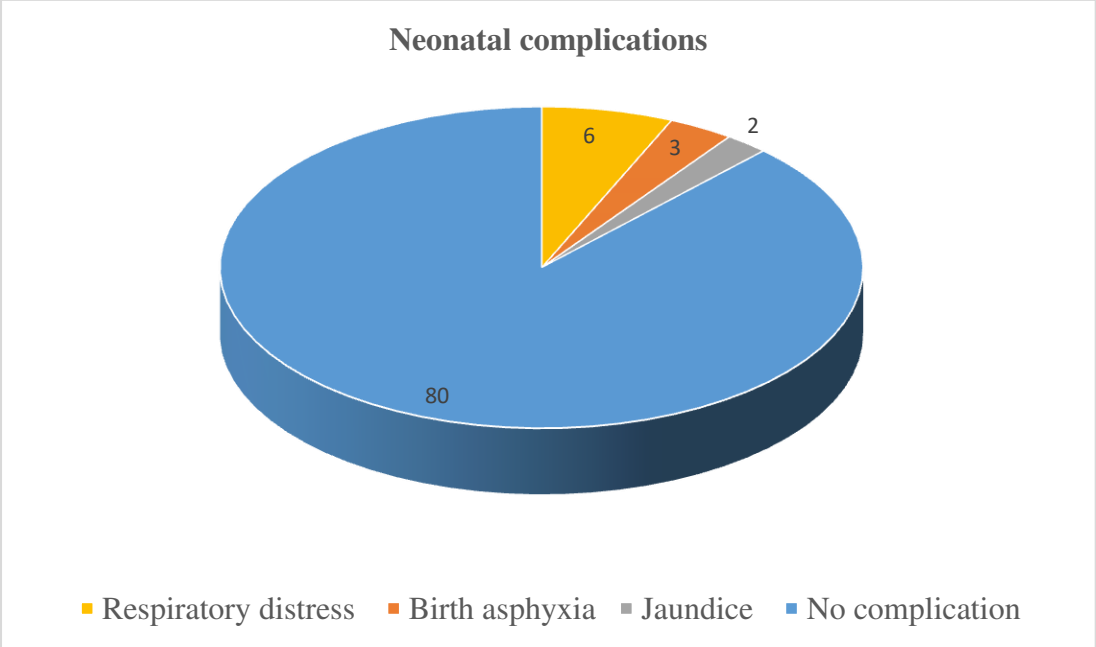
| Degree of thrombocytopenia | IUD |
|---|---|
| Mild | 2 |
| Moderate | 7 |
| Severe | 6 |
| Total | 15 |




Majority of intrauterine deaths were associated with moderate and severe degree of thrombocytopenia.

**T-16: Distribution based upon neonatal complications.**

| Neonatal complication | No. of cases | Percentage |
|---|---|---|
| Respiratory distress | 6 | 6.59 |
| Birth asphyxia | 3 | 3.30 |
| Jaundice | 2 | 2.20 |
| No complication | 80 | 87.91 |
| Total | 91 | 100 |



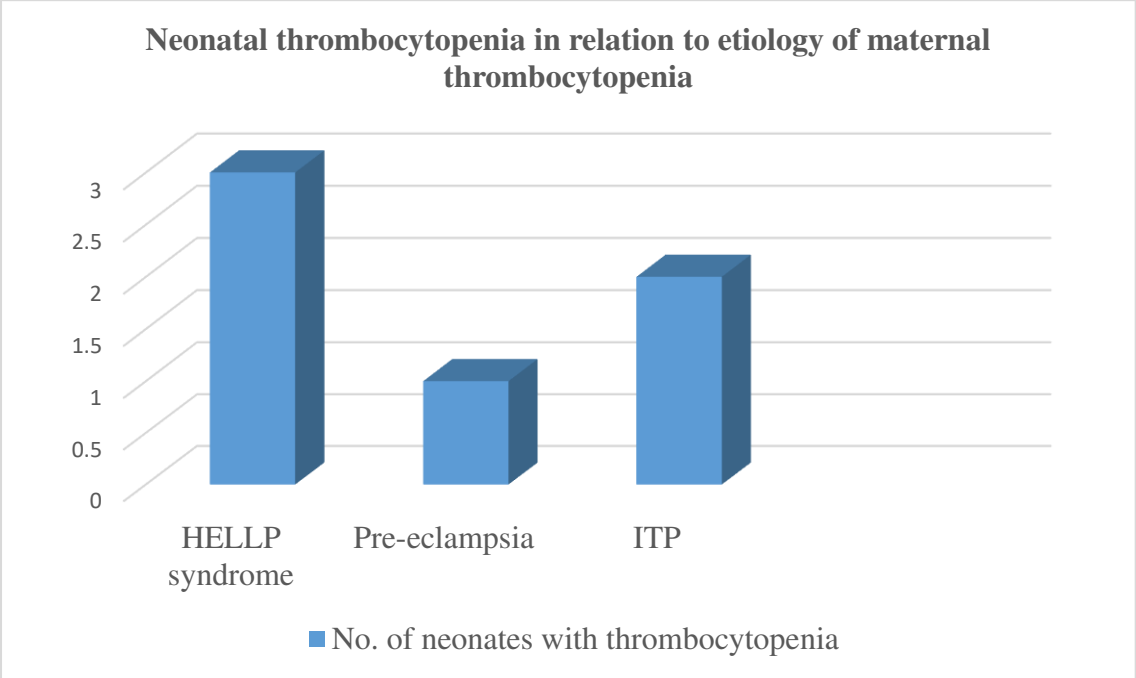

Majority of the neonates had no complications i.e., 87.91% (80/91) after delivery. Respiratory distress was seen in 6 cases (6.59%) followed by birth asphyxia i.e., 3.30% (3/91) and jaundice i.e., 2.20% (2/91).

Hence, maternal thrombocytopenia mainly presents with no neonatal complications. Respiratory distress birth asphyxia and jaundice were rarely encountered.

## NEONATAL THROMBOCYTOPENIA

**T-17: Neonatal platelet count in relation to etiology of maternal thrombocytopenia.**

| Etiology of maternal thrombocytopenia | No. of neonates with thrombocytopenia | Percentage |
|---|---|---|
| HELLP syndrome | 3 | 50 |
| Pre-eclampsia | 1 | 16.67 |
| ITP | 2 | 33.33 |
| Total | 6 | 100 |




Out of 91 new born babies only 6 neonates had thrombocytopenia which were associated with maternal conditions like HELLP syndrome, pre-eclampsia and ITP. Neonatal thrombocytopenia and gestational thrombocytopenia were not seen to be related.

# DISCUSSION

Thrombocytopenia in pregnancy is a common physiological condition seen during the 3rd trimester of pregnancy. This physiological decline in platelet count is attributed to hemodilution, increased platelet consumption and increased platelet aggregation due to increased levels of thromboxane A2.

However, when it manifests secondary to pregnancy specific conditions such as pregnancy induced hypertension or immunologic disorders such as ITP it poses high morbidity and mortality to both the mother and foetus.

The goal of this study was to determine the causes of pregnancy-related thrombocytopenia. Estimation of platelet count is a regular procedure that can be completed at each antenatal visit.

## PREVALANCE OF MATERNAL THROMBOCYTOPENIA

**T-18: Comparison of prevalence of maternal thrombocytopenia**

| Studies | Prevalence % |
|---|---|
| Singh et al (2012)[127] | 8.8 |
| Onisai et al (2012)[128] | 11.11 |
| Lin et al (2013)[129] | 4.3 |
| Brohi et al(2013)[130] | 1.9 |
| Chauhan et al(2016)[131] | 8.4 |
| Present study (2022) | 6.9 |

In our study, the prevalence of maternal thrombocytopenia was 6.9%, similar results were seen in Singh et al. (2012)[127]'s finding of 8.8% and Chauhan et al. (2016)[131]'s finding of 8.4%.

Prevalence of 6.9% in our region could be because of better antenatal care and early nutritional awareness.

**MATERNAL AGE**

**T-19: Comparison of maternal age**

| Studies | Mean age (years) |
|---|---|
| Suri et al (2006)[138] | 27 |
| Borna et al (2006)[133] | 28 |
| Turgot et al (2010)[134] | 27.6 |
| Chauhan et al (2016)[131] | 25.7 |
| Present study (2022) | 26.25 |

Most of the cases in the current study belonged to the 28-32 years age range. The mean age in the present study was 26.25 years identical to research done by Suri et al (2006)[138] i.e., 27 years and Chauhan et al (2016)[131] i.e., 25.7 years.

**MATERNAL GRAVIDITY STATUS**

**T-20: Comparison of maternal gravidity status**

| Studies | Primigravidae (%) | Multigravidae (%) |
|---|---|---|
| Won et al (2005)[135] | 51.6 | 48.4 |
| Bhat et al (2008)[136] | 65 | 35 |
| Brohi et al (2013)[130] | 40.3 | 59.7 |
| Chauhan et al (2016)[131] | 53.8 | 46.2 |
| Present study (2022) | 41.75 | 58.25 |

Primigravidae made up 41.75% of the cases in our analysis, whereas multigravidae made up 58.25% of the cases. This was also noted in research by Brohi et al (2013)[130].

In multigravidae prevalence of thrombocytopenia could be more because of repeated pregnancy with nutritional deficiency.

**MATERNAL GESTATIONAL AGE**

**T-21: Comparison of maternal gestational age at the time of delivery**

| Studies | Gestational age (weeks) |
|---|---|
| Bouzari et al (2013)[139] | 35.83 ± 1.34 |
| Lin et al (2013)[129] | 39.21 ± 1.35 |
| Kasai et al (2015)[140] | 38.6 ± 1.36 |
| Chauhan et al (2016)[131] | 38.6 ± 1.34 |
| Present study (2022) | 36.92 ± 2.65 |

The mean gestational age at delivery in the current study was 36.92 weeks, which was consistent with studies done by Bouzari et al (2013)[139], Kasai et al (2015)[140] and Chauhan et al (2016)[131] i.e., 35.83, 38.6, and 38.6 weeks respectively.

This is because the commonest cause is gestational thrombocytopenia which is commonly physiological.

**T-22: Comparison of degree of severity of maternal thrombocytopenia**

| Studies | Mild | Moderate | Severe |
|---|---|---|---|
| Borna et al(2006)[133] | 54% | 30% | 16% |
| Singh et al(2012)[127] | 74.7% | 17.9% | 7.4% |
| Chauhan et al(2016)[131] | 63.1% | 34.5% | 1.5% |
| Present study (2022) | 72% | 23% | 8% |

In this study, 72 % of cases had mild thrombocytopenia which was consistent with studies done by Singh et al (2012)[127] and Chauhan et al (2016)[131]i.e.,74.7% and 63.1% respectively.

Thus, in our study and the above-mentioned other studies mild thrombocytopenia was common followed by moderate thrombocytopenia. very few cases presented with severe thrombocytopenia.

## ETIOLOGY OF THROMBOCYTOPENIA IN PREGNANCY

**T-23: Comparison of etiology of thrombocytopenia**

| Studies | Causes of thrombocytopenia | | | |
|---|---|---|---|---|
| | **Gestational thrombocytopenia** | **Pre-eclampsia/ Eclampsia** | **HELLP syndrome** | **DIC** |
| Katke et al (2014)[142] | 30.1% | 21% | 5.8% | 0.76% |
| Somani et al (2015)[143] | 53.97% | 20.3% | 11.11% | 7.94% |
| Chauhan et al (2016)[131] | 68.2% | 26.3% | 1.5% | 0% |
| Vishwekar et al (2017)[144] | 68.46% | 18.46% | 7.69% | 1.53% |
| Present study (2022) | 65.05 | 22.33 | 4.85 | 1.94 |

In the current study, gestational thrombocytopenia accounted for 65.05% (67/103) of all cases of maternal thrombocytopenia, followed by pre-eclampsia and eclampsia 22.33% (23/103) and HELLP syndrome 4.85% (5/103).

Similar results were found in studies conducted by Somani et al (2015)[143], chauhan et al (2016)[131] and Vishwekar et al (2017)[144].

**MATERNAL PLATELET COUNT**

**T-24: Comparison of mean maternal platelet count of the present study with other studies.**

| Studies | Platelet count /mm³ |
|---|---|
| Singh et al (2012)[127] | 1,10,320 ± 21345.40 |
| Chauhan et al (2016)[131] | 1,06,907.7 ± 30136.52 |
| Present study (2022) | 64,000 ± 32475.92 |

The mean platelet count of pregnant ladies, in our research was 64,000 ± 32475.92/mm³ which was lower than the studies done by Singh et al (2012)[127] and Chauhan et al (2016)[131].

**Gestational thrombocytopenia**

Current study showed that maternal thrombocytopenia was the most frequently caused by gestational thrombocytopenia. Burrows et al (1990)[145] attributed this decrease in the maternal platelet count to hemodilution, elevated thromboxane A2 levels, and accelerated platelet destruction.

Gestational thrombocytopenia is the most prevalent kind of maternal thrombocytopenia, according to Burrows et al. (1990)[145], and it provides negligible risk to the mother or the newborn both in labour and after delivery.

**Pre-eclampsia, eclampsia and HELLP syndrome**

Second common cause of thrombocytopenia in pregnancy in this study was pre-eclampsia, eclampsia and HELLP syndrome.

Pre-eclampsia is a disorder characterized by maternal endothelial dysfunction and increased lipid peroxidation causing hypertension, proteinuria and platelet activation resulting in a hypercoagulable state.

Similar to studies by Katke et al. (2014)[142], Somani et al. (2015)[143], Chauhan et al. (2016)[131], and Vishwekar et al. (2017)[144], the current study had 22.33% cases of pre-eclampsia and eclampsia.

HELLP syndrome can develop as pre-eclampsia progresses. Red cell fragmentation brought on by the high-velocity passage of erythrocytes through the injured endothelium results in microangiopathic haemolytic anaemia and thrombocytopenia from increased platelet consumption.

This was demonstrated microscopically by the presence of schistocytes (fragmented red blood cells), contracted red blood cells with spicules known as burr cells and presence of polychromatic RBCs.

In this study, HELLP syndrome was seen in (5/103) cases i.e., 4.85% of cases similar to researches of Katke et al (2014)[142] and Somani et al (2015)[143].

**DIC**

Our study showed 1.94% which was one of the least common causes of thrombocytopenia this was correlated with katke vishweker et al (2014)[142] 1.53%.
Several conditions, including placental abruption, amniotic fluid embolism, uterine rupture, and retained foetal products that rupture and release tissue factor-rich material into the mother's circulation, can result in DIC. Thus, activating coagulation with consumption of coagulation factors and hypofibrinogemia and thrombocytopenia.

**Acute fatty liver of pregnancy**

In this study, only one patient of acute fatty liver of pregnancy was reported and this condition was Characterized by hypoglycaemia, low fibrinogen and prolonged prothrombin time and moderate thrombocytopenia. Studies by Barton JR et al (2004) reported conclusions which were similar.[146]

**Comparison of etiology of maternal thrombocytopenia with degree of thrombocytopenia in this study with other studies.**

In investigations conducted by Burrows et al (1990)[145], Singh et al (2012)[127], and Chauhan et al (2016)[131], platelet counts between 100000-150000 (mild thrombocytopenia) were found in 62 out of 67 cases with gestational thrombocytopenia, or 92.53% of the cases.

According to research by Shehata et al. (1999)[148], moderate to severe thrombocytopenia was linked to pre-eclampsia, eclampsia, HELLP syndrome, and DIC.

The current investigation found an association between ITP and severe thrombocytopenia, which was consistent with research by Cook et al. (2000)[147] and Wang et al. (2017)[138].

**1) MATERNAL OUTCOME**

**MATERNAL COMPLICATIONS**

The majority of the cases (75/103) or 72.81% did not experience any significant thrombocytopenia-related bleeding problems.

Antepartum haemorrhage was the bleeding sign that was identified in cases most frequently (10.68%), followed by petechiae, ecchymosis, and purpura (8.74%). Somani et al. (2015)[143] observed findings that were comparable.

The most common maternal complication in this study, post-partum haemorrhage, affected 4/103 (3.88%) of the women. The majority of these cases, 2/4 (50%) from HELLP syndrome, and 1/4 (25%) from DIC. They all had thrombocytopenia that ranged from moderate to severe.

In their study, Barton JR et al. (2004)146 discovered that women with HELLP syndrome and coagulopathy linked to deceased foetus were more likely to experience postpartum haemorrhage.

**T-25: Comparison of incidence of post-partum haemorrhage**

| Studies | Post-partum haemorrhage% |
|---|---|
| Singh et al (2012)[127] | 9.89 |
| Brohi et al (2013)[130] | 23 |
| Somani et al (2015)[143] | 17.4 |
| Arora et al (2016)[149] | 4.3 |
| Vishwekar et al (2017)[144] | 5.3 |
| Wang et al (2017)[138] | 3.6 |
| Present study (2022) | 3.88 |

Post-partum haemorrhage was observed in 3.88% (4/103) of patients in the present study which was in concordance to Arora et al (2016)[149] and Wang et al (2017)[138].

However, higher incidence of post-partum haemorrhage was reported by Brohi et al (2013)[130] and Somani et al (2015)[145].

Wang et al (2017)[138] explained in his study that patients with severe thrombocytopenia were at a high risk for post-partum haemorrhage and the reason for declining rates of post-partum haemorrhage in severe thrombocytopenic cases over the recent years could be due to administration of effective treatment before termination of pregnancy. He also found that post-partum haemorrhage was associated with disorders related to abnormal coagulation.

**MATERNAL MORTALITY**

**T-26: Comparison of incidence of maternal mortality**

| Studies | Maternal mortality % |
|---|---|
| Brohi et al (2013)[130] | 28.1 |
| Katke et al (2014)[142] | 7.76 |
| Somani et al (2015)[143] | 0 |
| Singh et al (2012)[127] | 5.26 |
| Present study (2022) | 1.94 |

In the present study only 2 maternal fatalities (1.94%) were reported.

In their study, Somani etal. (2015)143 did not find any maternal losses. However, higher maternal deaths were observed by Brohi et al (2013)[130] i.e., 28.1%. One case of DIC and one case of acute fatty liver of pregnancy died in this study at 30-32 weeks of gestation. Both of them died before delivery and had intra-uterine foetal deaths.

Brohi et al (2013)[130] in his study observed high maternal mortality and foetal morbidity from cases of HELLP syndrome and DIC. These findings were also reported by Parnas et al (2006)[150] and Mc Crae et al (2010)[151].

Cejudo et al (2000)[152] in his study of 12 cases of acute fatty liver of pregnancy over a period of 7 years also observed 1 maternal death. He concluded that acute fatty liver of pregnancy needed medical attention and intensive care unit treatment because of increased complications associated with DIC, hypoglycaemia, acidosis, acute kidney failure, encephalopathy and still births.

Fesenmeier MF et al (2005)[89] in his study of 16 cases of acute fatty liver of pregnancy reported 12.5% maternal deaths and 15% foetal deaths.

**ROUTE OF DELIVERY**

**T-27: Comparison of maternal route of delivery**

| Studies | Vaginal delivery | Caesarean delivery |
|---|---|---|
| Singh et al (2012)[127] | 64% | 36% |
| Chauhan et al (2016)[131] | 72.30% | 27.7% |
| Vishwekar et al (2017)[144] | 62.54% | 37.5% |
| Present study (2022) | 63.37% | 36.63% |

Vaginal delivery was the commonest mode of delivery in this study (63.37%) which was in concordance with all the studies mentioned above in Chauhan et al (2016)[131] and Vishwekar et al (2017)[144].

**POST-PARTUM THROMBOCYTOPENIA**

**T-28: Comparison of post-partum thrombocytopenia in the present study with other study.**

| Study | Post-partum thrombocytopenia |
|---|---|
| Singh et al (2012)[127] | 3.33% |
| Present study (2022) | 6.62% |

Nadine Shehata et al [149] in her study reported that in gestational thrombocytopenia, platelet levels returned to normal within 6 weeks following delivery.

None of the cases of gestational thrombocytopenia had thrombocytopenia persisting after delivery. Similar findings were also reported by Burrows et al (1990)[145] and Singh et al (2012)[127].

Post-partum platelet counts were checked up to one-week post-partum.

Majority of the cases i.e., 90/101 cases (89.11%) in the present study had normal platelet counts following delivery and only 11/101cases i.e. (6.62%) of cases had persistence of low platelet counts after delivery.

Post-partum thrombocytopenia persisted in all 5 cases of HELLP syndrome, Both the case of ITP and one case of megaloblastic anemia.

Thus, all the cases of HELLP syndrome and ITP should be followed up closely during post-partum period.

Mc. Crae KR et al (2010)[151] in his study also observed that cases with pre-eclampsia and in particular HELLP syndrome commonly presented with persistence

of thrombocytopenia following delivery and elevated LDH levels for several weeks following delivery.

**2) FETAL OUTCOME**

This study documented 15 intrauterine fatalities (14.56%) among 103 thrombocytopenic women.

Similar findings were reached by Khuman V et al (2015)[153], who found that preterm infants of eclamptic women were more likely to experience respiratory distress and needed intensive care.

Fetal consequences from HELLP syndrome, including placental abruption, preterm births, and intrauterine foetal fatalities, have been documented by Parnas et al. (2006)[150], Mc Crae et al. (2010)[151], and Brohi et al. (2013)[130].

11 new-borns (12.09%) out of 91 new-borns were hospitalised in the NICU due to problems such birth asphyxia, respiratory distress, jaundice, etc. These results were also noted in the Agarwal et al. (2016)[154] study.

**T-29: Comparison of fetal maturity born to thrombocytopenic mothers**

| Studies | Preterm | Term |
|---|---|---|
| Onisai et al (2012)[128] | 28.57% | 71.5% |
| Brohi et al (2013)[130] | 21% | 79% |
| Katke et al (2014)[142] | 21% | 79% |
| Vishwekar et al (2017)[144] | 25% | 75% |
| Present study (2022) | 20.79% | 78.22% |

In this study, 21/101 cases (20.79%) cases were associated with pre-term delivery, similar results seen by Brohi et al (2013)[130] and Katke et al (2014)[142] in their research.

In pre-eclampsia and HELLP syndrome since there are associated medical and obstetric complications the foetus are delivered pre term as a part of management of the above conditions.

**T-30: Comparison of mean birth weight of new-borns according to the etiology of maternal thrombocytopenia**

| **STUDY** | **Mean birth weight of neonates in gestational thrombocytopenia cases** | **Mean birth weight of neonates in pre-eclampsia/ eclampsia cases** | **Mean birth weight of neonates in HELLP syndrome cases.** |
|---|---|---|---|
| Onisai et al (2012)[128] | 3.2 ± 0.37 kg | 2.46 ± 0.79 kg | 1.64 ± 0.49 kg |
| Present study (2022) | 2.9 ± 0.75 kg | 2.2 ± 0.79 kg | 1.66 ± 0.60 kg |

In this study, the mean birth weight of neonates in gestational thrombocytopenia cases was 2.9 kg, in neonates of pre-eclampsia and eclampsia cases it was 2.2 kg, and in neonates of HELLP syndrome cases it was 1.66 kg. Similar findings were reported by Onisai et al (2012)[128].

This explains that the mean birth weight of neonate decreases with the severity of the maternal disease causing thrombocytopenia.

**T-31: Comparison of intra-uterine deaths of fetuses in maternal thrombocytopenic cases**

| Studies | IUD cases% |
|---|---|
| Brohi et al (2013)[130] | 28.1 |
| Katke et al (2014)[142] | 14 |
| Somani et al (2015)[143] | 14.29 |
| Vishwekar et al(2017)[144] | 6 |
| Present study (2022) | 14.56 |

Higher incidence of intrauterine fetal deaths in cases with maternal thrombocytopenia is a predictor of poor fetal outcome.

In this study, 15/103 thrombocytopenic mothers (14.56%) had intra uterine fetal deaths which is similarly seen in Katke et al (2014)[142] and Somani et al (2015)[143]'s researches.

Among 8 cases with severe maternal thrombocytopenia, 6/8 cases reported to have intra-uterine deaths of fetuses.

Hence, intra-uterine death of fetus was correlated with severe thrombocytopenia of the mother similar results were also seen in the researches done by Katke et al (2014)[142] and Somani et al (2015)[143].

Higher incidence of IUD was seen in cases of eclampsia 2/4 cases (50%), pre-eclampsia 8/19 (42.11%) and in HELLP syndrome 2/5 cases (40%). In cases of DIC both 2/2 cases (100%) had intra- uterine fetal deaths. Similar findings were reported by Brohi et al (2013)[130]

**T-32: Comparison of incidence of neonatal thrombocytopenia**

| Studies | Incidence % |
|---|---|
| Parnas et al (2006)[15] | 3.51 |
| Bhat et al (2008)[136] | 36 |
| Singh et al (2012)[127] | 1.09 |
| Somani et al (2015)[143] | 6.35 |
| Chauhan et al (2016)[131] | 3.10 |
| Vishwekar et al (2017)[144] | 7 |
| Wang et al (2017)[138] | 7.7 |
| Present study (2022) | 6.59 |

In this study, the incidence of neonatal thrombocytopenia (6/91) 6.59% which was comparable to studies by Somani et al (2015)[143], Vishwekar et al (2017)[144] and Wang et al (2017)[138].

However, much higher incidence of neonatal thrombocytopenia was observed by Bhat et al (2008)[136].

**Neonatal thrombocytopenia and fetal outcome in relation to etiology of maternal thrombocytopenia.**

Mothers with HELLP syndrome (3/5 cases) and pre-eclampsia (1/23 cases) were associated with neonatal thrombocytopenia in this study 60% and 4.35% respectively.

These results were similar to studies done by Dwivedi et al (2012)[155] and Arora et al (2016)[149]. They also established that pre- term neonates born to pre eclamptic mothers had increased risk to develop neonatal thrombocytopenia and resulting bleeding complications.

Two cases of ITP were noted in our study of whose offsprings also presented with neonatal thrombocytopenia.

# SUMMARY

From January 2021 to December 2021, a tertiary care hospital's Department of Pathology conducted the current prospective study.

Fifteen hundred pregnant women were studied who visited hospitals during the study period, and 103 of them experienced thrombocytopenia in the third trimester of pregnancy. In this study, maternal thrombocytopenia was 6.9% prevalent.

Mild thrombocytopenia was seen in 69.90% (72/103) cases, moderate thrombocytopenia was seen in 22.33% (23/103) cases and severe thrombocytopenia was seen in 7.77 % (8/103) cases.

Mean age of the study group was 26.25 years. Most patients i.e. 100/103 (97.09%) were < 32 years of age whereas only 3 patients (2.91%) were > 32 years old.

Most patients in this study were gravida two or more (58.25%) and 41.75% cases were primigravidae. Maximum cases delivered after full gestational age.

Platelet count in gestational thrombocytopenia on average was 72,000/$mm^3$, in pre-eclampsia was 73,000/$mm^3$, in eclampsia was 62,500/mm3, in HELLP syndrome it was 46,000/$mm^3$ and in DIC it was 36,000/$mm^3$.

Causes of maternal thrombocytopenia were mainly gestational thrombocytopenia (65.05%), followed by pre-eclampsia (18.45%), eclampsia (3.88%), HELLP syndrome (4.85%), DIC and ITP (1.94%) cases.

Among 67 cases of gestational thrombocytopenia 92.53% had mild thrombocytopenia, and the remaining 7.46% had moderate thrombocytopenia.

Out of 67 cases of gestational thrombocytopenia, 95.52% cases had term deliveries and only 2.98% cases had pre- term delivery. Only one case in our study

had post term delivery. Hence, gestational thrombocytopenia was seen associated with term deliveries and did not affect the fetal maturity.

The mean birth weight of neonates in cases of gestational thrombocytopenia was 2.9 kg.

Out of 67 cases of gestational thrombocytopenia 88.57% had new-borns with normal birth weight and only 11.43% gave birth to low birth weight babies. One term twin delivery with normal birth weight and 1 term triplet delivery with low birth weight were also observed. Hence, gestational thrombocytopenia cases were associated with normal birth weight.

Pre-eclampsia cases with mild thrombocytopenia (47.37%) and moderate thrombocytopenia (52.63%) were more common.

In 50% of eclampsia cases, the thrombocytopenia was moderate, and 50% of instances, it was severe.

Among 4 cases of eclampsia, 75% delivered preterm. Hence, it can be concluded that eclampsia cases were seen associated with fetal prematurity.

Low birth weight was observed in 52.63% patients of preeclampsia and 75% of eclampsia patients.

There were 4.85% cases of HELLP syndrome, among these 60% cases showed moderate thrombocytopenia and 40% cases showed severe thrombocytopenia.

Since 80% of the five cases of HELLP syndrome resulted in low-birth-weight babies and 80% of the cases were linked to preterm deliveries, the syndrome had a significant impact on birth weight and prematurity.

Both the cases of DIC in our study had severe thrombocytopenia One case died before delivery and both the cases had IUDs.

One case of 30 years of age died who had acute fatty liver of pregnancy.

Total of 2 death i.e., 1.94% fatality was noted in our study.

Vaginal delivery (62.13%) was the most common route of delivery in this study followed by Caesarean delivery (35.92%). Two cases died before the delivery in our study.

The major maternal complication seen in 3.88% of cases was post-partum haemorrhage. PPH was seen in 60% cases of HELLP syndrome and one case of DIC (50%). All the PPH cases had moderate to severe thrombocytopenia in mother.

Out of 101 cases, 78.22% were term deliveries and 20.79% were pre-term deliveries. only 0.99% (1 case) had post term delivery.

Out of 21 pre-term deliveries 52.38% neonates had moderate thrombocytopenia in mother and 28.57% had severe thrombocytopenia in mother and only 19.05% had mild thrombocytopenia in the mother. Hence, the preterm deliveries were associated with moderate to severe maternal thrombocytopenia.

Majority of neonates 73.08% had normal birth weight and only 26.92% presented with low birth weight.

In pregnant ladies with pre-eclampsia and eclampsia, the mean birth weight was 2.1 kg and 2.3 kg, respectively and in patients with HELLP syndrome it was 1.66 kilogram. It was found that the mean birth weight decreases with the severity of maternal disease causing thrombocytopenia.

Among 28 low birth weight neonates, 46.43% were born to mothers having moderate thrombocytopenia and 17.86% were born to mothers having severe thrombocytopenia. Thus, low birth weight correlated with the degree of thrombocytopenia.

Intra-uterine fetal deaths reported in our study were 14.15%. Thus, 91/106 babies were live born. Among 15 intra-uterine fetal deaths 40% had severe

thrombocytopenia in mother and 46.67% had moderate thrombocytopenia in mother. Hence, intrauterine deaths correlated with severity of the degree of thrombocytopenia.

The most common cause of IUD in this study was pre-eclampsia 53.33% followed by eclampsia 13.33% and HELLP syndrome 13.33%. Both the cases of DIC and one case of acute fatty liver of pregnancy had intra-uterine fetal deaths.

Majority of the cases 89.11% had normal platelet counts after delivery and only 10.89% had low platelet counts persisting after delivery.

In our study, 87.91% neonates had no complications. Respiratory distress was the common neonatal complication (6.59%) followed by birth asphyxia (3.30%).

Incidence of neonatal thrombocytopenia in our study was 6.59% i.e. (6/91).

Most common cause of neonatal thrombocytopenia in this study was HELLP syndrome (50%).

Among 5 cases of HELLP syndrome, 60% gave birth to neonates presenting with thrombocytopenia.

Two cases of maternal ITP with severe thrombocytopenia were reported of which the offsprings also presented with neonatal thrombocytopenia

# CONCLUSION

Pregnancy-related thrombocytopenia is uncommon. The most common reason for maternal thrombocytopenia was gestational thrombocytopenia. It appears in the 3rd trimester of pregnancy and typically causes no complications for the mother or the foetus.

Disorders associated with pregnancy-induced hypertension, or HELLP syndrome, were the second most frequent cause of maternal thrombocytopenia and was attributed to maternal morbidity and potentially fatal maternal complications such postpartum haemorrhage. It was also associated with foetal morbidities like prematurity, low birth weight and intra-uterine foetal deaths.

This leads to the conclusion that the aetiology and severity of thrombocytopenia during pregnancy play a significant role in the outcome of pregnancy.

Platelet count estimation and peripheral blood smear testing can minimize both maternal and foetal issues if the condition causing maternal thrombocytopenia is identified and treated at the earliest of the illness. Serial quantitative platelet estimation in thrombocytopenic pregnant ladies thus significantly reduces foetal and maternal morbidity and death.

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# ANNEXURE I

## INFORMED CONSENT

## "PREVALENCE OF THROMBOCYTOPENIA IN PREGNANCY-A HOSPITAL BASED STUDY"

**Purpose of the study:** You are being asked to enroll in this study as you are eligible for participation in this study. The present study is undertaken to know the prevalence of thrombocytopenia in our population and its possible etiological factors which is of great diagnostic value and has therapeutic implications.

**Procedure:** During this study, you will be asked questions regarding age and obstetric history and you are supposed to answer to the best of your knowledge. The principal investigator of the study is REG.NO. BN0120006 Patel under the guidance of Dr. _____.

If you agree to enroll yourself in this study, you will be interviewed regarding your present, past, obstetric and family history and your clinical manifestations.

**Risks and benefits**: There are no risks involved in taking part in this study and benefit is we will be able to judge the nature and prognosis of the disease which is essential for providing appropriate treatment.

**Alternatives:** Taking part in this study is voluntary. You may choose not to take part in this study or if you decide to take part now, you can later change your mind and withdraw from the study. The study doctor or sponsor may terminate your participation in this study anytime.

**Privacy and confidentiality:** All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study will be published but your identity will be confidential in any publication. No information about you or

information provided by you during research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.

2. If required by law.

**Financial incentives for participation:** You will not be paid / offered any gift incentives for participating in this study.

**Authorization to publish results:** The results of this study would be forwarded to the KLE University, Belagavi as a part of requirement towards the completion of MD degree, review and publishing.

**Questions:** In case you have any questions related to the study in future you can contact:

1. REG.NO. BN0120006, Department of Pathology, J.N. Medical College.

2. Dr. _____Professor, Department of Pathology, J.N. Medical College.

3. If you have any queries about your rights as a study subject, you may call Dr Harsha Hegde, Chairman of J.N. Medical College Institutional Ethical Committee of Human Subjects Research, Ph No-9480422500, at J.N. Medical College, Belagavi

## माहितीपूर्ण संमती पत्र

गरोदरपणात थ्रोम्बोसाइटोपेनियाची व्याप्ती - एक हॉस्पिटल आधारित अभ्यास

अभ्यासाचा उद्देश:

आपण या अभ्यासामध्ये सहभागास पात्र आहात म्हणून आपणास या अभ्यासामध्ये नावनोंदणी करण्यास सांगितले जाते. सध्याचा अभ्यास आमच्या लोकसंख्येमध्ये थ्रोम्बोसाइटोपेनियाचा प्रसार आणि त्याच्या संभाव्य एटिओलॉजिकल घटकांबद्दल जाणून घेण्यासाठी हाती घेण्यात आला आहे जे निदानात्मक मूल्यांचे आहे आणि त्यावर उपचारात्मक परिणाम आहेत.

प्रक्रियाः

या अभ्यासादरम्यान, आपल्या मुलाचा नैदानिक इतिहास नोंदविला जातो, हेमोलिटिक अनेमीयाच्या प्रकाराचे निदान करण्यासाठी हेमेटोलॉजिकल आणि बायोकेमिकल चाचण्या केल्या जातील. डॉ. _____(मार्गदर्शक) यांच्या मार्गदर्शनाखाली REG.NO. BN0120006 या अभ्यासाचे मुख्य तपासनीस आहेत.

आपण या अभ्यासामध्ये आपल्या मुलाची नावनोंदणी करण्यास सहमती दर्शविल्यास, आपल्या अहवालाचा उपयोग संशोधनाच्या उद्देशाने केला जाईल

जोखीम आणि फायदे

या अभ्यासामध्ये भाग घेण्यात कोणताही धोका नाही आणि त्याचा फायदा म्हणजे योग्य उपचार उपलब्ध करुन देण्यासाठी आवश्यक असलेल्या आजाराच्या स्वरूपाचा आणि रोगाचा पूर्वनिदान आम्ही करू शकू.

विकल्पः

या अभ्यासामध्ये भाग घेणे ऐच्छिक आहे. आपण या अभ्यासामध्ये भाग न घेण्याची निवड करू शकता किंवा आपण आता भाग घेण्याचा निर्णय घेतल्यास आपण नंतर आपले मत बदलू आणि अभ्यासापासून दूर जाऊ शकता.

गोपनीयता

या अभ्यासाच्या दरम्यान आपल्याबद्दल संकलित केलेली सर्व माहिती कायद्याद्वारे परवानगी असलेल्या मर्यादेपर्यंत गोपनीय ठेवली जाईल. कोड नंबर आपल्याला या संशोधन रेकॉर्डमध्ये ओळखतील. या अभ्यासाची माहिती प्रकाशित केली जाईल परंतु आपली ओळख कोणत्याही प्रकाशनात गोपनीय असेल. आपल्याबद्दल किंवा संशोधनादरम्यान प्रदान केलेली माहिती किंवा इतर माहिती आपल्या लिखित परवानगीशिवाय इतरांना उघड केली जाणार नाहीः

1. आपत्कालीन परिस्थितीत आपले हक्क आणि कल्याण संरक्षित करण्यासाठी.
2. कायद्याने आवश्यक असल्यास.

सहभागासाठी आर्थिक प्रोत्साहनः

या अभ्यासामध्ये भाग घेण्यासाठी आपल्याला कोणतीही भेट / प्रोत्साहन दिले जाणार नाही.

परिणाम प्रकाशित करण्यासाठी अधिकृतताः

या अभ्यासाचे निकाल एमएडी पदवी, आढावा आणि प्रकाशन पूर्ण करण्याच्या आवश्यकतेचा भाग म्हणून काहेर, बेलागावीकडे पाठविला जाईल.

प्रशनावळी:

भविष्यात अभ्यासाशी संबंधित काही प्रश्न असल्यास आपण संपर्क साधू शकताः

1. REG.NO. BN0120006,पॅथॉलॉजी विभाग, जे.एन. मेडिकल कॉलेज.

2. डॉ_____, पॅथॉलॉजी विभाग, जे.एन. मेडिकल कॉलेज.

3. आपल्याकडे अभ्यासाचा विषय म्हणून आपल्या हक्कांबद्दल काही शंका असल्यास आपण डॉ. हर्षा हेगडे चेअरपर्सन जे.एन.एम.सी. आय.ई.सी. आणि सायन्टीस्ट डी आय.सी.एम.आर. राष्ट्रीय संस्था पारंपारिक औषध बेलगावी 9480422500

संमती विधान

मी खाली स्वाक्षरी करून या अभ्यासात भाग घेण्यास स्वेच्छेने सहमत आहे. मी केव्हाही माघार घेऊ शकतो. या फॉर्मवर सही करून मी कोणतेही कायदेशीर हक्क सोडत नाही. खाली माझी स्वाक्षरी सूचित करते की मी हा संपूर्ण संमती फॉर्म वाचला आहे किंवा माझ्या कडून वाचविला गेला आहे आणि माझ्या सर्व प्रश्नांची उत्तरे दिली आहेत

प्रधान अन्वेषक:

मार्गदर्शन:

सहभागीचे नाव: (स्वाक्षरी / अंगठाचा ठसा)

साक्षीदाराचे नाव: (सही / अंगठाचा ठसा)

चौकशीचे नाव: (स्वाक्षरी)

तारीख:

ತಿಳುವಳಿಕೆಯುಳ್ಳ ಒಪ್ಪಿಗೆ ಪತ್ರ

ಗರ್ಭಾವಸ್ಥೆಯಲ್ಲಿ ಥ್ರಂಬೋಸೈಟೋಪೆನಿಯಾದ ಹರಡುವಿಕೆ - ಆಸ್ಪತ್ರೆ ಆಧಾರಿತ ಅಧ್ಯಯನ

ಅಧ್ಯಯನದ ಉದ್ದೇಶ:
ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಅರ್ಹರಾಗಿರುವುದರಿಂದ ಈ ಅಧ್ಯಯನಕ್ಕೆ ಸೇರಲು ನಿಮ್ಮನ್ನು ಕೇಳಲಾಗುತ್ತದೆ. ನಮ್ಮ ಜನಸಂಖ್ಯೆಯಲ್ಲಿ ಥ್ರಂಬೋಸೈಟೋಪೆನಿಯಾದ ಹರಡುವಿಕೆ ಮತ್ತು ಅದರ ಸಂಭವನೀಯ ರೋಗಶಾಸ್ತ್ರೀಯ ಅಂಶಗಳು ಹೆಚ್ಚಿನ ರೋಗನಿರ್ಣಯದ ಮೌಲ್ಯವನ್ನು ಹೊಂದಿವೆ ಮತ್ತು ಚಿಕಿತ್ಸಕ ಪರಿಣಾಮಗಳನ್ನು ಹೊಂದಿವೆ ಎಂದು ತಿಳಿಯಲು ಪ್ರಸ್ತುತ ಅಧ್ಯಯನವನ್ನು ಕೈಗೊಳ್ಳಲಾಗಿದೆ.

ವಿಧಾನ:
ಈ ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ, ನಿಮ್ಮ ಮಗುವಿನ ಕಲಿನಿಕಲ್ ಇತಿಹಾಸವನ್ನು ಗುರುತಿಸಲಾಗಿದೆ, ಹೆಮೋಲಿಟಿಕ್ ರಕ್ತಹೀನತೆಯ ಪ್ರಕಾರವನ್ನು ಪತ್ತೆಹಚ್ಚಲು ಹೆಮಟೊಲಾಜಿಕಲ್ ಮತ್ತು ಜೀವರಾಸಾಯನಿಕ ಪರೀಕ್ಷೆಗಳನ್ನು ಮಾಡಲಾಗುತ್ತದೆ.
ಡಾ._____ (ಮಾರ್ಗದರ್ಶಿ) ಅವರ ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ಅಧ್ಯಯನದ ಪ್ರಮುಖ ತನಿಖಾಧಿಕಾರಿ REG.NO. BN0120006.
ನಿಮ್ಮ ಮಗುವನ್ನು ಈ ಅಧ್ಯಯನಕ್ಕೆ ದಾಖಲಿಸಲು ನೀವು ಒಪ್ಪಿದರೆ, ನಿಮ್ಮ ವರದಿಗಳನ್ನು ಸಂಶೋಧನಾ ಉದ್ದೇಶಕ್ಕಾಗಿ ಬಳಸಲಾಗುತ್ತದೆ

ಅಪಾಯ ಮತ್ತು ಪ್ರಯೋಜನಗಳು
ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಲ್ಲಿ ಯಾವುದೇ ಅಪಾಯಗಳಿಲ್ಲ ಮತ್ತು ಸೂಕ್ತ ಚಿಕಿತ್ಸೆಯನ್ನು ಒದಗಿಸಲು ಅಗತ್ಯವಾದ ರೋಗದ ಸ್ವರೂಪ ಮತ್ತು ಮುನ್ನರಿವನ್ನು ನಾವು ನಿರ್ಣಯಿಸಲು ಸಾಧ್ಯವಾಗುತ್ತದೆ.

ಪರ್ಯಾಯಗಳು:
ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದು ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸದಿರಲು ನೀವು ಆಯ್ಕೆ ಮಾಡಬಹುದು ಅಥವಾ ನೀವು ಈಗ ಭಾಗವಹಿಸಲು ನಿರ್ಧರಿಸಿದರೆ, ನೀವು ನಂತರ ನಿಮ್ಮ ಮನಸ್ಸನ್ನು ಬದಲಾಯಿಸಬಹುದು ಮತ್ತು ಅಧ್ಯಯನದಿಂದ ಹೊರ ಸರಿಯಬಹುದು. ಅಧ್ಯಯನದ ವೈದ್ಯರು ಅಥವಾ ಪ್ರಾಯೋಜಕರು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆಯನ್ನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಕೊನೆಗೊಳಿಸಬಹುದು.

ಗೌಪ್ಯತೆ

ಈ ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ನಿಮ್ಮ ಬಗ್ಗೆ ಸಂಗ್ರಹಿಸಲಾದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಕಾನೂನಿನಿಂದ ಅನುಮತಿಸುವ ಮಟ್ಟಿಗೆ ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ. ಈ ಸಂಶೋಧನಾ ದಾಖಲೆಯಲ್ಲಿ ಕೋಡ್ ಸಂಖ್ಯೆಗಳು ನಿಮ್ಮನ್ನು ಗುರುತಿಸುತ್ತವೆ. ಈ ಅಧ್ಯಯನದ ಮಾಹಿತಿಯನ್ನು ಪ್ರಕಟಿಸಲಾಗುವುದು ಆದರೆ ಯಾವುದೇ ಪ್ರಕಟಣೆಯಲ್ಲಿ ನಿಮ್ಮ ಗುರುತು ಗೌಪ್ಯವಾಗಿರುತ್ತದೆ. ನಿಮ್ಮ ಲಿಖಿತ ಅನುಮತಿಯಿಲ್ಲದೆ ನಿಮ್ಮ ಬಗ್ಗೆ ಯಾವುದೇ ಮಾಹಿತಿ ಅಥವಾ ಸಂಶೋಧನೆಯ ಸಮಯದಲ್ಲಿ ನೀವು ಒದಗಿಸಿದ ಮಾಹಿತಿಯನ್ನು ಇತರರಿಗೆ ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ:

1. ನಿಮ್ಮ ಹಕ್ಕುಗಳು ಮತ್ತು ಕಲ್ಯಾಣವನ್ನು ರಕ್ಷಿಸಲು ತುರ್ತು ಪರಿಸ್ಥಿತಿಯಲ್ಲಿ.
2. ಕಾನೂನಿನ ಪ್ರಕಾರ ಅಗತ್ಯವಿದ್ದರೆ.

ಭಾಗವಹಿಸುವಿಕೆಗೆ ಆರ್ಥಿಕ ಪ್ರೋತ್ಸಾಹ:
ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಿಮಗೆ ಯಾವುದೇ ಉಡುಗೊರೆ / ಪ್ರೋತ್ಸಾಹ ಧನ ನೀಡಲಾಗುವುದಿಲ್ಲ.

ಫಲಿತಾಂಶಗಳನ್ನು ಪ್ರಕಟಿಸಲು ಅಧಿಕಾರ:
ಈ ಅಧ್ಯಯನದ ಫಲಿತಾಂಶಗಳನ್ನು ಎಂಡಿ ಪದವಿ, ವಿಮರ್ಶೆ ಮತ್ತು ಪ್ರಕಟಣೆಯ ಪೂರ್ಣಗೊಳಿಸುವಿಕೆಯ ಅವಶ್ಯಕತೆಯ ಭಾಗವಾಗಿ ಬೆಳಗಾವಿಯ ಕಾಹೇರ್‌ಗೆ ರವಾನಿಸಲಾಗುತ್ತದೆ.

ಪ್ರಶ್ನೆಗಳು
ಭವಿಷ್ಯದಲ್ಲಿ ನೀವು ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗಳನ್ನು ಹೊಂದಿದ್ದರೆ ನೀವು ಸಂಪರ್ಕಿಸಬಹುದು:

1. REG.NO. BN0120006, ರೋಗಶಾಸ್ತ್ರ ವಿಭಾಗ, ಜೆ.ಎನ್. ವೈದ್ಯಕೀಯ ಕಾಲೇಜು.

2. ಡಾ._____ರೋಗಶಾಸ್ತ್ರ ವಿಭಾಗ, ಜೆ.ಎನ್. ವೈದ್ಯಕೀಯ ಕಾಲೇಜು.

3. ಅಧ್ಯಯನದ ವಿಷಯವಾಗಿ ನಿಮ್ಮ ಹಕ್ಕುಗಳ ಬಗ್ಗೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಗಳನ್ನು ಹೊಂದಿದ್ದರೆ,, ಡಾ. ಹರ್ಷ ಹೆಗಡೆ, ಅಧ್ಯಕ್ಷರಾದ ಜೆ.ಎನ್.ಎಂ.ಸಿ, ಐ.ಇ.ಸಿ ಮತ್ತು ವಿಜ್ಞಾನಿ ಡಿ, ಐ.ಸಿ.ಎಂ.ಆರ್, ನಿಯಾಷನಲ್ ಇನಿಸೆಟಿಯೂಟ್ ಆಫ್ ಟಿರೆಡಿಶನಲ್ ಮೆಡಿಸಿನ್ ಬೆಲಗವಿ 9480422500

ಒಪ್ಪಿಗೆಯ ಹೇಳಿಕೆ

ಕೆಳಗೆ ಸಹಿ ಮಾಡುವ ಮೂಲಕ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪುತ್ತಿದ್ದೇನೆ. ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಹೆಂತೆಗೆದುಕೊಳ್ಳಬಹುದು. ಈ ಫಾರ್ಮಗೆ ಸಹಿ ಮಾಡುವ ಮೂಲಕ ನಾನು ಯಾವುದೇ ಕಾನೂನು ಹಕ್ಕುಗಳನ್ನು ಬಿಟ್ಟುಕೊಡುತ್ತಿಲ್ಲ. ಕೆಳಗಿನ ನನ್ನ ಸಹಿ ನಾನು ಓದಿದ್ದೇನೆ, ಅಥವಾ ಅದನ್ನು ನನಗೆ ಓದಿದೆ, ಈ ಸಂಪೂರ್ಣ ಒಪ್ಪಿಗೆಯ ರೂಪ ಮತ್ತು ನನ್ನ ಎಲ್ಲಾ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರಿಸಿದೆ ಎಂದು ಸೂಚಿಸುತ್ತದೆ

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ:

ಮಾರ್ಗದರ್ಶಿ:

ಭಾಗವಹಿಸುವವರ ಹೆಸರು: (ಸಹಿ / ಹೆಬ್ಬೆರಳು)

ಸಾಕ್ಷಿಯ ಹೆಸರು: (ಸಹಿ / ಹೆಬ್ಬೆರಳು)

ತನಿಖಾಧಿಕಾರಿಯ ಹೆಸರು: (ಸಹಿ)

ದಿನಾಂಕ:

## ANNEXURE II

## PROFORMA

Case no:

Name:

Age/Sex:

IP/OPD No:

Gravida: Parity: Abortion: Living: Dead:

LMP: EDD:

Slide no:

ON EXAMINATION.

- BP
- Pulse
- Temperature
- CVS
- RS
- PA.

CLINICAL EXAMINATION

- Icterus-
- Petechiae/ bruising-
- Gum bleeding-
- Hematuria-

HISTORY OF

- HTN
- Headache
- Blurring of vision

• Epigastric pain
• DM
• Thrombocytopenia in previous pregnancy
• Delayed clotting post trauma
• Viral infections
• Drug usage

HEMATOLOGICAL TESTS:-

• Platelet count
• PT
• aPTT
• LFT
• Kidney Function Test

Mode of delivery-

Maternal complication if any-

NEONATE

B/O:

Age/Sex:

DOB:

CLINICAL DETAILS:

Gestational age: Preterm Term / Post term

Type of delivery Vaginal/Caesarian-

Neonatal Platelet count-

Neonatal complication if any-

NICU admission-

## ANNEXURE III

### KEY TO MASTER CHART

GT-Gestational thrombocytopenia

PE- Pre-eclampsia

HELLP- HELLP Syndrome

EC- Eclampsia

AFLP- Acute fatty liver of pregnancy

MA- Megaloblastic anemia.

G- Gravida

LFT- Liver function tests

INC- Increased

BRB- Bilirubin

LSCS- Lower segment caesarean section

PEP-Petechiae/ ecchymosis / purpura

GB- Gum bleeding

APH- Ante partum hemorrhage

PPH- Post-partum hemorrhage

EPI- Epistaxis

POST- Post term

PRE- Pre-term

FULL- Full term

RD- Respiratory distress

BA- Birth asphyxia

IUD- Intra-uterine death

| SR NO | IP NO | AGE | GRAVIDITY | GESTATIONAL AGE | BLOOD PRESSURE | PLATELET COUNT | BIOCHEMICAL TESTS | DIAGNOSIS | MODE OF DELIVERY | MATERNAL OUTCOME | POST PARTUM PLATELET COUNTS | BIRTH WEIGHT | FETAL MATURITY | FETAL OUTCOME | NEONATAL OUTCOME | NEONATAL PLATELET COUNT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1061370 | 32 | G2 | 39 | 120/80 | 82,000 | | GT | LSCS | | N | 3.1 | FULL | | | N |
| 2 | 1061727 | 22 | G3 | 39 | 120/80 | 1,27,000 | | GT | LSCS | | N | 2.8 | FULL | | | N |
| 3 | 1062089 | 24 | G1 | 39 | 120/80 | 1,33,000 | | GT | LSCS | | N | 2.9 | FULL | | | N |
| 4 | 1062450 | 30 | G1 | 29 | 170/90 | 95,000 | | PE | VAGINAL | | N | 1 | PRE | IUD | | |
| 5 | 1062666 | 29 | G3 | 37 | 120/80 | 1,47,000 | | GT | LSCS | | N | 2.6 2.8 | FULL | | | N |
| 6 | 1062760 | 24 | G1 | 34 | 200/110 | 20,000 | | EC | VAGINAL | PEP | 1,75,00 | 3 | PRE | IUD | | N |
| 7 | 1062815 | 21 | G1 | 38 | 120/80 | 1,41,000 | | GT | VAGINAL | | N | 2.4 | FULL | | | N |
| 8 | 1062836 | 32 | G2 | 38 | 120/80 | 1,20,000 | | GT | LSCS | | N | 2 | FULL | | | N |
| 9 | 1063213 | 24 | G3 | 38 | 120/80 | 1,44,000 | | GT | LSCS | | N | 3 | FULL | | | N |
| 10 | 1063274 | 20 | G1 | 33 | 140/90 | 1,42,000 | | PE | VAGINAL | | N | 3.3 | PRE | | | N |
| 11 | 1063829 | 24 | G3 | 38 | 120/80 | 79,000 | | GT | VAGINAL | APH | N | 3.3 | FULL | | | N |
| 12 | 1064135 | 24 | G1 | 35 | 120/80 | 1,11,000 | | GT | VAGINAL | | N | 2 | PRE | | | N |
| 13 | 1064732 | 29 | G1 | 37 | 120/80 | 1,35,000 | | GT | LSCS | | N | 1.5 1.8 1.1 | FULL | | | N |
| 14 | 1065090 | 30 | G3 | 39 | 120/80 | 1,37,000 | | GT | LSCS | | N | 3.7 | FULL | | | N |
| 15 | 1065107 | 28 | G4 | 37 | 120/80 | 1,07,000 | | GT | LSCS | | N | 3 | FULL | | | N |
| 16 | 1065332 | 23 | G1 | 39 | 120/80 | 82,000 | | GT | VAGINAL | | N | 3 | FULL | | | N |
| 17 | 1065823 | 22 | G1 | 37 | 120/80 | 66,000 | | GT | LSCS | | N | 2.7 | FULL | RD | | N |
| 18 | 1065974 | 21 | G2 | 39 | 120/80 | 1,16,000 | | GT | VAGINAL | | N | 3.1 | FULL | | | N |
| 19 | 1067598 | 25 | G3 | 31 | 150/90 | 55,000 | | PE | VAGINAL | PPH | N | 1.4 | PRE | IUD | | |
| 20 | 1068368 | 28 | G4 | 40 | 120/80 | 1,21,000 | | GT | VAGINAL | | N | 2.8 | PRE | | | N |
| 21 | 1068447 | 25 | G2 | 38 | 120/80 | 1,31,000 | | GT | LSCS | | N | 2.8 | FULL | | | N |
| 22 | 1068460 | 30 | G3 | 37 | 120/80 | 90,000 | | DENGUE | LSCS | | N | 2.6 | FULL | | | N |
| 23 | 1068701 | 23 | G1 | 40 | 120/80 | 1,46,000 | | GT | VAGINAL | | N | 3.3 | FULL | | | N |
| 24 | 1068755 | 32 | G1 | 30 | 170/80 | 30,000 | LFT INC | HELLP | VAGINAL | PEP/APH/PPH | 1,05,000 | 0.7 | PRE | IUD | | |
| 25 | 1069498 | 23 | G2 | 40 | 120/80 | 1,40,000 | | GT | LSCS | | N | 2.7 | FULL | | | N |
| 26 | 1069578 | 30 | G3 | 39 | 120/80 | 54,000 | | GT | VAGINAL | PEP | N | 3.2 | FULL | | | N |
| 27 | 1069883 | 27 | G1 | 38 | 160/90 | 1,36,000 | | PE | LSCS | | N | 2.9 | FULL | | | N |
| 28 | 1069931 | 20 | G1 | 36 | 120/80 | 1,24,000 | | GT | VAGINAL | | N | 2 | FULL | | | N |
| 29 | 1070518 | 24 | G2 | 36 | 120/80 | 1,38,000 | | GT | LSCS | | N | 2.9 | FULL | | | N |
| 30 | 1071013 | 24 | G2 | 36 | 180/90 | 88,000 | | PE | VAGINAL | | N | 2.2 | PRE | | RD | N |
| 31 | 1071099 | 24 | G1 | 39 | 120/80 | 95,000 | | DENGUE | VAGINAL | | N | 2.7 | FULL | | | N |
| 32 | 1071337 | 28 | G1 | 39 | 120/80 | 1,11,000 | | GT | VAGINAL | | N | 2.6 | FULL | | | N |
| 33 | 1072056 | 27 | G2 | 38 | 120/80 | 1,40,000 | | GT | VAGINAL | | N | 2.9 | FULL | | | N |
| 34 | 1072238 | 39 | G1 | 40 | 120/80 | 1,46,000 | | GT | LSCS | | N | 3.6 | FULL | | | N |
| 35 | 1072277 | 26 | G2 | 40 | 150/90 | 8,000 | LFT INC | HELLP | LSCS | PEP | 1,40,000 | 3 | FULL | IUD | | |
| 36 | 1072424 | 25 | G2 | 39 | 120/80 | 1,48,000 | | GT | VAGINAL | | N | 3.4 | FULL | | | N |
| 37 | 1072509 | 26 | G2 | 36 | 150/90 | 1,20,000 | | PE | LSCS | | N | 2.6 | FULL | | | N |
| 38 | 1072973 | 21 | G1 | 37 | 120/80 | 1,38,000 | | GT | VAGINAL | | N | 2.8 | FULL | | | N |
| 39 | 1073089 | 25 | G3 | 35 | 130/80 | 51,000 | LFT INC | HELLP | VAGINAL | PEP | 1,03,000 | 1.6 | PRE | | RD | 69,000 |
| 40 | 1073559 | 26 | G2 | 36 | 120/80 | 1,44,000 | | GT | VAGINAL | | N | 2.8 | FULL | | | N |
| 41 | 1073987 | 28 | G2 | 37 | 120/80 | 1,46,000 | | GT | VAGINAL | | N | 2.9 | FULL | | | N |
| 42 | 1073990 | 32 | G1 | 37 | 120/80 | 1,33,000 | | GT | LSCS | | N | 2.6 | FULL | | | N |
| 43 | 1074520 | 30 | G2 | 36 | 160/90 | 1,41,000 | | PE | LSCS | | N | 2.7 | FULL | | | N |
| 44 | 1074733 | 28 | G4 | 32 | 180/90 | 58,000 | | PE | VAGINAL | EPI | N | 1.8 | PRE | IUD | | |
| 45 | 1074897 | 20 | G1 | 35 | 150/90 | 65,000 | | PE | LSCS | | N | 1.7 | PRE | | JAUNDICE | 90,000 |
| 46 | 1075012 | 23 | G3 | 38 | 120/80 | 1,31,000 | | GT | VAGINAL | | N | 3 | FULL | | | N |
| 47 | 1075231 | 29 | G4 | 36 | 120/80 | 1,24,000 | | GT | VAGINAL | | N | 3 | FULL | | | N |
| 48 | 1075236 | 23 | G1 | 40 | 130/80 | 1,45,000 | | GT | LSCS | | N | 3.3 | FULL | | | N |
| 49 | 1075300 | 23 | G2 | 38 | 120/80 | 1,25,000 | | MA | VAGINAL | | 1,38,000 | 2.8 | FULL | | | N |
| 50 | 1075303 | 30 | G3 | 35 | 120/80 | 45,000 | | ITP | LSCS | PEP | 80,000 | 2 | PRE | | | 47,000 |
| 51 | 1075371 | 22 | G1 | 33 | 170/110 | 42,000 | | DIC | LSCS | APH/PPH | N | 2 | PRE | IUD | | |
| 52 | 1075707 | 26 | G3 | 37 | 130/81 | 1,02,000 | | GT | LSCS | | N | 2.6 | FULL | | | N |
| 53 | 1075718 | 27 | G2 | 38 | 120/80 | 1,31,000 | | GT | VAGINAL | | N | 2.4 | FULL | | | N |
| 54 | 1076080 | 24 | G2 | 40 | 180/90 | 88,000 | | PE | VAGINAL | | N | 2.9 | FULL | | | N |
| 55 | 1076114 | 21 | G1 | 39 | 190/90 | 1,19,000 | | PE | VAGINAL | | N | 3 | FULL | | | N |
| 56 | 1076114 | 21 | G1 | 39 | 140/90 | 93,000 | | PE | VAGINAL | | N | 3.4 | FULL | | | N |
| 57 | 1077823 | 24 | G1 | 32 | 170/90 | 63,000 | | PE | VAGINAL | APH | N | 1.6 | PRE | IUD | | |
| 58 | 1077823 | 24 | G1 | 32 | 120/80 | 21,000 | | ITP | LSCS | PEP/APH | 70,000 | 1.1 | PRE | | | 30,000 |
| 59 | 1077851 | 27 | G2 | 39 | 130/82 | 1,39,000 | | GT | LSCS | | N | 3.4 | FULL | | | N |
| 60 | 1078337 | 21 | G1 | 35 | 160/110 | 45,000 | | EC | LSCS | PEP/APH | 1,60,000 | 2.1 | PRE | IUD | | N |
| 61 | 1078529 | 23 | G1 | 35 | 150/100 | 90,000 | | EC | LSCS | GB | 1,80,000 | 1.8 | PRE | | JAUNDICE | N |
| 62 | 1078756 | 28 | G3 | 38 | 140/90 | 1,02,000 | | PE | LSCS | | N | 2.5 | FULL | | | N |
| 63 | 1079393 | 29 | G3 | 39 | 150/90 | 1,02,000 | | PE | VAGINAL | | N | 2.9 | FULL | | | N |
| 64 | 1079393 | 29 | G3 | 39 | 130/84 | 1,02,000 | | GT | VAGINAL | | N | 2.9 | FULL | | | N |
| 65 | 1079467 | 28 | G1 | 37 | 130/93 | 1,18,000 | | GT | VAGINAL | | N | 2.7 | FULL | | | N |
| 66 | 1079616 | 23 | G2 | 34 | 120/80 | 66,000 | LFT,BRB INC | HELLP | VAGINAL | PEP | 1,35,000 | 1.8 | PRE | | BA,RD | 88,000 |
| 67 | 1079619 | 25 | G1 | 30 | 150/90 | 1,33,000 | | PE | VAGINAL | | N | 1.2 | PRE | IUD | | |
| 68 | 1079630 | 21 | G1 | 39 | 130/91 | 1,28,000 | | GT | VAGINAL | | N | 2.9 | FULL | | | N |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 69 | 1079656 | 19 | G1 | 38 | 130/92 | 1,20,000 | | GT | VAGINAL | | N | 2.6 | FULL | | | N |
| 70 | 1079659 | 30 | G3 | 38 | 120/80 | 1,46,000 | | GT | LSCS | | N | 2.8 | FULL | | | N |
| 71 | 1079787 | 29 | G2 | 37 | 130/85 | 1,42,000 | | GT | VAGINAL | | N | 3.2 | FULL | | | N |
| 72 | 1079800 | 22 | G2 | 40 | 120/80 | 1,39,000 | | GT | LSCS | | N | 3.1 | FULL | | | N |
| 73 | 1079801 | 25 | G1 | 38 | 120/80 | 1,19,000 | | GT | LSCS | | N | 2.7 | FULL | | | N |
| 74 | 1079831 | 22 | G1 | 36 | 120/80 | 1,36,000 | | GT | VAGINAL | | N | 3.2 | FULL | | | N |
| 75 | 1079847 | 24 | G1 | 41 | 140/80 | 1,27,000 | | GT | VAGINAL | | N | 2.8 | POST | | | N |
| 76 | 1079990 | 30 | G3 | 37 | 110/80 | 1,32,000 | | GT | VAGINAL | | N | 3.5 | FULL | | | N |
| 77 | 1080002 | 29 | G3 | 37 | 110/80 | 1,26,000 | | GT | VAGINAL | | N | 3.3 | FULL | | | N |
| 78 | 1080194 | 25 | G2 | 39 | 120/80 | 1,33,000 | | GT | VAGINAL | | N | 2.7 | FULL | | | N |
| 79 | 1080196 | 26 | G3 | 38 | 120/80 | 1,45,000 | | GT | VAGINAL | | N | 2.6 | FULL | | | N |
| 80 | 1080627 | 28 | G2 | 39 | 130/87 | 1,29,000 | | GT | VAGINAL | | N | 3 | FULL | | | N |
| 81 | 1080648 | 28 | G2 | 36 | 130/86 | 1,20,000 | | GT | VAGINAL | | N | 3 | FULL | | | N |
| 82 | 1081480 | 27 | G2 | 39 | 120/80 | 1,18,000 | | GT | LSCS | | N | 2.7 | FULL | | | N |
| 83 | 1081709 | 29 | G3 | 36 | 120/80 | 1,46,000 | | GT | VAGINAL | | N | 3.4 | FULL | | | N |
| 84 | 1081709 | 30 | G2 | 38 | 130/96 | 1,08,000 | | GT | VAGINAL | | N | 2.9 | FULL | | | N |
| 85 | 1081755 | 27 | G2 | 38 | 120/80 | 1,19,000 | | GT | LSCS | | N | 3 | FULL | | | N |
| 86 | 1081976 | 29 | G1 | 38 | 130/94 | 1,07,000 | | GT | VAGINAL | | N | 2.8 | FULL | | | N |
| 87 | 1082028 | 24 | G1 | 39 | 120/80 | 1,19,000 | | GT | VAGINAL | | N | 2.8 | FULL | | | N |
| 88 | 1082066 | 30 | G1 | 39 | 130/95 | 1,13,000 | | GT | VAGINAL | | N | 2.9 | FULL | | | N |
| 89 | 1082185 | 35 | G1 | 38 | 130/88 | 1,30,000 | | GT | VAGINAL | | N | 2.8 | FULL | | | N |
| 90 | 1082382 | 28 | G2 | 37 | 110/70 | 1,42,000 | | GT | VAGINAL | | N | 3.2 | FULL | | | N |
| 91 | 1082394 | 29 | G2 | 38 | 110/70 | 1,38,000 | | GT | VAGINAL | | N | 3 | FULL | | | N |
| 92 | 1082406 | 31 | G3 | 38 | 130/80 | 1,30,000 | | GT | VAGINAL | | N | 2.9 | FULL | | | N |
| 93 | 1082454 | 30 | G4 | 33 | 130/80 | 75,000 | LFT INC | HELLP | VAGINAL | APH/PPH | 1,20,000 | 1.2 | PRE | | BA RD | `1,05,000 |
| 94 | 1082535 | 28 | G1 | 37 | 120/80 | 1,42,000 | | GT | LSCS | | N | 2.6 | FULL | | | N |
| 95 | 1082808 | 26 | G2 | 36 | 150/100 | 95,000 | | EC | LSCS | | N | 2.4 | FULL | | RD | N |
| 96 | 1082985 | 22 | G1 | 37 | 130/89 | 1,41,000 | | GT | VAGINAL | | N | 2.7 | FULL | | | N |
| 97 | 1083100 | 22 | G1 | 40 | 130/90 | 1,39,000 | | GT | VAGINAL | | N | 2.8 | FULL | | | N |
| 98 | 1083913 | 32 | G4 | 38 | 130/83 | 1,35,000 | | GT | VAGINAL | | N | 3.1 | FULL | | | N |
| 99 | 1084108 | 32 | G2 | 38 | 170/90 | 53,000 | | PE | VAGINAL | GB | N | 0.9 | FULL | IUD | | |
| 100 | 1085005 | 30 | G1 | 30 | 128/80 | 88,000 | LFT, BRB - INC | AFLP | EXPIRED | GB | | | PRE | IUD | | |
| 101 | 1085557 | 23 | G2 | 37 | 180/90 | 1,10,000 | | PE | VAGINAL | PEP | N | 2.6 | FULL | IUD | | |
| 102 | 1086255 | 34 | G3 | 29 | 160/90 | 72,000 | | PE | VAGINAL | | N | 0.6 | PRE | IUD | | |
| 103 | 1086854 | 23 | G1 | 32 | 180/100 | 30,000 | LFT,BRB INC | DIC | EXPIRED | PEP/APH | | | PRE | IUD | | |