

**Review Article**

**IMMUNE THROMBOCYTOPENIC PURPURA: A HAEMATOLOGICAL DISORDER**

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**ABSTRACT**

Immune (idiopathic) thrombocytopenic purpura (ITP) is an autoantibody-mediated condition characterised by an unusually low level of platelets in the bloodstream. When thrombopoiesis was not occurring quickly enough to counteract the increased rate of platelet destruction, rapid antibody-mediated platelet destruction was initially thought to be the cause of ITP. However, recent research has concentrated on the creation of therapies that boost platelet production as it has emerged that insufficient or inadequate platelet production is also a factor in low platelet counts. ITP can be acute or chronic and affects both children and adults. Because the clinical manifestation of ITP can differ greatly from patient to patient, a thorough assessment of the signs and symptoms must be done in order to manage and treat ITP effectively. Due to the lack of data on clinical and laboratory characteristics, the diagnostic method for ITP now relies heavily on a process of exclusion. Obtaining the patient's medical history and conducting a physical examination are common diagnostic techniques used on both children and adults. Patients with suspected ITP have standard laboratory tests, such as a complete blood count and a peripheral blood smear. With various levels of success, a number of specialised laboratory assays have been created. There is still room to streamline and enhance the diagnostic procedure for detecting ITP.

**Keywords:** Immune (idiopathic) thrombocytopenic purpura, Autoimmune response, Pathophysiology, Thrombocytopenia, Cellular mechanism, Diagnosis, Treatment therapy

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**INTRODUCTION**

An autoimmune condition called Immune thrombocytopenic purpura is characterised by mucocutaneous haemorrhage and a low platelet count. The estimated incidence is 100 cases per 1 million people per year, with children accounting for nearly half of these cases. Immune thrombocytopenic purpura is categorised as acute (lasting six months or less) or chronic, primary or due to an underlying illness. There are pronounced differences between immune thrombocytopenic purpura that develops in adults and children. Young and previously healthy children who are affected generally present with the rapid onset of petechiae or purpura a few days or weeks following an infectious infection (peak age, around five years) [1]. Girls and boys are both equally impacted. Whether or not they receive therapy, the sickness goes away in more than 70% of children within six months. In contrast, immune thrombocytopenic purpura in adulthood tends to be persistent, with an often-silent start, and affects roughly twice as many women as men. The diagnosis and treatment of primary immune thrombocytopenic purpura are the main topics of this review [2, 3] ITP has been widely recognised to be an autoimmune condition with rapid platelet deterioration. Platelet phagocytosis is brought on by the immune system's induction of auto antibodies and cytotoxic T cells as a result of the normal surface proteins on platelets acting as antigens [4, 5] Recent studies have shown that ITP is connected to inadequate megakaryocytes maturation and death due to substances in the plasma, which results in decreased platelet formation [6].

Isolated thrombocytopenia without bone marrow alterations and in the absence of other thrombocytopenia-causing conditions is what is meant by primary Immune Thrombocytopenic purpura (ITP) [7]. In contrast to ITP secondary to other conditions, such as autoimmune disease (like systemic lupus erythematosus), viral infections (like chronic hepatitis C virus), lymph proliferative neoplasms, etc., primary ITP is distinguished by solitary thrombocytopenia.

Less than three months have passed since the diagnosis of acute ITP, which has since been replaced with newly diagnosed ITP. Immune thrombocytopenia with an evolution of 3 mo to 1 y is referred to as persistent ITP, whereas ITP with an evolution of more than 12 mo is chronic ITP. With a high risk of bleeding, refractory ITP refers to instances that did not respond to splenectomy or relapsed following surgery, necessitating continued therapy [8].

In order to understand ITP's effects on medicine and public health, one must be aware of its incidence, although studies on this topic are scarce [9]. The fact that ITP is a condition that may have numerous pathogenetic processes [10] and that there are no clinical or laboratory markers to reliably verify its diagnosis [11] presents a challenge for investigations on ITP. This makes it challenging to diagnose ITP because other causes of isolated thrombocytopenia must be ruled out [12]. Despite these challenges, it is crucial to establish the prevalence of ITP because the creation of novel therapeutic drugs has brought more attention to clinical studies on the disease.

**Pathophysiology**

More than 50 y of research have been devoted to understanding the pathophysiology of ITP. Initial research revealed that healthy volunteers in normal conditions developed thrombocytopenia after receiving blood or plasma transfusions from patients with chronic ITP [13]. This gave compelling proof that ITP was an antibody-mediated disease. Studies conducted later revealed that antiplatelet auto antibodies identified in the blood of ITP patients bind to circulating platelets and destroy them [14, 15]. The development of transient thrombocytopenia in healthy recipients following the passive transfer of plasma, including (Immunoglobulin G) IgG-rich fractions, from patients with immune thrombocytopenic purpura confirmed this suspicion since transient thrombocytopenia affects newborns born to affected women. IgG autoantibody-coated platelets are rapidly cleared by tissue macrophages, primarily in the spleen and liver, that express Fcγ (Fc-gamma) receptors. In most patients, a rise in platelet production serves as a compensating mechanism. Others show a reduction in platelet synthesis, possibly as a result of megakaryocytopoiesis suppression or intramedullary macrophage destruction of antibody-coated platelets [16]. Because of the normal megakaryocyte bulk, the level of thrombopoietin is not elevated [17].

The specificity of auto antigens has been examined in-depth elsewhere [18]. The failure of immune thrombocytopenic purpura antibodies to adhere to platelets with genetically defective glycoprotein IIb/IIIa complexes led to the discovery of the first antigen. Since then, a variety of other platelet determinants and

antibodies have been identified, [19-21] and it is common for individuals to have antibodies against several different antigens [20]. The destruction of platelets within antigen-presenting cells, which is most likely, but not always, triggered by an antibody, may produce a series of neoantigens that trigger enough antibody production to result in thrombocytopenia.

Both naturally occurring antibodies against glycoprotein IIb/IIIa and antibodies made from phage-display libraries exhibit highly limited utilisation of the VH gene and clonal restriction in the use of the light-chain [23]. These antibodies' antigen-combining domains have been sequenced, and this data shows that somatic mutation and antigen-driven affinity selection are what gave rise to them from a small number of B-cell clones [25]. Adults with immunological thrombocytopenic purpura frequently show elevated levels of soluble interleukin-2 receptors, (human leukocyte antigen-DR) HLA-DR+T cells, and a cytokine profile that suggests the activation of precursor helper T and type 1 helper T cells [26]. In these patients, glycoprotein IIb/IIIa fragment exposure triggers T cells to increase antibody production, while exposure to genuine proteins does not [24]. The origin of these obscure epitopes *in vivo*, as well as the cause of persistent T-cell activation are unknown.

### Molecular and cellular mechanisms of itp

#### T-cell imbalance

Patients with ITP have been reported to have abnormal T cells, such as increased T helper cell reactivity against platelets, decreased frequency of circulating CD4+CD25+FoxP3+Tregs, CD4+Th0, and Th1 activation patterns [27-30]. Only 60% of ITP patients show detectable plasma and/or platelet-bound autoantibodies, which suggests that ITP does not have an antibody-mediated mechanism. In connection with this, cytotoxic CD8+T cells were discovered in the blood of patients [32], and a related discovery was made in an active murine model of ITP. *In vitro*, these CD8+T cells can lyse platelets directly [32], and they can gather in the bone marrow where they can prevent thrombopoiesis [33]. Additionally, when compared to healthy people, CD3+T cells from ITP patients have a lower rate of apoptosis and a higher rate of clonal expansion, which results in abnormal cytokine secretion, such as (Interleukin-2, interferon, interleukin-10)IL-2, INF-, and IL-10 [34]. This may explain why active disease patients have lower levels and functions of CD4+CD25+FoxP3+Tregs [33].

#### Megakaryocytes

Anti-platelet autoantibodies that bind to (glycoprotein IIb/IIIa) GPIIb and GPIIbIIIa in ITP are obviously targeting MKs, which leads to morphological and physiological abnormalities [35, 36]. A decrease in granules, together with vacuolization of the cytoplasm and smoothening of the plasma membrane, are some of these modifications [35, 37]. Also impacted and appearing to be apoptotic are immature MKs (megakaryocytes) and mesenchymal stem cells (MSC), which support MK maturation and pro-platelet creation [38]. On the other hand, MKs control other BM niche cells, such as plasma cells, which make antibodies. This suggests that they may indirectly influence the pathogenesis of the disease. For instance, MSC and MKs and their significant immunomodulatory functions, such as the suppression of T-cell activation and the generation of IL-10, may have an impact on the entire BM niche in ITP [39]. Along with megakaryopoiesis defects, MSC do not appear to grow and lose their capacity to inhibit CD8 T cell proliferation in individuals with ITP [35, 36, 40]. It appears that individuals with chronic ITP have a damaged vascular niche in their bone marrow, which inhibits the interaction of MKs with the endothelial cells and plasma cells that make up the niche milieu. These findings show that MKs are directly impacted by ITP, and the entire BM is compromised, speeding up the disease's course. However, the precise processes, notably the function of TPO, are still unknown.

#### B cells and auto antibodies

Anti-platelet IgG antibodies (and less frequently IgM or IgA antibodies) are produced by ITP patients and bind to platelets to flag them for phagocytic breakdown in the spleen and liver [40]. However, it's possible to find no detectable antibodies in up to 30%

to 40% of patients [44]. It is currently unclear if the absence of antibodies in patient's results from the accuracy of the antibody tests employed or possibly from a process that is solely T cell-mediated. It is noteworthy that patients with anti-platelet antibodies have also been found to have antibodies against cytosolic proteins [45], which may indicate that platelets are subjected to protein degradation by antigen presenting cells (APC) before being presented with antigen by T cells [56]. In addition, additional processes, such as antigenic cross-reactivity (mimicry), somatic mutation [46], and deficiencies in the eradication of auto reactive B-cell clones [16], have been postulated to be involved in antibody production in ITP. It's also possible that oxidative stress, which encourages the creation of autoantibodies, is at play. In mice at least, the type of epitope that autoantibodies target may also be a sign of disease severity and, to some extent, of responsiveness to therapy [47].

Plasma cells, which have been linked to higher levels of auto reactive antibodies in ITP patients [48], as well as the B cell regulator and B cell-activating factor (BAFF, also known as B cell stimulator (BlyS), which plays a crucial role in B cell selection, survival, and proliferation, all secrete auto reactive antibodies. In fact, in a murine ITP model and in people, (B-cell activating factor) BAFF promoter area polymorphisms and its up-regulation in the plasma have been substantially linked to ITP. Additionally, it was shown that the number of B lymphocytes was elevated in the red pulp of the spleens from ITP patients, where they also appeared to proliferate at a higher rate [49].

Together, these findings show that pathogenic antibodies are produced in ITP patients due to defective plasma cells, Bregs, and B cells. These antibodies cause platelet destruction in the spleen and liver as well as faulty megakaryopoiesis through platelet and MK opsonisation [50].

#### Dendritic cells

APC continuously search their environment to process and transmit foreign antigens to immune cells, including DCs (Dendritic Cells), macrophages, and, in some circumstances, B cells [51]. Their function can change under specific conditions, such as those associated with inflammation, and aberrant processing and greater self-antigen presentation have been linked to the onset of autoimmune disorders. The most effective APC are DCs, and studies have demonstrated that they are impaired in ITP. For instance, *in vitro* platelet antigen presentation was stimulated by DCs from ITP patients, most likely due to enhanced DC CD86 expression [53]. Moreover, plasmacytoid DCs (pDCs), which are a particular subset of DCs specialized in type I interferon production (INF- $\alpha$  and INF- $\beta$ ), are also affected in ITP. Patients with primary ITP or secondary ITP caused by *H. pylori* were shown to have reduced pDCs levels. It appeared that the quantity of circulating pDCs was substantially associated with platelet counts in these individuals, supporting their involvement in ITP pathophysiology.

As a result, APCs, particularly DCs, are also compromised in ITP, which may indicate that aberrant self-antigen presentation occurs, increasing the formation of pathogenic antibodies and advancing the course of the disease [54].

#### Diagnosis

The platelet number is connected with the clinical characteristics. Low platelet counts (less than 20,000/l) are associated with an increased risk of menorrhagia, petechiae, and ecchymosed, particularly at the extremities [59]. Under 10,000/l, mucosal spontaneous bleeding is possible; the bleeding period also lengthens. ITP patients may experience serious hemorrhagic consequences, such as subarachnoid, intracerebral, intestinal, or other internal bleedings, in extreme cases when platelet count is below 5,000/l [58].

The most common clinical feature in ITP patients is bleeding into the skin, mucosae, gastrointestinal system, or any other organ. The "dry purpura" typically develops in the absence of a trigger. Gum bleeding, menorrhagia, epistaxis, and digestive haemorrhage are among manifestations of mucosal haemorrhage [60]. Oral haemorrhage lesions are a common symptom of severe

thrombocytopenia, however, the condition can also emerge clinically as severe hemorrhagic symptoms. The cerebral haemorrhage is the most serious complication of ITP, occurring with a platelet count lower than 10,000/l, and is more common in adults than in children [61].

Immune thrombocytopenic purpura is still diagnosed on the basis of exclusion. Secondary forms of the disease occur in association with systemic lupus erythematosus, antiphospholipid syndrome, immunodeficiency states (IgA deficiency and common variable hypogammaglobulinemia), lymphoproliferative disorders (chronic lymphocytic leukaemia, large granular lymphocytic leukaemia, and lymphoma), infection with human immunodeficiency virus and hepatitis C virus, and therapy with drugs such as heparin and quinidine. Passively acquired autoimmune or alloimmune thrombocytopenia must be ruled out in children younger than three months old. Immune thrombocytopenic purpura can appear to be hereditary nonimmune thrombocytopenia [55].

Isolated thrombocytopenia (ITP) is characterised by normal CBC (complete blood count) and normal morphology. A diagnosis of an inherited platelet condition, such as macrothrombocytopenia in the presence of the (Myosin heavy polypeptide) MYH9 mutation, should be made if aberrant platelet morphology is evident [62]. The necessary criteria include an otherwise healthy person presenting with isolated thrombocytopenia, a peripheral smear that is otherwise unremarkable, a physical exam that only reveals bleeding consistent with the platelet count, and the exclusion of other thrombocytopenia-causing conditions if there is cause for suspicion. These include exposure to foods, medications, herbs, or other substances (such as quinine) known to cause secondary immune thrombocytopenia, pseudo thrombocytopenia, or giant platelets, as well as family histories that are consistent with inherited thrombocytopenia.

The necessity of bone marrow aspiration is one of the most disputed topics. According to the American Society of Haematology's recommendations, a bone marrow test is not necessary in persons under the age of 60 if the presentation is typical but is necessary before splenectomy is carried out [56]. Our standard procedure is to examine the bone marrow in individuals who are over 40, show unusual characteristics (such as extra cypoenias), or do not respond quickly or effectively to treatment.

Antiplatelet antibody measurements are not used to confirm or rule out an ITP diagnosis. Although some contend that the methods currently used to identify platelet antigen-specific antibodies are now sufficiently specific to confirm the diagnosis, antibodies have also been found in 10% to 20% of patients with specific "nonimmune" thrombocytopenia's (for example, chronic liver disease, Myelodysplastic Syndromes), the populations in which testing would be most beneficial. These tests' interlaboratory repeatability is weak, and their sensitivity is insufficient to rule out a diagnosis of ITP [57].

We contend that the purpose of therapy must be tailored to each patient's unique set of indications and symptoms, treatment tolerance, way of life, and preferences. Our standard procedure is to start off with a little higher platelet count (for example, 30 000 109/l) while getting to know the patient in order to build a history of bleeding, compliance, and risk management that will allow us to gradually lower the barrier for treatment.

### Specialized laboratory assays in the diagnosis of ITP

#### Assays for anti-platelet antibodies

Indirect testing of the patient's plasma against donor platelets is of little value in the investigation of suspected ITP because the sensitivity and specificity are even lower than for direct testing. The direct platelet immunofluorescence test (PIFT) is used to investigate referred samples for the presence of platelet-associated immunoglobulin (PAIg). Most ITP patients have elevated platelet-associated IgG (PAIgG) levels, but these measurements are not sensitive or specific enough to support routine use of these assays in patients with suspected ITP (patients with non-immune thrombocytopenia's, such as septicaemia, frequently have positive results).

Although their routine use in the diagnosis of ITP is not seen to be warranted, they may be helpful in difficult instances to differentiate

between immune and non-immune thrombocytopenia. In people with diabetes, platelet autoantibodies may be useful to investigate:

- The combination of immune-mediated thrombocytopenia and bone marrow failure
- ITP patients who have not responded to first-and second-line therapies
- DDITP (drug-dependent immune thrombocytopenia)
- Other (rare) diseases, such as acquired autoantibody-mediated thrombasthenia and monoclonal gammopathies [64].

#### Reticulated platelets

Platelet maturity can be determined by measuring platelet RNA using flow cytometry and thiazole orange labelling. In comparison to children without ITP and children with other forms of thrombocytopenia, such as acute leukaemia and aplastic anaemia, children with ITP have much more reticulated platelets, which indicates enhanced platelet production [63]. Although its usage is not currently advised, the specific function of the reticulated platelet test has not been determined.

#### Helicobacter pylori infection

*H. pylori* has been found in patients with autoimmune diseases, including ITP, according to a number of investigations. Although some studies have produced contradictory results, in certain series antibiotic therapy intended to eradicate *H. pylori* has improved ITP in patients resistant to other therapies [65]. Despite this, it is worthwhile to do breath tests and serological assays targeted at finding the microorganism in individuals who are resistant to medication (Evidence level III).

#### Treatment management of ITP

General note: Few randomised controlled studies have been carried out in ITP to this point. Each patient should receive a unique treatment plan.

The morbidity and mortality rates in ITP patients are higher than in the general population, particularly if the platelet count is below 30,000/l during the time they receive treatment [39, 56]. Haemorrhage and infections both have an impact on mortality [56]. The therapy of ITP in adults is more complicated because the majority of cases progress to chronic disease and the risk of haemorrhage is higher than in children [36, 39]. The goal of treatment is to reduce drug toxicity while achieving a platelet count that is regarded to be hemorrhage-risk-free, between 20 and 30,000/l [56]. Treatment is not required if the platelet count is over 50,000/l; the indication is determined by the patient's age, lifestyle, and risk of haemorrhage.

Treatment plans focus on boosting platelet synthesis to raise platelet counts, lengthening platelet half-lives, and reducing the immune responses reactivity by preventing the development of reactive antibodies and destroying platelets.

Corticosteroids with or without intravenous IVIg and anti-D are first-line therapy [65, 66]. Splenectomy and/or immune-suppressive drugs like the B cell-depleting anti-CD20 drug Rituximab are regarded as second-line medicines. TPO receptor agonists like Romiplostim and Eltrombopag are considered third-line therapies [67].

#### First-line treatment

The most popular therapy is corticosteroids. At least 80% of ITP patients respond at first, however, many patients relapse when their corticosteroid dosage is cut back [68]. Studies have been done to see whether giving newly diagnosed ITP patients a higher dose of corticosteroids extends their remission time [69]. According to Cheng's study's findings, 50% of the patients who received 40 mg of dexamethasone daily for four days had a sustained response-a platelet value exceeding 50,000/l-six months after treatment [70]. According to Mazzucconi's study, newly diagnosed patients who had 4-6 cycles of dexamethasone given every two weeks had a 15 mo survival rate without relapse [69].

In a side-by-side comparison research, Zaja demonstrated the efficacy of combining Rituximab and dexamethasone over dexamethasone as a single medicine, resulting in a better response in 6 mo. For a longer observation time, these differences became uninteresting [71].

### **Intravenous immunoglobulin (IVIG) and intravenous Anti-RhD immune globulin**

Another typical first-line or rescue therapy frequently used when a patient arrives with substantial bleeding is intravenous immunoglobulin (IVIG). It can be used alone, in combination with corticosteroid therapy, or when corticosteroids are contraindicated to boost platelet count more quickly. It is advised to provide IVIG at a dose of 0.4 g/kg daily for up to 5 d (low dose) or 1 g/kg daily for 1-2 d (high dose) [72]. Inhibiting the IgG Fc receptor, which is essential for bridging the innate and adaptive immune systems, phagocytosis, and the suppression and/or eradication of platelet autoantibodies are just a few of the intricate methods by which IVIG works to reduce inflammatory processes [73].

For non-splenectomized, Rh (+) individuals, intravenous anti-RhD immune globulin (given at a dose of 50 mcg/kg to 75 mcg/kg daily) [74, 75], is an alternative to IVIG. To stop autoantibody-coated platelets from being destroyed, anti-D coated RBCs are considered to saturate macrophage Fc receptors. In one trial, there was no statistically significant difference in the cumulative response and remission rates between IVIG and IV anti-RhD immune globulin therapy for individuals with ITP [76]. The majority of patients who get anti-RhD immune globulin experience a controlled hemolysis with a 0.5–2.0 g/dl reduction in haemoglobin concentration 3–7 d after infusion, returning to baseline within 3 w of treatment. Rarely, disseminated intravascular coagulation, a life-threatening condition, can develop from this hemolysis [77].

### **Second-line treatments**

Second-line medicines are required to control ITP in patients who relapse after failing first-line therapies. For instance, because the activation of platelet-reactive T and B cells and the destruction of platelets occur most frequently in the spleen in ITP, [78] Before the development of steroid therapy in 1950, splenectomy was a common technique for extending the survival of antibody-coated platelets. Although the effector of platelet death is removed, opsonisation still occurs; hence the treatment is not exactly "curative." It is not unexpected that a splenectomy is still the go-to treatment for ITP patients who have failed other treatments to get their physiological platelet levels back.

About 60% of patients do experience a complete remission, and a further 15% exhibit a partial response [80]. However, as with any surgical operation, splenectomy has some risk, and complications connected to surgery have been documented in up to nearly 25% of cases [80], including a 1% fatality rate. It is well recognised, for instance, that splenectomy increases the risk of sepsis and the occurrence of vascular problems [81]. Despite these dangers, this surgical surgery is still regarded as the best option for people with ITP who want to see a long-term increase in platelet counts.

Patients with severe thrombocytopenia, especially those who have just been diagnosed, must stay in a hospital. The goal of treatment is to quickly raise platelet value. Corticotherapy and immunoglobulin are given intravenously, and platelet concentrate infusions can be used to temporarily boost the amount of platelets in emergency cases. The simultaneous delivery of immunoglobulin can extend the survival of the transfused platelets in some patients. Splenectomy was carried out as an ITP therapeutic strategy in patients with significant cerebral haemorrhage in order to very quickly boost the platelet number [90].

Rituximab is a chimeric antibody that is directed against the CD20 antigen on B cells and almost eradicates them *in vivo* when administered [82]. It is hypothesised that it causes antibody-dependent cellular cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC) to cause B cell apoptosis or destruction in the spleen [83]. Decreases in anti-platelet antibody titers and, intriguingly, normalisation of the T cell deficiencies seen in people

with chronic ITP and in murine ITP are the outcomes of the ensuing B cell depletion [84]. These data imply that the T cell compartment may actually be indirectly regulated as the rituximab's mode of action. The treatment's actual benefits, however, are still debatable. In fact, Rituximab produces a short-term response in around 50% of resistant chronic ITP patients, and this platelet surge lasts for 6 mo or more in roughly 30% of the cases [85]. About 21% of adults experience long-term reaction as a result. Although a dose of 100 mg/m<sup>2</sup> has a similar effectiveness, the suggested dose is 375 mg/m<sup>2</sup> once a week for 4 w [86].

### **Third-line treatment**

TPO-receptor agonists can be used to treat patients who respond poorly to splenectomy or Rituximab. Both Eltrombopag and Romiplostim stimulate platelet formation by activating TPO receptors on MKs through the JAK2 and STAT5 kinase pathways, and both treatments have shown to be effective in the majority of ITP patients who are refractory to other treatments. Additionally, it seems that even after 24 w without receiving TPO medication, almost one-third of Romiplostim-treated patients are still in remission [87]. Romiplostim appears to be able to reverse the Treg shortage seen during active illness in addition to its clear effect in promoting MK proliferation. It was demonstrated that Treg function was elevated, and platelet counts and circulating TGF-levels connected [88], which may be associated to an increase in platelet bulk. Similar to this, Bregs were also reported to rise in non-splenectomized ITP patients receiving this medication, along with a decrease in pro-inflammatory monocytes and an increase in CD16+monocytes' ability to modulate B cell immunity. These data demonstrate that TPO-receptor agonists may indirectly influence the immune system, possibly by influencing both Tregs and Bregs [89]. They may also directly stimulate thrombopoiesis.

### **Immune thrombocytopenic purpura during pregnancy**

The development of automatic blood cell counters for routine platelet counts brought attention to the fact that mild to moderate thrombocytopenia occurs often in healthy pregnant women. The majority of these women, excluding those with inflated counts brought on by EDTA-induced *in vitro* platelet aggregation, have "gestational thrombocytopenia" (GT), a benign, self-limiting condition with no appreciable risk of bleeding for the mother or the foetus. To tell GT apart from idiopathic (autoimmune) thrombocytopenia (ITP), in which the transmission of platelet antibodies through the placenta has the potential to result in foetal or neonatal thrombocytopenia and haemorrhage, may be challenging or impossible. A number of less frequent acquired or congenital diseases, as well as serious pregnancy problems such as pre-eclampsia or disseminated intravascular coagulation (DIC), may also be indicators of maternal thrombocytopenia. As a result, the evaluation of each case of thrombocytopenia in pregnancy focuses on ruling out significant secondary causes and balancing the risks of maternal and foetal bleeding with the dangers of diagnostic and therapeutic measures.

### **Therapy during pregnancy**

#### **Mother**

Even though corticosteroids should be reduced to the lowest dose that still allows for a safe platelet count, they are appropriate in cases of severe thrombocytopenia. Since it is unclear how steroids would affect foetal survival, they are only given when the mother's life is in danger. Along with the normal adverse effects, eclampsia, hypertension, and psychosis are frequent, and the foetus may experience adrenal suppression. Patients with refractory illness may have a splenectomy, but the advantages must be considered against the higher foetal mortality. Avoid using immunosuppressive medications.

#### **Foetus**

The primary danger of vaginal delivery-which can be avoided by having the baby delivered via caesarean section-is bleeding into the central nervous system. The mother's platelet count and splenic condition can be used to empirically assess whether this surgery is

necessary. If the spleen is absent, regardless of the mother's platelet level, or if the spleen is present but the mother's platelet count is less than 100,000 per cubic millimetre, a caesarean delivery is advised. Recently, a technique for measuring the foetal platelet count directly was published. Foetal counts of more than 50,000 per cubic millimetre allowed for safe vaginal birth.

After birth, the newborn should be closely watched. Severe bleeding may occur even though neonatal thrombocytopenia is self-limited and only lasts for three to four weeks at most. If petechiae or purpura appear, one should start taking corticosteroids (prednisone orally, 1 mg per kilogramme per day, initially with intravenous hydrocortisone, 10 mg every 12 h). Platelet transfusions (two platelet packs every six to eight hours) will typically stop active bleeding if it happens. Although exchange transfusions are typically unnecessary, they can be used in life-threatening situations.

## CONCLUSION

ITP, an autoantibody-mediated illness marked by an exceptionally low quantity of platelets in the bloodstream, is short for immune (idiopathic) thrombocytopenic purpura. To correctly diagnose and treat patients with ITP, a thorough evaluation of the ITP's signs and symptoms must be carried out. ITP patients present with a wide range of clinical signs and symptoms; hence, the diagnostic strategy should focus on ruling out other thrombocytopenia-causing conditions. In order to help with the diagnosis of ITP in complex patients, a variety of specialised laboratory assays have also been devised, however, many of these are still ineffective. Several tried-and-true first-line treatments, primarily corticosteroids and IVIG, as well as more recent treatments, are used in the modern treatment of ITP in adults. ITP still has unfulfilled needs despite the fact that there are now far more options for management than there were even only recently.

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## AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

## CONFLICT OF INTERESTS

Declared none

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