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Review Article

Thrombocytopenia

Immune Thrombocytopenia (Itp) In Emergency Medicine

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Abstract: Immune Thrombocytopenia (ITP) is an autoimmune disorder characterised by a low platelet countless than 100? ×? 10^9/L, purpura, and hemorrhagic episodes induced by antiplatelet autoantibodies without anemia or leukopenia. Immune thrombocytopenia (ITP) occurs in 2 to 4/100? 000 adults. A wide range of signs and symptoms, from modest mucocutaneous petechiae to severe, life-threatening organ haemorrhage, are seen in ITP patients. they may present to the emergency department (ED) with life-threatening bleeding as a result of their thrombocytopenia. ITP has two distinct clinical syndromes, manifesting as an acute condition in children and a chronic condition in adults. IgG autoantibodies make circulating platelets more sensitive. It causes these cells to be removed more quickly by antigen-presenting cells (macrophages) of the spleen, and occasionally the liver or other components of the monocyte-macrophage system.Current evidence supports alternatives to splenectomy for second-line management of patients with persistently low platelet counts and bleeding. By increasing platelet production, bone marrow compensates for platelet breakdown. Immune Thrombocytopenia most commonly arises within a few weeks after a viral infection in healthy children and young adults. Immunosuppressive treatment is usually effective in treating ITP. Many patients with ITP require no emergent treatment.However, the emergency physician should start treatment with a platelet transfusion, corticosteroids, and intravenous immune globulin (IVIG) as soon as the patient with suspected ITP arrives at the ED with serious haemorrhage. .The diagnosis is usually made by ruling out all known causes of thrombocytopenia. This review aims to summarize current evidences regarding prevalence, causes, diagnosis and management of immune thrombocytopenia.

Keywords: ITP, Symptoms, Diagnosis, Treatment

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1. INTRODUCTION

Immune thrombocytopenia (ITP) formerly known as immune thrombocytopenic purpura, is an autoimmune syndrome distinguished predominantly by immune-mediated enhanced platelet damage by autoantibodies and inhibited platelet manufacture in the bone marrow in the lead to cutaneal and mucosal bleeding [1]. Also, it was once known as idiopathic thrombocytopenic purpura until it was discovered that the pathophysiology of the thrombocytopenia involved the host immune system [2]. The most important characteristic of this pathology is heightened peripheral destruction of platelets, most patients showing anti-platelet membrane glycoproteins antibodies, platelet destruction via antiplatelet antibodies which may also affect marrow megakaryocytes [3]. ITP is characterized by platelet counts less than 100 × 10^9/L [4]. In ITP, thrombocytopenia happens secondary to antiplatelet antibodies that are produced in the spleen. These antibodies first bind to platelets, followed by phagocytosis of the platelet/antibody complex by the reticuloendothelial system [5, 6]. It represents 0.18 % of all hospital admissions [7]. Patients with ITP appear with a broad variation signs and symptoms ranging from minor mucocutaneous petechiae to severe life-threatening organ bleeding. Patients may present in critical situations, with cutaneous and/or mucous bleeding and conceivably dangerous organ hemorrhages (cerebral, digestive, etc.) Consequently, quick diagnosis and therapeutic involvement are obligatory [3]. ITP has two distinct clinical syndromes, manifesting as an acute condition in children and a chronic condition in adults [8]. Roughly 80% of ITP witnessed in children is acute, adults are usually affected with the chronic form [9]. The disease is thought chronic if the thrombocytopenia continues longer than 6-12 months without another discovered etiology. However, acute ITP naturally resolves within 6-12 months and often happens shortly after an infection or a vaccination [9,10]. Also, ITP was clinically classified to 3 phases according to an international working group on ITP [11]. Recently identified ITP (newly diagnosed) identifies the first 3 months post-diagnosis. The second phases called Persistent ITP suggests symptoms remaining for 3–12 months. The third phase called Chronic ITP indicates to symptoms long-lasting longer than 12 months. A supplementary phase is called refractory ITP, which consists of cases that fail to resolve with splenectomy and require further therapeutic intervention [3, 11, 12].

1.1 Prevalence

Immune thrombocytopenic (ITP) is an autoimmune condition that affects nearly 1:10,000 people in the world [13]. The epidemiology of ITP is varied and heterogeneous. ITP affects patients of all genders, races, and ages, it affects both children and adults [14]. children, the occurrence of ITP is about 1.9–6.4 per 100,000 children per year [15]. Studies from Scandinavia suggest a prevalence of ITP ranging from 4.6 to 5.3 cases per 100,000 children [16]. ITP was present in 9.5 per 100,000 children aged 1 to 5, 7.3 per 100,000 children aged 6 to 10, and 4.1 per 100,000 children aged 11 to 14, according to research that examined data from the Maryland Health Care Commission [17]. In a huge prospective study, 78% of pediatric ITP patients were identified between ages 0–7 with a minor male superiority [18]. According to an analysis of the General Practice Research Database (GPRD) in the United Kingdom (UK), occurrence of ITP was greater in boys between the ages of 2 and 5 (9.7 cases compared to 4.7 cases in girls per 100,000 patient-years, respectively) compared to that in teenagers between ages 13-17 (2.4 cases per 100,000 patient-years, with equal sex distribution) [19]. Regarding adults, one large review of published articles reported the incidence of ITP to be around 3.3 per 100,000 per year [15]. Primary ITP has a prevalence of 9.5:100,000 in adults with an occurrence of 3.3:100,000 per year [12]. As ITP is commonly a chronic disease in adults, the prevalence is greater than the incidence, and one study described the prevalence of ITP to be 12.1 per 100,000 adults per year [20]. A prospective, population-based study of patients older than 16 years old with newly diagnosed ITP revealed an annual report incidence 1.6 cases per 100,000; the incidence was a little greater in females between 45-49 years but otherwise no gender differences existed [21]. A Scandinavian study discovered an ITP incidence of between 2.25 and 2.68 per 100,000 individuals/year; the incidence was greater in females (female: male ratio 1.7) and the elderly [22]. Additional reports have indicated a prevalence of ITP in adults ranging from 4.0 to 23.6/100,000 patient years [23]. Generally, the male to female ratio in children decreases with increasing age, and reverses in adulthood. Female preponderance is clearly recognized in adults with ITP. Increased general occurrence of autoimmune diseases in adult females is believed to be a factor. Together male and female incidence of ITP increases with increasing age [24].

1.2 Causes

The pathogenesis of ITP includes harm of tolerance to glycoproteins expressed on platelets and megakaryocytes [25]. ITP develops by two processes either immune-mediated increased destruction of platelets or decreased production of platelets that leading to a complete reduction in circulating platelets [26]. Generally, Immune thrombocytopenia (ITP) is idiopathic in 80% of cases, and primary ITP is often supposed of as an autoimmune disorder due to pathogenic anti-platelet autoantibodies, T cell-facilitated platelet destruction and decreased megakaryocyte (MK) function [27, 28, 29]. Nevertheless, 20% of cases of ITP can existing secondary to other causes [12]. Viral infections containing human immunodeficiency virus (HIV), hepatitis C virus (HCV), cytomegalovirus (CMV), varicella zoster virus (VZV), auto immune diseases such as systemic lupus erythematosus (SLE) and lymphoproliferative disorders like chronic lymphocytic leukemia (CLL) are the furthermost common causes of secondary autoimmune platelet destruction [3]. In the infectious cases, it might be that a viral antigen is familiar as being like a platelet antigen, a process called molecular mimicry, which afterward gives rise to cross-reactive anti-platelet autoantibodies [30]. In the case of thrombocytopenia related to drug exposure (with the exclusion of myelosuppressive chemotherapy), the term "drug-induced" was preferred [31]. Quinine was the first drug to be identified as causing immune-mediated thrombocytopenia [32]. Some more widely used medications that are known to cause drug-induced immune thrombocytopenia include carbamazepine, ceftriaxone, ibuprofen, mirtazapine, penicillin, trimethoprim-sulfamethoxazole, and vancomycin [32].

1.3 Clinical presentation and symptoms

Patients with ITP present with a wide variety signs and symptoms ranging from minor mucocutaneous petechiae to severe life-threatening organ bleeding. The symptoms of ITP are reliant upon the intensity of thrombocytopenia. Signs and symptoms usually begin appearing with platelet counts less than 100 × 109/L, but bleeding is extraordinary till platelet counts decline lower than 30 × 109/L [33]. Platelet counts below

20,000/μ l raise the risk of spontaneous bleeding like epistaxis or gum hemorrhage and menorrhagia, petechiae or ecchymoses, especially at the extremities [34]. Mucosal bleeding may occur under 10,000/μ l; the bleeding time also growths while dangerous hemorrhagic cases such as intracranial, intestinal, or other internal bleeding typically occurs with platelet counts less than 10 × 10 [3]. Outside of bleeding-related symptoms, a couple of other symptoms are worth mentioning. Fatigue is a frequent symptom in both adults and pediatric patients with ITP which appearing in roughly 22% of children, and 22 to 39% of adults [35]. Whereas the primary symptoms of ITP include bleeding, thrombosis is more popular in patients with ITP as compared to controls [36]. Numerous patients with ITP are symptomless, and their decreased platelet count is often noticed parenthetically.

1.4 Pathophysiology

Our knowledge of the pathophysiology of ITP has considerably increased during the past several years. The thrombocytopenia caused by pathologic antiplatelet antibodies[37] defective megakaryocytopoiesis,[38] and T-cell-mediated destruction of platelets [39], each of which plays a different role in each patient with Primary ITP, is now understood to be an acquired immunological illness. Other underlying conditions including autoimmune disease (systemic lupus erythematosus or rheumatoid arthritis), HIV, Helicobacter pylori, or immunological dysregulation syndromes like common variable immunodeficiency are linked to secondary ITP. [40] Approximately 80% of persons with ITP have main ITP. Although certain patients with secondary ITP and severe disease may need ITP-like therapy to stabilise the platelet count while other treatment is started, secondary ITP treatment and pathophysiology are typically centred on the underlying disorder and are not the focus of this article. The evidence also implies that many ITP patients have poor platelet production. Megakaryocytes from ITP patients are aberrant, and electron microscopic changes in cell culture with ITP plasma revealed improper apoptosis and hindered megakaryocyte proliferation. [41,42] Additionally, the serum thrombopoietin levels in ITP patients are hardly ever high. These data are somewhat validated by the fact that TPO receptor agonists are effective. [43]

1.5 Diagnosis

The diagnosis of Immune thrombocytopenia ITP is one of exclusion. It is characterized by isolated thrombocytopenia, with normal morphology and else normal CBC. Corresponding to an International Working Group consensus panel of both adult and pediatric experts, ITP is characterized as a platelet count less than 100 × 109/L in the absence of other causes of thrombocytopenia [11]. diagnosis of ITP is validated by a discovering of thrombocytopenia in a blood smear. A sensible examination of the peripheral blood smear (PBS) is essential to eliminate other reasons of thrombocytopenia, such as the microangiopathic disorders, platelet satellitism or pseudo thrombocytopenia [23]. Bone marrow examination is not commonly required in ITP. It is recommended to be performed if another hematological pathology is suspected (other anomalies on the CBC, unexpected systemic signs, and symptoms, such as adenopathies, organ enlargement, etc.), if patients are over 60 years old, and before splenectomy [44]. Furthermore, amongst patients with ITP, it is essential to differentiate primary and secondary ITP. In particular, the physician should completely review the patient's recent medications as drug-induced immune thrombocytopenia is often clinically undifferentiated from primary ITP, so it may be ignored even if the suitable diagnostic tests are required [45.] Generally, Primary ITP is a diagnosis of exclusion by carefully ruling out causes of pseudo thrombocytopenia, secondary ITP, and inherited ITP. Getting a precise history come together with a complete blood count and a thorough evaluation of the blood smear is the first and most important step [26.] Harmonizing nomenclature and terminologies for ITP has advanced significantly in recent years, allowing recommendations to be made that are applicable to many ITP patients. The best way to manage patients is questionable, however, due to considerable gaps in the information that is currently accessible (such as the absence of information or a lack of agreement on second-line medicines and best practises for managing chronic ITP). The assessment of a peripheral smear, appraisal of the patient's history, and physical examination are typically used to make the diagnosis of ITP. All ITP patients should undergo a few extra tests, according the IWG's recommendations , including tests for hepatitis C, HIV, H pylori, direct antiglobulin, and blood type [46] Similar testing, with the exception of H pylori testing, is advised by the ASH recommendations for adults with ITP (only recommended for some geographic areas and if treatment of eradication is possible). The ASH guidelines suggest that bone marrow tests may not be necessary in any patient population, which is supported by some population studies, in contrast to the recommendations made by the IWG to perform bone marrow investigations in patients >60 years old with newly diagnosed ITP. [47]

1.6 exampels of Utility of various evaluations in the diagnosis of ITP

Basic evaluation (Patient/family history)

Tests of potential utility (Glycoprotein-specific antibody), Tests of unproven benefit (Thrombopoietin)

Basic evaluation (Physical examination)

Tests of potential utility (Antiphospholipid antibodies (including anticardiolipin and lupus anticoagulant), Tests of unproven benefit (Reticulated platelets)

Basic evaluation (Complete blood count and reticulocyte count)

Tests of potential utility (Antithyroid antibodies and thyroid function), Tests of unproven benefit (Platelet-associated immunoglobulin G)

Basic evaluation (Peripheral blood film)

Tests of potential utility (Pregnancy test in women of childbearing potential), Tests of unproven benefit (Bleeding time)

Basic evaluation (Quantitative immunoglobulin level measurement)

Tests of potential utility (Antinuclear antibodies), Tests of unproven benefit (Platelet survival study)

Basic evaluation (Bone marrow examination (in selected patients)

Tests of potential utility (Viral PCR for parvovirus and CMV), Tests of unproven benefit (Serum complement) [46]

1.7 Treatment

The most important objective for treatment of ITP is to provide a safe platelet count (e.g., one that prevents major bleeding) rather than improving the platelet count to normal levels [48]. Treatment of patients with ITP should consider the seriousness of the illness and the age of the patient because the bleeding risk and the hemorrhagic fatality rate increase with age [31]. Recent guidelines recommend that treatment should be introduced in the occurrence of bleeding symptoms [49]. Treatment is usually reserved for those with symptomatic ITP. The target is to achieve a hemostatic platelet count, which is around 20-30 x 109L, while this differs by person. Most ITP cases are self-limiting and need no treatment because most often the event responsible for antiplatelet antibody production is a viral illness. At present, most treatment protocols focus on the diminution of platelet destruction, and the drugs used are usually immunosuppressives [50]. Treatment of ITP can be divided into medical and surgical management. Medical management is further divided into first line and second-line pharmacotherapy. Medical options for front-line drug therapy are corticosteroids, intravenous (IV) immunoglobulin (Ig), and IV Rh anti-D [26]. Corticosteroids are the most extensively used treatment. Firstly, at least 80% of the ITP patients respond, a high percentage of patients decline when attempting to reduce the corticosteroid doses [37]. Dexamethasone and prednisone have been shown to modulate B-cell and dendritic cell activation, leading to a decrease in immune-mediated destruction of platelets [12]. In steroid-resistant patients, the addition of intravenous immunoglobulin (IVIG) or Rh_o (D) immune globulin (anti-RhD) can be used to improve the treatment effect. Furthermore, these two treatments can be used in patients when corticosteroids are contraindicated [51]. IVIG is also suggested when platelet counts need to be increased quickly, such as in cases of active and severe bleeding, and can be used in combination with corticosteroids in select patients. Anti-RhD can be useful in combination with corticosteroids in patients who are RhD positive [50]. If patients with ITP fail first-line treatments or relapse, second-line treatments are required to control the disease. Second-line therapies involve splenectomy and/or immune-suppressive agents such as the B cell-depleting anti-CD20 agent Rituximab [37]. In fact, the ASH 2011 guidelines still suggest splenectomy as the next option in therapy after failure of remission with corticosteroids, IVIG, and anti-RhD [51]. Splenectomy is still the golden model for repairing physiological platelet counts in patients with ITP, and it persists the method of choice in refractory patients with ITP [52]. monoclonal antibody against the CD20 antigen (anti-CD20), rituximab, is one new choice for the treatment of chronic and persistent ITP. It is supposed to cause either B cell apoptosis or destruction in the spleen via either complement-dependent cytotoxicity or antibody-dependent cellular cytotoxicity (ADCC). The resulting depletion of B cells results in decreases of anti-platelet antibody titers and, remarkably, in the normalization of the T cell impairments detected in patients with chronic ITP [53], [54]. Patients who fail splenectomy or Rituximab can be treated with TPO-receptor agonists. Both Eltrombopag and Romiplostim activate TPO receptors on MKs and induce platelet production via the JAK2 and STAT5 kinase pathways, and both therapies have proven efficacious in most refractory patients with ITP [55], [56]. Whether an ITP is primary or secondary affects how it is managed. We will talk about possible treatments in the remaining portion of this section for either primary or secondary ITP. If a patient has secondary ITP, addressing the underlying condition or stopping the medicine if it was caused by it is crucial. Regardless of the ITP's underlying cause, the aim of treatment is to stop or stop substantial bleeding, not to return the platelet count to normal. In the ED, this is especially true. Due to the paucity of significant randomised trials, the treatment of ITP is mostly relied on low quality evidence and expert opinion.As a result, we manage ITP in accordance with the 2019 American Society of Hematology clinical practise recommendations and a 2019 global consensus report. [57],[58] Treatment Strategies for ITP Based on Platelet Count and Symptoms. These Recommendations are Primarily Based on the 2019 Clinical Practice Guidelines from the American Society of Hematology and a 2019 International Consensus Report: [59],[60]

-Platelet Count (>30 x 10^9/L) ,Symptoms (None or minor mucocutaneous bleeding.) ,ED Treatment (No medications; counsel patient to avoid medications or activities that increase bleeding risk.)
-Platelet Count (20–30 x 10^9/L) ,Symptoms (None or minor mucocutaneous bleeding.) ,ED Treatment (Consider corticosteroids; consult hematologist.)
-Platelet Count (<20 x 10^9/L) ,Symptoms (None or minor mucocutaneous bleeding.) ,ED Treatment (Consult hematologist,Adults: Corticosteroids,Children: Consider corticosteroids.)
-Platelet Count (<20 x 10^9/L) ,Symptoms (Severe* (but not critical) bleeding.),ED Treatment (Corticosteroids and IVIG; consider platelet transfusion; consult hematologist.)
-Platelet Count (<20 x 10^9/L) ,Symptoms (Critical bleeding) ,ED Treatment (Corticosteroids and IVIG; platelet transfusion; consult hematologist)

1.8 Emergency Treatment of ITP

Patients with dangerous thrombocytopenia, especially those with newly diagnosed ITP should be hospitalized. The aim of therapy is to enhance the platelet value as soon as possible. Corticotherapy or immunoglobulins are administered IV. Platelet transfusion provides transient increases in the platelet count in emergent situations, and concurrent infusion of IVIg may prolong survival of transfused platelets in some patients [61]. In some patients, the life span of the transfused platelets can be raised by the simultaneous administration of immunoglobulins [62]. To increase the platelet number very rapidly, splenectomy may be used; it was performed as an ITP treatment method in patients with severe intracranial hemorrhage [63].

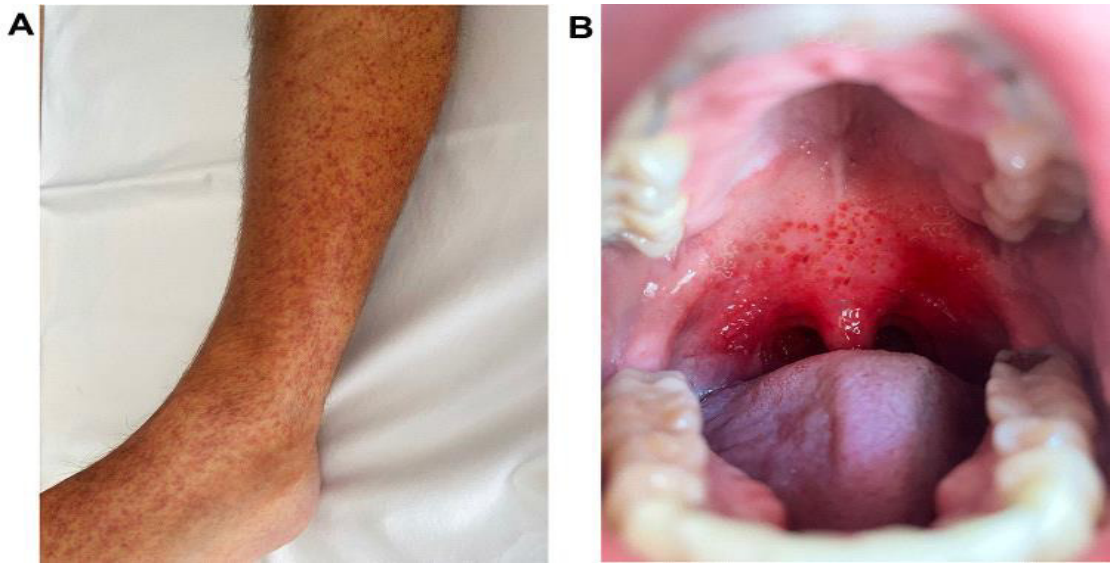

Fig :1 A) Example of cutaneous purpura. (B) Example of oral ("wet") purpura.

1.1 Diagnostic Tests to Avoid or Defer in the ED

In general, no additional testing in the ED is necessary if the diagnostic tests are compatible with main ITP. Antiplatelet antibody testing is one particular procedure to avoid in the ED. The sensitivity of antiplatelet antibody testing was reported to be 53% [64] in a prospective research intended to find platelet-bound autoantibodies reactive against GPs IIb/IIIa, Ib/IX, or Ia/IIa; this is probably too low for the test to be effective. Furthermore, while bone marrow testing may occasionally be used to rule out malignancy or myelodysplastic syndrome in atypical or resistant instances of suspected ITP, it is not advised in the vast majority of cases and does not need to be scheduled in the ED. Immunologic tests (like antinuclear antibodies) may be beneficial for patients with joint pain, malar rash, or other symptoms that could indicate a rheumatologic condition, but since a definitive diagnosis of a rheumatologic condition in the ED is unlikely, it may be best for the emergency physician to defer immunologic tests to the outpatient setting or a specialist.

1.2 Symptoms Not Due to Bleeding

There are a few additional symptoms worth addressing in addition to those connected to bleeding. Both adult and juvenile ITP patients commonly experience fatigue, but adults are more likely to experience it. According to one study, fatigue was the most prevalent symptom and was experienced by 58% of adult patients who had been diagnosed with ITP more than a month after the onset of symptoms.[65] In the meantime, 22% of paediatric patients are said to experience weariness.[66] Although bleeding is one of the main symptoms of ITP, people with ITP have a higher rate of thrombosis than controls. [67]-[69] Because thrombosis in ITP is still quite uncommon, the emergency physician should refrain from looking for it unless there is a clinical suspicion of it. Patients with ITP have a 1.5-fold higher overall mortality rate compared to the general population, as well as a noticeably higher risk of infection. [70]

1.3 ITP in Pregnancy

With an estimated incidence of 1 in 1000 to 1 in 10,000 pregnancies, ITP can develop during pregnancy. [71] Low platelet counts in pregnancy are still most frequently caused by gestational thrombocytopenia (GT), which can be challenging to distinguish from ITP. Both conditions are exclusion diagnoses, but GT's platelet count seldom dips below 70 10-9/L and often does not result in bleeding. ITP, on the other hand, raises the risk of maternal and newborn haemorrhage and can result in a significantly decreased platelet count. [71] When patients are treated appropriately medically, cases of maternal or neonatal haemorrhage are uncommon.The incidence of foetal loss appears to be higher in women with ITP who are diagnosed before becoming pregnant (11.2% vs. 3.9% in women diagnosed during pregnancy), and the foetal birth weight appears to be lower (17.9% vs. 9.7%). Premature birth rates have also reportedly increased. [72]

1.4 Thrombocytopenia

Patients with COVID-19 may experience pharmaceutical side effects, sepsis, or disseminated intravascular coagulation that results in thrombocytopenia. 73 Furthermore, COVID-19 is now a well-researched cause of ITP. [73-75] Bhattacharjee and Banerjee reported that 71% of COVID-19-induced ITP was detected in elderly individuals, and that moderate to severe COVID-19 was present in 75% of cases. [75] The platelet count often does not drop below 100 109/L in COVID-19 patients with thrombocytopenia. 76 Severe bleeding has been rare in affected people, despite reduced platelet counts being linked to an increased risk of mortality and severe illness in COVID-19 patients. [77],[78] The vast majority of COVID-19-related ITP cases have good prognoses, and the majority of patients respond favourably to the typical ITP therapies outlined below.[74,75,77]

2. CONCLUSION

Immune thrombocytopenia can be diagnosed at any age; however, it is most common in early childhood and late adulthood. Platelet levels are frequently reduced abruptly, but they normally return to normal within weeks to months. The majority of children experience spontaneous remission within a few weeks or months, and splenectomy is rarely required. However, spontaneous remissions necessitating splenectomy in young adults are uncommon in the first several months following diagnosis.

3. AUTHOR CONTRIBUTION STATEMENT

All the authors read and approved the final version of the manuscript.

4. CONFLICT OF INTEREST

Conflict of interest declared none.

5. REFERENCES

1. Stasi R, Evangelista ML, Stipa E, et al. Idiopathic thrombocytopenic purpura: current concepts in pathophysiology and management. Thromb Haemost. 2008;99(1):4–13.
2. Lusher JM, Zuelzer WW. Idiopathic thrombocytopenic purpura in childhood. J Pediatr 1966;68:971-9.
3. Onisâi, Minodora, Vlădăreanu, Ana-Maria, Spînu, Andreea, Găman, Mihaela and Bumbea, Horia. "Idiopathic thrombocytopenic purpura (ITP) – new era for an old disease" Romanian Journal of Internal Medicine, vol.57, no.4, 2019, pp.273-283. https://doi.org/10.2478/rjim-2019-0014
4. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019;3(23):3829-3866. PMID: 31794604s
5. Moller DE, Goldstein K. Hemarthrosis and idiopathic thrombocytopenic purpura. J Rheumatol 1987 Apr;14(2):382-3.
6. George JN, Woolf SH, Raskob GE, Wasser JS, Aledort LM, Ballem PJ, et al. Idiopathic Thrombocytopenic Purpura: A Practice Guideline Developed by Explicit Methods for The American Society of Hematology. Blood 1996;88:3-40.
7. Portielje JE, Westendorp RG, Kluin-Nelemans HC, et al. Morbidity and mortality in adults with idiopathic thrombocytopenic purpura. Blood. 2001;97(9):2549–54.
8. Cooper N, Ghanima W. Immune Thrombocytopenia. N Engl J Med. 2019 Sep 5. 381 (10):945-955. [QxMD MEDLINE Link].
9. Kuhne T. Idiopathic thrombocytopenic purpura of childhood: a problem-oriented review of the management. Transfus Apher Sci 2003 Jun;28(2):243-8.
10. Fargangi H, Ghasemi A, Banihashem A, Badiei Z, Jarahi L, Esami G, Langaee T. Clinical Features and Treatment Outcomes of Primary Immune Thrombocytopenic Purpura in Hospitalized Children Under 2-Years Old. Iran J Ped Hematol Oncol. 2016; 6(1): 24-31.
11. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. Blood. 2009;113(11):2386. doi: 10.1182/blood-2008-07-162503
12. Zufferey A, Kapur R, Semple J. Pathogenesis and therapeutic mechanisms in immune thrombocytopenia (ITP). JCM. 2017;6(2):16. doi: 10.3390/jcm6020016
13. Samson M, Fraser W, Lebowitz D. Treatments for Primary Immune Thrombocytopenia: A Review. Cureus. 2019 Oct 6;11(10):e5849. doi: 10.7759/cureus.5849. PMID: 31754584; PMCID: PMC6830854.
14. Fogarty PF, Segal JB. The epidemiology of immune thrombocytopenic purpura. Curr Opin Hematol. 2007;14(5):515–519.
15. Terrell DR, Beebe LA, Vesely SK, Neas BR, Segal JB, George JN. The incidence of immune thrombocytopenic purpura in children and adults: a critical review of published reports. Am J Hematol. 2010;85(3):174–180. doi: 10.1002/ajh.21616
16. Zeller B, Rajantie J, Hedlund-Treutiger I, et al. Childhood idiopathic thrombocytopenic purpura in the Nordic countries: epidemiology and predictors of chronic disease. Acta Paediatr. 2005;94(2):178–184.
17. Segal JB, Powe NR. Prevalence of immune thrombocytopenia: analyses of administrative data. J Thromb Haemost. 2006;4(11):2377–2383.
18. Zeller B, Rajantie J, Hedlund-Treutiger I, et al. Childhood idiopathic thrombocytopenic purpura in the Nordic countries: epidemiology and predictors of chronic disease: childhood ITP in the Nordic countries. Acta Paediatrica. 2007;94(2):178–184. doi: 10.1111/j.1651-2227.2005.tb01887.x [
19. Yong M, Schoonen WM, Li L, et al. Epidemiology of paediatric immune thrombocytopenia in the General Practice Research Database. Br J Haematol. 2010;149(6):855–864.
20. Terrell DR, Beebe LA, Neas BR, Vesely SK, Segal JB, George JN. Prevalence of primary immune thrombocytopenia in Oklahoma. Am J Hematol. 2012;87(9):848–852. doi: 10.1002/ajh.23262
21. ` Neylon AJ, Saunders PW, Howard MR, Proctor SJ, Taylor PR On behalf of the Northern Region Haematology Group. Clinically significant newly presenting autoimmune thrombocytopenic purpura in adults: a prospective study of a population-based cohort of 245 patients. Brit J Haematol. 2003;122:966–974.
22. Frederiksen H, Schmidt K. The incidence of idiopathic thrombocytopenic purpura in adults increases with age. Blood. 1999;94(3):909–913.
23. Kistangari G, McCrae KR. Immune thrombocytopenia. Hematol Oncol Clin North Am. 2013 Jun;27(3):495-520. doi: 10.1016/j.hoc.2013.03.001. PMID: 23714309; PMCID: PMC3672858.
24. Despotovic JM, Grimes AB. Pediatric ITP: is it different from adult ITP? Hematology Am Soc Hematol Educ Program. 2018;2018(1):405–411. doi: 10.1182/asheducation-2018.1.405
25. Stasi R. Immune thrombocytopenia: pathophysiologic and clinical update. Semin Thromb Hemost. 2012;38(5):454–462.
26. Warrier R, Chauhan A. Management of immune thrombocytopenic purpura: an update. Ochsner J. 2012 Fall;12(3):221-7. PMID: 23049459; PMCID: PMC3448244.

27. The ITP syndrome: pathogenic and clinical diversity. Cines DB, Bussel JB, Liebman HA, Luning Prak ET. Blood. 2009;113:6511–6521.
28. Olsson B., Andersson P.O., Jernas M., Jacobsson S., Carlsson B., Carlsson L.M., Wadenvik H. T-cell-mediated cytotoxicity toward platelets in chronic idiopathic thrombocytopenic purpura. Nat. Med. 2003;9:1123–1124. doi: 10.1038/nm921.
29. Khodadi E., Asnafi A.A., Shahrabi S., Shahjahani M., Saki N. Bone marrow niche in immune thrombocytopenia: A focus on megakaryopoiesis. Ann. Hematol. 2016;95:1765–1776. doi: 10.1007/s00277-016-2703-1.
30. Zhang W., Nardi M.A., Borkowsky W., Li Z., Karpatkin S. Role of molecular mimicry of hepatitis C virus protein with platelet GPIIIa in hepatitis C-related immunologic thrombocytopenia. Blood. 2009;113:4086–4093. doi: 10.1182/blood-2008-09-181073.
31. Rodeghiero, Francesco, et al. "Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group." Blood, The Journal of the American Society of Hematology 113.11 (2009): 2386-2393.
32. Vayne C, Guery E, Rollin J, Baglo T, Petermann R, Gruel Y. Pathophysiology and diagnosis of drug-induced immune thrombocytopenia. J Clin Med. 2020;9(7):2212. doi: 10.3390/jcm9072212
33. Despotovic JM, Grimes AB. Pediatric ITP: is it different from adult ITP? Hematology Am Soc Hematol Educ Program. 2018;2018(1):405–411. doi: 10.1182/asheducation-2018.1.405
34. KISTANGURI G, MCCRAE K. Immune Thrombocytopenia. Hematol Oncol Clin North Am. 2013; 27(3):495–520.
35. Newton JL, Reese JA, Watson SI, et al. Fatigue in adult patients with primary immune thrombocytopenia. Eur J Haematol. 2011;86(5):420–429.
36. Nørgaard M, Cetin K, Maegbaek ML, et al. Risk of arterial thrombotic and venous thromboembolic events in patients with primary chronic immune thrombocytopenia: a Scandinavian population-based cohort study. Br J Haematol. 2016;174(4):639. doi: 10.1111/bjh.13787
37. Shulman NR, Marder VJ, Weinrach RS. Similarities between known antiplatelet antibodies and the factor responsible for thrombocytopenia in idiopathic purpura. Physiologic, serologic and isotopic studies. Ann N Y Acad Sci. 1965;124(2):499-542.
38. Khodadi E, Asnafi AA, Shahrabi S, Shahjahani M, Saki N. Bone marrow niche in immune thrombocytopenia: a focus on megakaryopoiesis. Ann Hematol. 2016;95(11):1765-1776.
39. Olsson B, Andersson PO, Jernås M, et al. T-cell-mediated cytotoxicity toward platelets in chronic idiopathic thrombocytopenic purpura. Nat Med. 2003;9(9):1123-1124.
40. Cines DB, Bussel JB, Liebman HA, Luning Prak ET. The ITP syndrome: pathogenic and clinical diversity. Blood. 2009;113(26):6511-6521.
41. Nugent D, McMillan R, Nichol JL, Slichter SJ. Pathogenesis of chronic immune thrombocytopenia: increased platelet destruction and/or decreased platelet production. Br J Haematol. 2009;146(6):585-596.
42. Malara A, Abbonante V, Di Buduo CA, Tozzi L, Currao M, Balduini A. The secret life of a megakaryocyte: emerging roles in bone marrow homeostasis control. Cell Mol Life Sci. 2015;72(8):1517-1536.
43. Makar RS, Zhukov OS, Sahud MA, Kuter DJ. Thrombopoietin levels in patients with disorders of platelet production: diagnostic potential and utility in predicting response to TPO receptor agonists. Am J Hematol. 2013;88(12):1041-1044.
44. Provan D, Stasi R, Newland Ac, Blanchette Vs, Bolton-Maggs P, Bussel JB, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010; 115:168–186.
45. Zitek T, Weber L, Pinzon D, Warren N. Assessment and Management of Immune Thrombocytopenia (ITP) in the Emergency Department: Current Perspectives. Open Access Emerg Med. 2022 Jan 29;14:25-34. doi: 10.2147/OAEM.S331675. PMID: 35125895; PMCID: PMC8809484.
46. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010;115(2):168-186.
47. Purohit A, Aggarwal M, Singh PK, et al. Re-evaluation of need for bone marrow examination in patients with isolated thrombocytopenia contributors [published correction appears in Indian J Hematol Blood Transfus. 2016;32(2):197]. Indian J Hematol Blood Transfus. 2016;32(2):193-196.
48. DM Arnold, JG Kelton Current options for the treatment of idiopathic thrombocytopenic purpura. Semin Hematol, 44 (2007), pp. S12-S23
49. British Committee for Standard in Haematology General Haematology Task Force Guidelines for the investigation and management of idiopathic thrombocytopenic purpura (ITP) in adults, children and in pregnancy. Br J Haematol, 120 (2003), pp. 574-596 2003
50. Samson M, Fraser W, Lebowitz D. Treatments for Primary Immune Thrombocytopenia: A Review. Cureus. 2019 Oct 6;11(10):e5849. doi: 10.7759/cureus.5849. PMID: 31754584; PMCID: PMC6830854.
51. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Neunert C, Lim W, Crowther M, Cohen A, Solberg L, Jr. Jr., Crowther MA. Blood. 2011;117:4190–4207.
52. Cuker A., Prak E.T., Cines D.B. Can immune thrombocytopenia be cured with medical therapy? Semin. Thromb. Hemost. 2015;41:395–404.
53. Rudnicka D., Oszmiana A., Finch D.K., Strickland I., Schofield D.J., Lowe D.C., Sleeman M.A. Rituximab causes a polarization of B cells that augments its therapeutic function in NK-cell-mediated antibody-dependent cellular cytotoxicity. Blood. 2013;121:4694–4702. doi: 10.1182/blood-2013-02-482570.
54. Audia S., Samson M., Guy J., Janikashvili N., Fraszczak J., Trad M., Ciudad M., Leguy V., Berthier S., Petrella T., et al. Immunologic effects of rituximab on the human spleen in immune thrombocytopenia. Blood. 2011;118:4394–4400. doi: 10.1182/blood-2011-03-344051.
55. Erickson-Miller C.L., DeLorme E., Tian S.S., Hopson C.B., Stark K., Giampa L., Valoret E.I., Duffy K.J., Luengo

J.L., Rosen J., et al. Discovery and characterization of a selective, nonpeptidyl thrombopoietin receptor agonist. Exp. Hematol. 2005;33:85–93. doi: 10.1016/j.exphem.2004.09.006.
56. Cohn C.S., Bussel J.B. Romiplostim: A second-generation thrombopoietin agonist. Drugs Today. 2009;45:175–188. doi: 10.1358/dot.2009.45.3.1343793.
57. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019;3:3829. doi: 10.1182/bloodadvances.2019000966
58. Provan D, Arnold DM, Bussel JB, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. Blood Adv. 2019;3:3780. doi: 10.1182/bloodadvances.2019000812
59. Arnold DM, Cuker A. Immune thrombocytopenia (ITP) in adults: clinical manifestations and diagnosis. UpToDate. Available from: https://www.uptodate.com/contents/immune-thrombocytopenia-itp-in-adults-clinical-manifestations-and-diagnosis?search=immune%20thrombocytopenia&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H21. Accessed October 22, 2021.
60. Tintinalli JE. Tintinalli's Emergency Medicine. 8th ed. McGraw-Hill Companies; 2015:1491
61. Spahr JE, Rodgers GM. Treatment of immune-mediated thrombocytopenia purpura with concurrent intravenous immunoglobulin and platelet transfusion: a retrospective review of 40 patients. Am J Hematol. 2008;83(2):122–125.
62. BRYNES RK, ORAZI A, VERMA S, BRAINSKY K, BAILEY CK, BAKSHI K. Evaluation of bone marrow reticulin in patients with chronic immune thrombocytopenic purpura (ITP) treated with Eltrombopag-data from the EXTEND study. Blood. 2011; 118.
63. KISTANGURI G, MCCRAE K. Immune Thrombocytopenia. Hematol Oncol Clin North Am. 2013; 27(3):495–520.
64. Davoren A, Bussel J, Curtis BR, Moghaddam M, Aster RH, McFarland JG. Prospective evaluation of a new platelet glycoprotein (GP)-specific assay (PakAuto) in the diagnosis of autoimmune thrombocytopenia (AITP). Am J Hematol. 2005;78(3):193–197. doi: 10.1002/ajh.20309
65. Kuhne T, Berchtold W, Michaels LA, et al. Newly diagnosed immune thrombocytopenia in children and adults: a comparative prospective observational registry of the Intercontinental Cooperative Immune Thrombocytopenia Study Group. Haematologica. 2011;96(12):1831–1837. doi: 10.3324/haematol.2011.050799
66. Onisâi M, Vlădăreanu A-M, Spînu A, Găman M, Bumbea H. Idiopathic thrombocytopenic purpura (ITP) – new era for an old disease. Rom J Intern Med. 2019;57(4):273–283
67. Sarpatwari A, Bennett D, Logie JW, et al. Thromboembolic events among adult patients with primary immune thrombocytopenia in the United Kingdom general practice research database. Haematologica. 2010;95(7):1167–1175. doi: 10.3324/haematol.2009.018390
68. Nørgaard M, Severinsen MT, Lund Maegbaek M, Jensen AØ, Cha S, Sørensen HT. Risk of arterial thrombosis in patients with primary chronic immune thrombocytopenia: a Danish population-based cohort study. Br J Haematol. 2012;159(1):109. doi: 10.1111/j.1365-2141.2012.09231.x
69. Nørgaard M, Cetin K, Maegbaek ML, et al. Risk of arterial thrombotic and venous thromboembolic events in patients with primary chronic immune thrombocytopenia: a Scandinavian population-based cohort study. Br J Haematol. 2016;174(4):639. doi: 10.1111/bjh.13787
70. Frederiksen H, Maegbaek ML, Nørgaard M. Twenty-year mortality of adult patients with primary immune thrombocytopenia: a Danish population-based cohort study. Br J Haematol. 2014;166(2):260–267. doi: 10.1111/bjh.12869
71. Care A, Pavord S, Knight M, Alfirevic Z. Severe primary autoimmune thrombocytopenia in pregnancy: a national cohort study. BJOG. 2018;125(5):604–612. doi: 10.1111/1471-0528.14697
72. Lambert MP, Gernsheimer TB. Clinical updates in adult immune thrombocytopenia. Blood. 2017;129(21):2829–2835. doi: 10.1182/blood-2017-03-754119
73. Bomhof G, Mutsaers PGNJ, Leebeek FWG, et al. COVID- 19- associated immune thrombocytopenia. Br J Haematol. 2020;190(2). doi: 10.1111/bjh.16850
74. Murt A, Eskazan AE, Yılmaz U, Ozkan T, Ar MC. COVID- 19 presenting with immune thrombocytopenia: a case report and review of the literature. J Med Virol. 2021;93(1):43–45. doi: 10.1002/jmv.26138
75. Bhattacharjee S, Banerjee M. Immune thrombocytopenia secondary to COVID-19: a systematic review. SN Compr Clin Med. 2020;2(11):2048–2058. doi: 10.1007/s42399-020-00521-8
76. Sahu KK, Siddiqui AD, Rezaei N, Cerny J. Challenges for management of immune thrombocytopenia during COVID- 19 pandemic. J Med Virol. 2020;92(11):2277–2282. doi: 10.1002/jmv.26251
77. Mahévas M, Moulis G, Andres E, et al. Clinical characteristics, management and outcome of COVID-19- associated immune thrombocytopenia: a French multicentre series. Br J Haematol. 2020;190(4). doi: 10.1111/bjh.17024
78. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis. Clin Chim Acta. 2020;506:145–148. doi: 10.1016/j.cca.2020.03.022