Thrombocytopenia, A Comprehensive Study of Causes, Diagnostic Approaches, and Therapeutic Options

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Abstract

Background

Thrombocytopenia, explained a platelet count below 150 × 10⁹/L, is a frequent hematological abnormality with complex etiologies. Its clinical scope ranges from incidental findings to life-threatening hemorrhage. International societies, which includes the **BSH**, **ISTH**, and **ASH**, highlight systematize diagnostic methods and evidence-based treatment techniques.

Objectives

To review the major causes, diagnostic methods, and treatment techniques for thrombocytopenia, while consolidating recommendations from BSH, ISTH, and ASH instructions.

Methods

A systematic literature searches from 2000 to 2024 was held by using PubMed, Embase, and Cochrane databases. Articles were assessed according to **GRADE methodology**, lined up with the foundation of BSH, ISTH, and ASH. Evidence was synthesized into diagnostic and therapeutic recommendations.

Results

Thrombocytopenia emerge from decreased platelet production, increased destruction, splenic sequestration, or other dilutional effects. Immune thrombocytopenia is the most frequent earned cause, while bone marrow failure syndromes are major causes of production failure. Diagnostics include CBC, peripheral smear, bone marrow biopsy, and immune or viral testing. Treatment differ by etiology and severity: corticosteroids and IVIG are first-line for ITP, while extreme bleeding needs platelet transfusion.

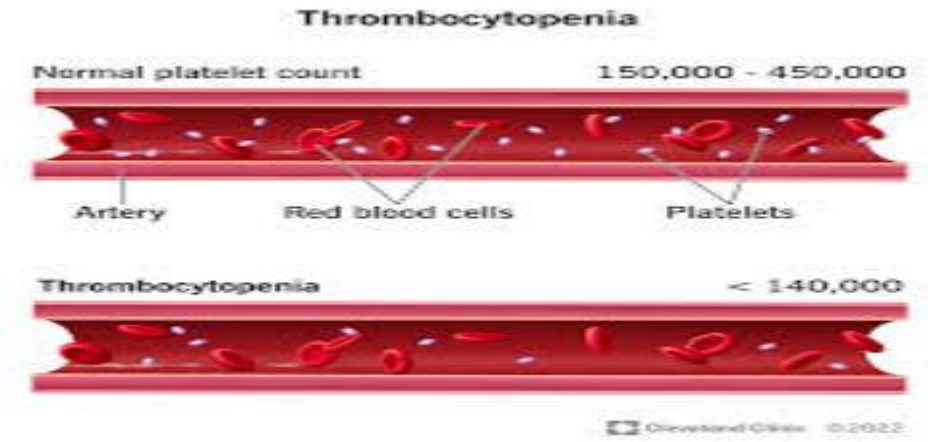
Conclusion

International instructions agree that diagnosis of thrombocytopenia must accompany a structured approach, with treatment modified to cause and severity. Advances includes thrombopoietin receptor agonists and shared decision-making models improve long-term management.

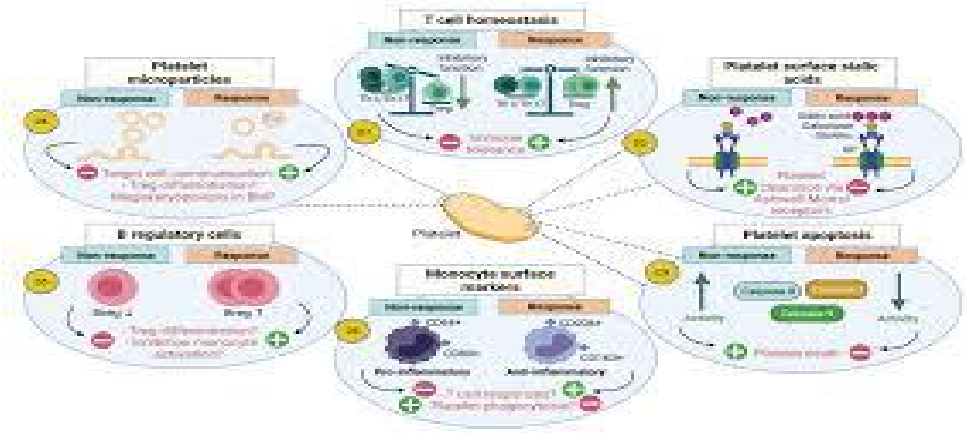
Keywords: Thrombocytopenia; Diagnosis; Immune Thrombocytopenia; Platelet Disorders; Guidelines

Introduction

Thrombocytopenia, distinguished by a platelet count below 150 × 10⁹/L, is a clinically remarkable condition that can lead to bleeding complications extended from petechiae and mucosal hemorrhage to extreme gastrointestinal or intracranial bleeding [1]. The disorder may be asymptomatic and accidentally diagnosed, or it may show as a hematological emergency needing quick intervention [2].



According to the **British Society of Hematology (BSH)**, **International Society on Thrombosis and Hemostasis (ISTH)**, and **American Society of Hematology (ASH)**, the assessment of thrombocytopenia should follow an arranged diagnostic pathway, with management instructed by both etiology and clinical presentation [3]. The pathophysiology of thrombocytopenia widely falls into four different categories: **Reduced platelet production**, **Increased destruction or consumption**, **Splenic sequestration**, and **Dilutional effects [4]**. Reduced production is linked with bone marrow failure syndromes includes aplastic anemia, myelodysplastic syndromes, or chemotherapy-induced suppression. Increased destruction happens in immune-mediated conditions like ITP, micro-angiopathic processes includes thrombotic thrombocytopenic purpura, distributed intravascular coagulation, or drug-induced mechanisms [5]. Splenic sequestration is specifically linked with portal hypertension and splenomegaly, whereas dilutional thrombocytopenia can occur following massive transfusion [6].



The **diagnostic approach**, as endorsed by BSH, ISTH, and ASH, begins with a **complete blood count** and **peripheral blood film**, which exclude pseudo thrombocytopenia and reveal morphologic abnormalities. Further tests may include bone marrow aspiration/biopsy, viral serology (HIV, HCV, EBV), autoimmune testing, and coagulation profiles [7]. Importantly, international guidelines emphasize correlating laboratory findings with clinical history, exposure to drugs, and comorbid conditions to identify the underlying cause accurately. Treatment strategies vary according to severity and etiology. **Immune thrombocytopenia**, the most common acquired form, is typically managed with corticosteroids, intravenous immunoglobulin (IVIG), or anti-D immunoglobulin [8]. For refractory cases, second-line options such as rituximab, thrombopoietin receptor agonists, or splenectomy are recommended. For bone marrow failure-related thrombocytopenia, transfusional support and consideration of stem cell transplantation may be necessary [9]. Platelet transfusion is indicated in patients with severe thrombocytopenia ($<10 \times 10^9$/L) or active bleeding, in line with international guidance. This review consolidates evidence from BSH, ISTH, and ASH guidelines, providing an integrated framework for the causes, diagnostic evaluation, and treatment strategies of thrombocytopenia.

Methodology

A systematic review was conducted using PubMed, Embase, and the Cochrane Library, covering publications from **January 2000 to February 2024**. Keywords included *"thrombocytopenia," "immune thrombocytopenia," "diagnosis," "platelet transfusion," "management,"* and *"guidelines."* Studies included randomized controlled trials, systematic reviews, meta-analyses, and guideline documents. The **GRADE (Grading of Recommendations, Assessment, Development, and Evaluation)** approach was applied, consistent with **BSH**, **ISTH**, and **ASH** practices. Recommendations were categorized based on the quality of evidence (high, moderate, low) and strength (strong, conditional). Final synthesis incorporated consensus across international guidelines.

Results

Thrombocytopenia was most commonly caused by immune-mediated destruction (ITP) and drug-induced mechanisms, followed by bone marrow suppression syndromes. Diagnostic workup begins with CBC and smear, with bone marrow biopsy reserved for cases suggestive of production failure.

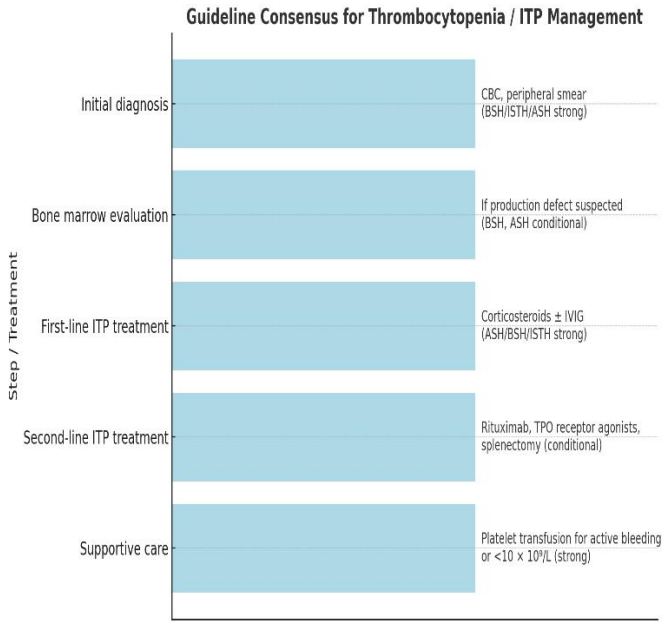
Table 1: Common Causes of Thrombocytopenia

Mechanism	Examples

Mechanism	Examples
Reduced platelet production	Aplastic anemia, myelodysplastic syndromes, chemotherapy, radiation
Increased destruction	ITP, TTP, DIC, drug-induced (heparin, antibiotics), viral infections (HIV, HCV)
Splenic sequestration	Splenomegaly, portal hypertension
Dilutional	Massive blood transfusion

Table 2: Diagnostic and Treatment Recommendations (BSH, ISTH, ASH Integrated)

Step / Treatment	Recommendation (Guideline Consensus)
Initial diagnosis	CBC, peripheral smear (BSH/ISTH/ASH strong recommendation)
Bone marrow evaluation	If production defect suspected (BSH, ASH conditional)
First-line ITP treatment	Corticosteroids ± IVIG (ASH/BSH/ISTH strong recommendation)
Second-line ITP treatment	Rituximab, thrombopoietin receptor agonists, splenectomy (conditional)
Supportive care	Platelet transfusion for active bleeding or <10 × 10⁹/L (strong)



Discussion

Thrombocytopenia is a multifactorial condition with diverse clinical implications, requiring a systematic diagnostic and therapeutic approach [10]. Across **BSH**, **ISTH**, and **ASH** guidelines, several points of consensus emerge, reflecting the strength of current evidence. First, the **diagnostic pathway** universally begins with CBC and blood smear, ensuring exclusion of pseudo thrombocytopenia and initial morphologic assessment [11]. International guidelines concur that bone marrow examination should be reserved for atypical presentations or suspected production failure, avoiding unnecessary invasive testing

[12]. Viral and autoimmune testing is emphasized by both ISTH and ASH, particularly in endemic regions or when clinical suspicion arises. Second, there is strong agreement regarding **treatment of immune thrombocytopenia [13]**. Corticosteroids remain the preferred first-line therapy across all societies. IVIG is recommended in patients with severe thrombocytopenia or bleeding, especially when rapid platelet count elevation is needed. Second-line treatments diverge slightly: ASH emphasizes patient-centered shared decision-making, particularly when selecting between rituximab, thrombopoietin receptor agonists, or splenectomy; BSH highlights long-term efficacy and safety of thrombopoietin receptor agonists; ISTH underscores the importance of individualized therapy in special populations (e.g., pregnancy, pediatric patients) [14]. Third, supportive care, especially **platelet transfusion**, is uniformly recommended in patients with life-threatening bleeding or platelet counts below 10×10^9/L. However, guidelines caution against prophylactic transfusion in stable, non-bleeding patients due to alloimmunization risk. Importantly, ISTH guidelines emphasize **shared decision-making** and incorporation of patient preferences, reflecting a growing recognition of quality of life outcomes in thrombocytopenia management [15]. Similarly, ASH has developed **clinical decision-support tools and pocket guides** to aid clinicians in real-world settings, highlighting a practical orientation to implementation. BSH guidelines remain particularly strong in providing detailed laboratory diagnostic algorithms, ensuring early identification of underlying etiologies [16]. Despite consensus, research gaps persist. Long-term safety data on thrombopoietin receptor agonists, optimal treatment sequencing in refractory ITP, and strategies for thrombocytopenia in complex settings (e.g., pregnancy, malignancy) remain priorities [17]. Future guidelines should further integrate biomarker-driven approaches to personalize therapy and reduce complications. Overall, while variations exist in emphasis, the BSH, ISTH, and ASH guidelines collectively provide a robust framework for thrombocytopenia management, combining diagnostic precision with individualized, evidence-based therapy.

Conclusion

Thrombocytopenia is a clinically significant disorder arising from multiple mechanisms, requiring careful evaluation and tailored therapy. International guidelines from **BSH, ISTH, and ASH** converge on a structured diagnostic pathway and emphasize corticosteroids and IVIG as first-line ITP therapy, with thrombopoietin receptor agonists, rituximab, and splenectomy as subsequent options. Platelet transfusions remain central for bleeding emergencies. Integration of patient preferences, diagnostic accuracy, and evidence-based therapeutics are key to improving outcomes. Continued refinement of guidelines will ensure more personalized and effective management of thrombocytopenia in diverse clinical settings.

References:

1. Martínez-Carballeira, D., Bernardo, Á., Caro, A., Soto, I., & Gutiérrez, L. (2024). Pathophysiology, clinical manifestations and diagnosis of immune thrombocytopenia: contextualization from a historical perspective. *Hematology Reports*, *16*(2), 204-219.
2. Sharma, A., Raut, S. S., Dhikale, P., Khushboo, & Mishra, A. (2024). Navigating the Landscape of Cancer-Induced Thrombocytopenia: Current Challenges and Emerging Advances. *Industrial Microbiology and Biotechnology: A New Horizon of the Microbial World*, 435-463.
3. Dahiphale, S. M., Dewani, D., Agrawal, M., Dahiphale, J. M., Jyotsna, G., & Desale, R. (2024). Navigating primary immune thrombocytopenia during pregnancy with management strategies and considerations: a comprehensive review. *Cureus*, *16*(8).
4. Mazumder, A., Das, S., Atri, A., Singh, K., & Singh, M. Immune Thrombocytopenia: an Updated Review From Etiopathophysiology, Laboratory Investigations and Current Therapy. *International journal of health sciences*, *6*(S5), 8499-8526.
5. Kalantari, A., Karimizadeh, Z., Jafari, L., Behfar, M., & Hamidieh, A. A. (2025, August).

Thrombocytopenia after Hematopoietic Stem Cell Transplantation in Pediatrics and Adults; A Narrative Review Including Etiology, Management, Monitoring and Novel Therapies. In *Seminars in Thrombosis and Hemostasis*. Thieme Medical Publishers, Inc..

6. Nasreddine, G. M., Farhat, S., Hammoud, Z. M., Saad, F., Saad, W., Hammoud, Z., & Saad, W. A. (2024). Chronic Myelomonocytic Leukemia-Associated Immune Thrombocytopenic Purpura: A Report of a Rare Case and a Review of Literature. *Cureus*, *16*(3).
7. Kos, M., Tomaka, P., Mertowska, P., Mertowski, S., Wojnicka, J., Błażewicz, A., ... & Bojarski, K. (2024). The Many Faces of Immune Thrombocytopenia: Mechanisms, Therapies, and Clinical Challenges in Oncological Patients. *Journal of Clinical Medicine*, *13*(22), 6738.
8. Tirelli, C., Rondinone, O., Italia, M., Mira, S., Belmonte, L. A., De Grassi, M., ... & Centanni, S. (2024). The genetic basis, lung involvement, and therapeutic options in Niemann–Pick disease: A comprehensive review. *Biomolecules*, *14*(2), 211.
9. Ryu, M. O., Kim, J. K., An, J. H., Seo, K. W., Oh, Y. I., & Youn, H. Y. (2024). Romiplostim for treatment of thrombocytopenia in dogs: A retrospective assessment and clinical outcomes. *Journal of Veterinary Internal Medicine*, *38*(4), 2158-2164.

10. Igrutinovic, N., Pantovic, J., Markovic, B., Medovic, M., Cekerevac, M., Markovic, V., ... & Medovic, R. (2025). The Prognostic Value of Platelet Kinetics Assessment in Pediatric Chronic Idiopathic Thrombocytopenic Purpura. *Diagnostics*, *15*(14), 1790.
11. Pektaş, G., Uncu, İ. A., Dere, Y., Öncü, Ş., Kızılkaya, M. B., Sadi, G., & Pektaş, M. B. (2024). Retrospective Evaluation of Survival and Prognostic Factors in Immune Thrombocytopenia: A Single-Center and Cross-Sectional Study. *Medicina*, *60*(7), 1153.
12. Sato, D., Kirikae, H., Nakano, T., Katayama, S., Yaoita, H., Takayama, J., ... & Sasahara, Y. (2024). Comprehensive genetic analysis for identification of monogenic disorders and selection of appropriate treatments in pediatric patients with persistent thrombocytopenia. *Pediatric Hematology and Oncology*, *41*(8), 541-556.
13. Pranja, G., Sooriyakumar, T., & Pragalathan, E. (2025). A Single-Center Experience of Immune Thrombocytopenic Purpura: Disease Characteristics, Treatment Options, Response to Treatment, and Side Effects. *Jaffna Medical Journal*, *37*(1).
14. Soresina, A., Rondelli, R., Notarangelo, L. D., Locatelli, F., Aiuti, A., Biffi, A., ... & Fulvio, F. (2025). Long-term outcome in Wiskott-Aldrich syndrome and X-linked thrombocytopenia patients: an observational-prospective multi-center study of the Italian Primary Immune Deficiency Network (IPINET). *EClinicalMedicine*, *84*.
15. Inatomi, A., Tokoro, S., Katsura, D., Sawai, T., & Murakami, T. (2025). The Critical Importance of Diagnosing Atypical Hemolytic Uremic Syndrome in Postpartum Renal Dysfunction in a Patient With Systemic Lupus Erythematosus: A Case Report and Comprehensive Review. *Cureus*, *17*(2).
16. Asano, T., Noma, K., Mizoguchi, Y., Karakawa, S., & Okada, S. (2024). Human STAT1 gain of function with chronic mucocutaneous candidiasis: A comprehensive review for strengthening the connection between bedside observations and laboratory research. *Immunological Reviews*, *322*(1), 81-97.
17. Müller, L., Dabbiru, V. A., Schönborn, L., & Greinacher, A. (2024). Therapeutic strategies in FcγIIA receptor-dependent thrombosis and thromboinflammation as seen in heparin-induced thrombocytopenia (HIT) and vaccine-induced immune thrombocytopenia and thrombosis (VITT). *Expert Opinion on Pharmacotherapy*, *25*(3), 281-294.