ITP and Thrombosis

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Abstract

Immune Thrombocytopenia (ITP) is a condition characterized by an abnormally low platelet count due to auto-antibodies attacking platelet antigens. We researched the epidemiology, pathogenesis, and clinical presentation of ITP, highlighting its impact on bleeding and thrombotic risks. The diagnosis is based on exclusion, given the necessity of multiple laboratory tests, while treatment involves corticosteroids, immunosuppressive agents, and supportive care. Importantly, despite its association with bleeding, ITP also increases the risk of thrombosis, necessitating careful management to balance thrombotic and bleeding complications.

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Introduction

Platelets (thrombocytes, Figure 1) are small, colorless cell fragments in blood are made in the bone marrow that form clots and stop or prevent bleeding. Their primary function is to prevent and stop bleeding. If a blood vessel is damaged, the body sends signals to platelets which cause them to travel to the injured area. At the site of injury, they clump together to form a clot that helps stop bleeding.

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Figure 1: Platelets

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Platelets and low platelet count

- Normal range: 150,000 to 400,000 platelets per mcL
- Thrombocytopenia is a condition the blood platelet count is low
  - Three levels of thrombocytopenia resulting in varying degrees of clinical severity.
    - Mild: (100-150K/mcL): Typically no increased risk of bleeding.
    - Moderate (50-100K/mcL): Typically no risk of increased bleeding
    - Severe (<50K/mcL): Increased risk of bleeding.
    - If <10K, then high risk of life threatening bleeding
- Thrombocytosis is a disorder in which the body produces too many platelets.
- Classification of ITP, refer to Figure 2

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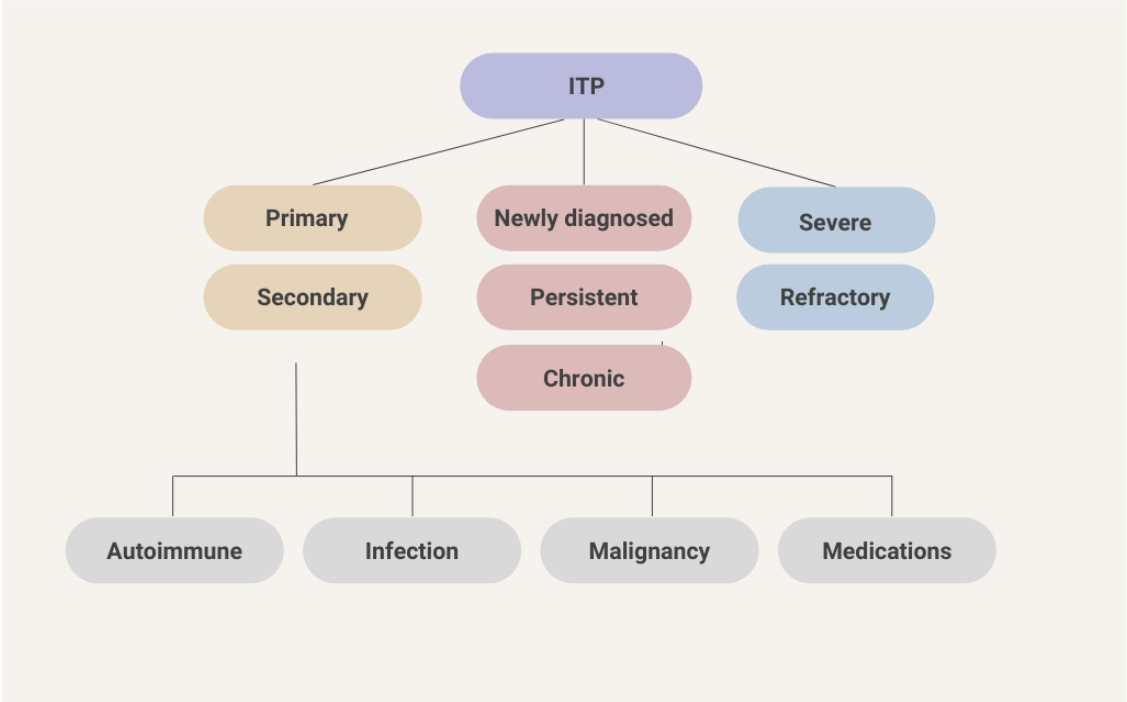

Figure 2: Classification of ITP

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Causes of ITP

- Major causes of thrombocytopenia include decreased platelet production, peripheral platelet destruction or consumption in thrombi, dilution from fluid resuscitation or massive transfusion, and sequestration of platelets in the spleen.
- Primary immune thrombocytopenia (ITP)
  - An acquired thrombocytopenia caused by autoantibodies against platelet antigens (most common cause).
- Other causes include:
  - Inability of the bone marrow to produce enough platelets
    - Drugs: quinine, sulfa drugs, tagamet, chemotherapy medications
    - Infections: HCV, HIV,
    - Medical conditions: autoimmune disorders (lupus, cirrhosis, leukemia and other bone marrow cancer)
  - Removal (consumption)/ Sequestration (trapped platelets)
    - Increased splenic platelet sequestration can occur in various disorders

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Epidemiology

Prevalence/Incidence:

- Commonly acquired bleeding disorder
- Incidence of ITP in adults is 66/1,000,000, and in children it is 50/1,000,000.
- US prevalence 8/100,000 (children), 12/100000 (adults)
- Incidence increases with age (Figure 3).
- Most serious complication is hemorrhage, with a mortality rate of 1% in children and 5% in adults.
- In Acute ITP male to female ratio is nearly equal, but in Chronic ITP 72% of patients >10 years of age are female. Ratio is 2.6:1

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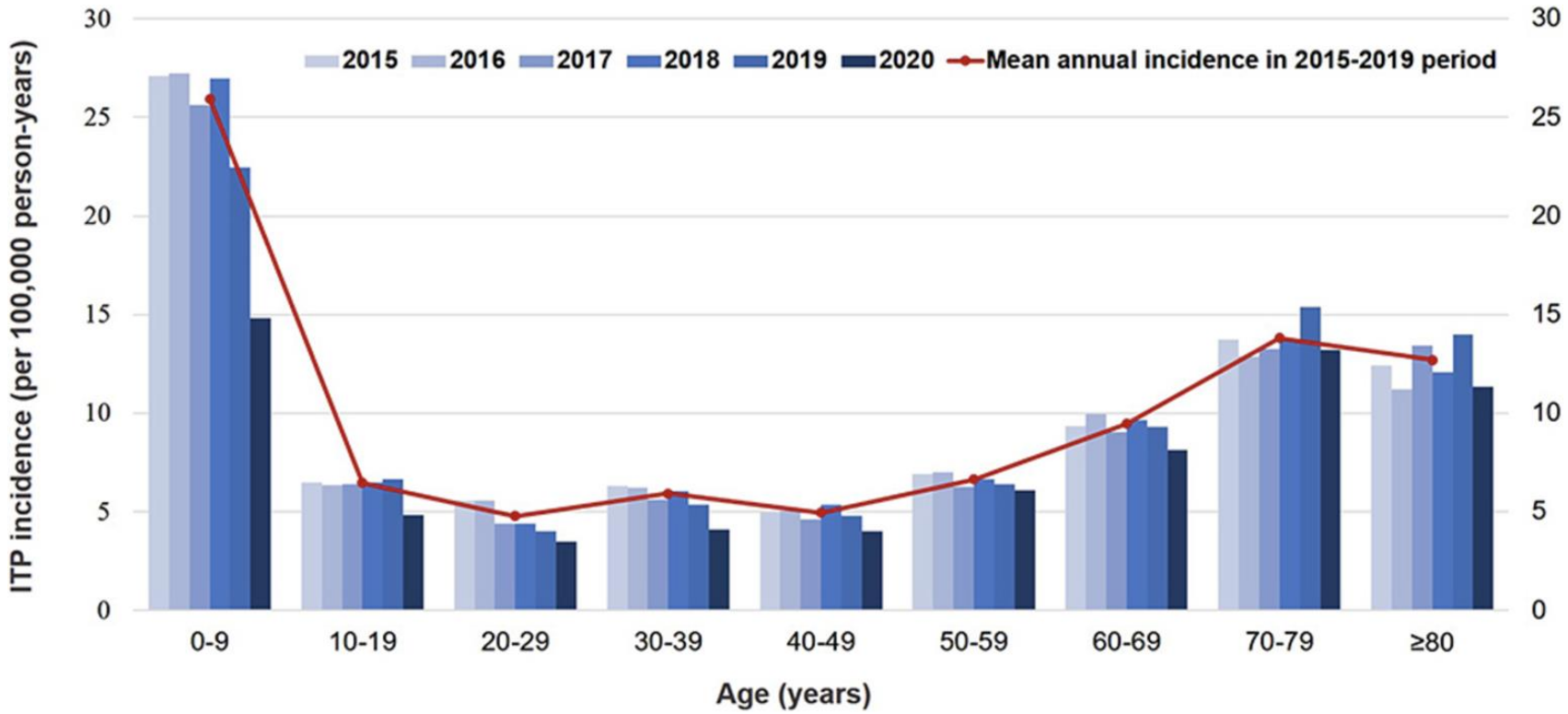

Figure 3: Incidence of ITP by age

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Pathogenesis of ITP

- Principle mechanism: specific autoantibodies (IgG) against platelet membrane proteins
- Pathogenesis of ITP is not fully understood by medicine yet.
- Familial ITP has been explored but is very rare, only 2%.
- The principal mechanism is thought to be IgG or other antibodies attacking platelets, specifically their membrane glycoproteins.
- In some cases, there seems to be events inciting the ITP, and secondary ITP can be caused by a number of chronic and infectious diseases, such as Chronic Lymphocytic Leukemia, Antiphospholipid System, Hepatitis C.

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Diagnosis of ITP

- History and Physical:
  - Review prior platelet counts, family history, medications.
  - Examine for bleeding: petechiae or bruising, hepatosplenomegaly, lymphadenopathy
- Lab testing-CBC, Peripheral blood smear, CBC, HIV/HCV testing, Thyroid function, immunologic testing (ANA,It has been well recognised that ANA can be detected in some patients with primary ITP who do not meet the diagnostic criteria for any defined CTD.)
- Bone marrow examination:
  - Rule out leukemia, myelodysplastic syndrome or aplastic anemia.
  - Patients with secondary ITP often may have associated conditions like vitamin B12 deficiency that may further contribute to thrombocytopenia.
- No single laboratory result or clinical finding can establish a diagnosis of ITP; it is a diagnosis by exclusion

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Symptoms of ITP

- Varies: Asymptomatic to severe
- Patients may present with (Figure 4):
  - petechiae (superficial bleeding into skin appearing as spots)
  - Purpura (petechiae join together forming red, purple or brown spots on your skin. The spots are larger than petechiae but smaller than a bruise. This happens when small blood vessels under your skin leak blood).
  - Mucosal bleeding: nosebleeds (epistaxis), blood in urine or stool
  - Excessive bruising
  - Severe cases can lead to life threatening bleeding such as intracranial hemorrhage

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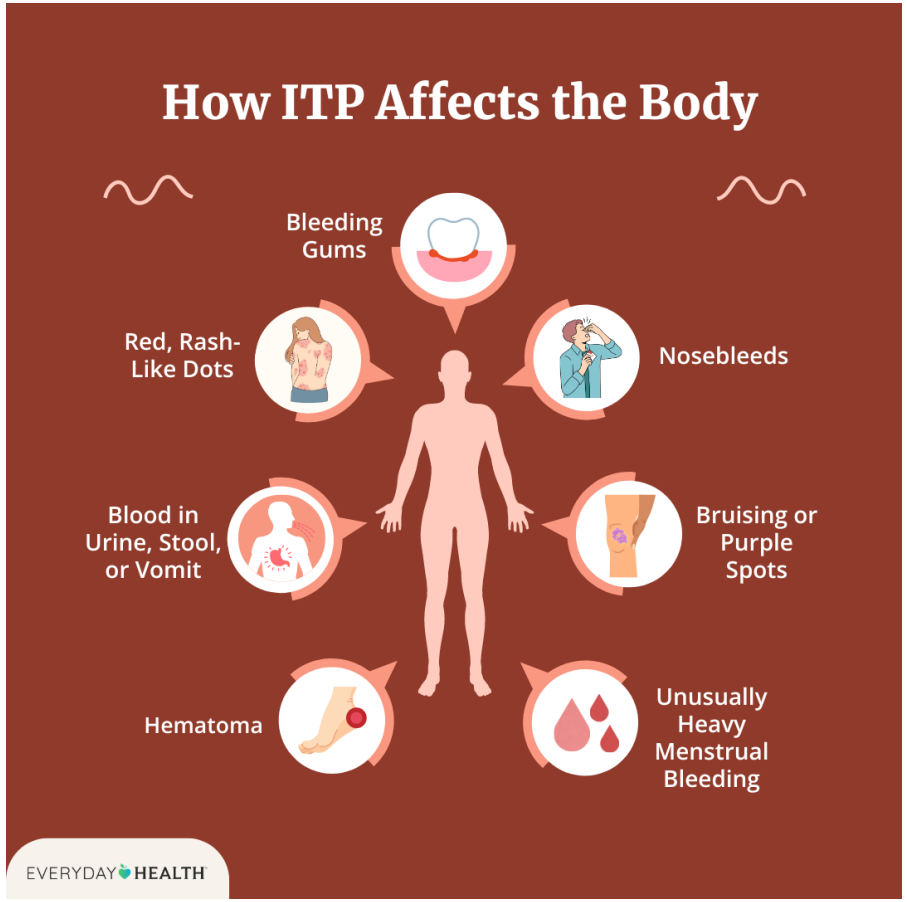

Figure 4: Organs Affected By ITP

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Complications of ITP

- Patients with ITP are at increased risk of bleeding complications.
- Long-term use of corticosteroids and immunosuppressive agents while treating ITP carries risks of infections, and other adverse effects. Splenectomy carries increased risk of pneumococcal infections.
- Most fatal complication is severe hemorrhage, with a mortality rate of 1% in children and 5% in adults.

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Treatment of ITP

- Corticosteroids are first-line therapy for acute management to suppress immune response.
- Second-line treatments include immunosuppressive agents like rituximab, thrombopoietin receptor agonists (TPO-RA), and splenectomy for refractory cases.
- Supportive care includes platelet transfusions and antifibrinolytic agents for bleeding episodes.
    - Controlling severe hemorrhage requires platelet transfusion, dosage of 4-6 U of platelet concentrate (should raise Plt count by 100-150K)
        - Outpatient: appropriate if Plt >20K and patient remains asymptomatic
        - Inpatient: If Plt <20K or if active bleeding.

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Thrombosis in ITP

- While not intuitive, thrombocytopenia from ITP does not prevent thrombosis from occurring as risk for thrombosis is increased as well.
  - pathogenesis is not well understood:
    - may involve increased platelet activation and aggregation
    - May be due to inflammation
    - Antiphospholipid antibodies in some patients
    - Effects of treatments: (steroids, splenectomy, Thrombopoietin receptor agonists)
    - There have been cases of ITP following both the COVID-19 infection as well as the vaccination, the demographics and outcome of COVID-19 infection-associated ITP may differ from COVID-19 mRNA vaccine-associated ITP.

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Thrombosis Management in ITP

- Must balance between preventing further thrombotic events and avoiding bleeding complications.
  - Anticoagulation remains the cornerstone of treatment for thrombotic events in ITP patients, irrespective of their platelet count
    - Low molecular weight heparin or direct oral anticoagulants are often used with care monitoring for bleeding
    - Some treatments of ITP can increase risk of thrombosis as well, so balancing is important in treating ITP itself and in treating thrombotic events in ITP patients.

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Conclusion

ITP is an immune disorder targeting the membrane glycoproteins of platelets, and is not very well understood in terms of pathogenesis. While it is a disorder causing excess bleeding, it still causes an increased risk of thrombosis. Treatment of thrombosis depends upon the severity of ITP.

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References

1. https://my.clevelandclinic.org/health/diseases/5726-immune-thrombocytopenia
2. https://www.ccjm.org/content/88/12/664#:~:text=Outpatient%20management%20can%20be%20considered%20for%20patients%20with%20a%20platelet,or%20epistaxis%20on%20nose%2Dblowing.
3. https://emedicine.medscape.com/article/779545-clinica
4. https://www.uptodate.com/contents/immune-thrombocytopenia-itp-in-adults-clinical-manifestations-and-diagnosis?csi

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