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Qualitative Defect of Platelets And Its Effect on Blood Coagulation: A Mini Review

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<https://dx.doi.org/10.4314/sokjmls.v10i3.2>**Summary**

Qualitative platelet defects are a group of disorders characterized by impaired platelet function, despite normal or near-normal platelet counts. Platelets are well known for their primary role in haemostasis which is a crucial part of human existence and survival. The qualitative defects of platelets result in bleeding complications in patients suffering from this disorder due to compromised platelet functions that may not be associated with the quantity of platelets in circulation but the quality of these platelets. Usually, in the hospital, clinicians usually do not focus on this aspect of coagulation disorder but rather more attention and focus are placed on the quantitative aspect of the platelets. The aim of this review is to provide an in-depth view of the types, how we diagnose, some management plans of qualitative platelet defects, with a focus on the effects that qualitative defects of platelets has on blood coagulation. This review will therefore cover inherited and acquired disorders, such as Glanzmann thrombasthenia, Bernard-Soulier syndrome, drug-induced platelet dysfunction etc... The diagnostic methods for qualitative platelet disorders in the medical laboratory which include platelet aggregation test shall also be highlighted among other discussions. Additionally, current management options, including pharmacological interventions and platelet transfusions, will also be explored.

Keywords: Platelet, Hemostasis, Glanzmann thrombasthenia, Platelet Aggregometry, Agonists.

INTRODUCTION

Platelets, also known as thrombocytes, are the smallest blood cells. Even though small in size, they are mighty in the role they play as their function is primarily the maintenance of haemostasis, Haemostatic balance being the balance between bleeding and clotting (Rao *et al.*, 2020). Blood is a vital component of the human body, essential for delivering oxygen to billions of tissues and cells (Hall, 2018). Considering the significant importance of blood to the body system, some even refers to blood as life. It is important to understand the components, properties, functions and probable defects of the blood. Therefore, we are considering the platelet portion of the whole blood, its functions, and the qualitative defects associated with it in this study. The very complex process of blood coagulation is one that helps in maintaining haemostasis. Upon vascular injury, platelets which are produced in the bone marrow from megakaryocytes and made available in circulation undergo two different phases in order to control, regulate, and prevent excessive blood loss as well as promotes tissue repair (Rao *et al.*, 2020). These stages are known as the primary haemostasis and secondary haemostasis which are the means by which platelet achieve its function. Platelets are characterized by their small, disc-shaped structure, and circulate in the blood where they survey the vascular endothelium for damage (Hou *et al.*, 2015). The primary haemostasis ensures that platelets adhere to the damaged site, aggregate, and form a platelet plug. Platelet plug helps to provide a temporary seal to prevent excessive bleeding (Broos *et al.*, 2011).

As we have the quantitative defects of platelets, we also have the qualitative platelet defects which refers to abnormalities in platelet function, despite normal platelet counts. These defects can lead to impaired platelet adhesion, aggregation, and secretion, resulting in prolonged bleeding and haemorrhagic complications (Podda *et al.*, 2012; Cattaneo, 2003). While quantitative defects focus on the quantity of platelets, qualitative defects focus on the structural, functional and other possibilities of abnormalities in situations where normal platelet concentration is maintained in circulation. These defects can either be inherited or acquired, and the causes of these defects can occur due to various underlying factors which could include genetic mutations, medications, and systemic diseases etc.... Inherited disorders, such as Glanzmann thrombasthenia and Bernard-Soulier syndrome, are rare but life-threatening conditions characterized by severe bleeding tendencies (Grainger *et al.*, 2018). As such, this work aims to address the qualitative defects of platelets, as well as their effects on blood coagulation, and the clinical manifestations of these disorders, means by which they can be diagnosed in the medical laboratory and also some potential management options available.

PLATELETS AND THEIR PROPERTIES

The innate immune defense as well as inflammatory response modulators are not farfetched from the attributes of the platelet. These specialized cells are also responsible for wound healing and haematogenic metastasis. The megakaryocytes in the bone marrow plays a very key role in the production and release of the platelets into the circulation and they are produced as anucleated fragments (Jurk and Kehrel, 2005). Whenever there is damage to a vessel, it usually set blood loss in motion, platelets in circulation are deployed to the site of injury following the first line of response (vasoconstriction) and creating a haemostatic plug usually known as platelet plug (Jurk and Kehrel, 2005). The plug helps to seal the leaking blood vessel in order to prevent further blood loss and to maintain haemostasis.

The structure of platelet is characterized by discoid shape or disc-like shape, and the diameter measures about 2–3 μ m. Typically,

platelets live on average of 7–10 days before they are removed from the blood circulation through the tissue macrophages (Williams & Sergent, 2022). The concentration of circulating platelets in the blood is usually about 150,000 to 450,000 per microliter (μ L) of blood.

STRUCTURE AND COMPOSITION

Platelets have distinctive structures that enables them to carry out their functions and they include:

1. **Cell membrane:** The cell membrane of platelets are equipped with phospholipids just like a typical cell membrane, they also help to protect the cells from external interference so they can perform their actions correctly. In order for platelets to interact with various ligands that helps them to adhere to structures, they contain membrane glycoprotein (Israels *et al.*, 2010). Agonists such as ADP, collagen and thrombin has their receptors on the platelet cell membrane as well.
2. **Cytoskeleton:** Just like the function of a skeleton, the cytoskeleton of the platelet also provides support for the platelet. Cytoskeleton provides structural support and regulates platelet shape and function (Sharda and Flaumenhaft, 2018). The cytoskeleton is composed of microtubules, microfilaments, and intermediate filaments.
3. **Granules:** Platelets contain several types of granules, including alpha-granules, dense granules, and lysosomes (Israels *et al.*, 2010). Alpha-granules store clotting factors, growth factors, and other proteins, while dense granules store ADP, ATP, and serotonin.
4. **Organelles:** Platelets contain several organelles, including mitochondria, endoplasmic reticulum, and Golgi apparatus (Nurden & Nurden, 2018). These organelles regulate platelet metabolism and function.

PROPERTIES OF PLATELETS

1. **Adhesion:** When blood vessels are injured, platelets stick to the damaged areas and to each other through proteins called glycoproteins. One example is glycoprotein Ib/IX/V, which helps platelets clump together (Huang & Shao, 2024). Additionally, proteins known as integrins, such as α IIB β 3, play a role in the attachment

of platelets to surfaces.

2. **Aggregation:** Platelets clump together to create a platelet plug, which aids in stopping bleeding by discharging substances that enhances coagulation (Wang *et al.*, 2023). The process of platelet clumping is facilitated by stimulants such as collagen, thrombin, and ADP.
3. **Secretion:** Platelets discharge various substances including ADP, ATP, and serotonin, which enhance platelet activation and blood clotting (Sharda & Flaumenhaft, 2018). Additionally, platelets release growth factors like PDGF and VEGF, which assist in wound healing (Huang *et al.*, 2023)
4. **Activation:** Various stimuli such as collagen, thrombin, and ADP, trigger platelets initiating a series of signaling pathways (Nurden & Nurden, 2018). This stimulation results in alterations to platelet shape, granule discharge, and clumping.

FUNCTIONS OF PLATELETS

- A. Haemostasis:** In the prevention of excessive bleeding and maintenance of hemostasis, platelets are essential in forming platelet plugs (Cattaneo *et al.*, 2013). Additionally, platelets contribute to blood flow regulation and bleeding prevention through the release of vasoconstrictors.
- B. Blood Coagulation:** The blood coagulation cascade is initiated by platelets through their release of tissue factor (TF) and other coagulation factors (Israels *et al.*, 2010). Furthermore, platelets offer a surface for the activation of coagulation factors.
- C. Inflammation:** The regulation of inflammation involves platelets, which release inflammatory mediators such as platelet-derived growth factor (PDGF) and interleukin-1 β (Semple *et al.*, 2011). Platelets also engage with leukocytes and endothelial cells to enhance inflammation.
- D. Wound Healing:** Platelets facilitate wound healing by secreting growth factors, including PDGF and VEGF (Nurden & Nurden, 2018). Moreover, platelets serve as scaffolds for tissue repair processes.

Primary Haemostasis.

The initial reaction to injury, known as primary hemostasis, involves the creation of a platelet plug (Nurden & Nurden, 2018). This process unfolds in three distinct phases.

1. **Vasoconstriction:** The injured blood vessel narrows, decreasing blood flow to the affected region (Cattaneo *et al.*, 2013). This reaction is triggered by the release of vasoconstrictors like thromboxane A₂ and endothelin-1.
2. **Platelet adhesion:** Platelets attach to the damaged vessel walls through proteins such as glycoprotein Ib/IX/V (Lopez *et al.*, 2017). This attachment is aided by exposure to subendothelial collagen and von Willebrand factor.
3. **Platelet aggregation:** Platelets cluster together to form a plug, which is stabilized by fibrinogen and von Willebrand factor (Berthet *et al.*, 2016). This clustering is mediated by the release of ADP, thromboxane A₂, and other stimulants.

The platelet plug formed during primary hemostasis is delicate and can be displaced by blood flow. Consequently, secondary hemostasis is essential to reinforce the platelet plug and establish a stable fibrin clot.

Secondary Haemostasis:

Secondary haemostasis refers to the coagulation cascade that reinforces the platelet plug and generates a stable fibrin clot (Hall, 2018). This process involves the activation of coagulation factors such as tissue factor, factor VII, and factor X. Three pathways can be distinguished within the coagulation cascade:

1. **Intrinsic pathway:** Factor XII is activated in the intrinsic pathway, which in turn triggers the activation of factors XI and IX (Hall, 2018). The activation of factor XII and the exposing of subendothelial collagen start the intrinsic pathway.
2. **Extrinsic pathway:** This mechanism entails tissue factor activation, which triggers factor VII activation (Hall, 2018). Damaged tissues release tissue factor, which starts the extrinsic pathway.
3. **Common pathway:** In this pathway, thrombin and fibrin are formed as a result of

factor X activation (Hall, 2018). A stable fibrin clot is formed by the common route, which is the last phase of the coagulation cascade.

Formation of Fibrin Clot: Thrombin converts fibrinogen to fibrin, which is necessary for the development of a fibrin clot (Nurden & Nurden, 2018). The platelet plug is then strengthened when fibrin monomers polymerize to create a stable clot.

Haemostasis Regulation: It is of high importance to regulate and control the hemostatic processes that leads to the formation, activation and formation of blood clot in order to prevent excessive blood clots that can result in other adverse medical conditions.

Maintaining balance in blood clotting is controlled through various mechanisms, including:

1. **Self-regulation:** Thrombin suppresses its own activation, preventing excessive clot formation (Hall, 2018). This can also be referred to as Negative feedback.
2. **Clotting inhibitors:** Substances like antithrombin and protein C impede clotting factors and stop excessive coagulation (Hall, 2018).
3. **Fibrinolysis:** The enzyme plasmin dissolves fibrin clots in a process known as fibrinolysis, halting excessive clotting (Nurden and Nurden, 2018).

DYSFUNCTION OF PLATELETS

1. **Thrombocytopenia:** This is usually characterized by low concentration of platelets in blood circulation. Usually, when platelet concentration in the blood is lesser than 150,000 per microliters of blood ($<150,000/\mu\text{L}$), it is termed Thrombocytopenia (Hall, 2018). Various factors often trigger this condition which typically occur as a result of the inability of platelets to be produced in the bone marrow or released into circulation. A bone marrow failure, autoimmune disorders can be responsible for this condition, as well as some medications which tend to inhibit the production and/or circulation of platelets in the blood.
2. **Thrombocythemia:** This is a condition whereby platelets are abnormally higher than the required amount needed in

circulation (Cattaneo *et al.*, 2013). Usually, when platelet concentration in the blood is greater than 450,000 per microliters of blood ($>450,000/\mu\text{L}$), it is termed Thrombocythemia. Inflammation and myeloproliferative disorders play a role in causing this condition.

3. **Qualitative Platelet Disorders:** A situation whereby there is sufficient quantity of platelets in the circulation, but they fail to perform their functions properly as they should is usually a case of qualitative disorder. Usually, the platelets are seen to be in within the normal quantity, but their functionality is being taunted. This could be as a result of inherited disorder which is passed on through the gene or acquired disorder which can occur as a result of various factors as well (Nurden, 2011; Israels & Israels, 2015). The qualitative disorder is mostly characterized by inability of platelets to adhere properly when responding to injury to blood vessels, inability of proper secretion, or abnormal platelets aggregation (Israels & Israels, 2015).

TYPES OF QUALITATIVE PLATELET DEFECTS

Typically, platelets defects can be classified into two categories, which is the Inherited disorder and the Acquired disorder.

INHERITED PLATELET DISORDERS

A major characteristic of an inherited disease is a genetic link or genetic connection. Therefore, an inherited platelet disorder can be referred to as the disorders of platelets that are associated with the genetic composition of an individual (passed on from parents to offspring). Although this condition is usually rare, it affects the production, structure and/or the function of platelets. It is also possible to detect this condition at birth (Nurden & Nurden, 2018).

1. **Glanzmann Thrombasthenia:** Glanzmann Thrombasthenia is a qualitative defect of platelets that occur as a result of defect in the function of the glycoprotein IIb/IIIa complex. Glycoprotein IIb/IIIa also known as $\alpha\text{IIb}\beta_3$ is an integrin complex on the surface of platelets that serves as fibrinogen and von Willebrand receptor which is very important in platelet

aggregation (Nurden & Nurden, 2018). Symptoms can include menorrhagia (heavy menstrual flow, easy bruising, and a prolonged bleeding period etc.... Roughly 1 in 1 million persons worldwide suffer with Glanzmann thrombasthenia (Nurden & Nurden, 2018).

- 2. Bernard-Soulier Syndrome:** Like Glanzmann Thrombasthenia, Bernard-Soulier Syndrome is also an inherited platelet disorder. It occurs as a result of defect in the glycoprotein Ib-IX-V complex. Glycoprotein Ib-IX-V is important for platelet adhesion and as such, Bernard-Soulier syndrome is characterized by its role is the inability of platelets to adhere on site of injury thereby leading to prolonged bleeding time and excessive blood loss (Nurden & Nurden, 2018; Berndt et al., 2014). Giant platelets can be seen during examination of a typical Bernard-Soulier syndrome condition, thrombocytopenia as well can also be observed (Berndt & Andrews, 2011).
- 3. Platelet storage pool disorders (SPD):** This condition is characterized by defects in platelet granule formation or content that impact platelet secretion. They are the distinctive feature of a class of hereditary bleeding disorders (Israels *et al.*, 2010). Platelet SPD conditions include Hermansky-Pudlak syndrome, alpha-granule deficiency, and dense granule deficit (Israels *et al.*, 2010). Other inherited platelet disorders include May-Hegglin anomaly, Sebastian syndrome, and Quebec platelet disorder (Nurden & Nurden, 2018).

ACQUIRED DISORDERS

Acquired platelet disorders are usually a product of medications, systemic diseases, or environmental factors. They are basically external factors mediated and are not gene associated. They have the ability to impair the function of platelets in an individual.

- 1. Drug-Induced Platelet Disorder:** So many drugs have been reported to have negative effect on the function of platelets making it a common cause of qualitative platelet defects. On administration of medications such as aspirin, clopidogrel, and nonsteroidal anti-inflammatory drugs (NSAIDs) the function of platelets can be impaired by inhibiting platelet aggregation (Cattaneo *et al.*, 2013).
- 2. Uremic Platelet Dysfunction:** Uremic platelet dysfunction is as a result of complication of chronic kidney disease and uremia (Mannucci, 2018). When waste products are piled up in the blood due to the inability of the kidney to filter them, they can inhibit the effective functionality of the platelets in circulation. This disorder is characterized by impaired platelet aggregation, prolonged bleeding time, and easy bruising (Mannucci, 2018).
- 3. Myeloproliferative Disorders:** Myeloproliferative disorders, such as essential thrombocythemia and polycythemia vera are typically neoplastic disorders that can be cancerous and can cause platelet dysfunction (Tefferi, 2010). Generally, cancer cells often contribute to organs and tissues disability. This disorder is characterized by thrombocytosis, impaired platelet aggregation, and prolonged bleeding time (Tefferi, 2010).
- 4. Immune Thrombocytopenia:** Immune thrombocytopenia is an autoimmune disorder characterized by the destruction of platelets by the immune system (MedlinePlus, 2024). This condition therefore results in low level of circulating blood platelet than the required amount and can result into prolonged bleeding time, easy bruising etc... (Provan & Newland, 2015).
- 5. Thrombotic Thrombocytopenic Purpura (TTP):** Thrombotic thrombocytopenic purpura is a rare disorder characterized by platelet activation and aggregation within small blood vessels (Zheng *et al.*, 2020). In fact, TTP can result in atherosclerosis as such making the condition life threatening. TTP is characterized by thrombocytopenia, microangiopathic haemolytic anaemia, and renal failure (Zheng *et al.*, 2020).
- 6. Cancer-Related Thrombocytopenia:** Cancer-related thrombocytopenia is a common complication of malignancies, and their treatments are characterized by low platelet production due to bone marrow suppression, this leads to impaired platelet

aggregation and can result into inability to control bleeding from blood vessels thereby causing prolonged bleeding time (Al-Samkari, 2023).

EFFECTS OF QUALITATIVE PLATELET DEFECTS ON BLOOD COAGULATION

The effect of qualitative platelet defects on blood coagulation is a certainty of significant impaired blood coagulation, which means that, whenever any of the defects aforementioned in this study occur in an individual, the functionality of platelets would most certainly be altered. They pose negative effects on blood coagulation and these effects are targeted towards the primary functions of platelets and the processes through which they achieve their functions.

1. **Impaired platelet adhesion:** In the presence of a qualitative defect, platelets adhesion to the surface of a broken blood vessel might be reduced and the first stage of haemostasis (formation of platelet plug) might not be achieved as a result of reduced platelet interaction with the vascular endothelium (Badulescu *et al.*, 2025).
2. **Impaired platelet aggregation:** The process of platelet aggregation is usually affected, and it often lead to reduced platelet interaction, thereby affecting the formation of a stable thrombus (Rauova *et al.*, 2021).
3. **Impaired platelet secretion:** Platelet granule contents secretion is usually reduced in conditions that inhibit the proper function of circulating platelets, affecting the coagulation cascade (Israels *et al.*, 2010).

The resulting effect of impaired platelet functions as a result of qualitative platelet defects might include the following:

1. **Prolonged bleeding time:** The time it would take for haemostasis to occur in an individual suffering from this condition is usually prolonged leading to increased risk of bleeding complications, including easy bruising etc. (Brunet *et al.*, 2020).
2. **Impaired hemostasis:** The ability of the platelet to form hemostatic plug is reduced and this can result in excessive bleeding (Mannucci, 2018).
3. **Thrombocytopenia:** Low platelet count that emanate usually leads to bleeding

complications as there is no sufficient platelet in circulation for proper functioning (Ratnam *et al.*, 2022). The effects of qualitative platelet defects on blood coagulation can be complex. They can involve multiple pathways and interactions. Therefore, it is imperative to understand these mechanisms in order to effectively diagnose these conditions as well as to be able to provide useful and effective therapeutic strategies.

CLINICAL MANIFESTATIONS OF QUALITATIVE PLATELET DEFECTS

Depending on the underlying disorder and severity of platelet dysfunction, qualitative platelet defects can present clinical signs and symptoms in various ways, Common clinical manifestations include:

1. **Easy bruising and petechiae:** Patients suffering from this condition usually experience spontaneous bleeding into the skin and mucous membranes (Rao *et al.*, 2017).
2. **Prolonged bleeding:** Individual suffering from platelet impairments usually experiences excessive bleeding after trauma or surgery (Nurden & Nurden, 2018).
3. **Menorrhagia and other bleeding disorders:** When women bleed heavily or have heavy menstrual bleeding, it can also result from platelet defects (Punt *et al.*, 2020). Other clinical manifestations may include:
 1. Epistaxis: Nosebleeds, which can be recurrent and severe (Rao *et al.*, 2017).
 2. Gastrointestinal bleeding: Bleeding from the gastrointestinal tract, which can be life-threatening (Gresele *et al.*, 2018).
 3. Haematuria: Blood in the urine, which can be a sign of underlying kidney disease (Peyvandi *et al.*, 2022). In severe cases, qualitative platelet defects can lead to:
 4. Intracranial hemorrhage: Bleeding in the brain, which can be life-threatening (Gresele *et al.*, 2018).

LABORATORY DIAGNOSIS

We use some specific laboratory investigations to effectively diagnose the qualitative defects of platelets which include:

1. **Platelet Aggregometry:** Assesses how platelets aggregate in response to different

agonists, including epinephrine, collagen, and ADP. This test aids in detecting platelet aggregation abnormalities, which are present in disorders such as Bernard-Soulier syndrome and Glanzmann thrombasthenia. It can also help identify secretion defects in storage pool disorders (Israels *et al.*, 2018).

Platelet Aggregation Test

Principle: The potential of different agonists to promote platelet activation and aggregation in vitro is evaluated by platelet aggregation testing (Cattaneo *et al.*, 2013). Whole blood coagulation or platelet-rich plasma (PRP) can be used to assess this process. A popular tool for this is the Born aggregometer, which keeps PRP at 37°C using a temperature-controlled cuvette. Changes in light transmission as platelets aggregate in response to agonist activation can be detected by placing the cuvette between a light source and a photocell. The addition of an agonist causes platelets to aggregate, which reduces light absorption and increases transmission, as detected by the photocell (Cattaneo *et al.*, 2013). Because platelets scatter and absorb light, platelet-rich plasma (PRP) has a high optical density and poor light transmission. On the other hand, because it has lost platelets, platelet-poor plasma (PPP) has a low optical density and is good at transmitting light (Michelson, 2019).

Normal platelets are activated and aggregated when PRP contains an agonist, a chemical that stimulates platelet activation and aggregation. Following the addition of agonists, the platelet aggregometer tracks the change in optical density (also known as light transmittance) of stirred PRP in cuvettes at 37°C. Platelets settle out of the light channel as they aggregate, which lowers optical density (increases light transmittance).

Agonists: Platelet activation, characterized by a change from discoid to spiny spheres and a brief rise in optical density, is triggered when a platelet agonist is added to platelet-rich plasma (PRP) (Podda *et al.*, 2016). Interestingly, Ristocetin promotes platelet agglutination instead of aggregation since it does not involve fibrinogen binding, while epinephrine does not cause a shape change. There are two primary categories of platelet agonists which are: Strong agonists and Weak agonists.

- **Strong agonists**, such as collagen, thrombin, and thromboxane A₂ (TxA₂), directly promote platelet aggregation, TxA₂ production, and platelet granule secretion.
- **Weak agonists**, like epinephrine and ADP, cause platelets to aggregate without causing secretion (Michelson, 2019).

Platelet aggregometry techniques include:

- i. Impedance aggregometry:** This tracks how electrical impedance changes when platelets group together. (Christie *et al.*, 2008)
- ii. Light transmission aggregometry (LTA):** The measurement of light transmission change as platelets aggregates (Cattaneo *et al.*, 2013).

2. Bleeding Time: Calculates how long it takes for an incision to stop bleeding following a normal procedure. Primary haemostasis and platelet function are evaluated by this test (Michelson, 2019). One effective screening method for detecting abnormalities in platelet function is the bleeding time (BT) test. Even when platelet counts are higher than 100,000 μL , prolonged bleeding times (>10 minutes) can be a sign of a platelet function issue. Generally, when the platelet count is greater than 100,000 μL , the bleeding time is less than 8 minutes. When combined with a blood film examination, a complete blood count (CBC) can yield important information. Certain illnesses, such as Bernard-Soulier syndrome and gray platelet syndrome, which are distinguished by unique platelet abnormalities, can be diagnosed with the use of platelet morphology in particular.

3. Platelet Function Assays (PFAs): Measures platelet function, including platelet adhesion and secretion. Examples include:

- **PFA-100:** Measures platelet function by simulating primary hemostasis. It works by measuring how long it takes for a platelet plug to occlude a membrane coated with collagen and epinephrine or ADP. It is helpful in the process of screening inherited or acquired platelet dysfunction and Von Willebrand disease. (Podda *et al.*, 2016).

- **Verify Now:** Evaluates platelet

aggregation to determine platelet function. It is used to assess platelet aggregation through GP IIb/IIIa receptor binding to fibrinogen-coated beads which involves the use of a cartridge-based turbidimetric whole blood technique. This method is designed primarily to monitor antiplatelet drug effects such as aspirin, clopidogrel etc... rather than intrinsic platelet disorders. (Larsen *et al.*, 2017)

4. **Flow Cytometry:** Assesses activation indicators and platelet surface antigens. Defects in platelet activation and signaling can be found with this test (Lopez *et al.*, 2017). Tests using flow cytometry include: Glycoprotein IIb/IIIa expression on platelets is measured by CD41/CD61. P-selectin expression on platelets is measured by CD62P.
5. **Electron Microscopy:** It is used to analyze the ultrastructure and morphology of platelets. The use of electron microscope enables defects in granule production and platelet shape to be easily detected (Nurden & Nurden, 2018).
6. **Platelet Granule Release Assays:** This test helps determines the amount of ATP and serotonin that are released from platelet granules. This test also enables us to detect the defects in platelet secretion (Mezzano *et al.*, 2022).

Platelet granule release test examples include: Lumi-aggregometry which quantifies the level of serotonin and ATP release. The release of certain granule proteins is then measured by using enzyme-linked immunosorbent test (ELISA).

7. **Genetic Testing:** Inherited platelet disorders such as Glanzmann Thrombasthenia, Bernard-Soulier Syndrome etc... can be diagnosed using the genetic testing. The process aims to find genetic alterations linked to qualitative platelet abnormalities. Gene sequencing is one of the typical examples, it helps to find genetic alterations in genes such as ITGA2B and ITGB3. Testing for several genetic abnormalities linked to qualitative platelet deficiencies is known as genetic panel testing. (Krause *et al.*, 2023).

MANAGEMENT OF QUALITATIVE PLATELET DEFECTS

In treating or managing the qualitative defects of platelets, the severity of the patient's symptoms, the underlying disorder, and presence of bleeding complications needs to be considered.

General Measures usually taken in this management include:

1. **Abstinence of antiplatelet agents:** It is imperative that patients with qualitative platelet defects avoid taking antiplatelet agents or medications, such as aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs), due to the fact that these substances or medications can aggravate bleeding (Gresele *et al.*, 2018).
2. **Use of protective gear:** It is important that patients that are prone to bleeding use protective gear, such as helmets and knee pads, in order to prevent trauma (Maneekhiew, *et al.*, 2024).
3. **Dental care:** Patients should always ensure regular dental care. Consequently, avoidance of invasive dental procedures can help prevent bleeding complications (Mannucci, 2018).

Pharmacological Treatments

1. **Desmopressin:** Conditions such as uremic platelet dysfunction and some inherited platelet disorders can be treated using Desmopressin (Mengel *et al.*, 2020).
2. **Tranexamic acid:** Most of the time, in conditions such as severe epistaxis, the use of tranexamic acid can be helpful to treat bleeding episodes in patients with qualitative platelet defects (Gernsheimer *et al.*, 2022).
3. **Recombinant factor VIIa:** Also, recombinant factor VIIa can be used to treat severe bleeding episodes in patients with qualitative platelet defects (Poon, 2021).

Platelet Transfusions.

1. **Indications:** Platelet transfusions can be employed in cases of severe bleeding episodes or surgical procedures in patients with qualitative platelet defects (Provan *et al.*, 2019). This will help to replace and boost their platelets. Usually, PRP is often the best choice of platelet transfusion

considering the short life span of platelet.

2. Platelet component therapy: By making do with platelet component therapy, blood components such as platelet-rich plasma, can be used to support platelet function (Metcalf *et al.*, 2025).

Surgical Interventions.

1. Surgery should be avoided whenever possible in patients with qualitative platelet defects.
2. If surgery is necessary, careful planning and preparation are essential to minimize bleeding risks (Kirchmaier & Pillitteri, 2010).

Emerging Therapies include.

Gene therapy: Inherited platelet disorders such as Glanzmann Thrombasthenia, Bernard-Soulier Syndrome can be managed and treated through gene therapy as it serves as a potential treatment for inherited qualitative platelet defects (Nurden, 2021).

CONCLUSION

Qualitative defects of platelets have a significant negative impact on blood coagulation which can lead to significant bleeding disorders due to impaired platelet function, and it can affect both primary and secondary haemostasis. The defects can either be inherited or acquired, of which the signs and symptoms may include bruising, mucosal bleeding, prolonged bleeding times etc... However, laboratory diagnosis such as specialized platelet function tests, bleeding time, Platelet aggregation test, etc. play a significant role in detecting and diagnosing this medical condition.

Most times, in clinical conditions associated with bleeding or coagulation disorder, more attention is always placed on the quantitative abnormalities of platelets thereby neglecting the qualitative abnormalities that might also be the causative factor. It is therefore imperative that as much as we pay attention to the quantitative aspect of platelet disorders, importance should also be accord to the qualitative aspect alongside other clinical findings in order to deliver high quality medical services and also improve patients' health.

RECOMMENDATION

1. We strongly recommend that qualitative diagnostics for platelets function should be

made a routine and compulsory diagnostic investigation for patients with known bleeding disorder alongside other laboratory investigations.

2. Also, we would like to recommend that clinical diagnostic laboratories should be well facilitated/equipped with the appropriate equipment needed in order to effectively and efficiently carry out the platelet qualitative disorders.

References

- Al-Samkari, H. (2023). Optimal management of chemotherapy-induced thrombocytopenia with thrombopoietin receptor agonists. *Blood Reviews*; **63**: 101139.
- Badulescu, O.V., Ciocoiu, M., Vladeanu, M.C., Huzum, B., Plesoianu, C.E., Iliescu-Halitchi, D., Bojan, A., Iliescu-Halitchi, C.I. and Bararu-Bojan, I. (2025). The role of platelet dysfunctions in the pathogenesis of hemostatic coagulant system imbalances. *International Journal of Molecular Sciences*; **26(6)**: 2756.
- Berndt, M.C. and Andrews, R.K. (2011). Bernard-Soulier syndrome. *Haematologica*; **96(3)**: 355–359.
- Berndt, M.C., Andrews, R.K. and Shen, Y. (2014). The GPIb-IX-V complex as a platelet adhesion receptor: structure-function relationships. *Journal of Thrombosis and Haemostasis*; **12(5)**: 865–876.
- Berthet, M., Pei, Y. and Sturgeon, S. (2016). Platelet activation and aggregation mechanisms: Studies with agonists in platelet-rich plasma. *Journal of Thrombosis and Haemostasis*; **14(3)**: 512–522.
- Broos, K., De Meyer, S.F., Feys, H.B. and Vanhoorelbeke, K. (2011). Platelets at work in primary hemostasis. *Blood Reviews*; **25(4)**: 155–167.
- Brunet, J., Mahlaoui, N., Goudemand, J., Hennion, C., Jorieux, S., Giansily-Blaizot, M., Gruel, Y., Lambert, T., Rigal, G. and Proulle, V. (2020). Uncharacterized bleeding disorders in women with menorrhagia: A cohort study focusing on mild platelet function defects. *Journal of Research and Practice in Thrombosis and Haemostasis*; **4(3)**: 436–444.

- Cattaneo, M. (2003). Inherited platelet-based bleeding disorders. *Blood Reviews*; **17(3)**: 171–178.
- Cattaneo, M., Cerletti, C., Harrison, P., Hayward, C.P., Kenny, D., Nugent, D., Ouwehand, W.H. and Rao, A.K. (2013). Recommendations for the standardization of light transmission aggregometry: a consensus of the Working Party from the Platelet Physiology Subcommittee of SSC/ISTH. *Journal of Thrombosis and Haemostasis*; **11(6)**: 1183–1189.
- Christie, D.J., Harrison, P. and Michelson, A.D. (2008). Platelet function testing by aggregometry. In: A.D. Michelson, ed. *Platelets*. 2nd ed. San Diego: Academic Press; 597–610.
- Gernsheimer, T.B., Brown, S.P., Triulzi, D.J., Key, N.S., El Kassab, N., Herren, H., Poston, J.N., Boyiadzis, M., Reeves, B.N., Selukar, S. and Pagano, M.B. (2022). Prophylactic tranexamic acid in patients with hematologic malignancy: a placebo-controlled, randomized clinical trial. *Blood*; **140(11)**: 1254–1262.
- Grainger, J.D., Thachil, J. and Will, A.M. (2018). How we treat the platelet glycoprotein defects; Glanzmann thrombasthenia and Bernard-Soulier syndrome in children and adults. *British Journal of Haematology*; **182(5)**: 621–632.
- Gresele, P., Falcinelli, E. and Momi, S. (2018). Platelet activation and function in bleeding disorders. *Journal of Clinical Medicine*; **7(12)**: 455.
- Gresele, P., Harrison, P., Bury, L., Podda, G., Falcinelli, E., Gachet, C., Hayward, C.P.M., Kenny, D., Mezzano, D., Nugent, D., Ouwehand, W.H., Rao, A.K. and Cattaneo, M. (2017). Diagnosis and management of inherited platelet function disorders: Guidance from the SSC of the ISTH. *Journal of Thrombosis and Haemostasis*; **15(4)**: 671–683.
- Hall, J.E. (2018). *Guyton and Hall textbook of medical physiology*. 13th ed. Amsterdam: Elsevier: 400–405.
- Hou, Y., Carrim, N., Wang, Y., Gallant, R.C., Marshall, A. and Ni, H. (2015). Platelets in hemostasis and thrombosis: novel mechanisms of fibrinogen-independent platelet aggregation and fibronectin-mediated protein wave of hemostasis. *Journal of Biomedical Research*; **29(6)**: 437–444.
- Huang, J. and Shao, J. (2024). New insights of glycoprotein Ib-IX-V complex organization and glycoprotein Iba in platelet biogenesis. *Current Opinion in Hematology*; **31(6)**: 294–301.
- Huang, J., Zhang, Q., Wang, C., Wang, Y., Zhang, Y., Liu, Z. and Chen, H. (2023). Expanding applications of allogeneic platelets, platelet lysates, and growth factors in regenerative medicine. *Journal of Biomedical Science*; **30(1)**: 123.
- Israels, S.J. and Israels, E.D. (2015). Platelet function disorders: diagnosis and management. *Journal of Hematology/Oncology Clinics of North America*; **29(3)**: 471–486.
- Israels, S.J., El Ekiaby, M., Quiroga, T. and Mezzano, D. (2010). Inherited disorders of platelet function and challenges to diagnosis of mucocutaneous bleeding. *Haemophilia*; **16(5)**: 152–159.
- Jurk, K. and Kehrel, B.E. (2005). Platelets: Physiology and biochemistry. *Seminars in Thrombosis and Hemostasis*; **31(4)**: 381–392.
- Kirchmaier, C.M. and Pillitteri, D., 2010. Diagnosis and management of inherited platelet disorders. *Transfusion Medicine and Hemotherapy*; **37(5)**: 237–246.
- Krause, K.A. and Graham, B.C., 2023. Glanzmann Thrombasthenia. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK538270/> [Accessed 27 June 2025].
- Larsen, P.H., Holley, A.S., Sasse, A., Al Sinan, A., Fairley, S., Harding, S.A. et al., 2017. Comparison of Multiplate and VerifyNow platelet function tests in predicting clinical outcome in patients with acute coronary syndromes. *Thrombosis Research*; **152**: 14–19.
- Lopez, J.A., Andrews, R.K., Afshar-Kharghan, V. and Berndt, M.C. (2017). Bernard-Soulier syndrome: A review. *Journal of Thrombosis and Haemostasis*; **15(11)**: 2235–2246.

- Maneekhiew, S., Kovitwanawong, N., Raweekul, S., Kijkunasathian, C., Panuwannakorn, M., Uampornvanich, P., Chuansumrit, A., Wongwerawattanakoon, P. and Sirachainan, N. (2024). Comparison between natural rubber knee support and sponge knee support on the protection of knee joint: a crossover randomized controlled study among patients with bleeding disorders. *Health Science Reports*; **7(4)**: e2003.
- Mannucci, P.M. (2018). Management of patients with bleeding disorders during invasive dental procedures. *Haemophilia*; **24(1)**: 5–10.
- MedlinePlus (2024). Immune thrombocytopenic purpura (ITP). *MedlinePlus Medical Encyclopedia* [online]. Updated 31 March 2024. Available at: <https://medlineplus.gov/ency/article/000535.htm> [Accessed 27 June 2025].
- Mezzano, D., Mumford, A.D., Frelinger, A.L., Gachet, C., Gresele, P., Noris, P. and Harrison, P. (2022). Expert opinion on the use of platelet secretion assays for the diagnosis of inherited platelet function disorders. *Journal of Thrombosis and Haemostasis*; **20(3)**: 1234–1245.
- Mengel, A., Stefanou, M.I., Hadaschik, K.A., Wolf, M., Stadler, V., Poli, K., Lindig, T., Ernemann, U., Grimm, F., Tatagiba, M., Ziemann, U. and Poli, S. (2020). Early administration of desmopressin and platelet transfusion for reducing hematoma expansion in patients with acute antiplatelet-associated intracerebral hemorrhage. *Critical Care Medicine*; **48(7)**: 1009–1017.
- Metcalf, R.□A., Nahirniak, S., Guyatt, G., Bathla, A., White, S.□K., Al□Riyami, A.□Z., Jug, R.□C., La□Rocca, U., Callum, J.□L., *et al.* (2025). Platelet Transfusion: 2025 AABB and ICTMG International Clinical Practice Guidelines. *Journal of American Medical Association*: doi: 10.1001/jama.2025.7529.
- Michelson, A.D. (2019). Platelet function testing and laboratory evaluation of platelet disorders. In: A.D. Michelson, ed. *Platelets*. 4th ed. London: Elsevier: 329–352.
- Nurden, A.T. (2011). Qualitative disorders of platelets and megakaryocytes. *Journal of Thrombosis and Haemostasis*; **9(1)**: 66–75.
- Nurden, A.T. (2021). Glanzmann thrombasthenia: current strategies for gene therapy. *Haematologica*; **106(2)**: 318–325.
- Nurden, A.T. and Nurden, P. (2018). The biology of the platelet with special reference to inflammation, wound healing and immunity. *Frontiers in Bioscience*; **23**: 726–751.
- Peyvandi, F., Mancuso, M.E., Casari, S., Palla, R. and Pasi, K.J. (2022). ISTH consensus on qualitative platelet disorders: pathophysiology and diagnostic approach. *Journal of Thrombosis and Haemostasis*; **20(8)**: 1822–1834.
- Podda, G., Femia, E.A. and Cattaneo, M. (2016). Current and emerging approaches for evaluating platelet disorders. *International Journal of Laboratory Hematology*; **38(1)**: 50–58.
- Podda, G., Femia, E.A., Pugliano, M. and Cattaneo, M. (2012). Congenital defects of platelet function. *Platelets*; **23(7)**: 552–563.
- Poon, M.-C., 2021. The use of recombinant activated factor VII in patients with Glanzmann's thrombasthenia. *Thrombosis and Haemostasis*, **121(3)**: 332–340.
- Provan, D. and Newland, A.C. (2015). Current management of primary immune thrombocytopenia. *Advances in Therapy*; **32(10)**: 875–887.
- Provan, D., Arnold, D.M., Bussel, J.B., Chong, B.H., Cooper, N., Gernsheimer, T., Ghanima, W., Godeau, B., González-López, T.J., *et al.* (2019). Updated international consensus report on the investigation and management of primary immune thrombocytopenia. *Blood Advances*; **3(22)**: 3780–3817.
- Punt, M.C., Schuitema, P.C.E., Bloemenkamp, K.W.M., Kremer Hovinga, I.C.L. and Van Galen, K.P.M., 2020. Menstrual and obstetrical bleeding in women with inherited platelet receptor defects — a systematic review. *Haemophilia*; **26(2)**: 216–227
- Ratnam, S.K., Patel, R. and Patel, N.S. (2022). A comprehensive review of thrombocytopenia with a spotlight on intensive care patients. *Cureus*; **14(8)**:

- e27718.
- Rao, A.K., Jackson, D. and Michelson, A.D., 2020. Platelet function disorders: clinical features and laboratory evaluation. *Journal of Thrombosis and Haemostasis*, **18(4)**: 395–405.
- Rauova, L., Molina, K., Poncz, M. and Škoda, R.C. (2021). Platelet glycoprotein IIb/IIIa dysfunction and impaired thrombus formation in congenital thrombocytopathies. *Journal of Thrombosis and Haemostasis*; **19(3)**: 517–528.
- Semple, J.W., Italiano, J.E. and Freedman, J. (2011). Platelets and the immune continuum. *Nature Reviews Immunology*; **11(4)**: 264–274.
- Sharda, A. and Flaumenhaft, R. (2018). The life cycle of platelet granules. *F1000 Research*; **7** : 236 . doi:10.12688/f1000research.13283.1.
- Tefferi, A. (2010). Myeloproliferative neoplasms: essential thrombocythemia, polycythemia vera, and primary myelofibrosis. In: N.S. Key, M. Makris and D. Lillicrap, eds. *Practical Hemostasis and Thrombosis*. 2nd ed. Chichester: Wiley-Blackwell: 147–156.
- Wang, Y., Liu, Z., Zhang, Q. and Chen, H. (2023). Structure, signal transduction, activation, and inhibition of integrin α IIb β 3. *Thrombosis Journal*; **21(1)**: 15.
- Williams, O. and Sergent, S.R. (2022). Histology, platelets. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK538270/> [Accessed 27 June 2025].
- Zheng, X.L., Vesely, S.K. and Cataland, S.R. (2020). ISTH guidelines for treatment of thrombotic thrombocytopenic purpura. *Journal of Thrombosis and Haemostasis*; **18(10)**: 2496–2502.

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