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Comparison Of Red Cell Indices And Coagulation Profile In Thrombocytopenia Patients

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Abstract

Background: Thrombocytopenia is a common blood disorder that is characterized by a decrease in the number of platelets. In addition to this fall, patients tend to acquire red blood cell index variations and disruptions of their coagulation pattern. The changes are capable of affecting bleeding risk, severity of diseases, and clinical decision-making. But, there is not much local data telling about the variations of such parameters in different grades of thrombocytopenia of the Pakistani population.

Objective: To compare the red cell indices and coagulation parameters in patients with thrombocytopenia and to find out the relationship between change and the degree of platelet reduction.

Methodology: This cross-sectional research involved 100 patients who were diagnosed with thrombocytopenia and were selected in a number of diagnostic laboratories in Lahore. The sample was homogenous (52% men and 48% women). Measures were made of red cell indices (MCV,

MCH, MCHC) and of coagulation (PT, aPTT, INR, fibrinogen, D-dimer). Patients were clustered as per the level of platelet severity, and non-normal data distribution was observed, which necessitated the use of Kruskal-Wallis test.
Results: Red blood cell indices and coagulation parameters exhibited a notable varying result according to groups of thrombocytopenia degrees of severity ($p < 0.001$). Severe thrombocytopenic patients reported reduced MCV, MCH, and MCHC values, which were of a hypochromic and marginally microcytic nature. There was marked abnormality of coagulation markers, increased PT and aPTT, increased INR and D-dimer and significantly decreased fibrinogen levels. The trend of increased D-dimer and low fibrinogen was a good indication of continuing coagulopathy of consumption in the worst case scenarios.
Conclusion: The research points at the fact that the red blood cell indices and coagulation parameters decline proportionally to the decrease in the number of platelets. Severe thrombocytopenia can thus hardly exist on its own and most commonly indicates more hematological or inflammatory malfunction. These results support the importance of comprehensive hematological and coagulation examination of every patient with thrombocytopenia that is presented with the aim of diagnosing, properly monitored, and treated.

Introduction

A platelet count of less than 150 × 109/L is considered thrombocytopenia, a common clinical issue. However, many believe that a cutoff value of 100 × 109/L is more acceptable to diagnose clinically relevant thrombocytopenia.[1]

Primary hemostasis depends on platelets, and a low platelet count is clearly a major risk factor for bleeding.Therefore, bleeding is a common consequence and may be the reason for mortality in people with thrombocytopenia; however, bleeding does not always occur in thrombocytopenic patients.[2]

The contact between platelets and the vessel wall is known as primary hemostasis. Platelets are quickly involved in a series of functional responses at the site of vessel wall damage, including adhesion, spreading, shape change, aggregation, release reaction, exposure of a procoagulant surface, and clot retraction.The activated platelets create a hemostatic plug that blocks the site of injury to stop blood loss due to the quick development of these various abilities.[3]

Reduced platelet generation and accelerated platelet breakdown are the main causes of a lower platelet count. The BM failure syndromes (such as aplastic anemia, myelodysplastic syndromes, and chemotherapy-induced thrombocytopenia) are typical examples of the former, while disseminated intravascular coagulation (DIC) and thrombotic microangiopathies exhibit enhanced destruction.[4]

Numerous conditions, such as infections, certain drugs, autoimmune diseases, and blood problems, can result in thrombocytopenia. Bacterial or viral infections can cause the immune system to target platelets, destroying them. Thrombocytopenia can also be brought on by medications, such as blood thinners or certain antibiotics. Platelets may be inadvertently destroyed by the body as a result of autoimmune illnesses such as immune thrombocytopenic purpura (ITP). Furthermore, thrombocytopenia can also be caused by diseases such as liver disease, lymphoma, and leukemia.[5]

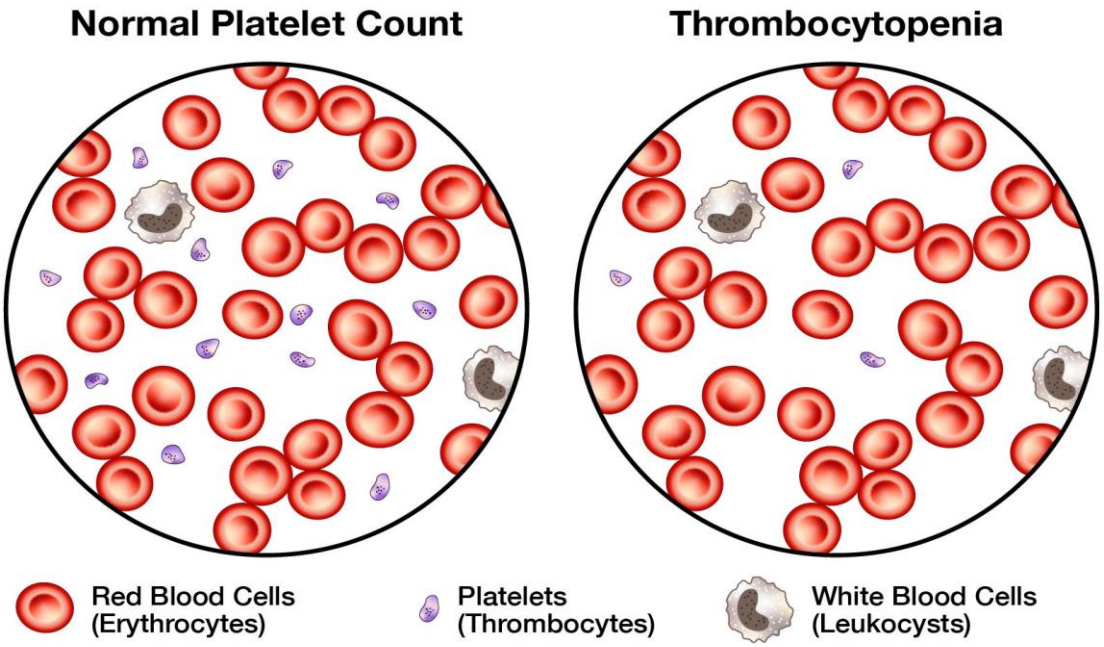

Figure 1 Platelet count in Normal and Thrombocytopenia Pateints adopted from USCF Benioff Children's Hospital

The most frequent hematological anomaly seen in individuals with chronic liver disease (CLD) is thrombocytopenia, which affects 64%–84% of patients with fibrosis or cirrhosis. Two Up to 35% of patients having bone marrow biopsies for thrombocytopenia of unclear cause have cirrhosis.Reduced thrombopoietin (TPO) levels and direct bone marrow suppression can also reduce platelet production.[6]

In 1929, Wintrobe proposed the terms mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) to describe the size (MCV) and hemoglobin content (MCH, MCHC) of red blood cells. These numbers are helpful in determining the cause of anemias and are referred to as red cell indices. Knowing the hemoglobin, hematocrit (packed cell volume), and red blood cell count numbers allows one to compute red cell indices. Since electronic cell counters are widely available, all blood count calculations now automatically measure red cell indices.[7]

Red cell indices in thrombocytopenia may exhibit hemolysis, anemia, or micro-angiopathic hemolysis. Reduced hemoglobin, hematocrit, MCV, or red blood cell count can all be signs of these alterations, as can schistocytes or other signs of red cell disintegration. Although thrombotic thrombocytopenic purpura (TTP) and hemolytic-uremic syndrome (HUS), which entail increased hemolysis of red blood cells, are linked to thrombocytopenia, it does not directly induce anemia. In some cases, thrombocytopenia can be associated with macrocytic anemia, which is anemia with large-sized red blood cells. This is often an outcome of other underlying diseases like vitamin B12 or folate deficiencies that may interfere with the production of red blood cells.[8]

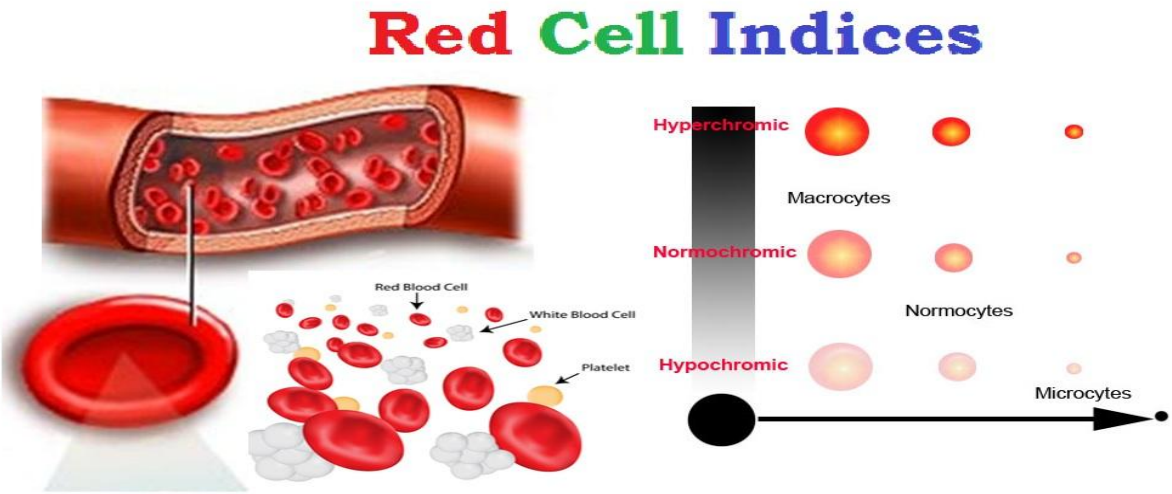

Figure 2 Red Cell Indices adopted from Medico Info

A coagulation profile (also known as a series of blood tests) is used to assess the ability of the body to form and dissolve blood clots. They usually include tests of fibrinogen, platelet count, International Normalized Ratio (INR), Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT). These are tests that were used to diagnose bleeding issues, monitor anticoagulant treatment, and determine the state of the coagulation cascade [9]

The risk of bleeding is very high when platelets lose their functionality or when their number reduce. Platelets are the essential mediators that trigger the mechanical pathway of coagulation cascade whenever blood artery injury takes place and are present in circulation within the blood.

Platelets promote primary hemostasis through three main mechanisms: adhesion, aggregation, and activation. The vascular sub-endothelium's different macromolecular components become visible and easily accessible to platelets when the vascular endothelium's integrity is compromised.[10]

Particularly in cases with more severe thrombocytopenia, thrombocytopenia can affect the coagulation profile and increase the risk of bleeding and prolonged bleeding duration. Activated coagulation time (ACT) may not be much changed by moderate thrombocytopenia, but it may be prolonged by severe thrombocytopenia. Moreover, thrombocytopenia and coagulation abnormalities can result from diseases such as disseminated intravascular coagulation (DIC). A prolonged PT may occasionally be linked to thrombocytopenia, particularly in situations such as liver illness or DIC. Studies indicate that severe thrombocytopenia, particularly in patients with underlying platelet dysfunction, can delay aPTT, even while mild thrombocytopenia may not have a substantial impact on ACT. Thrombocytopenia raises the risk of bleeding, particularly in cases when platelet deficits are more severe. The underlying reason and severity of the thrombocytopenia can affect this risk.[11]

Coagulation profile and red cell index comparison in the patients with thrombocytopenia may help to differentiate among the causes of thrombocytopenia, identify potential side effects, and guide therapeutic therapy. Therefore, the objective of the work is to compare and evaluate the coagulation pattern of patients who report thrombocytopenia to identify possible prognostic and diagnostic parameters that could help in managing the clinical decision-making process.

CHAPTER 2
LITERATURE REVIEW

A study conducted by Alvarez-Roman et al., (2016) also revealed that although patients with immune thrombocytopenia (ITP) have low platelet counts, the bleeding is often minimal, and it may denote that there are compensating procoagulants. Some individuals have a high risk of developing thrombosis. This study was aimed at identifying these variables and assessing the application of rotational thromboelastometry (ROTEM) in the hemostasis evaluation. The ITP patients had a procoagulant tendency because of high levels of platelets and red cells microparticles, resistance to protein C, and a fibrinolytic resistant clot caused by higher levels of plasminogen activator inhibitor-1, which indicated endothelial activation. The clotting period was prolonged, which was possibly due to anti-platelet antibodies, despite ROTEM showing higher clot stiffness and reduced lysis. These findings prove the need to provide personalized care and confirm the applicability of ROTEM in assessing hemostasis in ITP. [12]

The study conducted by Mohamed-Rachid et al., (2015) demonstrated that, despite the advanced automated analyzers, it is still difficult to count the number of platelets in individuals with thrombocytopenia. The present study involved 32 blood samples that contained platelet counts of less than 50x10[?]/L to compare four procedures optical, impedance, immunological, and manual. The impedance method failed in findings and highly inflated platelet counts in 15% of samples whose counts were less than 15x10[?]/L. The poor reliability of the impedance and immunological methods was even though most of the methods had good correlations. Bias analysis also demonstrated the biggest discrepancy with the impedance approach. In terms of low platelet count, those methods are more reliable than optical and immunological, and it is essential in cases when a decision is made regarding platelet transfusions.[13]

A study by Kim MJ et al., (2014) was able to minimize platelet production or maximize platelet breakdown as the causes of thrombocytopenia. The etiology of thrombocytopenia is now better comprehensible as a result of the advances of the automated blood cell analyzers that allow determination of the platelet parameters precisely. This study measured the significance of these features in thrombocytopenic patients. The individuals who had recently developed myeloid leukemia or primary immune thrombocytopenia and whose platelet counts were below 100 x 103/ul were considered. The percentage large platelets was calculated based on the measurement of platelet count, mean platelet volume, platelet distribution width, platelet crit, mean platelet component, mean platelet mass, and large platelet count. Moreover, a reference population was employed in making comparisons with these data. The patients with primary immune thrombocytopenia compared to those with myeloid leukemia showed large mean platelet volume, platelet distribution width, mean platelet component, mean platelet mass and large platelet percentage. This difference reveals that platelet production is not effective in leukemia but platelet destruction is increased in immune thrombocytopenia. Overall, the automated analyzer parameters help to more accurately assess the peripheral blood status and the production of bone marrow platelets in the clinical practice. [14]

Indora P et al., (2022) made a study that many maternal deaths are caused by hypertensive problems during pregnancy. Since activated platelets get bigger, platelet indices including mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (PLCR) can be used to show platelet activation. The coagulation profiles and platelet indices of women with pre-eclampsia, eclampsia, and normal pregnancies were compared in this study. From January to December 2021, it was carried out in the obstetrics and pathology departments of RNT Medical College. Prothrombin time, aPTT, and bleeding time all showed notable variations across the groups. Additionally, eclamptic and pre-eclamptic moms had significantly greater rates of NICU admissions. In general, basic coagulation tests and platelet indices

were helpful in determining the severity of hypertensive problems during pregnancy.[15]

The study made by Ebrahim H et al., (2021) indicated that Diabetes is a complicated condition of metabolism characterized by long term elevated blood sugar levels and seen to have significant vascular effects. In this research, basic coagulation tests and platelet parameters of patients with type 1 diabetes, type 2 diabetes, and healthy people were assessed. This was done with 180 subjects and their coagulation profiles and platelet indices were analyzed with the aid of standard laboratory equipment. The results revealed that prothrombin time (PT) and INR were significantly low in the type 2 diabetes patients and the control group as compared to the type 1 diabetes patients, which indicated the increased tendency towards the development of the clots. Platelet distribution width (PDW) and mean platelet volume (MPV) significantly increased in every type of diabetes, and this means more platelet activation. There was also a negative correlation between Fasting blood glucose and PT, INR and in some instances APTT. On the whole, these data indicate the importance of regular observation to avoid thrombotic risks of diabetes.[16]

A study conducted by Adam MA et al., (2017) noted that Regardless of the major progress, it is challenging to diagnose coronary syndrome (ACS). This paper evaluated the suitability of blood counts and coagulation indicators in the diagnosis of ACS and predicting the immediate implications. There was a comparison of 250 ACS patients and 250 healthy people. All the values (PT, APTT, MPV, WBC count, and RDW) were significantly high in patients with ACS. When outcomes were considered, the WBC, RDW, and MPV exhibited a significant increase in the patients who died within 30 days as compared to those who survived. Regression analysis showed substantial independent predictors of death to be RDW more than 16.53, MPV more than 11.25 FL, and WBC more than 10.55x10[?]/L. In this way, these criteria can be used to diagnose ACS early.[17]

Elderdery AY et al., (2022) made a study that Basic CBC parameters have clearly been impacted by COVID-19. 384 matched healthy controls and 384 confirmed COVID-19 cases were compared in this retrospective analysis. COVID-19 individuals were three to four times more likely to be anemic and almost five times more likely to be thrombocytopenic, indicating a considerable increase in both conditions. Leukopenia, MCV, WBC, lymphocyte, or basophil counts did not change significantly. More investigation is advised.[18]

Tiruneh T et al., (2024) made a study that Malaria is an intravascular parasite infection that can result in thrombocytopenia, coagulation issues, and bleeding issues. This study compared the platelet count and basic coagulation characteristics of 120 malaria patients with 120 healthy controls in order to better understand how malaria impacts coagulation. PT, APTT, INR, platelet count, and malaria parasitemia tests were performed on blood samples.

The majority of malaria patients exhibited extended PT, INR, and APTT, which indicated poor coagulation, according to the results. Additionally, about 25% of infected people had moderate thrombocytopenia. PT, INR, and APTT dramatically increased as parasitemia increased, yet the platelet count decreased. In general, extended clotting times and decreased platelets are closely linked to malaria infection.[19]

Sewify EM et al., (2013) made a study that By analyzing red cell microparticles (RMP), platelet microparticles (PMP), and specific coagulation factors, this study investigated whether chronic immunological thrombocytopenia (ITP) is associated with increased pro-thrombotic activity. Ten healthy controls and twenty-nine chronic ITP patients—eight of whom had had splenectomies were assessed. RMP, PMP, D-dimer, FVIII, FIX, and FXI levels were considerably higher in ITP patients, and aPTT was noticeably longer. Protein C did not differ significantly. The majority of coagulation factors had a negative connection with platelet count, and higher RMP levels were linked to shorter aPTT. Microparticle levels remained elevated even in

patients whose platelets were almost normal. Patients with splenectomies showed lower FIX and FXI and higher RMP. All things considered, these results point to a prothrombotic propensity in chronic ITP.[20]

Murray DJ et al., (1995) made a study that examined coagulation issues in surgical patients who undergo resuscitation mostly using packed red blood cells rather than whole blood after losing more than half of their blood volume. In order to maintain stable intravascular volume, 32 young patients having elective posterior spinal fusion were closely followed utilizing hemodynamic measures, urine output, and serial hematocrits. Of them, 17 experienced increased bleeding with inadequate clot formation, whereas 15 patients maintained normal surgical hemostasis. Laboratory tests, such as PT, aPTT, fibrinogen, platelet count, and factors V, VIII, and IX, were performed on these bleeding individuals.

Before results were available, fresh frozen plasma (FFP) was given empirically at 10 mL/kg to restore coagulation factor levels. Patients with abnormal bleeding showed higher PT and aPTT values and greater total blood loss than those without bleeding, while platelet counts and fibrinogen levels fell to a similar extent in both groups. Coagulation factors, especially V and IX, decreased as blood loss increased. FFP effectively corrected hemostatic abnormalities in most cases.

The findings indicate that, unlike emergency trauma settings where thrombocytopenia is common, elective surgeries with massive transfusion primarily develop coagulation factor deficiencies leading to impaired hemostasis.[21]

Dorgalaleh A et al., (2013) made a study that Thyroid hormones are essential for blood cell formation and metabolism. Anemia, leukopenia, thrombocytopenia, and changes to RBC indices such as MCV, MCH, MCHC, and RDW can all result from dysfunction. There were 118 healthy controls, 84 hyperthyroid patients, and 102 hypothyroid patients in this study. Complete blood counts and TSH levels were evaluated. WBC, platelets, and MCV were not significant ($P>0.05$), while RBC count, MCH, MCHC, RDW, hemoglobin, and hematocrit showed significant differences ($P<0.05$). Patients with unexplained blood abnormalities should have their thyroids evaluated. [22]

Roeloffzen WWH et al., (2010) made a study that A point-of-care technique called thrombelastography (TEG) evaluates hemostasis by measuring plasmatic coagulation factors and platelet function. 189 TEG studies, with a median of 11 tests per patient, were carried out in 16 patients with hematological malignancies in remission receiving chemotherapy in order to assess the effect of platelet count alone. 120 healthy persons' TEG findings from citrated and unaltered blood were compared. TEG clot strength (highest amplitude) and platelet count were found to be strongly correlated ($r=0.7$; $p<0.001$). Reaction time, clotting time, alpha angle, maximum thrombus formation, time to maximum thrombus generation, and total thrombus generation were all linked with platelet count. Important coagulation characteristics were partially obscured by citration. The platelet count affects every stage of plasmatic coagulation in addition to clot strength.[23]

Chang CK et al., (2009) made a study that Repairing an endovascular thoracoabdominal aortic aneurysm (TAAA) causes a significant coagulation and inflammatory reaction. In this study, postoperative changes in WBC, platelet count, PT, and renal indicators were assessed in 38 individuals. All patient ssignificant leukocytosis (139%), thrombocytopenia (56%), and elevated PT following stent-graft implantation. 32% of patients experienced renal insufficiency, which was linked to higher increases in WBC and greater decreases in platelet count. In a subgroup of nine patients, IL-6 drastically increased, indicating severe inflammation, whereas NGAL and cystatin C levels markedly increased, indicating early renal damage. In every instance, d-dimers rose while Protein C and Factor V declined. Stronger coagulopathic and inflammatory reactions were often associated with worse renal outcomes.[24]

Jubelirer SJ et al., (2002) made a study To ascertain if a bone marrow examination is required in patients suspected of having ITP, the study examined ten years' worth of information. Eighty-six patients with normal blood counts and smears but isolated thrombocytopenia were assessed. Marrow results, which showed normal or elevated megakaryocytes, supported ITP in 82 instances. Despite having fewer megakaryocytes, four patients reacted favorably to corticosteroids. None had another diagnosis over a median follow-up of 22 months. A review of 99 leukemia cases revealed characteristics that were distinctly different from ITP. Overall, the results indicate that when conventional tests and clinical evaluation reveal no abnormalities other than low platelets, bone marrow investigation is typically not required.[25]

Osuka A et al., (2019) made a study that White blood cell and platelet counts frequently decline early in severely burned individuals, though it's unclear how this relates to mortality. 280 significant burn patients (≥20% TBSA) treated in a Japanese burn hospital between 2006 and 2015 were examined in this retrospective cohort study. For thirty days following the injury, serial blood counts were kept on file. Every cell count was large at first and then decreased. RBCs gradually decreased, WBCs drastically decreased by day two before rebounding, and platelets hit their lowest point on day three. Low RBCs from days 1–5, lymphopenia on day 3, monocytopenia on day 10, and consistently low platelet counts from days 3–30 were significant predictors of 60-day death after controlling for age and burn size. A bad prognosis is indicated by early lymphopenia and thrombocytopenia.[26]

Jabeen S et al., (2022) made a study that Assessing coagulation profile alterations (PT, APTT, and D-dimer) in malaria patients and their relationship to parasitemia was the goal. From January to July of 2018, 92 patients at CMH Lahore participated in this cross-sectional study. 64.1% of cases were caused by Plasmodium vivax and 35.9% by P. falciparum. 54.3%, 28.3%, and 17.4% of cases had mild, moderate, and severe parasitemia, respectively.

Particularly in cases of P. falciparum, coagulation measures demonstrated a strong positive connection with parasitemia. Patients with bleeding issues need to be treated with extra care and caution.[27]

Muronoi T et al., (2016) made a study that the immature platelet fraction's (IPF) diagnostic and predictive significance in sepsis. Prospectively, 149 ICU patients (101 septic, 48 non-septic controls) with platelet counts $\geq 80\times10^3/\mu l$ were evaluated. IPF was assessed at arrival, and patients were tracked for 28-day mortality and a platelet fall (>30% reduction or $<80\times10^3/\mu l$ within 5 days). Platelet decrease was seen in 47 septic individuals. In comparison to controls and patients without deterioration, IPF was substantially greater in these patients. Higher IPF predicted coagulopathy, platelet consumption, and greater mortality, demonstrating substantial independent predictive significance even when AIPC was equal between groups.[28]

Koyama K et al., (2018) made a study that Sepsis frequently results in thrombocytopenia, however its underlying cause is yet unknown. Using absolute immature platelet counts (AIPC), this study examined thrombopoietic activity and assessed its relationship to the degree of thrombocytopenia and mortality in septic patients. Based on nadir platelet counts during the first week, 205 adult ICU patients with sepsis were divided into four groups in this retrospective observational study: severe ($\leq 40\times10^3/\mu L$), moderate ($41–80\times10^3/\mu L$), mild ($81–120\times10^3/\mu L$), and normal/increased ($>120\times10^3/\mu L$). The groups' AIPC values at admission were comparable. From days 2 to 7, the AIPC of patients who subsequently experienced severe thrombocytopenia significantly decreased, but the other groups' levels remained normal or increased. Reduced AIPC was independently linked to severe thrombocytopenia, according to multivariate analysis (day 3 OR 0.49; day 5 OR 0.59). Lower AIPC on days 3 and 5 was a significant predictor of 28-day mortality, according to Cox regression models. These results imply that poor outcomes and sepsis-induced thrombocytopenia are caused by decreased thrombopoiesis.[29]

Drews RE et al., (2003) made a study that Critically sick patients often have coagulopathy, thrombocytopenia, and anemia. Effective therapy of these hematologic abnormalities requires a systematic assessment. Clinicians must carefully balance the advantages against potential hazards, even though blood products might be necessary in some circumstances.

Transfusions of red blood cells (RBCs) increase the bulk of red blood cells and may be important to improve oxygen delivery in cases of unstable angina or myocardial infarction or to restore intravascular volume in cases of hemorrhage, but they may also be damaging in other situations. Although platelet transfusion helps lessen bleeding in cases of thrombocytopenia or platelet malfunction, it should not be used in cases of TTP-HUS or type II HIT as it may exacerbate thrombosis. Recombinant factor VIIa, PCC, or fresh frozen plasma (FFP) can be utilized to quickly treat coagulopathy.[30]

Valeri CR et al., (2007) made a study In order to better manage blood loss in injured patients, research at the Naval Blood Research Laboratory has looked at the preservation and function of red blood cells (RBCs), platelets (PLTs), and plasma-clotting proteins. Research investigated the effects of temperature, hematocrit, PLT count and function, and clotting proteins on nonsurgical blood loss and bleeding time (BT). In patients with anemia and thrombocytopenia, BT was highly linked with the amount of blood released and the intensity of bleeding. The results show that before giving functional PLTs to restore hemostasis, viable RBCs must be transfused to reach a hematocrit of roughly 35%. By lowering nitric oxide, releasing vasoconstrictors, and increasing thrombin production, red blood cells promote hemostasis. By reducing the need for preventive PLT transfusions, appropriate RBC transfusion can lessen hazards such alloimmunization and transfusion-related problems.[31]

CHAPTER 3

OBJECTIVE

To compare red cell indices and coagulation parameters among patients with thrombocytopenia and to determine how these changes relate to the severity of platelet reduction.

PROBLEM STATEMENT

Clinicians in Pakistan regularly manage patients with thrombocytopenia but lack clear local evidence on how red blood cell indices and coagulation parameters change as platelet counts drop. This gap makes it difficult to fully assess bleeding risk, predict complications, or tailor management beyond platelet count alone. Without understanding these linked hematological changes, we may miss early signs of systemic disorders like DIC or underestimate disease severity. This study directly addresses that gap by analyzing how red cell and clotting profiles shift across thrombocytopenia severity levels

OPERATIONAL DEFINITION

Thrombocytopenia: is a condition that occurs when the platelet count in your blood is too low. Platelets are tiny blood cells that are made in the bone marrow from larger cells. When you are injured, platelets stick together to form a plug to seal your wound. This plug is called a blood clot.

Red cell indices:

Mean Corpuscular Volume (MCV): Average volume of red blood cells, measured in femtoliters (fL); obtained from automated hematology analyzer.

Mean Corpuscular Hemoglobin (MCH): Average amount of hemoglobin per red cell, measured in picograms (pg); derived from CBC.

Mean Corpuscular Hemoglobin Concentration (MCHC): Average concentration of hemoglobin in red cells, measured in g/dL.

Coagulation Profile:
Prothrombin Time (PT): Time in seconds for plasma to clot after adding tissue factor; indicates extrinsic pathway function.
Activated Partial Thromboplastin Time (aPTT): Time in seconds to clot formation via the intrinsic pathway
International Normalized Ratio (INR): Standardized PT value for comparing across labs.
Fibrinogen Level: Concentration of fibrinogen in blood plasma, measured in mg/dL or g/L.
D-Dimer:D-dimer is a fibrin degradation product that is formed when a blood clot (fibrin clot) is broken down by the body's fibrinolytic system.

CHAPTER 4
Material and Methodology
Study Design
This was a cross-sectional observational study.

Study Setting
The study was conducted at several diagnostic laboratories and affiliated hospitals in Lahore. Both inpatient and outpatient subjects diagnosed with thrombocytopenia were included. After obtaining written informed consent, relevant clinical and laboratory data were collected to analyze the relationship between thrombocytopenia severity and changes in red cell indices and coagulation parameters.

Study Duration
The study was conducted for 4 months after the approval of the synopsis.

Sample Size
The data of 100 people was calculated by Cochran's formula .It will be collected from the Al-Hamd Lab Lahore.

$$n_0 = z^2 . p . (1-p) / e^2$$

Calculation:
With a 95% confidence level, the z-value is 1.96.
Expected Proportion (p): Patients with Type 2 Diabetes have a remarkably high prevalence of dyslipidemia The proportion (pp) was calculated to be 58% (0.58) based on earlier research carried out in comparable settings in Pakistan.
Margin of Error (e): A margin of error of 10% (0.10) was considered acceptable for this study, given the resource constraints.

$$n_0 = \frac{(1.96)^2 \cdot 0.58 \cdot (1 - 0.58)}{(0.10)^2}$$

$$n_0 = \frac{(3.8416) \cdot 0.58 \cdot 0.42}{0.01}$$

$$n_0 = \frac{0.936}{0.01} = 93.6$$

Result: The initial calculation yielded a minimum sample size of approximately **94 participants**. To account for potential non-response or incomplete data records, this number was rounded up. Therefore, a final sample size of **100 participants** was deemed sufficient and practical for this study.

Sampling Technique
Convenience sampling was used to recruit participants from the study settings during the data collection period.
Sample Selection
Inclusion Criteria
Adults (14 years and above) diagnosed with thrombocytopenia (platelet count < 150 × 10^3/µL).
Willing to provide written informed consent
No prior history of hematological malignancies or known inherited bleeding disorders.

Exclusion Criteria
Patients on anticoagulant therapy (e.g., warfarin, heparin) were excluded.
Known chronic liver disease, renal failure, or metastatic cancer was excluded.
Pregnancy or postpartum status were excluded.
Refusal to consent were excluded.

Equipment and Reagents
Automated hematology analyzer (for CBC and red cell indices)
Coagulation analyzer (for PT, aPTT, INR, fibrinogen, D-dimer)
Centrifuge, micropipettes, test tubes, EDTA and citrate tubes
Standard laboratory reagents for coagulation testing

Data Collection Procedure
Participant Recruitment and Consent
Eligible patients diagnosed with thrombocytopenia were approached, and written informed consent was obtained prior to enrollment.

Blood Sample Collection
Approximately 8 mL of venous blood was drawn under aseptic conditions.
3 mL was collected in an EDTA tube for complete blood count (CBC) and red cell indices.
5 mL was collected in a sodium citrate tube for coagulation profile testing.

Laboratory Analysis
A. Red Cell Indices (MCV, MCH, MCHC):
Determined with a computerized analysis of hematology (Sysmex XN-1000) as per the manufacturer guidelines Calibration and quality control were done daily.

Coagulation Profile:
Prothrombin Time (PT) and International Normalized Ratio (INR:) determined by the photo-optical technique on a photo-optical coagulation analyzer (STA Compact Max(r)). Thromboplastin reagent was applied according to the common protocol**.**
Activated Partial Thromboplastin Time (aPTT): aPTT, the time is measured by the use of ellagic acid and phospholipid reagents
Fibrinogen: Measured with Clauss methodology.
D-dimer: Measured with the aid of an immunoturbidimetric test.

Data Recording
A structured proforma was used to record:
Demographic details (age, gender)
Platelet count and thrombocytopenia severity grading (mild, moderate, severe)
Red cell indices (MCV, MCH, MCHC)
Coagulation parameters (PT, aPTT, INR, fibrinogen, D-dimer)

ETHICAL CONSIDERATIONS

The study was conducted in accordance with the ethical guidelines of Superior University, Lahore.
Written informed consent was obtained from all participants.
Confidentiality and anonymity were maintained throughout.
Participants were informed of their right to withdraw at any time without penalty.
Data was stored securely and accessed only by the research team.

DATA ANALYSIS

The data were put in Microsoft Excel and analyzed with SPSS. Variables were summarized using descriptive statistics (mean, SD, median, IQR). The normality was testing through the Shapiro-Wilk test. The Kruskal-Wallis test was used to compare the parameters based on the severity of thrombocytopenia due to non-normality. The p-value of less than 0.05 was taken as statistically significant.

GANTT CHART

Gantt Chart					
	May	June	July	August	September
Approval of Synopsis					
Data collection					
Data analysis					
Thesis Writing					
Publications					

CHAPTER 5
RESULTS

Descriptive Statistics of Study Population:

In this table, the descriptive statistics of demographic, hematological, and coagulation parameters are introduced covering 100 patients with thrombocytopenia. The mean age of the study population was 30.07 +- 9.52 years (=14-63 years). Lab results showed the mean platelet count of 79.18 +- 95.32 x103/uL which showed mid-range of thrombocytopenia. There were normocytic (MCV: 83.78 +- 6.09 fL) and borderline hypochromic erythrocyte features (MCH: 26.87 +- 2.51 pg). Coagulation profile demonstrated significant abnormalities with prolonged PT (17.21 ± 4.00 sec), elevated aPTT (42.72 ± 9.64 sec), increased INR (1.45 ± 0.42), markedly elevated D-dimer (1594.52 ± 1369.82 ng/mL), and low-normal fibrinogen levels (210.56 ± 68.74 mg/dL).

Table 1 Descriptive Statistics of Study Population

Parameter	**Mean ± SD**	**Minimum**	**Maximum**	**Reference Range**
Demographic				
Age (years)	30.07 ± 9.52	14.00	63.00	-
Red Cell Indices				
Mean Corpuscular Volume - MCV (fL)	83.78 ± 6.09	56.00	100.00	80-100
Mean Corpuscular Hemoglobin - MCH (pg)	26.87 ± 2.51	19.00	34.00	27-34
Mean Corpuscular Hemoglobin Concentration - MCHC (g/dL)	31.52 ± 1.52	27.00	35.00	32-36

Platelet Count				
Platelets (×10³/µL)	79.18 ± 95.32	8.00	310.00	150-450
Coagulation Tests				
Prothrombin Time - PT (seconds)	17.21 ± 4.00	11.00	28.00	11-14
Activated Partial Thromboplastin Time - aPTT (seconds)	42.72 ± 9.64	27.00	68.00	25-35
International Normalized Ratio – INR	1.45 ± 0.42	1.00	2.00	0.9-1.2
D-dimer (ng/mL)	1594.52 ± 1369.82	150.00	7000.00	<500
Fibrinogen (mg/dL)	210.56 ± 68.74	80.00	340.00	200-400

Frequency of Gender Distribution:

A total of 100 participants were involved in the study, of which the proportion of the male population (n = 52, 52.0) was slightly higher than that of the female population (n = 48, 48.0). This implies a relatively equal gender sample in the population of the study. The male and female representation will mean that the results about Coagulation profile and Red cell Indices in thrombocytopenia can be applied to both the male and female patients.

Table 2 Frequency of Gender Distribution

Gender	Frequency	Percent %
Male	52	52.0
Female	48	48.0
Total	100	100.0

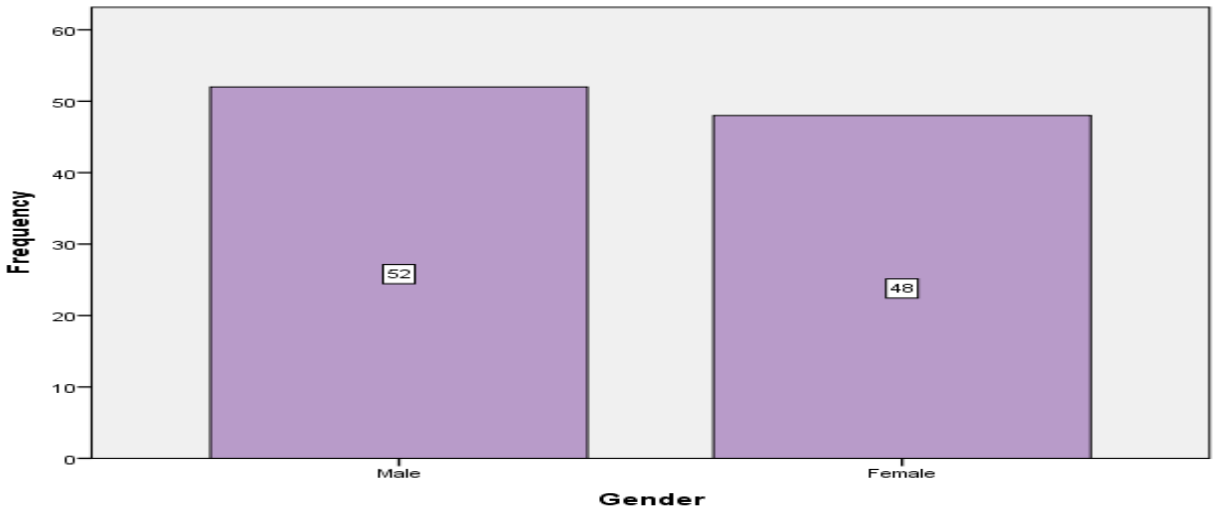

Figure 3 Frequency of Gender Distribution of Study Population

Age Categories And Its Frequency Distribution:
The age distribution showed that majority of the patients were youthful with 62% (n=62) being below 30 years, 34% (n=34) aged 31-50 years and only 4% (n=4) aged above 51 years. The average age was 30.07 +- 9.52 years (minimum: 14 years, maximum: 63 years).

Table 3 Frequency of Age Categories of Study Population

Age Categories	Frequency	Percent %
Less than 30	62	62.0
31-50	34	34.0
More than 51	4	4.0
Total	100	100.0

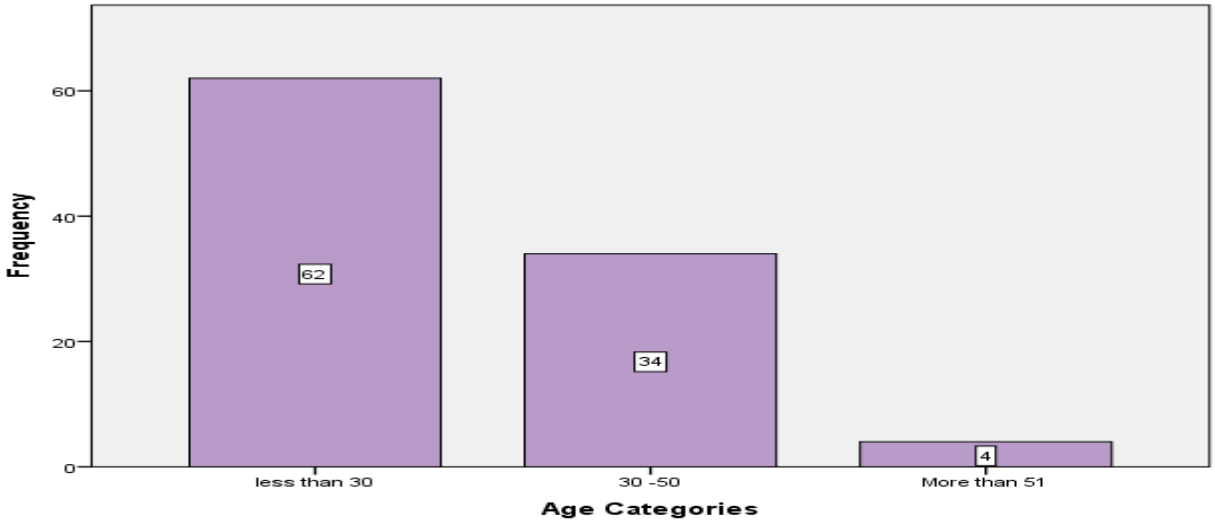

Figure 4 Frequency of Age Categories of Study population

Frequency Distribution of Platelets:
Out of 100 patients with thrombocytopenia, 62% had severe (<50, 000/uL), 17% moderate, 3% mild, and 18% normal platelet count, which forms discrete severity groups in subsequent red cell indices comparison.

Table 4 Frequency Distribution of Platelets

Thrombocytopenia	Frequency	Percent %
Severe	62	62.0
Moderate	17	17.0
Mild	3	3.0
Normal	18	18.0
Total	100	100.0

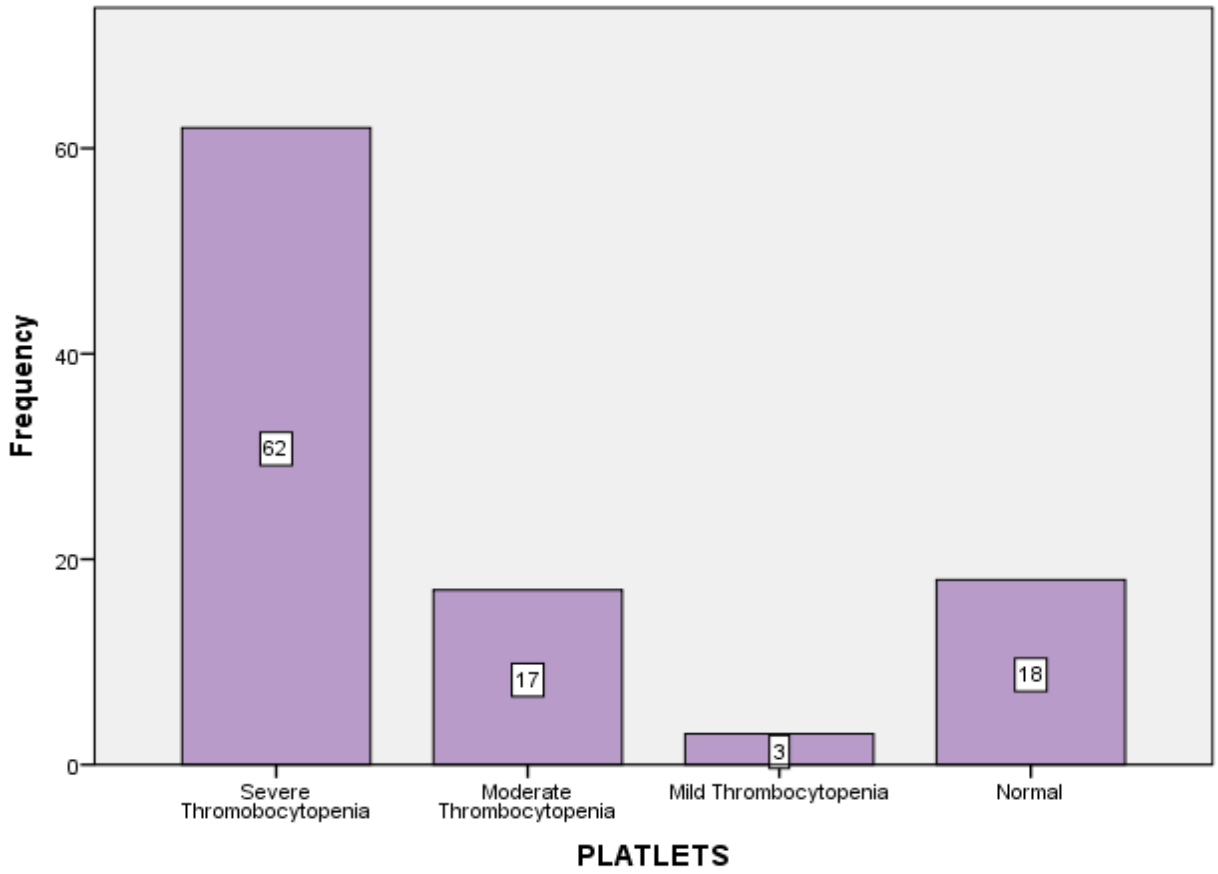

Figure 5 Frequency Distribution of Platelets

Frequency distribution of Red Cell Indices:
Frequency distribution indicated that there were abnormalities of red cell indices that were dominant in the study population. Microcytic abnormalities were observed in 31 patients (MCV less than 80 fL), whereas 57 Patient with low MCH (less than 27 pg) and 47 Patient with low MCHC were found. The normocytic indexes were found in 69 patient of MCV, 43 patient of MCH and 53 patient of MCHC. It is important to note that there was no presence of macrocytic and hyperchromic abnormalities in all three parameters on all patients.

Table 5 Frequency distribution of Red Cell Indices

Parameter	Abnormal/Low	Normal	High	Total
MCV	31	69	0	100
MCH	57	43	0	100
MCHC	47	53	0	100

Note: MCV abnormal = Microcytic RBC, MCH/MCHC abnormal = Low values

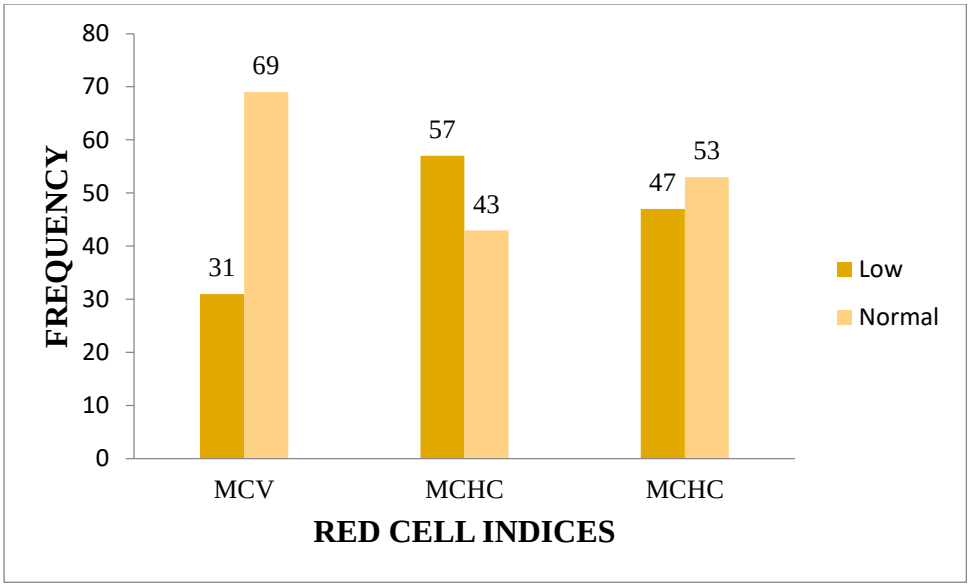

Figure 6 Frequency distribution of Red Cell Indices

Frequency distribution of Coagulation Parameters:

Coagulation studies showed that there were mostly normal coagulation tests. Prothrombin time was prolonged in only 19% of patients, activated partial thromboplastin time in 28%, while international normalized ratio was elevated in 41%. D-dimer levels were elevated in 25% of cases. Strikingly, fibrinogen deficiency was observed in nearly half (49%) of the cohort, representing the most prevalent coagulation abnormality in this thrombocytopenic population.

Table 6 Frequency distribution of Coagulation Parameters

Parameter	Prolonged	Normal	Total
PT	19	81	100
APTT	28	72	100
INR	41	59	100
D-Dimer	25	75	100
Fibrinogen	49	51	100

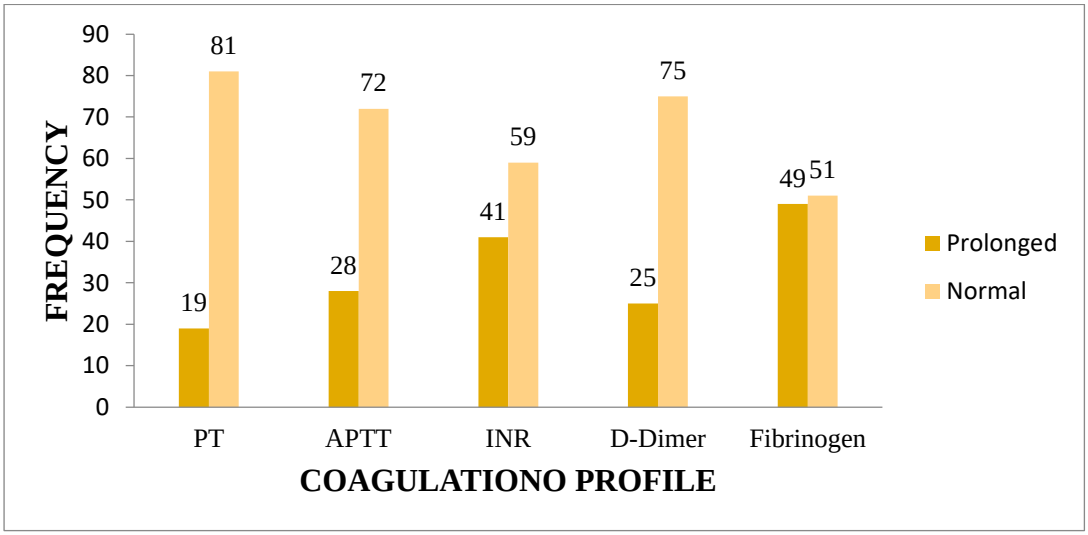

Figure 7 Frequency distribution of Coagulation Parameters

Test for Normal Distribution:

Normality assessment of continuous laboratory parameters using Shapiro-Wilk test. All variables demonstrated statistically significant deviations from normal distribution ($p < 0.05$), including platelet count ($p < 0.001$), red cell indices (MCV: $p = 0.001$, MCH: $p = 0.020$, MCHC: $p = 0.001$), and coagulation parameters (PT: $p = 0.001$, aPTT: $p = 0.010$, INR: $p < 0.001$, D-dimer: $p < 0.001$, fibrinogen: $p = 0.012$). Consequently, non-parametric statistical methods (Kruskal Wallis Test) were employed for all subsequent analyses

Table 7 Test for Normal Distribution

Lipid Parameter	Kolmogorov-Smirnov			Shapiro-Wilk		
	Statistic	Df	Sig.	Statistic	Df	Sig.
MCH	.131	100	.000	.970	100	.020
MCHC	.164	100	.000	.947	100	.001
PT	.122	100	.001	.951	100	.001
APTT	.077	100	.148	.965	100	.010
INR	.226	100	.000	.801	100	.000
D-Dimer	.146	100	.000	.850	100	.000
PLTs	.310	100	.000	.662	100	.000
Fibrinogen	.086	100	.065	.967	100	.012
MCV	.084	100	.076	.950	100	.001

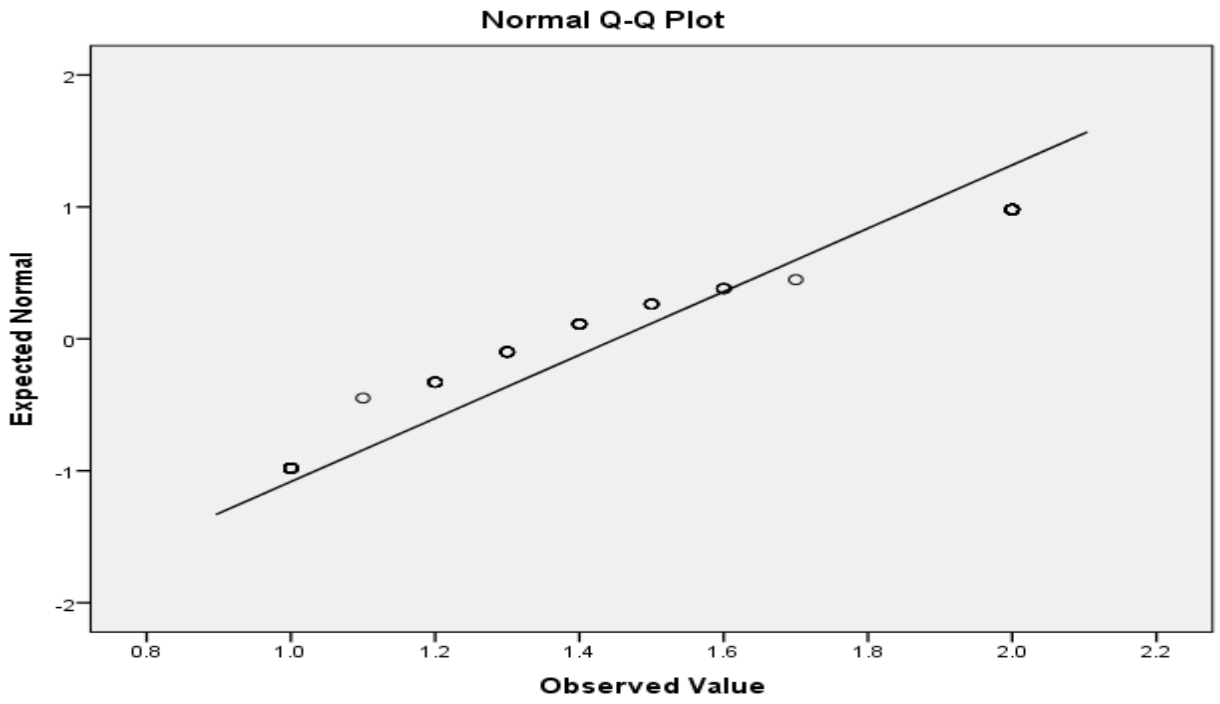

Figure 8 Normal QQ plot

Kruskal-Wallis Test:
Severe thrombocytopenia patients exhibited significantly lower median MCV (81.00 fL, IQR: 78.00-87.00) compared to normal platelet patients (88.00 fL, IQR: 85.75-88.25), representing a 7.9% reduction in red cell size. Similarly, hemoglobin content per cell (MCH) was reduced by 8.8% in severe cases (26.00 pg, IQR: 24.00-27.25 vs 28.50 pg, IQR: 28.00-29.25). Most strikingly, hemoglobin concentration (MCHC) showed a 6.1% decline in severe thrombocytopenia (31.00 g/dL, IQR: 30.00-32.00 vs 33.00 g/dL, IQR: 32.75-33.25). Kruskal-Wallis tests confirmed highly significant differences across all severity groups (all p-values <0.001), with MCHC displaying the strongest association (H=42.87).
This graded pattern of worsening red cell parameters with increasing thrombocytopenia severity suggests concomitant erythropoietic disturbances

Table 8 Red cell Indices Across Thrombocytopenia Severity Groups

Thrombocytopenia Severity	**N**	**MCV (fL)** Median (IQR)	**MCH (pg)** Median (IQR)	**MCHC (g/dL)** Median (IQR)
Severe (<50,000/µL)	62	81.00 (78.00-87.00)	26.00 (24.00-27.25)	31.00 (30.00-32.00)
Moderate (50,000-100,000/µL)	17	85.00 (83.50-86.50)	28.00 (27.00-29.00)	32.00 (32.00-33.00)
Mild (100,000-150,000/µL)	3	89.00 (56.00-)	30.00 (19.00-)	33.00 (31.00-)
Normal (>150,000/µL)	18	88.00 (85.75-88.25)	28.50 (28.00-29.25)	33.00 (32.75-33.25)
Statistical Test		Kruskal-Wallis	Kruskal-Wallis	Kruskal-Wallis
H statistic		H = 18.075	H = 23.779	H = 42.866
p-value		p < 0.001	p < 0.001	p < 0.001

Coagulation Profile across Thrombocytopenia Severity Groups
Coagulation parameters demonstrated progressive deterioration with worsening thrombocytopenia severity. Severe thrombocytopenia patients exhibited significantly prolonged prothrombin time (median: 18.00 sec, IQR: 15.00-22.00 vs normal: 12.00 sec, 11.75-12.00; H=43.02, p<0.001) and activated partial thromboplastin time (43.00 sec, 39.00-52.00 vs 30.00 sec, 29.00-31.25; H=48.40, p<0.001). International normalized ratio was elevated in severe cases (1.70, 1.20-2.00 vs 1.50, 1.40-1.60; H=39.29, p<0.001). Most strikingly, D-dimer levels were 7-fold higher in severe thrombocytopenia (1410.00 ng/mL, 965.00-2600.00 vs 200.00 ng/mL, 177.50-225.00; H=50.06, p<0.001), while fibrinogen concentrations were 38% lower (195.00 mg/dL, 133.75-235.00 vs 315.00 mg/dL, 307.50-330.00; H=42.16, p<0.001)

Table 9 Coagulation Profile Across Thrombocytopenia Severity Groups

Group	**N**	**PT (sec)** Median (IQR)	**aPTT (sec)** Median (IQR)	**INR** Median (IQR)	**D-dimer (ng/mL)** Median (IQR)	**Fibrinogen (mg/dL)** Median (IQR)
Severe	62	18.00 (15.00-22.00)	43.00 (39.00-52.00)	1.70 (1.20-2.00)	1410.00 (965.00-2600.00)	195.00 (133.75-235.00)
Moderate	17	17.00 (17.00-18.00)	47.00 (45.50-49.50)	1.50 (1.40-1.60)	1800.00 (1625.00-2050.00)	180.00 (170.00-197.50)
Mild	3	[Constant]	33.00	[Constant]	486.00	240.00

			(32.00-)		(369.00-)	(180.00-)
Normal	18	12.00 (11.75-12.00)	30.00 (29.00-31.25)	[Constant]	200.00 (177.50-225.00)	315.00 (307.50-330.00)
Statistical Test		Kruskal-Wallis	Kruskal-Wallis	Kruskal-Wallis	Kruskal-Wallis	Kruskal-Wallis
H statistic		H = 43.017	H = 48.396	H = 39.285	H = 50.064	H = 42.159
p-value		<0.001	<0.001	<0.001	<0.001	

Note: IQR = Interquartile Range (25th-75th percentiles). "Constant" indicates identical values within group.

CHAPTER 6
DISCUSSION

This study shows that red cell indices and the coagulation profile in different grades of thrombocytopenia in 100 patients with thrombocytopenia that reveals significant link between platelets count severity and the both erythrocyte morphology and hemostatic role. the demographic data shows a mean age of 30.07 ± 9.52 years with 62% of patients under 30 years, consistent with infectious etiologies common in Pakistan such as dengue fever, malaria, and viral infections. and the gender balanced distribution (52% male and 48 % female) suggests acquired rather than hereditary cause of thrombocytopenia

The level of severity distribution shows that 62% with severe thrombocytopenia (<50000), 17 % moderate, 3% mild, and 18% normal platelet counts, shows the hospital-based nature of this study the predominance of all patient who have severe cases requiring inpatient management. The mean platelets count of 79.18 ± 95.32 $\times 10^3/\mu L$ with wide range (8.00-310.00 $\times 10^3/\mu L$) demonstrates the heterogeneity captured in our cohort, spanning from life-threatening severe cases to patients in recovery phase

The red call indices show normocytic (mean MCV: 83.78 ± 6.09 Fl) and borderline hypochromic (mean MCH: 26.87 ± 2.51 pg.) characteristics on averages the frequency distribution shows 31% with microcytosis, 57% with hypochromic and the 47 % with reduced value of MCHC. The predominance of the hypochromic changes over the change which are microcytic suggest that hemoglobin synthesis impairment precedes red cell size reduction, consistent with iron-restricted erythropoiesis due to inflammation-mediated iron sequestration or true iron deficiency. the absence of the microcytic or the hyperchromic abnormalities show reflects the young age and disease process as vitamin B12 and the folate the deference required months to years to develop and very uncommon demographic

The Kruskal- Walli's study analysis show highly significant difference in all the red cell indices across thrombocytopenia severity group. serve the patient have thrombocytopenia exhibited median MCV of 81.00 FL (IQR: 78.00-87.00) vs 88.00 FL (IQR: 85.75-88.25) in normal platelet patients, representing 7.9% reduction. MCH showed 26.00 pg. (IQR: 24.00-27.25) versus 28.50 pg. (IQR: 28.00-29.25), an 8.8% reduction. MCHC demonstrated 31.00 g/dL (IQR: 30.00-32.00) versus 33.00 g/dL (IQR: 32.75-33.25), a 6.1% reduction. MCHC showed the strongest statistical association (H=42.87), it may suggest the most sensitive marker for the detection erythropoietic dysfunction in thrombocytopenic patients.

The moderate thrombocytopenia group consistently showed intermediate values (MCV: 85.00 FL, MCH: 28.00 pg., MCHC: 32.00 g/dL), establishing a clear dose-response relationship

This study finding indicated a graded, severity-dependent the relationship suggests multi-lineage the hematopoietic dysfunction instead of isolated megakaryocytic impairment. Some mechanism explains the link bone marrow suppression affect multiple cell line, systemic inflammatory states causing cytokine-mediated suppression and iron sequestration through hepcidin upregulation, consumptive

processes such as DIC causing both platelet consumption and hemolysis with iron dysregulation, or combined nutritional deficiencies affecting multiple cell lines.

The coagulation profile shows significant bassline abnormalities with mean PT 17.21 ± 4.00 seconds, aPTT 42.72 ± 9.64 seconds, INR 1.45 ± 0.42, D-dimer 1594.52 ± 1369.82 ng/mL, and fibrinogen 210.56 ± 68.74 mg/dL. Frequency distribution revealed PT prolongation in 19%, aPTTprolongation in 28 % INR elevation in 41%, D-dimer elevation in 25%, and most significantly, hypofibrinogenemia in 49% of patients, making it the most prevalent coagulation abnormality. The high prevalence of low level of fibrinogens combined with thrombocytopenia show dual hemostatic defects substantially amplifying bleeding risk

Kruskal-Walli'sfindingsshow highly significant differences across severity groups for all coagulation parameters (all $p<0.001$). PT increase from median 12.00 second. seconds (IQR: 11.75-12.00) in normal to 18.00 seconds (IQR: 15.00-22.00) in severe thrombocytopenia, a 50% prolongation (H=43.02)). apt increased from 30.00 seconds (IQR: 29.00-31.25) to 43.00 seconds (IQR: 39.00-52.00), a 43% prolongation (H=48.40). INR rose from 1.50 (IQR: 1.40-1.60) to 1.70 (IQR: 1.20-2.00; H=39.29. with these results severe cases approach levels indicate less than 50 percent normal clotting factors

This type of combinations of markedly increase D-dimer value and reduced fibrinogens in pathognomonic for consumption of coagulation activation leads to intravascular fibrin deposition and consuming platelets and clotting factors. the simultaneously activating fibrinolysis and generating D-dimer. This creates a paradoxical state where thrombosis and bleeding coexist: microvascular thrombosis causes organ dysfunction while consumption of hemostatic components causes bleeding diathesis. Common DIC triggers include sepsis, trauma, malignancy, and severe infectionsall plausible in our young patient population.

The link of findings hypochromic anemia, serve thrombocytopenia increase D-dimer and hypofibrinogenemia points which move toward specific disease process. Given Pakistani context and demographic, dengue hemorrhagic fever represents a highly plausible diagnosis, as it is endemic with annual epidemics, predominantly affects young adults, and characteristically causes thrombocytopenia through bone marrow suppression and platelet consumption, coagulopathy with elevated D-dimer and hypofibrinogenemia, and anemia of inflammation with iron sequestration.

The severe bacterial sepsis with which DIC could explain that the entire constellation among bone marrow suppression systemic inflammation with iron sequestration, and consumptive coagulopathy Malaria, particularly Plasmodium falciparum, causes thrombocytopenia through splenic sequestration, anemia through hemolysis and bone marrow suppression, and can trigger DIC. Hematological malignancies leading to marrow infiltration and secondary DIC are other considerations, but they are less likely due to an presentation. Strong biological relationships are suggested by the statistical strength, all the comparisons gave $p<0.001$ although the sample size is not huge. Application of Shapiro-Wilk test and subsequent non-parametric Kruskal-Walli analysis is to assure that the conclusions made are not biased by the failure to comply with the normality assumption. This regular tendency of gradual increasing severity of the situation reinforces the cause-and-effect argument, since dose-response correlations can be a strong point of causal implication of biological relationships.

These clinical results suggest that thrombocytopenia can never be considered alone but as a possible sign of systemic hematological malfunction. Every thrombocytopenic patient with moderate and severe thrombocytopenia should be fully evaluated with complete blood count with indices and full coagulation profile with fibrinogen. The extremely high frequency of hypofibrinogenemia (49% total) points to the state that fibrinogen measurement is not a choice, but a routine and the low concentration level significantly endangers the risk of bleeding and may necessitate a cryoprecipitate or fibrinogen concentrate A significant increase in D-dimer (>1000 ng/mL) must provide high suspicion of consumption coagulopathy and initiate DIC.

The decisions to do transfusion should not only take into account the platelet count but also coagulation parameters and fibrinogen level as combined defects need more aggressive approaches. Past research that have reported relationships between thrombocytopenia and anemia, but few have systematically assessed red cell indices in different severity levels that have shown unambiguous dose-response curves. The results of our study contribute to the quantitative data concerning multi-lineage hematopoeietic dysfunction in thrombocytopenia

The abnormalities of coagulation are in line with the observed reports of DIC complication of severe thrombocytopenia in critically ill and septic patients. Nevertheless, we have a quite high prevalence (49) of hypofibrinogenemia, which may be an indication of differences in the etiology of the disease, or presentations, or access to healthcare in our region.

CHAPTER 7
CONCLUSION

One thing is made evident in this study, that is, thrombocytopenia does not only impact platelet counts. With the decrease in the platelet counts, the alteration was also noticed in the coagulation profile of the patients as well as in the red cell indices. These alterations were enhanced by the increase in severity of thrombocytopenia. The severe thrombocytopenic patients had significant decreases in MCV, MCH and MCHC, which implies that the red blood cells of the patients were shrinking and were packed with lesser hemoglobin. This indicates that the bone marrow may not be functioning well or the body may be under stress due to inflammation, infection or there may be nutritional deficiencies. The coagulation profile was also significantly altered in accordance with the severity of the disease. There were severe cases with prolonged PT and aPTT, increased values of INR, ly increased levels of D-dimer, and decreased fibrinogen. High D-dimer and low fibrinogen are a very strong indication of consumption of clotting factors, which is commonly seen in such conditions as disseminated intravascular coagulation (DIC), severe infections, and dengue fever- all of which are prevalent in our area. When combined with the findings, they demonstrate that thrombocytopenia is not a very common issue on its own. It is oftentimes a manifestation of a larger disturbance of many blood cell sets and the clotting mechanism in the body. This is the reason why platelet count cannot be taken as a sufficient measure to determine the condition of the patient. Full hematologic and coagulation testing is necessary to inform diagnosis, disease issues and treatment planning. The research contributes to useful local data to clinicians in Pakistan where febrile diseases often cause coagulopathy and thrombocytopenia. With the knowledge of the trend in laboratory changes, the healthcare providers will be able to recognize high-risk patients beforehand and respond in a more efficient manner.

LIMITATIONS

Although informative, there are a number of limitations that exist with this study which need to be taken into consideration when interpreting the results. Since it was only carried out in a single center with relatively small sample particularly in mild and moderate thrombocytopenia groups, the results might not be entirely true to the overall patient population. The cross-sectional design also did not allow following changes in hematological and coagulation parameters over time and, therefore, did not allow any insight into the course of the disease or recovery. In addition, the patients were not sampled based on the cause of thrombocytopenia, and this could have produced some variability in the outcomes as dengue, malaria, sepsis, and ITP may have different hematological presentation. The lack of bone marrow analysis meant that the destruction of platelets with impaired production could not be distinguished. Other lab tests like iron, inflammatory, and nutritional tests were not conducted and this limited the scope of the explanation of how some red cell abnormalities were

obtained. No history of treatment and the duration of the disease were also recorded and this could have contributed to the laboratory results during the sampling period.

RECOMMENDATION

Based on the study outcomes, several recommendations can help enhance clinical practice and guide future research. Clinicians should routinely assess both red cell indices and coagulation profiles in all patients presenting with moderate to severe thrombocytopenia, as these parameters offer valuable information beyond platelet count alone. Early identification of hypofibrinogenemia and markedly elevated D-dimer levels is essential, and timely fibrinogen replacement or further evaluation for potential DIC should be considered when indicated. Bone marrow examination may be useful when the cause of thrombocytopenia remains unclear, helping distinguish between decreased production and increased destruction. Future studies should involve larger, multicenter cohorts and incorporate longitudinal follow-up to better understand how laboratory values evolve during different stages of illness. Researchers should also stratify patients based on confirmed diagnoses, include iron and inflammatory markers, and explore cost-effective screening strategies. Developing local risk-stratification tools that integrate platelet count, red cell indices, and coagulation markers could further improve early detection of high-risk patients and support more informed clinical decision-making.

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