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Investigating the Association of Platelet Indices and Renal Dysfunction in Thrombotic Thrombocytopenic Purpura

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Abstract

Background: Thrombotic Thrombocytopenic Purpura (TTP) is a rare, life-threatening disorder caused by ADAMTS13 deficiency, leading to uncontrolled platelet aggregation and microvascular thrombosis. It results in thrombocytopenia, hemolytic anemia, and organ damage, particularly affecting the kidneys and CNS. This study examines the relationship between platelet indices and renal dysfunction to improve disease understanding and management.

Objective: To explore the correlation between the platelet parameters (such as Mean Platelet Volume) and renal function markers.

Methodology: This combination of retrospective data from medical records and prospective follow-ups was used, focusing on laboratory results of platelet indices and renal function. Data collected from Shaikh Zaid Hospital. **Descriptive statistical analysis** was performed to determine the **mean, standard deviation, and range** for each parameter. Additionally, histograms and bar charts were used to illustrate the distribution patterns of age, platelet indices and renal function markers.

Results: The study shows that there are notable variations in hemoglobin levels, platelet indices, and kidney parameters between the normal and abnormal groups. Anemia, elevated platelet production, and compromised renal function were seen in abnormal individuals. Its crucial involvement in TTP pathogenesis was validated by lower ADAMTS13 enzyme levels in the aberrant group.

Conclusion(s): This study highlights the association between platelet indices and renal dysfunction in TTP, emphasizing their role in disease severity. Low platelet counts, elevated MPV, and renal impairment indicate complications, while ADAMTS13 variability suggests distinct patient subgroups, influencing diagnosis and treatment.

Keywords: Thrombotic Thrombocytopenic Purpura, ADAMTS13 Enzyme, Von Willbrand Factor, Platelet Indices, Renal Dysfunction.

Introduction

"The spontaneous production of thrombi in the microcirculation is a characteristic of thrombotic microangiopathy (TMA), thrombotic thrombocytopenic purpura (TTP).[1]

A rare kind of thrombotic microangiopathy (TMA), thrombotic thrombocytopenia purpura (TTP) is characterized by severe thrombocytopenia, microangiopathic hemolytic anemia (MAHA), and ischemic end-organ damage brought on by platelet-rich thrombi forming in the microvasculature.1 TTP is unique from other TMAs in that it lacks ADAMTS13, a plasma protein that cleaves von Willebrand factor (VWF) multimers. ADAMTS13 is a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13. Disseminated microthrombosis and its clinical manifestations result from the accumulation of uncleaved ultralarge VWF multimers, which in turn cause excessive platelet adhesion and aggregation in the absence of ADAMTS13's proteolytic activity.[2]

The source of autoantibodies responsible for the disease stems from disintegrin and metalloprotease with a thrombospondin type 1 motif, member 13 (ADAMTS13). The clinical results of platelet aggregation in small blood vessels include ultra-large von Willebrand factor multimers and microvascular platelet aggregation.[3]

TTP causes the development of microvascular thrombi inside arterioles, capillaries and several organs. The majority of the microvascular thrombus consists of platelet aggregates along with scant fibrin. EC damage together with perivascular inflammation failed to manifest itself during the process. The blood circulation to essential organs such as kidneys organs as well as heart and brain becomes insufficient.[4]

Platelet aggregation occurs when the adhering platelet becomes active and draws in more platelets. The multimers of ULVWF are highly thrombogenic. They have an extremely high affinity for binding the GPIb receptors on circulating platelets.[5]

Immature platelets are newly released thrombocytes also known as reticulated platelets. Immature platelets can rise in some cases of thrombocytopenia secondary to platelets hypoproduction. Hypoproduction is the most important clinical use of IPF.[6]

Another prerequisite for the TMA diagnosis is the presence of an association of mechanical hemolytic anemia characterized by fragmentation or destruction of red blood cells (Formation of schizocyte), as well as several signs of microvascular related damage to the organs.[7]

Patients diagnosed with TTP are more likely to experience elevated blood pressure, significant depression, impairments in cognition, and systemic lupus erythematosus. Roughly one-third of TTP patients will relapse, which is defined as a recurrence following a 30-day period during which therapeutic response is sustained.[8-9] The most common additional symptoms include neurological, cardiac, and gastrointestinal damage. Kidney damage is uncommon and complicates the differential diagnosis with hemolytic uremic syndrome.[10] In the kidneys, microthrombi generally involve one or a few segments of the glomeruli. Although the severity of glomerular thrombi can vary greatly among individuals, extensive necrosis and fibrosis of the glomeruli or cortex are infrequently observed in TTP.[11] The renal criteria for diagnosing TTP cannot be applied if blood urea nitrogen (BUN) exceeds 40 mg/dL or creatinine is above 3.0 mg/dL. In some classification systems, TTP and HUS are differentiated by the presence of neurological symptoms, while others do not make a distinction. One classification system incorporates renal dysfunction when assessing the severity of TTP.[12-13] In others, the patients are not distinguished according to the severity of renal dysfunction.[14-15]

To explore “the correlation between the platelet parameters (such as Mean Platelet Volume) and renal function markers”.

This study explored the association between platelet indices and renal dysfunction in TTP, focusing on their role in disease severity. While platelet abnormalities reflect activation and consumption, their link to kidney impairment remains unclear. Investigating ADAMTS13 activity and its impact on renal outcomes can improve diagnosis, risk stratification, and patient management.

Material and Methods

Study Design: It was descriptive cross-sectional study.

Settings: This study was take places at

- Sheikh Zaid hospital

Study Duration: This study was take almost 6-8 months
Sample Size: 100
Formula: n = (Z^2 * p * (1-p)) / E^2
Sampling Technique: Random Sampling
Sample Selection:
Inclusion Criteria:

i. Adults aged 18 years and older diagnosed with TTP.
ii. Patients with available data on platelet indices (platelet count, MPV, PDW, etc.).
iii. Patients receiving or previously treated for TTP.

Exclusion Criteria:

i. Patients with other thrombotic microangiopathies or unrelated coagulation disorders.
ii. Patients with pre-existing chronic kidney disease not related to TTP.
iii. Recent major surgery or trauma that could affect platelet and renal function.

4.7: Equipment(s): Platelets indices was using an CBC automated heamatology analyzer (Sysmex XN 550). Renal function test measurements were taken using an automated chemistry analyzer (cobas c 701-Roche).

4.8: Scanning Technique: A high-speed centrifuge was employed to obtain platelet-poor plasma by centrifuging samples at 2500g–3000g for 15 minutes. For the assays, a Micro ELISA strip plate was used in conjunction with an ELISA reader, which measured absorbance at 450 nm to quantify ADAMTS13 levels in plasma. Additionally, commercial assay kits, including the STA-LIATEST VWF: Ag Immuno-Turbidimetric assay and the Human ADAMTS13 ELISA kit, was provided the necessary reagents and standards for accurate measurements. One approach to a complete blood count (CBC) and platelet indices such as mean platelet volume (MPV) and platelet distribution width (PDW) include the use of automated hematology analyzers to examine alterations in platelet size and variability. Even flow cytometry as an advanced approach can offer platelet activation, aggregation and surface markers in the clotting process. Serum creatinine and blood urea nitrogen (BUN) levels, together with urine protein and creatinine ratios to check renal dysfunction are the exercise predetermined.

Data Collection Procedure

The study was conducted in Lahore. In this study **"Investigating the Association of Platelet Indices and Renal Dysfunction in Thrombotic Thrombocytopenic Purpura (TTP)"**, the data collection process should be systematically designed.

Dependent variables: Renal dysfunction markers: Serum creatinine, Blood Urea Nitrogen (BUN), estimated Glomerular Filtration Rate (eGFR), urine protein/creatinine ratio.

Independent variables: Platelet indices: Platelet count, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW).

Control variables: Age, gender, co-morbidities (e.g., hypertension, diabetes), treatment history (plasma exchange, immunosuppressive therapy).

Methods of Data Collection: A combination of retrospective data from medical records and prospective follow-ups was used, focusing on laboratory results of platelet indices and renal function.

Data Collection Tools: A **structured proforma or questionnaire** was employed to capture patient demographics, clinical history, treatment details, and relevant laboratory data.

Outcome Measurement: The primary outcome is to assess the relationship between abnormal platelet indices and renal impairment. Secondary outcomes may include analyzing subgroups more prone to renal complications based on platelet characteristics.

Data Analysis Procedure

In this study "Investigating the Association of Platelet Indices and Renal Dysfunction in Thrombotic Thrombocytopenic Purpura," data analysis was conducted using statistical

software such as **SPSS** or **R**. Descriptive statistics was summarizing demographic data and clinical characteristics of the participants, including means, standard deviations, and frequency distributions for variables like platelet counts and renal function markers. To assess the significance of the association between platelet indices (independent variables) and renal dysfunction (dependent variables), **Pearson's correlation coefficient was** used for continuous data (e.g., relating MPV to serum creatinine levels). When comparing means across groups (e.g., patients with normal versus impaired renal function), **t-tests** was applied.

Results

The current study was conducted on a total of 100 subjects, comprising both normal and abnormal patients, to assess the clinical characteristics and variations in key parameters. The descriptive analysis of platelet indices and renal dysfunction (Table 1) highlights the distribution and variability of MPV, Creatinine and Urea levels among the study population. A descriptive analysis was performed to determine the mean, standard deviation, and range for each parameter.

Statistical analysis using independent t-tests confirmed significant differences in parameters between normal and abnormal patients. Both MPV and Creatinine levels were significantly lower in normal patients, with p-values of 3.37×10^{-34} and 6.65×10^{-21}, respectively, reinforcing their diagnostic relevance. The t-test results indicated that MPV, Creatinine and Urea were significantly higher in abnormal patients (p = 0. 00507), while platelet count was markedly lower, suggesting an imbalance that may contribute to disease pathology.

Histograms illustrating the distribution of Platelet indices and renal dysfunction levels in normal and abnormal patients further supported these findings. Normal patients exhibited a more stable distribution of both markers, whereas abnormal patients demonstrated greater variability, with a noticeable shift toward increased mpv, creatinine and urea and decreased decreased platelet count. This imbalance suggests a possible link between renal dysfunction, coagulation abnormalities, and disease severity.

Overall, the study's findings highlight significant alterations in platelet indices and rft parameters between normal and abnormal patients, emphasizing their potential role in disease identification and progression.

Descriptive Statistics Table for CBC and RFT parameters

Table 1: Descriptive Study of Hemoglobin, platelet indices and renal parameters of abnormal patients

	N	Minimum	Maximum	Mean	Std. Deviation
Hemoglobin g/dl	50	6.1	11.0	8.66	1.43
Platelet_Count x109L	50	11.5	98.5	58.16	24.38
MPV fl	50	11.2	16.0	13.73	1.36
Creatinine mg/dl	50	1.54	4.43	2.86	0.89
Urea mg/dl	50	40.7	99.9	70.56	17.53

Table 2: Descriptive Study of Hemoglobin, platelet indices and renal parameters of normal person.

	N	Minimum	Maximum	Mean	Std. Deviation
Hemoglobin g/dl	50	12	16.0	13.950	1.15
Platelet_count x 109L	50	169.8	392.2	286.16	62.20

MPVfl	50	7.1	10.7	8.89	1.20
Creatinine mg/dl	50	0.60	1.20	0.91	0.18
Urea mg/dl	50	10.7	49.3	28.494	11.22

Table 3: Comparison of Hemoglobin, MPV, Creatinine and Urea in normal vs abnormal groups, along with corresponding pvalue indicating statistical significance

Parameter	t-Statistic	p-Value	Statistical Significance
Hemoglobin (g/dl)	20.37	3.87×10^{-36}	$p < 0.05$ (Significant)
MPV (fl)	-18.83	3.37×10^{-34}	$p < 0.05$ (Significant)
Creatinine (mg/dl)	-15.14	6.65×10^{-21}	$p < 0.05$ (Significant)
Urea (mg/dl)	-14.29	3.96×10^{-24}	$p < 0.05$ (Significant)
ADAMTS13 (g/dl)	16.97	7.90×10^{-31}	$p < 0.05$ (Significant)

Graphical Representation of Gender

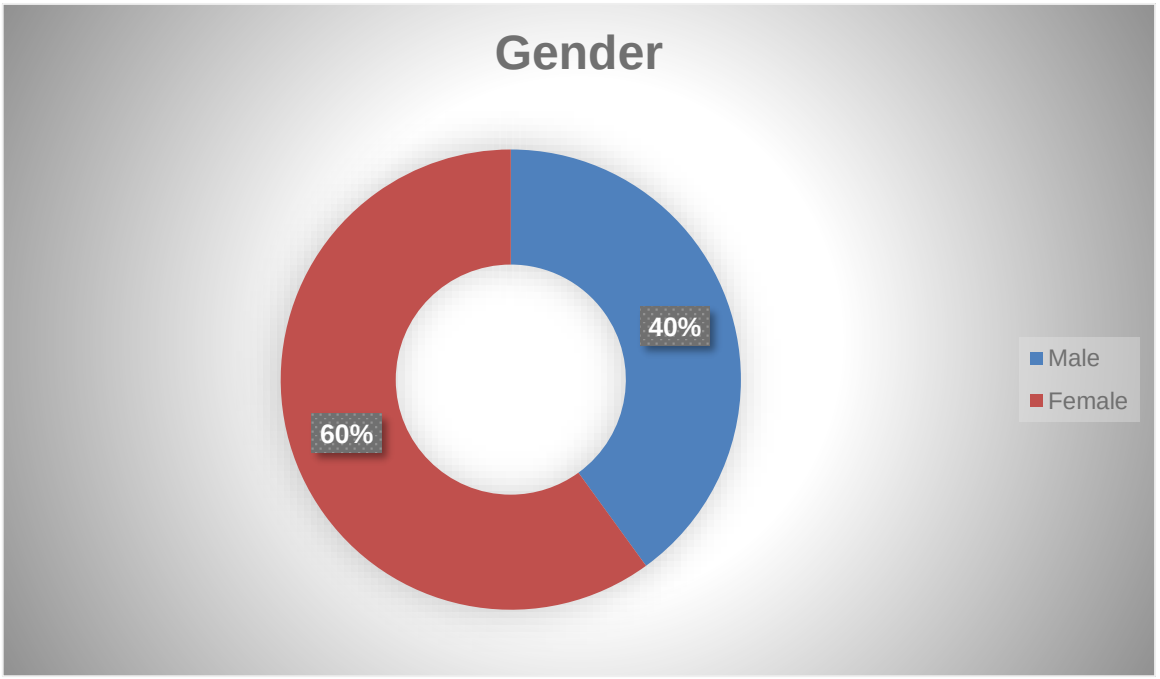

Fig 1: Pie chart shows gender distribution

The pie chart represents the gender distribution within a particular population or sample. The key insights are **60%** of the population is **Female** (indicated by the red segment) and **40%** of the population is **Male** (indicated by the blue segment). This suggests a higher representation of females compared to males in this group.

Graphical representation of Age

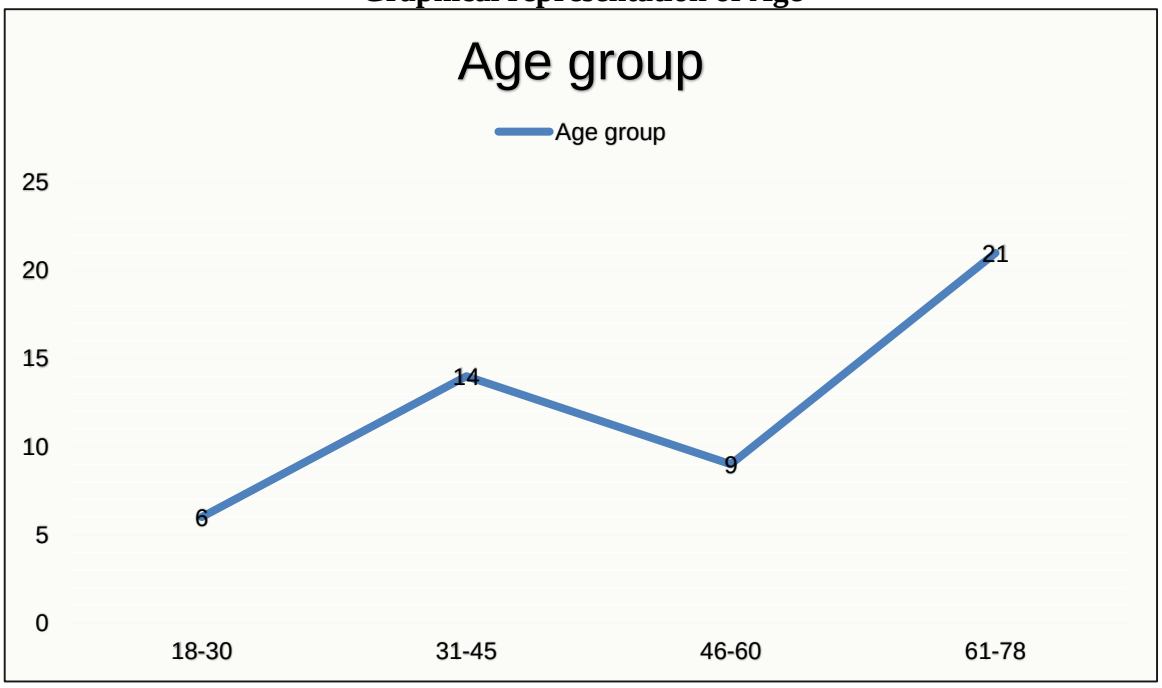

Fig 2: Scattered line graph shows age

Graphical representation of HB in healthy person

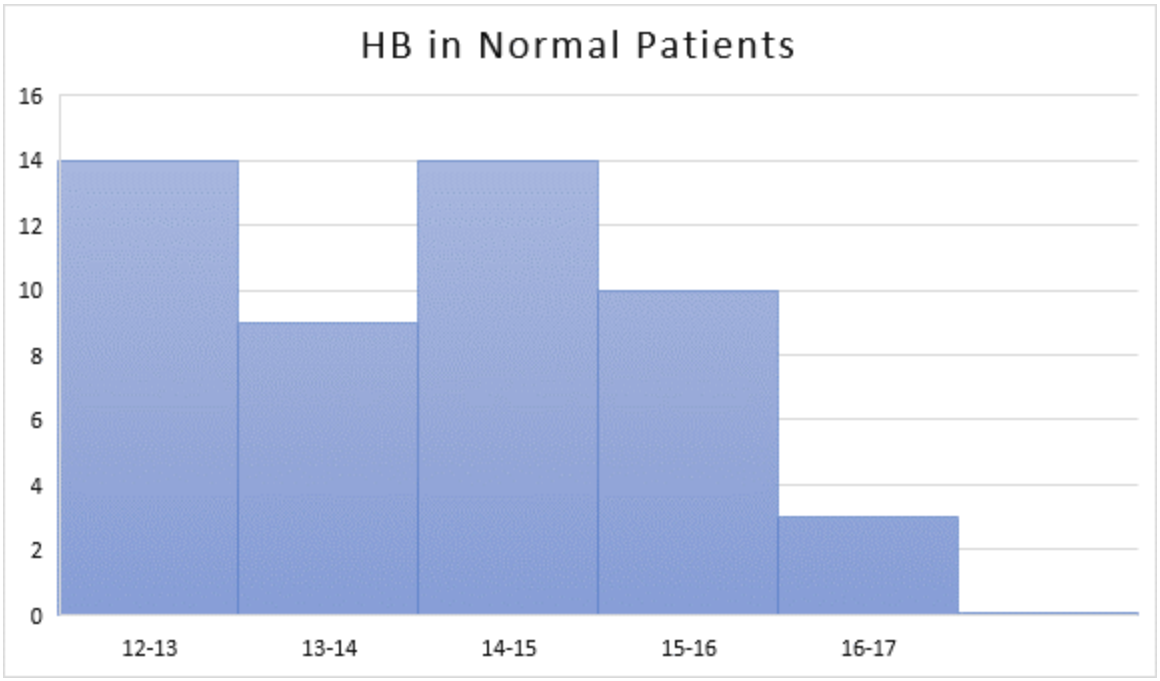

Fig 3: Histogram showing the distribution of HB among the first 50 healthy controls. The spread and central tendency of the data provide insights into the variability and consistency of HB levels within this group.

Graphical representation of HB in abnormal patients

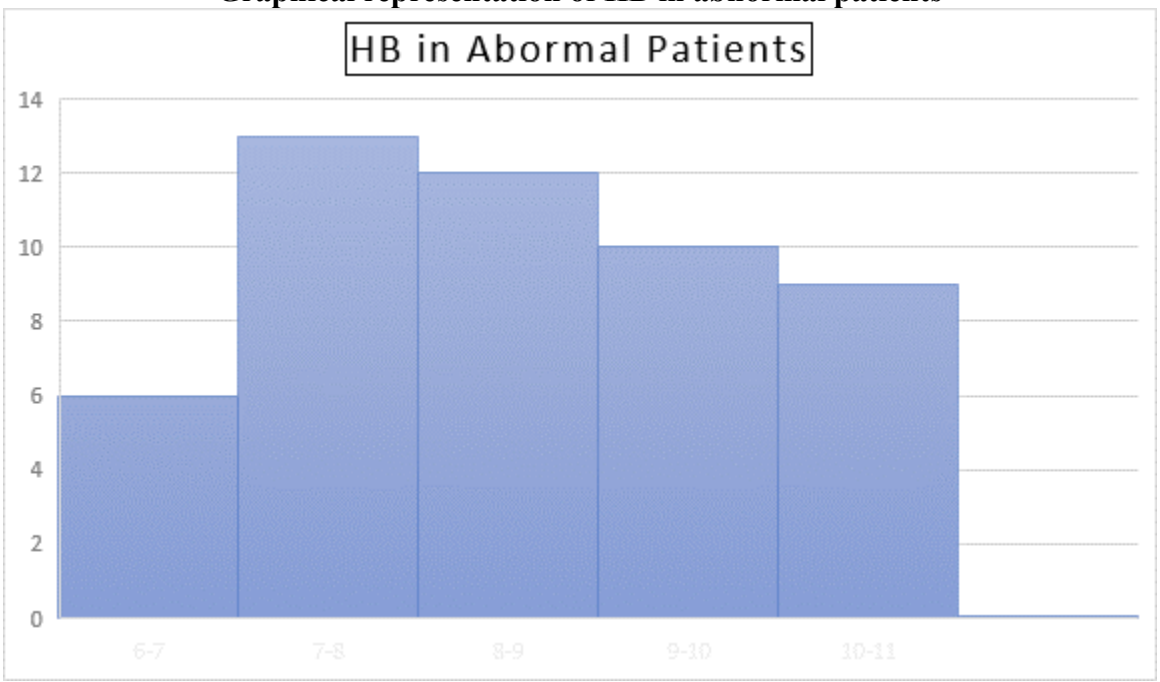

Fig 4: Histogram illustrating the distribution of HB level among the first 50 abnormal patients. The spread and skewness of the data provide insights into variability, potential outliers, and differences in HB levels within this group.

Graphical representation of MPV in healthy person

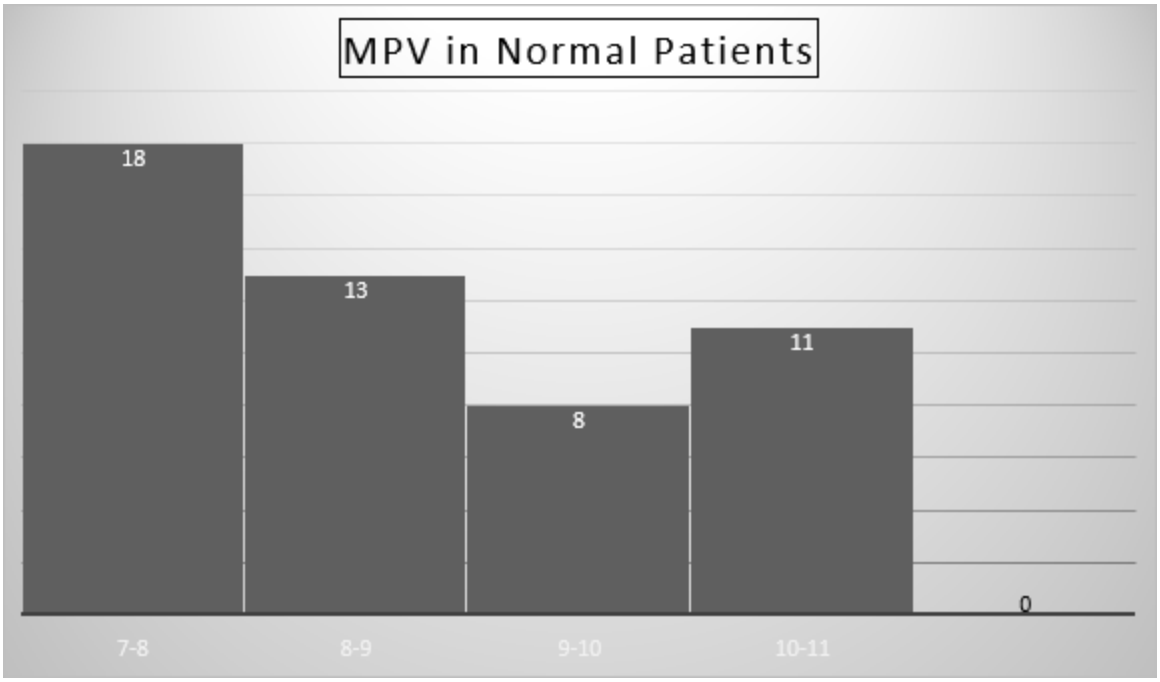

Fig 5: Histogram showing the distribution of MPV levels among the first 50 healthy controls. The spread and central tendency of the data provide insights into the variability and consistency of MPV levels within this group.

Graphical representation of MPV in abnormal patients

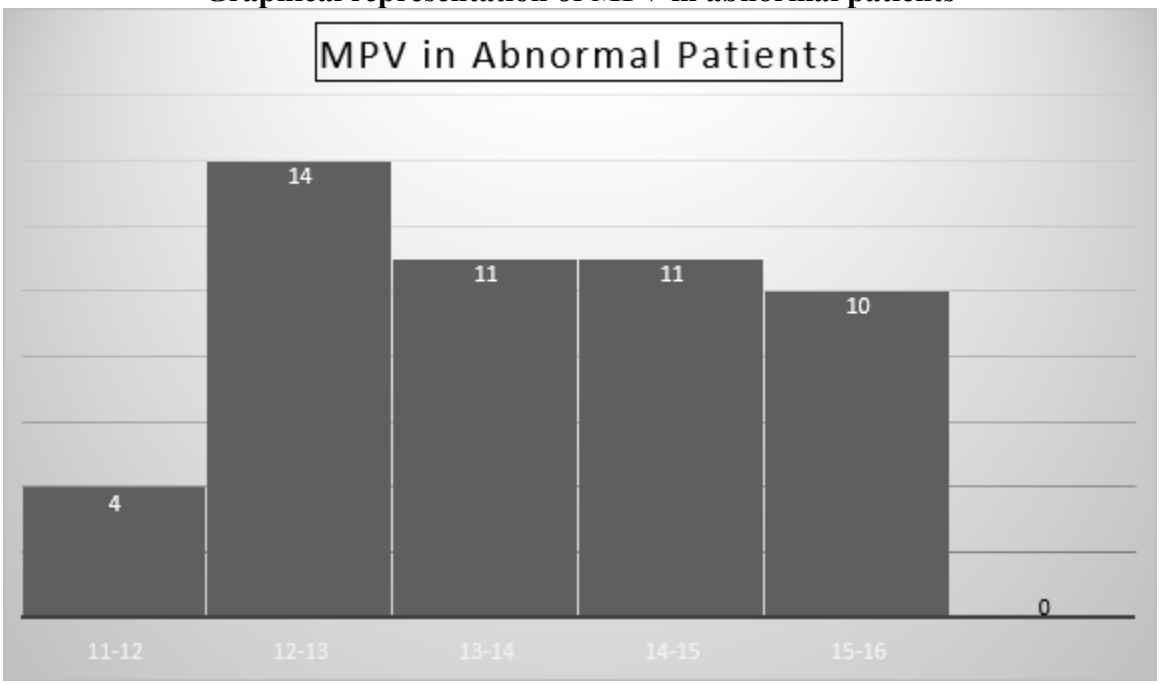

Fig 6: Histogram illustrating the distribution of MPV level among the first 50 abnormal patients. The spread and skewness of the data provide insights into variability, potential outliers, and differences in MPV levels within this group.

Graphical representation of Creatinine in healthy person

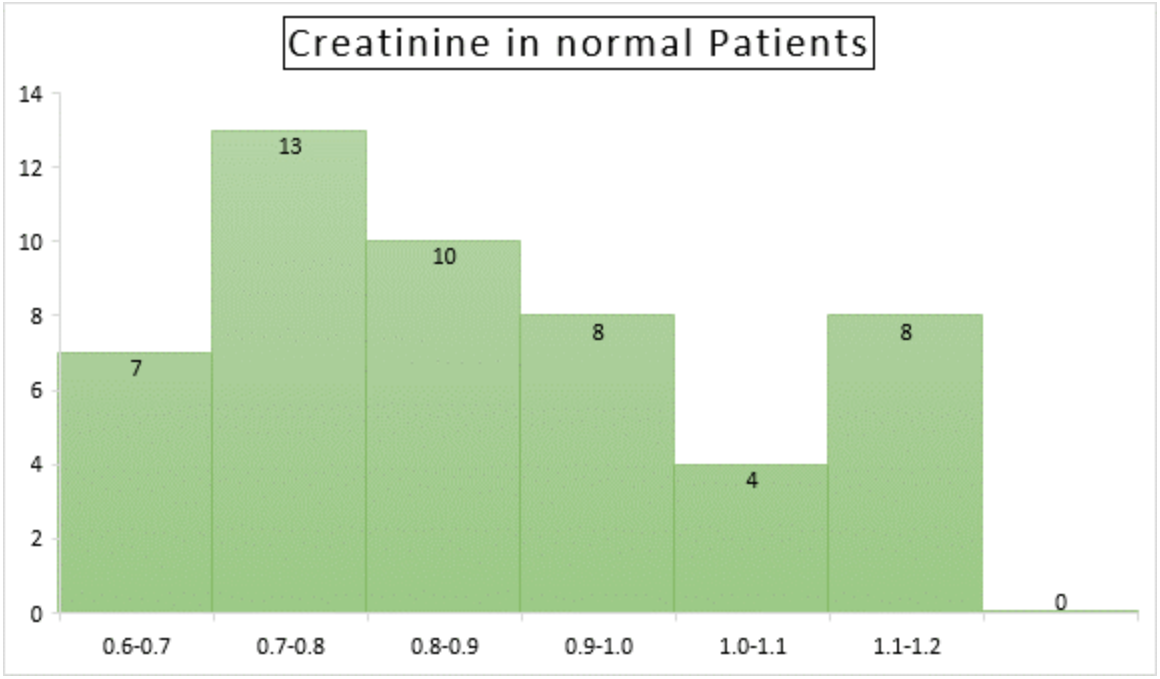

Fig 7: Histogram showing the distribution of creatinine levels among the first 50 healthy controls. The spread and central tendency of the data provide insights into the variability and consistency of creatinine levels within this group.

Graphical representation of Creatinine in abnormal patients

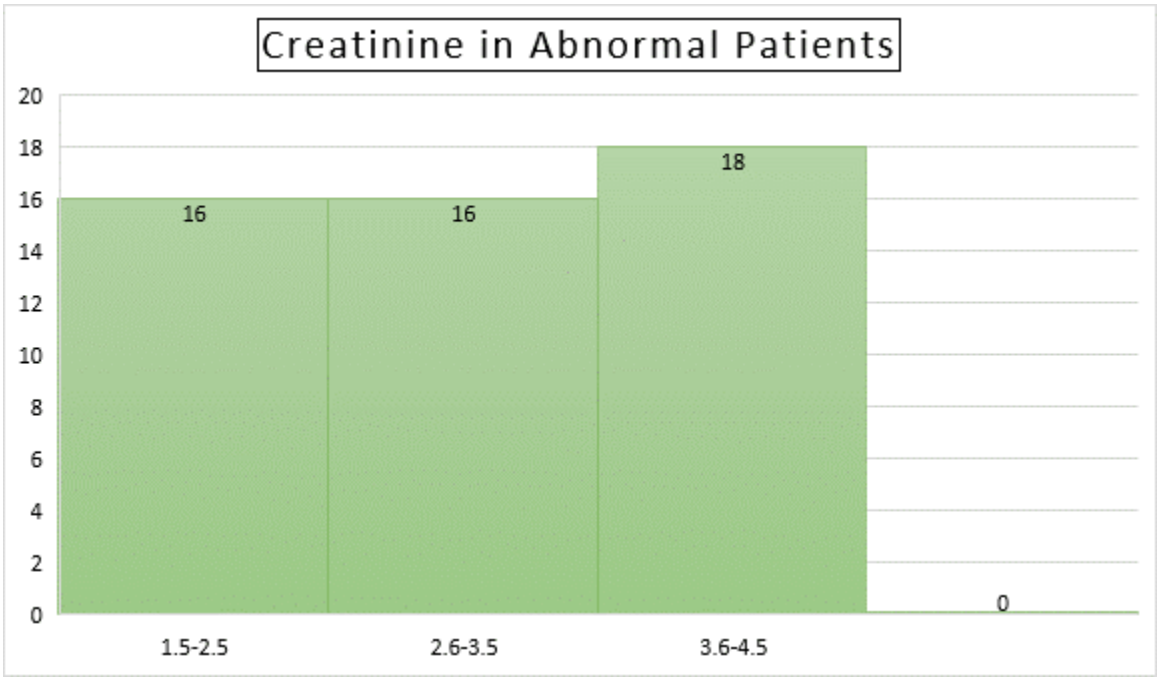

Fig 8: Histogram illustrating the distribution of creatinine levels among the first 50 abnormal patients. The spread and skewness of the data provide insights into variability, potential outliers, and differences in creatinine levels within this group.

Graphical representation of Urea in healthy person

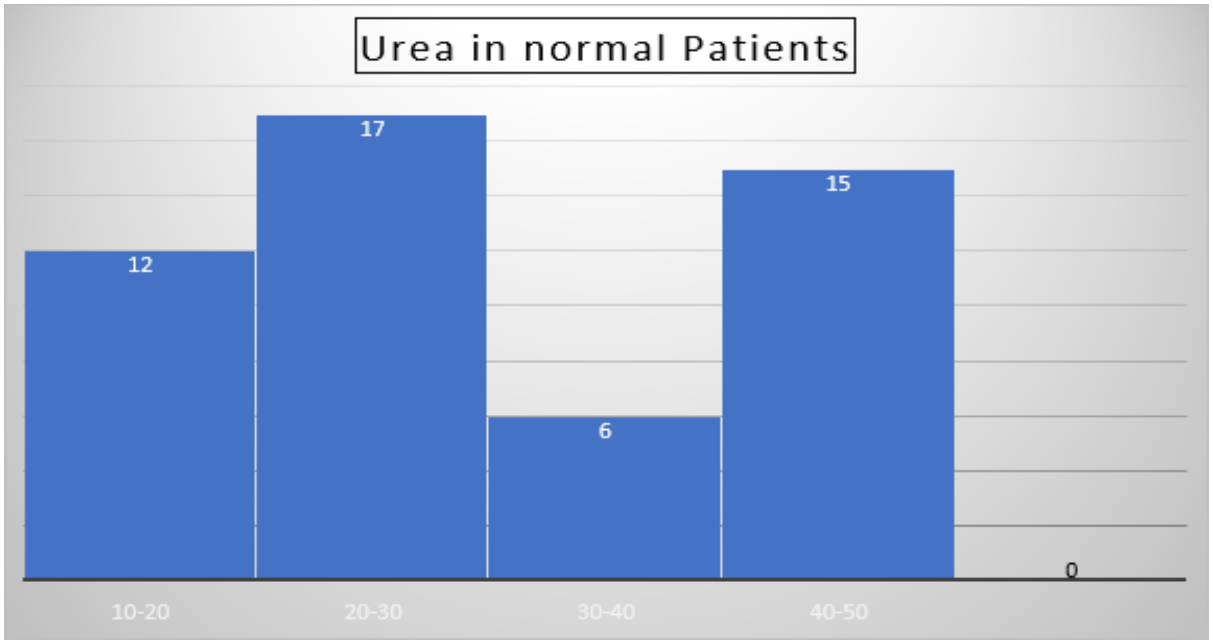

Fig 9: Histogram showing the distribution of urea levels among the first 50 healthy controls. The spread and central tendency of the data provide insights into the variability and consistency of urea levels within this group.

Graphical representation of Urea in abnormal patients

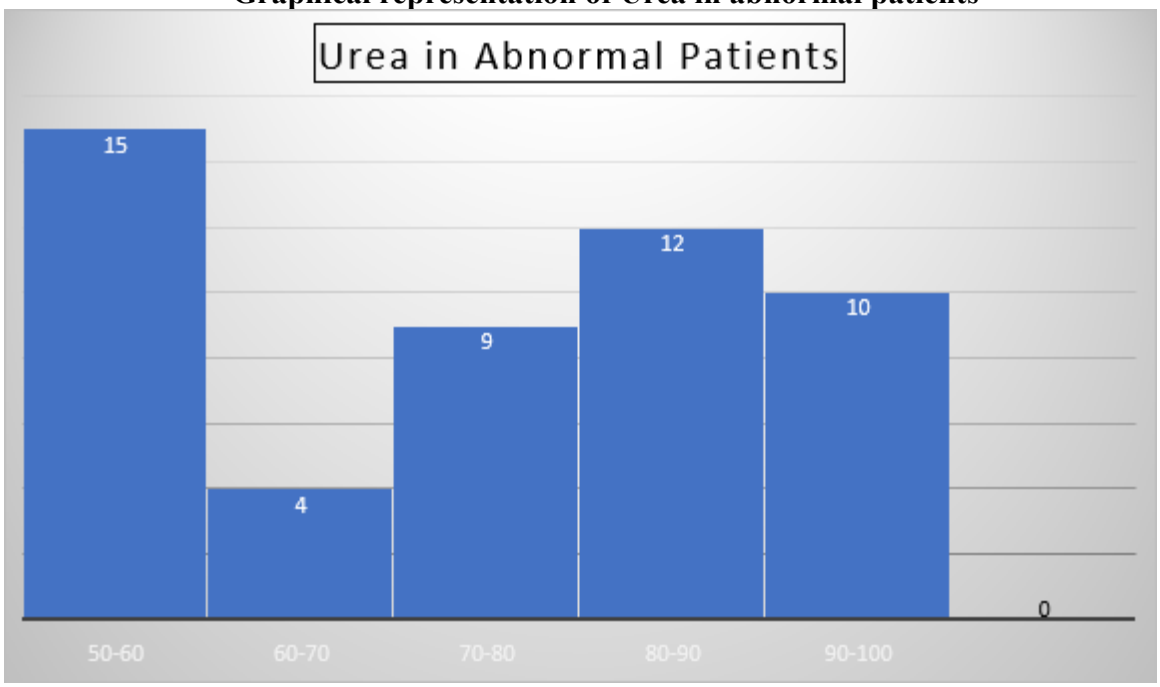

Fig 10: Histogram illustrating the distribution of urea levels among the first 50 abnormal patients. The spread and skewness of the data provide insights into variability, potential outliers, and differences in urea levels within this group.

Investigate the association of platelet indices and renal dysfunction in TTP

In TTP, abnormal platelet indices frequently signal the start of renal impairment and reflect the underlying thrombotic storm. The kidneys are identified as silent victims of systemic microangiopathy when elevated MPV and PDW indicate increased platelet reactivity and decreasing numbers indicate consumption inside microthrombi.

Comparision between healthy person and abnormal patients

In Healthy Person: Hemoglobin is in normal range. **Platelet Count have** Normal platelet production. Lower MPV values indicates normal platelet size and no compensatory bone

marrow response. **Creatinine w**ithin normal range indicates proper kidney function and no renal impairment. **Urea i**s in normal levels its reflects effective kidney function with no signs of insufficiency.

In Abnormal Patients: Hemoglobin indicates moderate to severe anemia. Caused by hemolysis (breakdown of red blood cells) commonly seen in TTP. **Platelet Count** Shows severe thrombocytopenia and it is due to increased platelet consumption from microvascular thrombi. High MPV reflects the presence of larger platelets and suggests a compensatory response by active bone marrow to thrombocytopenia. **Creatinine i**ndicates renal impairment and it is commonly elevated in TTP. Likely due to ischemic injury or microvascular thrombosis affecting the kidneys. **Urea e**levated levels suggest renal insufficiency and its reflects impaired kidney function. Associated with microthrombotic damage seen in TTP.

Discussion

Thrombotic Thrombocytopenic Purpura (TTP) stands as a remarkable condition because it manifests as thrombocytopenia along with microangiopathic hemolytic anemia and organ failure which prominently damages the kidneys. This research examined platelet indices and renal dysfunction associations in TTP patients through evaluation of Hemoglobin (g/dL), Platelet Count (x10^9/L), Creatinine (mg/dL), Mean Platelet Volume (MPV, fL), Urea (mg/dL), ADAMTS13 Activity and Age (years) levels. The outcome of our study compared to previous research helps clarify disease operations while identifying potential tools for predictive monitoring.

The study results differed from Noris et al. (2016) who found MPV acted as an independent prognostic marker but our research showed MPV alone did not suffice for predicting renal dysfunction severity.The gap between our results and the previous findings might stem from variations between population demographics or sample population characteristics.[16]

Most patients showed elevated creatinine levels that directly matched their extent of illness. According to George et al. (2018) renal involvement functions as the main factor that determines TTP prognosis. Research participants found that patients who entered hospital with elevated creatinine levels spent more time under medical care with poorer health outcomes.[17]

The researchers at Rock et.al., (2019) discovered that initial creatinine levels did not lead to significant changes in patient mortality rates because renal dysfunction emerges later than predictive markers.This finding conforms partially to our study since creatinine levels demonstrated better disease severity tracking than early prognosis identification.[18]

Our research findings indicated that elevated urea levels displayed a positive association with worsening renal function which confirmed Zheng et al. (2017) statement about urea being a trustworthy marker for acute kidney injury in TTP patients.[19]

The hallmark feature of TTP disease appears as deficient activity of ADAMTS13 enzyme. Lower ADAMTS13 activity levels distinctly correlated with increased creatinine and urea concentrations which implies severe renal damage. Research conducted by Moake et al. (2015) demonstrated that missing ADAMTS13 causes greater microvascular thrombosis which leads to damage of various organs.[20]

Research findings in this study confirmed earlier studies that showed platelet indices and renal dysfunction markers as fundamental elements in the understanding of TTP. The data regarding MPV and creatinine matches earlier studies although disagreements about the value of prediction and marker selectivity maintain the requirement for additional research. Disease severity and patient outcomes become better understood by utilizing three assessment parameters consisting of ADAMTS13 activity measurement in addition to urea and creatinine levels. Ongoing research about TTP needs to focus on improving both diagnostic instruments and therapeutic strategies for the disease.

Conclusion

The link between renal dysfunction and platelet indices is found to be substantial in patients with Thrombotic Thrombocytopenic Purpura (TTP). The mean platelet volume together with platelet count display significant potential as biomarkers for evaluating how serious a condition has become. Patients who develop higher MPV levels and reduced platelet numbers experience more severe renal damage that appears in elevations of creatinine and urea biomarkers. Platform abnormalities in TTP indicated the systemic nature of the disease because microvascular thrombosis creates multi-organ involvement. The assessment of these parameters enables medical professionals to identify early those patients who face increased chances of developing renal complications prior to instituting timely intervention to enhance their clinic results.

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