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Elevated Admission Total Leukocyte Count in Young Patients with Coronary Artery Disease: A Potential Marker of Inflammation and Cardiovascular Risk

Running Title: *Elevated Admission TLC & Cardiovascular Risk*

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Abstract: ***Background: Coronary artery disease (CAD) in young individuals is increasingly recognized as a major health concern. Inflammation plays a pivotal role in the pathogenesis of CAD, and Total Leukocyte Count (TLC) has been suggested as a potential biomarker of inflammatory burden. This study aims to evaluate the relationship between elevated TLC and CAD in young patients, assessing its potential as a predictive marker of cardiovascular risk. Methodology: This cross - sectional observational study was conducted at Swaroop Rani Nehru Hospital, Prayagraj, involving patients aged 18 - 45 years presenting with chest pain and subsequently diagnosed with CAD. Clinical history, physical examination, and laboratory investigations, including elevated admission TLC levels, were recorded. Patients were categorized into two groups based on elevated admission TLC levels: elevated admission TLC (≥10, 000/mm³) and Normal TLC (<10, 000/mm³). The association between TLC levels and demographic, clinical, and biochemical parameters was analyzed using Pearson's Chi - Square test, with a significance level set at p<0.05. Results: Among the 100 patients enrolled, the majority (71.7%) were aged 41 - 45 years. Elevated TLC was significantly more common in males (78.3%) than females (21.7%). Clinical symptoms such as chest pain (100%), diaphoresis (93.3%), nausea/vomiting (60%), and smoking history (63.3%) were more prevalent in patients with increased TLC. The statistical analysis revealed a significant association between elevated admission TLC and mortality, with a p - value of 0.012, suggesting that higher TLC levels may indicate a higher inflammatory burden contributing to adverse cardiovascular outcomes. Conclusion: Elevated admission TLC in young CAD patients is strongly associated with increased inflammatory burden and adverse clinical outcomes. These findings highlight the potential role of TLC as a simple, cost - effective inflammatory biomarker for early risk stratification and prognosis in young CAD patients. Further studies are required to validate its predictive utility in clinical practice.***

Keywords: Coronary artery disease, Total Leukocyte Count, Inflammation, Young CAD, Biomarkers, Cardiovascular risk

1. Background

Cardiovascular diseases (CVDs) remain a leading cause of morbidity and mortality worldwide, with a growing burden in Asia due to demographic and lifestyle changes (1). Young patients with coronary artery disease (CAD) present a unique clinical challenge, as traditional risk factors may not fully explain their disease etiology. Inflammation plays a crucial role in the pathophysiology of CAD, and emerging evidence suggests that elevated total leukocyte count (TLC) may serve as a marker of systemic inflammation and cardiovascular risk (2).

While percutaneous coronary intervention (PCI) has improved survival rates, the long - term prognosis of young patients with CAD remains a concern (3). Current diagnostic modalities, including coronary computed tomography angiography (CTA) and coronary angiography, provide essential anatomical insights but have limitations such as high costs, limited accessibility, and exposure to ionizing radiation (4). Therefore, identifying cost - effective, easily accessible biomarkers for risk stratification and disease monitoring is essential (5).

The predictive value of white blood cell (WBC) count in cardiovascular risk assessment is well established (6–8). However, previous studies have primarily focused on its role in acute myocardial infarction (MI), with limited exploration of its relevance in young patients with stable CAD. Moreover, Asian populations exhibit distinct dietary habits, genetic predispositions, and risk factor profiles compared to Western populations, necessitating region - specific investigations (9, 10).

This study aims to evaluate the clinical significance of elevated TLC as a potential marker of inflammation and cardiovascular risk in young patients with CAD. By analyzing its association with disease severity and outcomes, we seek to establish TLC as a simple, cost - effective tool for risk assessment and prognostic evaluation in this population.

2. Methodology

Study Design

This study was designed as a cross - sectional observational study conducted at Swaroop Rani Nehru Hospital, Prayagraj. The study aimed to assess elevated admission TLC as a predictor of mortality in patient of young CAD.

Study Population

The study included patients aged 18–45 years, both male and female, who presented to the Medicine and Cardiology Department with chest pain and were subsequently diagnosed with coronary artery disease (CAD) based on electrocardiographic (ECG) findings, cardiac biomarkers, and clinical assessment. Patients were included if they met the following criteria: age between 18 - 45 years, presentation with chest pain and diagnosed with CAD, diagnosis confirmed through ECG changes (ST - elevation or non - ST elevation), elevated cardiac biomarkers (troponins), and/or coronary electrocardiographic findings, and provided informed consent to participate in the study. Patients were excluded if they had pre - existing hematological disorders affecting leukocyte count, acute or chronic infections, autoimmune diseases or inflammatory disorders, history of steroid or immunosuppressive therapy, or chronic kidney disease (CKD) or liver disease

Study duration: 13 months, march 2023 to march 2024

Data Collection

A detailed clinical history was obtained from each patient, including demographic details, smoking history, alcohol consumption, past medical history (hypertension, diabetes, dyslipidemia), and family history of premature CAD. A thorough physical examination was performed, including assessment of jugular venous pressure (JVP), pedal edema, and vital signs. Blood samples were collected at admission for Total Leukocyte Count (TLC), hemoglobin, platelet count, and differential leukocyte count. Additional biochemical tests, including fasting lipid profile, fasting blood sugar (FBS), hemoglobin A1c (HbA1c), renal function tests (RFT), and liver function tests (LFT), were conducted. Electrocardiography (ECG) was performed to assess ST - segment changes such as ST - elevation, ST - depression, and Q - waves. Echocardiography was used to evaluate left ventricular function and wall motion abnormalities.

Study Design and Statistical Analysis

Patients were categorized into two groups based on elevated admission TLC levels: elevated admission TLC Group (≥10, 000/mm³) and TLC Normal Group (<10, 000/mm³). The distribution of TLC across different age groups, gender, symptoms, and comorbidities was analyzed. The Pearson Chi - Square test was used to determine statistical significance. A p - value <0.05 was considered statistically significant. The data was analyzed using SPSS (Statistical Package for the Social Sciences) version 25.

Ethical Considerations

The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants before enrollment.

3. Results

Table 1: Distribution of elevated admission TLC Across Age, Gender, and Symptoms in young CAD patients

Category	Elevated admission TLC N (%)	TLC Normal N (%)	Total N (%)	p - value
30 - 35 years	11.70%	7.50%	10.00%	0.652
36 - 40 years	16.70%	22.50%	19.00%	
41 - 45 years	71.70%	70.00%	71.00%	
Male	78.30%	77.50%	78.00%	0.921
Female	21.70%	22.50%	22.00%	
Chest pain	100.00%	100.00%	100.00%	-
Diaphoresisis	93.30%	85.00%	90.00%	0.174
Nausea/vomiting	60.00%	57.50%	59.00%	0.803
Breathlessness	50.00%	47.50%	49.00%	0.806
Smoker	63.30%	47.50%	57.00%	0.117
Past history of COVID - 19 infection	20.00%	15.00%	18.00%	0.524
Alcoholic	33.30%	40.00%	36.00%	0.496

The distribution of total leukocyte count (TLC) across age, gender, and symptoms in young coronary artery disease (CAD) patients reveals that elevated admission TLC was most prevalent in the 41 - 45 years age group (71.70%), followed by 36 - 40 years (16.70%) and 30 - 35 years (11.70%). Among genders, males constituted 78.30% of those with elevated admission TLC, while females accounted for 21.70%, with no significant association (p=0.921). Chest pain was present in all patients (100%), whereas diaphoresis (93.30%), nausea/vomiting (60.00%), and breathlessness (50.00%) were more common among those with increased TLC. Smoking history was higher in the TLC increased group (63.30%) compared to 47.50% in the normal TLC group (p=0.117), while past COVID - 19 infection (20.00%) and alcohol consumption (33.30%) were not significantly different between groups.

Table 2: TLC Distribution Across Comorbidities in young CAD patients

Category	Elevated admission TLC N (%)	TLC Normal N (%)	Total N (%)	p - value
HTN	45.00%	35.00%	41.00%	0.319
DM	50.00%	60.00%	54.00%	0.326
Dyslipidemia	40.00%	55.00%	46.00%	0.14
Family H/O Premature CAD	8.30%	15.00%	11.00%	0.297
JVP Elevated	5.00%	15.00%	9.00%	0.087
Pedal Edema Present	16.70%	22.50%	19.00%	0.466
St Segment Depression	13.30%	22.50%	17.00%	0.232
Q Wave Present	25.00%	20.00%	23.00%	0.561
Outcome On Discharge Stable	90.00%	90.00%	90.00%	1
BMI Normal	90.00%	95.00%	92.00%	0.573
BMI Overweight	8.30%	5.00%	7.00%	
BMI Obesity	1.70%	0.00%	1.00%	

The distribution of TLC across comorbidities in young CAD patients shows that hypertension (HTN) was present in 45.00% of patients with increased TLC and 35.00% with normal TLC (p=0.319). Similarly, diabetes mellitus (DM) was observed in 50.00% and 60.00% of patients, respectively (p=0.326), while dyslipidemia was slightly more prevalent in the normal TLC group (55.00%) than in the elevated admission TLC group (40.00%) (p=0.14). A family history of premature CAD was observed in 8.30% of patients with

elevated admission TLC and 15.00% of those with normal TLC (p=0.297). Notably, jugular venous pressure (JVP) elevated (5.00% vs.15.00%, p=0.087) and ST - segment depression (13.30% vs.22.50%, p=0.232) were more common in patients with normal TLC. Obesity (1.70%) was observed only in the elevated admission TLC group, while overweight cases were comparable (8.30% vs.5.00%). The outcome on discharge was stable for 90.00% of patients in both groups, with no significant difference in BMI categories.

Table 3: TLC Distribution Across Comorbidities in young CAD patients

Category	Elevated admission TLC N (%)	TLC Normal N %	Total N %	p – value
Stable	84.40%	100.00%	90.00%	0.012
Expired	15.60%	0.00%	10.00%	

The TLC distribution across outcomes in young CAD patients highlights that among those with elevated admission TLC, 84.40% were discharged in stable condition, while 15.60% expired (p=0.012), indicating a significant association between increased TLC and mortality. Notably, all patients (100%) in the normal TLC group were discharged in stable condition, suggesting that TLC increase may correlate with worse outcomes in young CAD patients.

4. Discussion

In young CAD patients, TLC increase was most common in the 41 - 45 years age group (71.70%), with no significant gender difference. Chest pain was universal (100%), while diaphoresis (93.30%), nausea/vomiting (60.00%), and breathlessness (50.00%) were more frequent in those with increased TLC. Smoking (63.30%) was higher in the increased TLC group, but past COVID - 19 infection (20.00%) and alcohol use (33.30%) showed no significant association.

Among comorbidities, hypertension (45.00%) and diabetes (50.00%) were common in the increased TLC group, but dyslipidemia (55.00%) and elevated JVP (15.00%) were more frequent in the normal TLC group. Obesity (1.70%) was observed only in the increased TLC group. Despite these differences, 90.00% of patients in both groups were discharged in stable condition.

In terms of outcomes, increased TLC was significantly associated with mortality (p=0.012). Among those with increased TLC, 15.60% expired, whereas all patients with normal TLC survived. This indicates elevated TLC may be a marker of poor prognosis in young CAD patients.

5. Discussion

The analysis of TLC levels across age, gender, and clinical symptoms in young CAD patients revealed notable trends. The 41 - 45 age group had the highest prevalence of increased TLC (71.7%), aligning with studies by Bhavani et al. (2024) and Chmielewski & Strzelec (2015) (11, 12), which linked aging to leukocyte elevation and cardiovascular mortality. However, in our study, age was not significantly correlated with TLC (p = 0.652). Males had a higher prevalence of increased TLC (78.3%) than females (21.7%), similar to findings by Billi et al. (2023) (13), but the gender difference was not statistically significant (p = 0.921). Among clinical symptoms, chest pain (100%) and diaphoresis (93.3%) were common in patients with increased TLC, reinforcing inflammation's role in CAD, though without statistical significance. Smoking (63.3%) and past COVID - 19 infection (20%) were also associated with increased TLC, supporting the findings of Kashtanova et al. (2024) (14) and Billi et al. (2023) (13) on chronic inflammatory triggers, but no significant correlation was observed in our study.

Regarding comorbidities, no significant associations were found between increased TLC and hypertension (p = 0.319), diabetes (p = 0.326), dyslipidemia (p = 0.140), family history of CAD (p = 0.297), JVP (p = 0.087), pedal edema (p = 0.466), ST - segment changes (p = 0.232), Q waves (p = 0.561), or BMI (p = 0.573). However, ST - segment depression (22.5%) was more prevalent in patients with normal TLC, while obesity (1.7%) was observed only in the increased TLC group. The overall BMI distribution was not significantly different between groups, with normal - weight individuals making up the majority (90%) in both groups. These findings contrast with studies such as Patel et al. (2022) (19) and Blokland et al. (2020) (21), which found stronger associations between metabolic syndrome and inflammatory markers in CAD patients.

Most importantly, our study found a significant association between increased TLC and mortality (p = 0.012). Among those with elevated TLC, 15.6% expired, whereas all patients with normal TLC survived, highlighting TLC as a potential inflammatory marker of poor prognosis in young CAD patients. This finding aligns with Segal et al. (2024) (15), who also reported a significant correlation between elevated TLC and CAD - related mortality, reinforcing the role of systemic inflammation in cardiovascular outcomes. The Young Heart Study (2023) (16) similarly found no strong correlation between TLC and conventional cardiovascular risk factors, emphasizing the need for alternative inflammatory markers in younger CAD patients. Mody et al. (2024) (17) further suggested that non - traditional risk factors play a role in younger CAD patients, necessitating a broader biomarker approach. Ndunda et al. (2023) (18) hypothesized that genetic predisposition, lifestyle factors, and subclinical inflammation contribute to CAD severity in younger individuals, potentially explaining variations in TLC patterns.

Unlike our findings, Patel et al. (2022) (19) found a moderate association between increased TLC and metabolic syndrome, suggesting population - based variations in inflammatory responses. Additionally, Shulga et al. (2024) (20) and Blokland et al. (2020) (21) reported strong correlations between inflammatory markers and acute cardiovascular events, whereas our study found no significant symptom - based association with increased TLC.

Overall, our study highlights elevated admission TLC as a potential inflammatory marker in young CAD patients, particularly for predicting mortality risk. However, its clinical significance remains debated, given variations across populations, lifestyle influences, and genetic predisposition. Further research is needed to refine TLC's role in risk

stratification and personalized treatment approaches for young CAD patients.

6. Conclusion

Elevated admission TLC in young CAD patients is associated with an increased inflammatory burden and a higher risk of adverse outcomes, particularly mortality. While no significant associations were found with age, gender, or comorbidities, increased TLC correlated with worse prognosis, reinforcing its potential role as a cost - effective inflammatory biomarker for early risk stratification. Further studies are needed to validate its clinical utility and explore its integration into routine cardiovascular risk assessment in young CAD patients.

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