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Study the Changes in Hematological Parameters Based on Sputum Smear in Men Suffering Pulmonary Tuberculosis Attending Quefia Specialized Hospital for Chest and Tuberculosis-Benghazi

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Abstract:

Background

Pulmonary tuberculosis (PTB) remains one of the most infectious diseases worldwide, with significant morbidity and mortality rates. It is caused by *Mycobacterium tuberculosis*, which primarily affects the lungs but can also infect other parts of the body. The Immune system reacts to this infection, and its response leads to either latent or active disease. The immune system's response to infection leads to changes in various hematological and inflammatory parameters, which can be useful as diagnostic markers.

Subjects and methods

This study aimed to evaluate hematological and inflammatory parameters based on sputum smear positivity in 32 male PTB patients attending Quefia Hospital-Benghazi. Blood samples were collected at two different time points corresponding to sputum smear conversion. The patients' ages ranged from 15 to 67 years, and their medical histories were recorded.

Results

The results demonstrated significant increases in lymphocyte count (Lymph), lymphocyte percentage (Lymph%), mid-cell percentage (Mid%), and total white blood cells (WBCs). Red blood cell (RBC) parameters, including red cell distribution width-standard deviation (RDW-SD) and mean corpuscular hemoglobin (MCH), increased significantly with sputum smear conversion, whereas mean corpuscular volume (MCV) showed a significant decrease. Platelet parameters did not exhibit significant variations. However, inflammatory indices such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) significantly decreased as the sputum smear converted to negative.

Conclusion

These findings support the potential role of these hematological parameters in diagnosing and monitoring PTB pathogenicity.

Keywords: Pulmonary Tuberculosis; Hematological Parameters; Sputum Smear; Inflammatory Markers; NLR; PLR; SII; Complete Blood Count; Tuberculosis Diagnosis; Treatment Response.

Introduction:

Tuberculosis (TB) is an ancient disease that remains a significant global health challenge, particularly in low- and middle-income countries (Delogo et al., 2013). The causative agent, *Mycobacterium tuberculosis* (MTB), is responsible for pulmonary tuberculosis (PTB), which primarily affects the lungs but can also involve other organs, resulting in extrapulmonary tuberculosis (EPTB) (Khan et al., 2019). Several environmental factors, such as overcrowded and poorly ventilated spaces, as well as high humidity, contribute to the transmission of TB (Mathema et al., 2017).

MTB forms granulomas—clusters of immune cells that encapsulate bacteria—limiting bacterial spread while simultaneously shielding the pathogen from immune responses (Pieters, 2008; Liu et al., 2017; Acharya et al., 2020). The disease can manifest as **latent tuberculosis infection (LTBI)** when the immune system contains the bacteria without causing significant symptoms. However, TB becomes **active** when the immune response fails to control bacterial proliferation, leading to increased bacterial load and heightened infectivity (Pieters, 2008; Liu et al., 2017; Acharya et al., 2020).

Despite the availability of vaccines and antibiotics, TB remains a widespread disease, necessitating improved diagnostic and monitoring strategies. The World Health Organization (WHO) emphasizes the importance of enhanced screening and preventive treatment for high-risk populations (Drain et al., 2018). Hematological changes, such as anemia and fluctuations in white blood cell (WBC) and platelet counts, have been recognized as potential diagnostic markers and indicators of treatment response in TB patients (Abay et al., 2018). Sputum smear microscopy remains the primary diagnostic tool in resource-limited settings due to its simplicity and cost-effectiveness (Desikan, 2013). However, recent studies suggest that blood-inflammatory markers may also provide valuable insights into TB severity, treatment outcomes, and patient recovery (Pieters, 2008; Liu et al., 2017; Acharya et al., 2020).

This study aims to analyze hematological and inflammatory markers in active TB patients based on sputum smear results and evaluate their potential role in monitoring disease progression.

Methods:

This study was conducted on 32 male patients diagnosed with pulmonary tuberculosis (PTB) at Quefia Specialized Hospital for Chest and Tuberculosis in Benghazi. All patients provided informed consent and completed a medical history questionnaire. The inclusion criteria required a positive Ziehl-Neelsen-stained sputum smear, confirming the presence of acid-fast bacilli (AFB). Patients with HIV/AIDS were excluded to avoid potential confounding effects on hematological parameters.

Blood samples were collected at two time points: before and after anti-TB treatment, to assess hematological changes. Laboratory analysis included a complete blood count (CBC), which was used to calculate inflammatory markers such as the Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Systemic Inflammation Index (SII). These markers were evaluated to assess changes in the inflammatory status of patients throughout the treatment period.

Data analysis was performed using SPSS version 26. The Shapiro-Wilk test was used to assess normality, and paired-sample t-tests were conducted to compare pre- and post-treatment values. Independent-sample t-tests were applied for group comparisons, and Pearson correlation analysis was used to examine relationships between hematological parameters. A p-value of ≤ 0.05 was considered statistically significant.

Results:

Demographic data: This study was conducted on male patients attending Quefia Specialized Hospital for Chest and Tuberculosis in Benghazi from November 2022 to June 2023. The analysis of the questionnaire revealed that the patients' ages ranged from 15 to 67 years, with a mean age of 37.06 ± 11.86 years. Of the study sample, 72% were Libyan, while 28.1% were foreigners from various nationalities. As shown in **Figure 1**, 82% of the patients resided in Benghazi, while the remaining patients were from areas near and far from Benghazi, as shown in **Figure 2**.

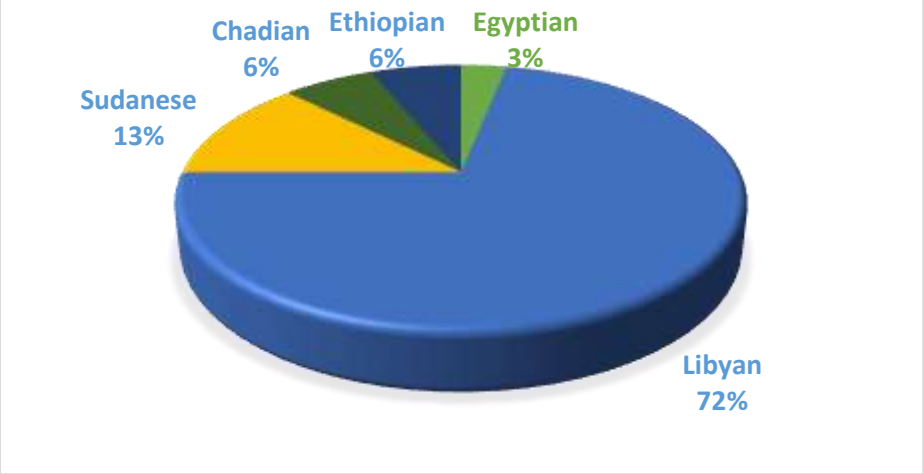

Figure 1: Distribution of Patient Nationalities in the Study Group

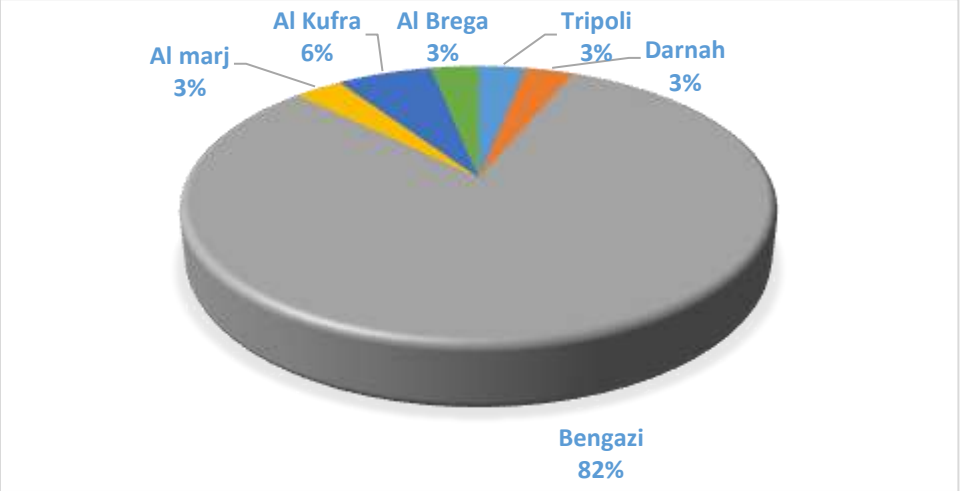

Figure 2: Distribution of Patient Residencies in the Study Group

As illustrated in **Figure 3,** the results of the patient-distributed survey showed that the majority of patients were self-employed, accounting for 62.5% of the study sample, followed by 9.4% working in the military or other official positions.

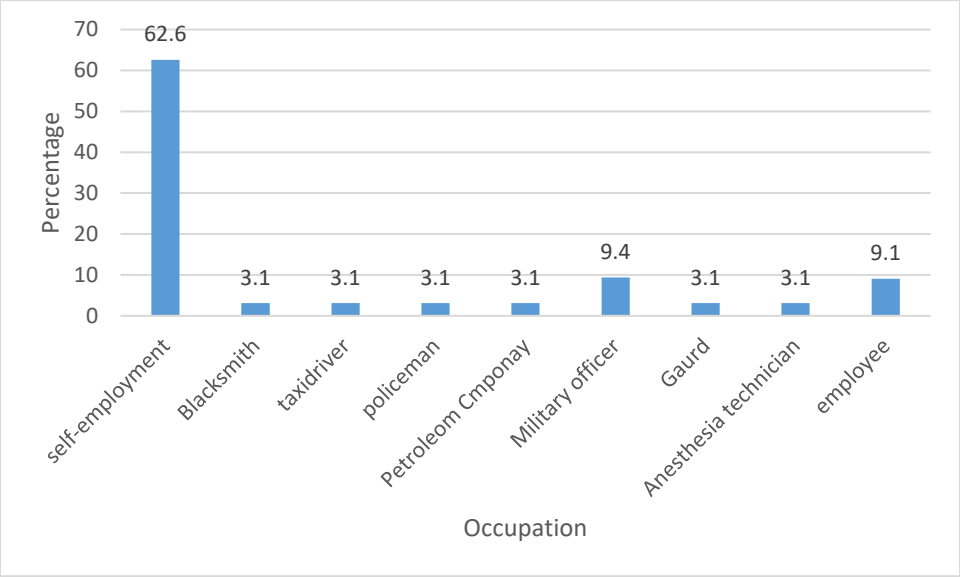

Figure 3: Percentage of Patients' Occupations in the Study Group

Medical History

All patients (100%) exhibited classic tuberculosis (TB) symptoms, including cough, fever, and appetite loss. Less common secondary symptoms included weight loss (37.5%), chest pain (18.8%), and night sweats (9.4%).

Regarding the medical history, the results showed that 12.5% of patients were smokers, 28.1% had diabetes, and 3.1% had hypertension. A family history of TB was reported in 18.8% of cases, while 9.4% had prior occupational exposure. Recurrent TB was observed in 12.5% of patients as illustrated in **Table1**

Table 1: Medical History and Infection Status of Patients in the Study Sample

Medical History	Number of Patients in the Study Sample (N, %)	
Previous family history of tuberculosis	6(18.8%)	Total 32(100%)
No previous family history of tuberculosis	23 (71.9%)	
Exposure to a work colleague or friend	3 (9.4%)	
Primary Infection	28 (87.5%)	Total 32 (100%)
Re-Infection	4 (12.5%)	

The results also showed that the highest incidence of tuberculosis among the studied patients occurred in young adults aged 26–35 years (40.6%), followed by those aged 36–45 years (25%) and 15–25 years (15.6%). The remaining percentages are listed in **Table 2**.

Table 2: Percentage Distribution of Tuberculosis Infection by Age Group

Age group (years)	Frequency (n)	Percentage (%)
15-25	5	15.6
26-35	13	40.6
36-45	8	25.0
46-55	2	6.3
56-65	3	9.4
66-75	1	3.1
Total	32	100.0

Hematological Findings

Blood samples taken before and after treatment showed significant variations in hematological parameters. Results were obtained once the patient was admitted to the hospital and diagnosed, and again after hospitalization and treatment, with an average duration of 35.56 days (ranging from 8 to 99 days). Hematological parameters, including WBC, neutrophils, lymphocytes, RBCs, Hb, and platelets, are compared between patients with negative and positive tuberculosis smears. The distribution of these parameters is presented across different levels compared to normal values for men (increase, normal, or decrease) to highlight variations between the two groups, as shown in **Table 3**.

Table 3: Hematological Parameters in Negative and Positive Smear Patients.

Parameters	Level	Positive smear Patients (N) %	Negative smear Patients (N) %
T WBC	Leukocytosis ⇧	**(12)** 37.5%	**(10) 31.25%**
	Normal range ⇔	**(17)** 53.2%	**(20) 62.5%**
	Leukopenia ⇩	**(3)** 9.4%	**(2) 6.25%**
Neutrophil	Neutrophilia ⇧	**(13)** 40.6%	**(10) 31.25%**
	Normal range ⇔	**(17)** 53.2%	**(20) 62.5%**
	Neutropenia ⇩	**(2)** 6.25%	**(2) 6.25%**
Lymphocyte	Lymphocytosis ⇧	**(6)** 18.75%	**(1) 3.1%**
	Normal range ⇔	**(26)** 81.25%	**(29) 90.6%**
	Lymphopenia ⇩	**(0)** 00%	**(2) 6.25%**
RBCs	Erythrocytosis ⇧	**(1)** 3.1%	**(0) 00%**
	Normal range ⇔	**(7)** 21.9%	**(9) 28.12%**
	Anemia ⇩	**(24)** 75%	**(23) 71.9%**
Hb	Polycythemia ⇧	**(0)** 00%	**(0) 00%**
	Normal range ⇔	**(5)** 15.63%	**(9) 28.12%**
	Anemia ⇩	**(27)** 84.37%	**(23) 71.9%**
Plt	Thrombocytosis ⇧	**(20)** 62.5%	**(24) 75%**
	Normal Range ⇔	**(12)** 37.5%	**(7) 21.9%**
	Thrombocythemia ⇩	**(00)** 0.00%	**(1) 3.1%**

White Blood Cells (WBCs): While total WBC count remained largely unchanged, Lymph, Lymph%, Mid%, and Mid values significantly increased after smear conversion ($p < 0.05$). As listed in **Table 4**.

Table 4: The variation in WBCs values in patients with positive and negative sputum smears.

parameters	Mean ± SD		P.value
	Patients with positive results	Patients with negative results	
WBC* 10^9/L	9.703±3.788	9.273±3.613	0.599
Lymph* 10^9/L	1.334 ±0.548	1.884±1.247	0.032*
Mid* 10^9/L	0.472±0.231	0.750±0.648	0.039*
Neut* 10^9/L	7.828±3.512	6.769 ±3.851	0.147
Lymph%	7.260±15.588	21.713±10.775	0.001*
Mid%	5.153±2.154	7.359 ±2.707	0.001*
Neut%	79.522 ±8.690	69.772 ±14.682	0.134

Red Blood Cells (RBCs): RBC count, hemoglobin (Hb), and hematocrit (HCT) remained relatively stable, but MCV decreased significantly ($p = 0.003$), while RDW-SD and MCH increased ($p < 0.001$), as shown in **Table 5.**

Table 5 The variation in RBCs values in patients with positive and negative sputum smears.

Parameters	Mean ± SD		P.value
	Patients with positive results	Patients with negative results	
RBC * 10^9/L	4.119±1.452	3.855±0.720	0.276
HGB (g/dl)	10.747 ±2.346	11.491±2.163	0.143
HCT (%)	34.772±5.907	36.744±6.060	0.120
MCV (ft)	89.900±7.729	59.775±10.322	0.003*
MCH (pg)	27.834±3.142	30.088 ±3.525	0.000*
MCHC (%)	31.072±1.625	31.244±1.221	0.590
RDW-SD (%)	51.900 ±9.942	58.775 ± 10.317	0.000*
RDW-CV (%)	15.906±3.472	17.409±3.982	0.070

Platelets: No significant changes were observed in platelet count (PLT), plateletcrit (PCT), mean platelet volume (MPV), or platelet distribution width (PDW). As illustrated in table 6.

Table 6: The variation in platelet values in patients with positive and negative sputum smears.

Parameters	Mean ± SD		P.value
	Patients with positive results	Patients with negative results	
PLT* 10^9/L	388.81±135.459	378.69±109.743	0.681
PCT (%)	0.293 ±0.097	0.288±0.079	0.771
MPV (ft)	7.525±1.682	7.456±1.318	0.840
PDW (%)	15.606±0.868	15.434±0.490	0.221

Inflammatory Markers: NLR, PLR, and SII significantly decreased following sputum smear conversion ($p < 0.05$), suggesting a reduction in inflammation with successful treatment, As shown in table 7.

Table7: The variation in inflammatory markers values in patients with positive and negative sputum smears.

Parameters	Mean ± SD		P.value
	Patients with negative results	Patients with negative results	
NLR	4.428±3.026	6.632±3.642	0.000*
PLR	248.968±118.096	329.313 ±139.600	0.006*
SII	1815.751±1433.221	2684.654±1846.607	0.003*

Discussion:

Tuberculosis (TB) causes nearly 700,000 deaths annually, which is more than the combined deaths caused by several other diseases. In some years, the death toll has surpassed 1.5 million, making TB one of the ten most dangerous causes of death worldwide. The World Health Organization (WHO) has outlined various strategies to reduce TB infections and ultimately eliminate the disease. One of the main strategies is to improve efforts in identifying individuals with active TB and treating them, as well as preventing the progression of latent TB into active cases. Despite the availability of several diagnostic methods, distinguishing between latent and active TB remains challenging with simple laboratory techniques in developing countries (De Martino et al., 2019; Christian et al., 2020).

This study, therefore, focused on the simplest laboratory methods, specifically blood count measurements, to analyze the changes in the blood profile of infected individuals. The significance of studying blood cells lies in their role as the primary cellular component of the immune system, which interacts with TB. The result of this interaction determines whether TB presents as latent or active (Delogu et al., 2013; Luies and Du Preez, 2020). This study's findings reflect how pulmonary TB impacts the blood profile and inflammatory markers—indicators of the immune system's response to TB bacteria—and how the immune system's reaction influences the course of the disease.

Key blood profile changes observed in patients with positive sputum smears included a decrease in hemoglobin concentration and a reduction in red blood cell count in 75.84% and 37.5% of study participants, respectively. Despite patients responding to treatment, the rate of anemia remained 71.9% in those with negative sputum results. These findings align with previous studies that reported a high prevalence of anemia in TB patients (Shareef and Amin, 2012; Monirozzaman, 2018). However, the anemia rates in this study (71.9%, 75%, 84.37%) were higher compared to those in other studies. Anemia was one of the most common blood disorders among participants, either due to low hemoglobin concentration or reduced red blood cell count, particularly among adult males.

No significant differences were observed in red blood cell indices based on sputum smear positivity, except for MCV, RDW-SD, and MCH, which is consistent with findings from several studies. This may be due to various factors, such as immune response products or the effects of treatment on red blood cells. A study conducted at Gondar University Hospital in India showed that immune response products like IL-6 and TNF-a could reduce erythropoietin production, leading to decreased red blood cell production or directly affecting iron metabolism and absorption (Abay et al., 2018). Anemia that appears after the patient's response to treatment and a negative sputum result may be attributed to the negative

impact of inflammatory mediators on red blood cell production, along with the effects of antimicrobial treatment. Overall, some studies suggest that the most notable impact on red blood cells is an increase in red blood cell count in most individuals, which was not observed in this study (Ştefanescu et al., 2021).
Regarding platelet count and related values, no significant changes were observed before and after treatment, and platelet levels were slightly elevated compared to normal values. Some studies suggest that this lack of significant elevation in platelets might be due to their involvement in inflammatory reactions, which could lead to a reduced platelet count in peripheral blood, explaining the lack of change in platelet-related blood values (Abay et al., 2018). In general, most patients had either normal or elevated platelet counts before treatment (37.5% and 62.5%, respectively). After treatment, 21.9% and 75% of patients had normal and elevated platelet counts, respectively. This platelet increases in our study contrasts with findings from Monirozzaman, which reported a decrease in platelet count in 71.4% of TB patients (Monirozzaman, 2018).
A significant decrease in MCV was noted in patients with negative sputum results compared to those with positive results, which could be attributed to the substantial changes in red blood cell count due to immune responses or the effects of antimicrobial treatment. This finding agrees with a study by Shah et al. (2020), which showed lower MCV than the normal range in pulmonary TB patients. Other studies reported varying results, such as normal MCV (Minchella et al., 2015; Kahase et al., 2020) or a significant increase in MCV (Devi et al., 2003). In contrast, this study found an increase in both RDW-SD and MCH above normal levels, possibly reflecting anemia and the impact of TB infection on red blood cells.
The total white blood cell count remained within normal ranges but showed a slight increase. Specifically, neutrophils and lymphocytes increased by 40% and 18%, respectively, likely due to the activation of the general immune response and specific cellular immunity in the form of increased lymphocyte counts. The results showed a positive correlation between elevated white blood cells, lymphocytes, neutrophils, and platelet count after the sputum smear result changed. Correlation analysis also revealed that platelets had a positive effect on the duration of hospital stay and positively impacted all inflammatory markers studied (PLR, NLR, SII), as well as PCT and WBC. In contrast, lymphocyte count, hemoglobin, and hematocrit showed an inverse correlation with platelet count.
The study results showed a significant decrease in all inflammatory markers after the sputum smear result changed, further emphasizing the importance of evaluating these markers and their potential use in monitoring patient progress. The increase in PLR in patients with positive sputum smears and its subsequent decrease after treatment, coinciding with bacterial clearance from the sputum, supports the potential use of this inflammatory marker as a diagnostic tool for pulmonary TB. The findings of this study align with the results of a study by Chen et al. (2022), which evaluated the use of inflammatory markers as diagnostic tools. Their study found elevated inflammatory markers, including PLR and NLR, in patients with tuberculous meningitis.
These findings also theoretically align with a study conducted in India (2011-2012) on newly diagnosed TB patients, which investigated the impact of TB on blood variables and hemostatic factors. This study concluded that TB directly affects blood variables, causing a reduction in red blood cell count and disturbances in platelet and white blood cell counts. Additionally, it found a heightened predisposition to thrombosis and elevated fibrinogen, factor VIII, and D-dimer levels, with immediate improvements upon treatment response (Kutiyal et al., 2017).

The results of this study also support findings from Wicaksono, who emphasized the importance of inflammatory markers as diagnostic factors. His study, which examined changes in inflammatory markers and the effects of treatment on drug-resistant TB, showed significant differences in markers (MLR, NLR, PLR) at diagnosis and after 30 days of treatment with drug-resistant TB. His study suggested that platelet count has diagnostic value compared to other markers (Wicaksono, 2018).

Conclusion This study underscores the importance of hematological parameters in diagnosing and monitoring PTB. Significant changes in RBC indices, WBC subpopulations, and inflammatory markers provide valuable insights into disease progression and treatment response. The observed decline in inflammatory indices following smear conversion suggests their utility in assessing treatment efficacy. Further large-scale studies are recommended to validate these findings and explore their clinical applications.

Recommendations:

- Conduct more studies across various centers with larger TB patient samples.
- Include phagocytic cell and platelet markers in future research due to their relevance to TB and immune response.
- Implement routine use of inflammatory markers (e.g., PLR, NLR, SII) to monitor pulmonary TB patients.
- Establish accurate patient data recording systems and databases in healthcare centers for research and analysis.
- Focus on statistical analysis of patient data and regularly monitor it for better treatment outcomes.
- Investigate the role of systemic inflammatory markers throughout TB treatment until full recovery.
- Address the lack of medical care in remote areas by improving monitoring of healthcare centers and ensuring consistent, accessible treatment for all patients.

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