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Original Article

Complete blood count indices as inflammatory markers in diabetic patients with active pulmonary tuberculosis

Pulmonology

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ABSTRACT

Background: The role of hematological-indices in follow-up of pulmonary tuberculosis (PTB) has not been extensively investigated.

Objectives: To evaluate the role of hematological-indices as inflammatory markers in PTB course in diabetes mellitus (DM) and non-diabetes mellitus (NDM) patients.

Methodology: The present prospective cohort study included a total of 90 active pulmonary tuberculosis patients. They were grouped into 30 uncontrolled (DM-TB), 30 controlled (DM-TB), and 30 (NDM-TB) patients. All have active smear-positive PTB. The following parameters were reported before starting anti-TB treatment (baseline), and at 1st, and2nd months after starting treatment; mean corpuscle volume (MCV), red blood cell distribution width (RDW), mean corpuscle hemoglobin (MCH), mean corpuscle hemoglobin concentration (MCHC), mean platelet volume (MPV),platelet distribution width (PDW),neutrophil-lymphocyte ratio (NLR), monocyte lymphocyte ratio (MLR) and platelet lymphocyte ratio (PLR).

Results: the MCV and RDW were significantly higher in the uncontrolled DM-TB group than in the other two groups, and in the controlled DM-TB group than in the NDM-TB group at baseline,1st and2nd months. The RDW was significantly decreased from baseline till 2nd month in the uncontrolled and controlled DM-TB groups. The MPV was significantly lower in uncontrolled DM-TB group than in the other two groups, and in controlled DM-TB group than in the NDM-TB group at baseline, 1st and 2nd months. PDW was significantly reduced in uncontrolled and controlled DM-TB groups than in the NDM-TB group at 2nd month. In the uncontrolled and controlled DM-TB groups, the MPV and PDW were significantly increased during follow-up. The NLR and PLR were significantly higher in uncontrolled DM-TB group than the other two groups and in controlled DM-TB group than in NDM-TB group at 1st month. MLR was significantly higher in uncontrolled DM-TB group than in the other two groups and in controlled DM-TB group than in NDM-TB group at 1st and 2nd months. In uncontrolled DM-TB and controlled DM-TB groups the NLR, PLR, and MLR were decreased during follow-up.

Conclusion: The MCV, RDW, MPV, PDW, NLR, PLR and MLR could have an important role in follow-up of PTB in diabetic patients and in predicting treatment outcome.

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Keywords: Complete blood count indices; tuberculosis; diabetes mellitus

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INTRODUCTION

Tuberculosis (TB) and diabetes mellitus (DM) represent two intersecting global epidemics with considerable implications for public health. DM is linked to a 3-fold increased risk of developing active TB, attributed largely to the deleterious impact of hyperglycemia on cell mediated immunity [1].

The World Health Organization (WHO) advised crucial intervention plans to mitigate the burden of DM-TB comorbidity. These strategies include starting collaboration between TB and DM control programs, identifying and treating TB in patients with DM, and identifying and managing DM in TB patients [2].

The DM was discovered to affect the manifestation of TB, resulting in increased cavitation, higher severity TB scores, and a greater likelihood of having smear or culture positive pulmonary TB (PTB). Also, diabetes enhances the bacterial load of mycobacterium TB with prolonged duration to negative results of TB cultures [3]. DM hampers the immune response of cells involved in fighting infections, while inadequate control of blood sugar levels negatively impacts the production of cytokines and disrupts the defense mechanisms of alveolar macrophages. Hyperglycemia impairs the ability of neutrophils to be recruited, the chemotactic movement of monocytes, and the phagocytic action of alveolar macrophages. Additionally, the release of interferon-gamma that is specific to the antigen is reduced due to the poor activation of T-helper cells. Furthermore, changes in the small blood vessels of the lungs and a lack of essential nutrients create favorable conditions for the spread and development of TB, as both the body's immune system and nutritional status are compromised. Chronic immunosuppression or an inadequate immune response makes individuals more susceptible to TB infection and increases the amount of TB bacteria in their bodies. [4].

Hematological abnormalities are commonly observed in DM-TB patients as a consequence of disordered hematopoiesis and immune dysfunction under glucotoxic conditions. Leukocyte counts are heavily impacted by the DM-TB state. Neutrophil and monocyte counts are typically elevated, resulting in elevated neutrophil-lymphocyte ratio (NLR) and monocyte-lymphocyte ratio (MLR). Lymphopenia arising from activation-induced apoptosis and sequestration at disease sites contributes to the imbalanced leukogram [5].

Hematological parameters, including mean corpuscular volume (MCV), red cell distribution width (RDW), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), and platelet distribution width (PDW) have been studied in the context of chronic inflammatory diseases, little is known about the correlation of these hematological parameters and incidence of TB especially among people in special situation as diabetic patients. Thus, this study was conducted aiming to evaluate the role of hematological indices as inflammatory markers in PTB course in diabetic and non- diabetic patients.

PATIENTS AND METHODS

This prospective cohort study was carried out in TB-sensitive wards of Mansoura chest hospital, during the period from August 2022 to February 2023.

Inclusion criteria: both male and female adult patients aged 18–- 62 years old, recently diagnosed with PTB. They were categorized into 3 groups:

- **Uncontrolled DM-TB group:** included 30 uncontrolled DM patients (HBA1c ≥ 6.5%) with smear-positive PTB.
- **Controlled DM-TB group:** included 30 controlled DM patients (HBA1c < 6.5%) with smear-positive PTB.
- **Non-DM-TB group:** included 30 non-diabetic patients with smear-positive PTB.

Exclusion criteria: Patients with extrapulmonary TB, smear-negative PTB, drug-resistant TB, hepatitis C virus, hepatitis B virus, chronic liver disease, chronic kidney disease, autoimmune diseases, as well as pregnant and lactating females were excluded from the study.

Methods

Data regarding age, sex, toxic symptoms e.g. night fever, night sweating, loss of appetite, and loss of weight were reported. Sputum smear conversion time / weeks which is the time from starting anti-TB medications till sputum smear microscopy became negative were recorded.

Microbiological diagnosis of PTB by Ziehl-Neelsen staining of sputum–and Gene expert was done for all studied participants.

The HBA1C was measured using HITACH9-911 TM autoanalyzer, Switzerland). It was done for diabetic patients to determine the levels of control: value ≤ 6.4% was considered controlled DM and value ≥ 6.5% or more was considered uncontrolled DM.

Complete blood count (CBC) was done before starting anti-TB treatment (baseline), one month after starting anti-TB treatment (1st month), and 2 months after starting anti-TB treatment (2nd month). It was done using a hematological analyzer (Sysmex XE-21N, Kobe, Japan). The following indices were reported; mean corpuscle volume (MCV), red blood cell distribution width (RDW), mean corpuscle hemoglobin (MCH), mean corpuscle hemoglobin concentration (MCHC), mean platelet volume (MPV), and platelet distribution width (PDW). Platelet count, neutrophil count and monocytes count were measured for calculation of neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), and platelet-lymphocyte ratio (PLR).

Ethical considerations

Before enrolling into the study, the participants were given a clear explanation of the study objectives and tools. Informed consent was obtained from all participants. The study protocol received approval from the research ethics committee of the faculty of medicine for girls, Cairo, Al-Azhar University, Egypt. All data has been encrypted and encoded to ensure the anonymity of participants. Participants could decline participation or withdraw from the study without providing a reason, and without impact their rights to medical care.

Statistical analysis

The analysis was carried out using SPSS, PASW statistics for Windows version 25, Chicago: SPSS Inc.

qualitative data were presented as number and percentages. The Kolmogorov-Smirnov test was applied to determine the normal distribution of the quantitative data, thereafter, it was presented as median and interquartile range (IQR) if not normally distributed, and as mean ± SD if normally distributed. Qualitative data between groups were compared using either Chi-Square test (x^2), Fisher exact test (FE), and Monte Carlo testing (MC), as appropriate. For comparison between the three studied groups, the Kruskal Wallis (KW) was for not normally distributed data, and One Way ANOVA test (F) was used for normally distributed data. For comparison between two independent groups, the Mann-Whitney U test (MW) was used for non-normally distributed data, and the Student t-test (t) was used for normally distributed data. Wilcoxon Signed Rank test was implemented to compare between two studied periods. Spearman's rank-order correlation is employed to ascertain the magnitude and direction of a linear association between two variables that are not regularly distributed, either continuous or ordinal. For all used statistical tests p-value < 0.05 was considered significant (95% confidence interval).

RESULTS

No statistically significant difference was detected among the studied groups regarding age and sex. The Prevalence of toxic symptoms was higher among uncontrolled DM-TB and NDM-TB cases compared to controlled DM-TB cases (p = 0.001). The conversion time was significantly longer in uncontrolled DM-TB group compared to controlled DM-TB and NDM-TB groups (p = 0.001) (table1).

The MCV was significantly higher among the uncontrolled DM-TB group than the other two groups at baseline, 1st and 2nd months (p<0.05). Regarding comparison within group, the MCV was significantly reduced at 2nd month than at baseline in NDM-TB group (p<0.05), while it was non-significantly differed during follow up in uncontrolled or controlled DM-TB groups (p > 0.05) (table 2).

The RDW was significantly higher among the uncontrolled DM-TB group than the other two groups at base line, 1st month, and 2nd month (p<0.05). Regarding comparison within group the RDW was significantly reduced at 1st and 2nd months than at baseline and at 2nd month than at 1st month in uncontrolled DM-TB group, while in controlled DM-TB group, the RDW was significantly lower at1st month than at baseline and at 2nd month than at 1st month (p < 0.05). In NDM-TB group the RDW was significantly lower at 2nd month than at both baseline and 1st month (p < 0.05) (table 2).

The MCH was not differed at baseline, 1st month and 2nd month between the three groups (p >0.05). Regarding comparison within group the MCH was significantly increased in uncontrolled DM-TB group at both 1st and 2nd months than at baseline (p<0.05), while in controlled DM-TB group and NDM-TB group, the MCH was not differed between the three measurements (p >0.05). The MCHC was not differed either between groups or within group during follow up (p >0.05) (table 2).

A statistically significant lower mean MPV was found in the uncontrolled DM-TB group than in the other two groups at baseline, 1st and 2nd months (p<0.05). Regarding comparison within group, in the uncontrolled DM-TB and NDM-TB group the MPV was significantly increased at 2nd month than at either baseline or 1st month (p<0.05). In the controlled DM-TB group there was significant increase in MPV at 2nd month than at 1st month (p<0.05) (table 3).

Table (1): Comparison of age, sex, toxic symptoms, and conversion time among groups

Item		Uncontrolled DM-TB n = 30	Controlled DM-TB n = 30	NDM-TB n = 30	Stat. test	p-value
Age (yrs.) [Mean ±SD]		49.63±16.59	42.93±15.13	41.47±13.07	F=2.53	0.09
Gender	Male [no. (%)]	27 (90%)	29 (96.7%)	30 (100%)	MC=3.66	0.160
	Female [no. (%)]	3 (10%)	1 (3.3%)	0 (0%)		
Toxic symptoms [no. (%)]		30 (100%)	21 (70%)	28 (93.3%)	X^2=13.88	0.001*
Conversion time (weeks)		7.32±0.86	4.82±2.56	3.03±0.89	F=50.25	0.001*

The statistical tests used were one-way ANOVA (F test) and chi-square test, *: Significant p-value (< 0.05).

The PDW was significantly lower in both uncontrolled DM-TB and controlled DM-TB groups than in the NDM-TB group at 2nd month (p<0.05). In both uncontrolled DM-TB and controlled DM-TB groups; there was significant increase in PDW at both 1st and 2nd months than at baseline, and at 2nd month than at ~~first~~ 1st month (p<0.05) (table 3).

NLR was significantly higher in the uncontrolled DM-TB group than other in the two groups and in the controlled DM-TB group than in the NDM-TB group at 1st month (p<0.05). Regarding comparison within group, the uncontrolled DM-TB group showed significant decreases in NLR at 2nd month than at baseline (p<0.05). In the controlled DM-TB and NDM-TB groups there was significant decrease in NLR at 2nd month than at either baseline or 1st month (p<0.05). The PLR was significantly higher in the uncontrolled DM-TB group than in the other two groups and in the controlled DM-TB group than in the NDM-TB group at 1st month (p<0.05). Regarding comparison within group, PLR was significantly reduced at 1st and 2nd months than at baseline in uncontrolled DM-TB group (p<0.05). The MLR was significantly higher in the

uncontrolled DM-TB group than in the other two groups and in the controlled DM-TB group than in the NDM-TB group at 1st and 2nd months (p<0.05). Regarding comparison within group, the MLR was significantly decreased at 1st and 2nd months than at baseline (p<0.05), and at 2nd month than at 1st month in NDM-TB group (p<0.05) (table 4).

In total diabetic patients, conversion time showed significant positive correlations with MCV, RDW, MCH, MCHC at baseline, 1st and 2nd months (p<0.05) (table 5). Also, it showed positive correlations with MPV and PDW at baseline, 1st and 2nd months (p<0.05) (table 6). Additionally, it showed significant positive correlations with NLR, PLR and MLR at baseline, 1st and 2nd months (p<0.05) (table7).

Table (2): Comparison of red blood cell indices among studied groups and within group before and after treatment

Red blood cell indices		Uncontrolled DM-TB n = 30	Controlled DM-TB n = 30	NDM-TB n = 30	Stat. test	Post hoc analysis between groups
MCV (fl/cell)	Baseline	90.61±5.83	79.76±6.31	75.28±4.97	F=50.2 p<0.001*	P4< 0.001 P5< 0.001 P6= 0.004
	1st month	85.48±4.65	77.85±6.72	73.37±4.47	F=29.68 p<0.001*	P4< 0.001 P5< 0.001 P6= 0.003
	2nd month	85.46±5.25	77.13±6.56	73.33±4.43	F=38.38 p<0.001*	P4< 0.001 P5< 0.001 P6= 0.004
Post hoc analysis within group		p1=0.299 p2=0.510 p3=0.106	p1=0.280 p2=0.084 p3=0.650	p1=0.07 p2=0.014* p3=0.948		
RDW (%)	Baseline	26(0.11-8)	19(1-39)	16(11-23)	KW=35.98 p<0.001*	P4< 0.001 P5< 0.001 P6= 0.005
	1st month	20.5(1.3- 16.4)	18(1.3-15.9)	14.5(12-23)	KW=21.53 p<0.001*	P4< 0.001 P5< 0.001 P6< 0.001
	2nd month	19(14-52)	17(1.2-39)	13(1.1-15)	KW=51.00 p<0.001*	P4< 0.001 P5< 0.001 P6< 0.001
Post hoc analysis within group		p1=0.005* p2=0.001* p3=0.038*	p1=0.01* p2=0.861 p3=0.013*	p1=0.691 p2<0.001* p3<0.001*		
MCH (pg/cell)	Baseline	24.58±2.76	25.68±2.98	24.65±3.55	F=1.19 p=0.310	
	1st month	25.48±2.65	25.89±2.79	25.45±2.09	F=0.294 p=0.746	
	2nd month	25.79±2.53	25.91±2.96	25.46±2.77	F=0.269 p=0.459	
Post hoc analysis within group		p1=0.004* p2=0.004* p3=0.468	p= 0.1	P= 0.2		
MCHC (g/dl)	Baseline	32.70±2.14	33.67±2.43	32.92±2.15	F=1.53 p=0.222	
	1st month	32.95±2.36	33.89±2.87	33.41±1.78	F=1.18 p=0.313	
	2nd month	32.69±2.05	33.79±2.59	33.59±1.95	F=2.09 p=0.129	
Post hoc analysis within group		p= 0.6	p= 0.5	p= 0.3		

MCV: Mean corpuscular volume, RDW: Red cell distribution width, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration. DM: Diabetes mellitus, TB: Tuberculosis, The statistical tests used were one-way ANOVA (F test) and Kruskal-Wallis test (KW), p1: Baseline vs. 1st month, p2: Baseline vs. 2nd month; p3: 1st vs. 2nd months; p4: Uncontrolled DM-TB group vs. controlled DM-TB group; p5: Uncontrolled DM-TB group vs. NDM-TB group, p6: Controlled DM-TB group vs. NDM-TB group, *: Significant p-value (< 0.05).

Table (3): Comparison of platelet indices among studied groups and within group before and after treatment

Platelet indices		Uncontrolled DM-TB n = 30	Controlled DM-TB n = 30	NDM-TB n = 30	Stat. test	Post hoc analysis between groups
MPV (fl/cell)	Baseline	6.29±0.99	6.95±0.66	8.13±1.19	F=15.8 p <0.001*	p4= 0.004* p5 < 0.001* p6 < 0.001*
	1st month	6.97±0.85	7.01±0.76	8.21±0.75	F=20.25 p <0.001*	p4= 0.004* p5 < 0.001* p6 < 0.001*
	2nd month	7.30±0.81	7.08±0.91	8.96±0.69	F=42.15 p <0.001*	p4= 0.045* p5 < 0.001* p6 < 0.001*
Post hoc analysis within group		p1=0.307 p2=0.002* p3=0.001*	p1=0.174 p2=1.0 p3=0.012*	p1=0.846 p2=0.002* p3=0.001*		
PDW(%)	Baseline	12.36±1.35	13.37±0.81	13.97±4.14	F=3.05 p=0.053	
	1st month	13.29±1.08	14.40±0.62	14.78±4.19	F=2.82 p=0.07	
	2nd month	14.39±0.53	14.92±4.08	16.02±0.50	F=12.5 p<0.001*	p4= 0.5 p5< 0.001 p6< 0.001
Post hoc analysis within group		p1<0.001* p2<0.001* p3<0.001*	p1<0.001* p2<0.001* p3<0.001*	p1=0.360 p2=0.733 p3=0.514		

MPV: Mean platelet volume, PDW: Platelets distribution width, DM: Diabetes mellitus, TB: Tuberculosis. F: One-way ANOVA test: KW: Kruskal Wallis test, p1: Baseline vs. 1st month, p2: Baseline vs. 2nd month; p3: 1st vs. 2nd months; p4: Uncontrolled DM-TB group vs. controlled DM-TB group; p5: Uncontrolled DM-TB group vs. NDM-TB group, p6: Controlled DM-TB group vs. NDM-TB group, *: Significant p-value (< 0.05).

Table (4): Comparison of NLR, PLR and MLR change among studied groups and within group before and after treatment

		Uncontrolled DM-TB n = 30	Controlled DM-TB n = 30	NDM-TB n = 30	Stat. test	Post hoc analysis between groups
NLR (median)	Baseline	5.91 (1.08-16.5)	4.83 (2.08- 24.33)	3.78 (1.08-10.94)	KW=2.15 p=0.07	
	1st month	4.92 (0.85-18.14)	4.35 (1.39-26)	3.59 (1.89-43)	KW=3.56 p=0.05*	p4= 0.01 p5< 0.001 p6< 0.001
	2nd month	3.46 (0.98-14.5)	4.21 (0.98-7.73)	3.18 (0.62-6.55)	KW=3.19 p=0.203	
Post hoc analysis within group		p1=0.131 p2=0.03* p3=0.600	P1=0.974 P2=0.001* P3=0.001*	P1=0.894 P2=0.03* P3=0.03*		
PLR (median)	Baseline	280.13 (68.08-616.67)	263.56 (77.33-691.43)	239.38 (68.08-482)	KW=0.350 p=0.839	
	1st month	230.55 (86.19-881.43)	227.76 (96.45-2250)	224.07 (78.42-2220)	KW=4.41 p=0.04*	p4< 0.001 p5< 0.001 p6< 0.001
	2nd month	218.33 (38.65- 533.33)	217.43 (38.65-450)	218.23 (27.7-454.17)	KW=2.49 p=0.288	
Post hoc analysis within group		P1=0.02* P2=0.01* P3=0.25	P1=0.600 P2=0.644 P3=0.558	P1=0.262 P2=0.517 P3=0.318		
MLR (median)	Baseline	0.635 (0.13-2.0)	0.508 (0.08-1.71)	0.445 (0.07-1.0)	KW=3.25 P=0.07	
	1st month	0.559 (0.0-1.29)	0.501 (0.12-2.0)	0.370 (0.11-1.23)	KW=6.51 p=0.02*	p4= 0.002 p5< 0.001 p6< 0.001
	2nd month	0.409 (0.19-1.45)	0.435 (0.07-1.22)	0.333 (0.07-0.86)	KW=10.2 p=0.003*	p4< 0.04 p5< 0.001

						p6< 0.001
Post hoc analysis within group	p= 0.09	p= 0.07	P1=0.03* P2=0.05* P3=0.01*			

NLR: Neutrophil to lymphocyte ratio, PLR: platelet to lymphocyte ratio, MLR: Monocyte to lymphocyte ratio. DM: Diabetes mellitus, TB: Tuberculosis. F: One-way ANOVA test: KW: Kruskal Wallis test, p1: Baseline vs. 1st month, p2: Baseline vs. 2nd month; p3: 1st vs. 2nd months; p4: Uncontrolled DM-TB group vs. controlled DM-TB group; p5: Uncontrolled DM-TB group vs. NDM-TB group, p6: Controlled DM-TB group vs. NDM-TB group, *: Significant p-value (< 0.05).

Table (5): Correlation of conversion time with RBCs indices in patients with DM and TB (n = 60)

Variables		Conversion time	
		r	p-value
MCV	Baseline	0.659	0.002*
	1st month	0.685	0.007*
	2nd month	0.721	0.001*
RDW	Baseline	0.458	0.04*
	1st month	0.512	0.03*
	2nd month	0.536	0.02*
MCH	Baseline	0.465	0.048*
	1st month	0.521	0.03*
	2nd month	0.634	0.001*
MCHC	Baseline	0.499	0.045*
	1st month	0.521	0.003*
	2nd month	0.721	0.001*

MCV: Mean corpuscular volume, RDW: Red cell distribution width, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, The statistical test used was Spearman's correlation r ,*: Significant p-value (< 0.05).

Table (6): Correlation of conversion time with platelet indices in patients with DM-TB (n= 60)

Variables		Conversion time	
		r	p-value
MPV	Baseline	0.512	0.04*
	1st month	0.524	0.039*
	2nd month	0.547	0.02*
PDW	Baseline	0.515	0.03*
	1st month	0.625	0.01*.
	2nd month	0.541	0.03*

MPV: Mean platelet volume, PDW: Platelet distribution width, The statistical test used was Spearman's correlation r, *: Significant p-value (< 0.05).

Table (7): Correlation of conversion time with inflammatory markers in patients with DM-TB (n = 60)

Variables		Conversion time	
		r	p-value
NLR	Baseline	0.611	0.02*
	1st month	0.704	<0.001*
	2nd month	0.712	<0.001*
PLR	Baseline	0.425	0.049*
	1st month	0.709	0.005*
	2nd month	0.584	0.03*
MLR	Baseline	0.634	0.02*
	1st month	0.559	0.02*
	2nd month	0.635	0.02*

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, MLR: Monocyte to lymphocyte ratio, The statistical test used was Spearman's correlation r, *: Significant p-value (< 0.05).

DISCUSSION

TB and DM are two distinct and significant illnesses that have been present in society and have a great impact on public health. TB has historically been associated with poverty, while DM has been seen as a condition linked to prosperity [6]. In the current study, patients with uncontrolled DM-TB and NDM-TB had more toxic symptoms than controlled DM-TB (p< 0.001). In agreement with the current results, its proposed that

hemoptysis in DM-TB patients is more common than in the NDM-TB patients [7]. Also, it was documented that the uncontrolled DM-TB patients presented more frequently with hemoptysis and toxic manifestations [8]. Moreover, another study demonstrated that 38.7% of DM-TB patients had hemoptysis in comparison to 31% in NDM-TB patients [8], [9]. On contrary, previous study found no significant differences between diabetics and non-diabetics tuberculous patients regarding severity of symptoms, and fever, cough, and weakness were the commonest in both groups [10].

In the present study, conversion time was significantly longer in uncontrolled DM-TB group than in the controlled DM-TB and NDM-TB groups, and in the controlled DM-TB group than in the NDM-TB group ($p< 0.001$). Similarly, previous study reported a longer conversion times among DM-TB patients than NDM-TB patients [11].

According to the present study, the uncontrolled DM-TB group had the highest MCV and RDW values, followed by the controlled DM-TB group ($p<0.001$). This was in agreement with Bhutto et al. [12] who reported that the increased MCV in DM-TB patients may be attributed to vitamin B-12 and folate deficiency which are more pronounced in uncontrolled DM-TB. Also, it was documented that the uncontrolled DM-TB patients had significantly higher MCV and RDW than the controlled DM-TB patients [12], [13].

Regarding follow-up of patients, the current study revealed that the MCV was significantly decreased at 2nd month than at baseline in NDM-TB group ($p<0.05$). Moreover, the RDW was progressively decreased from baseline to 1st and 2nd months in the three studied groups ($p < 0.05$). In contrary, previous study found that the MCV was increased significantly in TB patients during follow up, an effect attributed to that the anti-TB medications could affect vitamin B-12 level [14].

In the present study, the uncontrolled DM-TB patients had the lowest MPV and PDW followed by the controlled DM-TB with significant differences. In agreement with the present study, it was demonstrated that DM-TB patients had significantly lower MPV and PDW than NDM-TB patients [15]. Additionally, it was found that the TB patients had significantly lower MPV than the control group [15], [16].

The current study revealed that during follow up we found that the MPV and PDW were significantly increased progressively from baseline to 2nd month in the three studied groups. In agreement with the present study, one study showed that the MPV and PDW were increased significantly during follow-up due to deceased platelet count. On the contrary, it's showed that PDW and MPV had the highest values at baseline which showed significant reduction to normal levels after TB infection recovery [14], [17], [18].

The results of the current study revealed that the NLR was significantly higher in the uncontrolled DM-TB group than in the other two groups and in the controlled DM-TB group than in the NDM-TB group at 1st month ($p<0.05$). Moreover, it was decreased progressively during follow-up from baseline till 2nd month in the three studied groups ($p<0.05$). These findings may be attributed to that the successful anti-TB treatment leads to decrease of bacterial load with subsequent reduction of systemic inflammatory reaction that leads to reduction of NLR. This reliance could suggest the efficacy of assessing these ratios prior to and following anti-TB treatment in predicting clinical outcome. In agreement with the current study, a study that conducted on Romanian TB patients showed that NLR were decreased significantly after anti-TB treatment [14]. Rakotosamimanana et al. and Yin et al., reported that active TB patients had a marked decrease in lymphocyte count with an increase of neutrophil count [21], [23], thus NLR was high at baseline. Moreover, other studies reported that during follow up, there was significant rise in lymphocytic count with decrease in neutrophil count, thus NLR decreased significantly [19], [20].

The present results showed that PLR had the highest values in all studied groups at baseline with no significant differences between the studied groups in spite the highest value was found in uncontrolled DM-TB group followed by controlled DM-TB group. These ratios were decreased at 1st and 2nd months, with significant differences only in uncontrolled DM-TB group. Another study reported that the PLR decreased significantly in tuberculous patients after receiving anti-TB drugs secondary to rise in lymphocytic count as part of immune response to TB [14]. Another study documented significant reduction of PLR after anti-TB, and he explained this finding by reduction of platelet count after subsidence of the infection together with increased lymphocyte production [17].

The present study showed that MLR had the highest values in the uncontrolled DM-TB group than in the controlled DM-TB and NDM-TB groups with significant differences at 1st and 2nd months. The increase of MLR at baseline indicated the relative increase of monocytes and the relative decrease of lymphocytes. MLR was reported to show significant decrease after treatment and suppression of TB [19]. In contrary, other studies reported that MLR decreased significantly during follow-up of TB patients [14] [22]. Additionally, one study has demonstrated that a higher proportion of monocytes in the bloodstream and a higher MLR are linked to an increased likelihood of developing TB [21].

The strong positive correlations observed between conversion time and MCV, RDW, MCH, and MCHC suggest that alterations in these indices may be linked to delayed sputum conversion. The consistent increase in correlation strength over time indicates that these RBCs indices might serve as indicators of treatment response or disease progression. Notably, higher MCV, RDW, MCH, and MCHC values, which reflect changes in the size and hemoglobin content of RBCs, were associated with longer conversion times, potentially indicating the

impact of DM and TB comorbidity on erythropoiesis and hemoglobin metabolism. Similarly, the positive correlations between platelet indices (MPV and PDW) and conversion time highlight the role of platelet activation and heterogeneity in influencing treatment outcomes. The larger and more variable platelet sizes associated with prolonged conversion times may reflect a heightened inflammatory state or a dysregulated platelet response in DM-TB patients.

NLR which reflects neutrophil-driven inflammation, as well as PLR and MLR which indicate platelet and monocyte responses demonstrate positive correlation with conversion time implying that chronic inflammation and immune dysregulation in DM-TB patients may delay sputum conversion. Similar to our results, Zahorec identified the NLR as a marker of systemic inflammation, often associated with poorer outcomes in various diseases. This study further demonstrates that a higher NLR correlates with prolonged sputum conversion times, indicating that an intense inflammatory response, potentially exacerbated by DM may hinder effective TB treatment [23]. In the same context, the study by Imran et al. also found that elevated NLR levels were linked to worse prognosis in TB patients, particularly those with co-morbidities, reinforcing the association between heightened inflammation and delayed disease resolution. Our results expand on these findings by showing that this relationship becomes stronger as treatment progresses, highlighting the persistent impact of inflammation on treatment outcomes in DM-TB patients [24].

Regarding PLR, Feng, et al. found that poor glycemic control was associated with a higher risk of tuberculosis and poorer treatment outcomes, including a higher PLR in TB-DM patients compared to TB-only patients [25]. Finally, the consistent positive correlation between MLR and conversion time observed in our study aligns with Han et al. who noted that elevated MLR is associated with chronic inflammation and worse outcomes in TB and other infections. Our findings further suggest that the chronic inflammatory state reflected by a higher MLR in DM-TB patients may be a critical factor in delayed sputum conversion, emphasizing the importance of managing inflammation throughout the treatment course [26].

CONCLUSION

Toxic symptoms and longer sputum conversion times were linked to uncontrolled DM-TB. Hematological markers, such as MCV, RDW, MPV, NLR, PLR, and MLR demonstrated an important role in follow-up of PTB in DM patients and correlated with conversion times, therefore, they could serve as valuable prognostic tools in managing DM-TB patients. Emphasizing glycemic control and using hematologic and inflammatory markers for clinical utility in DM-TB patients are critical. It also calls for further research to validate these findings and explore potential interventions that could mitigate the impact of DM on TB treatment efficacy. Multidisciplinary care programs and follow-up with CBC are recommended for optimal management and monitoring.

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الملخص العربي

مؤشرات تعداد الدم الكامل كعلامات التهابية في مرضى السكري المصابين بالدرن الرئوي النشط

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ملخص البحث

الخلفية: لم يتم البحث بشكل كافي في دور مؤشرات الدم الكاملة كعلامات التهابية في مسار الدرن الرئوي.

الهدف: تقييم دور مؤشرات الدم الكاملة كعلامات التهابية في مرض الدرن الرئوي عند مرضى السكري وغير السكري.

الطرق: شملت الدراسة التتبعية المستقبلية على 90 مريضا مصابا بالدرن الرئوى النشط. و قد تم تقسيمهم الى 30 مريضًا بالسكري الغير متحكم فيه و الدرن الرئوي، و30 مريضًا ب السكري متحكم فيه و الدرن الرئوي، و30 مريضًا بالدرن الرئوي بدون السكرى. تم تسجيل المعايير التالية قبل بدء علاج الدرن ، وبعد الشهر الأول والثاني من بدء العلاج: متوسط حجم الخلية، عرض خلايا الدم الحمراء، متوسط محتوى الهيموجلوبين في الخلية، متوسط تركيز الهيموجلوبين في الخلايا الحمراء، متوسط حجم الصفائح الدموية، عرض الصفائح الدموية، نسبة عدد خلايا العدلات إلى عدد الخلايا الليمفاوية، و نسبة عدد الخلايا أحادية النواة إلى عدد الخلايا الليمفاوية.

النتائج: كانت قيم متوسط حجم الخلية، عرض خلايا الدم الحمراء أعلى بشكل ملحوظ في مجموعة السكري الغير متحكم فيه و الدرن مقارنة بالمجموعتين الأخريين، وفي مجموعة السكري متحكم فيه و الدرن مقارنة بمجموعة الدرن فقط في جميع الفترات. انخفض عرض خلايا الدم الحمراء بشكل ملحوظ من البداية حتى الشهر الثاني في مجموعتي السكري الغير متحكم فيه و المتحكم فيه مع الدرن. كان متوسط حجم الصفائح الدموية أقل بشكل ملحوظ في مجموعة السكري الغير متحكم فيه مع الدرن مقارنة بالمجموعتين الأخرتين، وفي مجموعة السكري المتحكم فيه و الدرن مقارنة بمجموعة الدرن فقط في جميع الفترات. كان توزيع عرض الصفائح الدموية أقل بشكل ملحوظ في مجموعتي السكري المتحكم فيه و الغير متحكم فيه مع الدرن مقارنة بمجموعة الدرن فقط في الشهر الثاني. زاد متوسط حجم الصفائح الدموية و توزيع عرض الصفائح الدموية بشكل ملحوظ خلال فترة المتابعة في مجموعتي السكري المتحكم فيه و الغير متحكم فيه مع الدرن. كانت نسبة عدد الخلايا العدلات إلى عدد الخلايا الليمفاوية و نسبة عدد الصفيحات الدموية إلى عدد الخلايا الليمفاوية اعلي بشكل ملحوظ في مجموعة السكري الغير متحكم فيه و الدرن مقارنة بالمجموعتين الاخرتين، وفي مجموعة السكري المتحكم فيه و الدرن مقارنة بمجموعة الدرن فقط في الشهر الأول. كانت نسبة عدد الخلايا أحادية النواة إلى عدد الخلايا الليمفاوية أعلى بشكل ملحوظ في مجموعة السكري الغير متحكم فيه و الدرن مقارنة بالمجموعتين الأخرتين، وفي مجموعة السكري المتحكم فيه و الدرن مقارنة بمجموعة الدرن فقط في الشهر الأول والثاني. انخفضت نسبة عدد الخلايا أحادية النواة إلى عدد الخلايا الليمفاوية و نسبة عدد الخلايا العدلات إلى عدد الخلايا الليمفاوية و نسبة عدد الصفيحات الدموية إلى عدد الخلايا الليمفاوية خلال فترة المتابعة في مجموعتي السكري المتحكم فيه و الغير متحكم فيه و الدرن.

الإستنتاجات: قد يكون لـمؤشرات الدم الكاملة كعلامات التهابية دور مهم في متابعة الدرن الرئوي عند مرضى السكري وفي التنبؤ بنتائج العلاج.

الكلمات المفتاحية: مؤشرات الدم الكاملة، الدرن، داء السكري.

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