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Development of Scoring and Stratification of Severe Lung Involvement in Multidrug-Resistant Pulmonary Tuberculosis Patients

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ABSTRACT

Background and Objective: The probability of the presence of risk factors and clinical outcomes in multidrug-resistant pulmonary tuberculosis subjects is undermined. A clinical prediction model was established based on radiological examination. To assess the effectiveness of the prediction model and strengthen both the diagnostic and prognostic applications, we developed and validated a scoring system employing radiological examination. **Materials and Methods:** The radiological grading categorized severe lung involvement. The study recorded the patient's hemogram and medical history. Radiological grading and clinical investigations were chosen as dependent variables and independent variables, respectively. Data were analyzed using bivariate logistic regression with $p<0.2$ and multivariate logistic regression analysis with $p<0.05$. Independent predictor variables and their regression coefficient (β) evaluated. The constant in this study was based on the Framingham study. **Results:** Hematological changes were observed in the grading of lung severity using ANOVA. The regression analysis identified a history of multidrug-resistant tuberculosis ($p = 0.0001$) and resistance to more than one anti-tubercular drug ($p = 0.026$) and a few parameters of hemogram as predictors for an intense lung infection. This study segregated the study subjects into risk categories and evaluated the performance of the scoring system. **Conclusion:** The score developed helps in stratifying the patients at severe risk of lung involvement alerting the healthcare professional for patients' better pharmaceutical care.

KEYWORDS

Anemia, clinical prediction, hemogram, multidrug-resistant pulmonary tuberculosis, radiological manifestations, lung grading, pharmaceutical care

INTRODUCTION

Pulmonary Tuberculosis (TB), a leading cause of death worldwide, ranks ninth above human immunovirus and acquired immunodeficiency. Approximately 10.4 million people were affected with TB in 2019 and more than 50% of cases were reported in India, Indonesia, China, the Philippines and Pakistan[1]. The existence of resistance-causing mutations in susceptible bacilli during anti-TB treatment has gradually become the dominant strain[2]. The frequency of single mutations can be prevented if appropriate

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combination therapy is prescribed and regularly monitored for medication adherence. Multidrug-Resistant Tuberculosis (MDRTB) refers to the resistance of an individual to at least two notable anti-TB drugs, isoniazid and rifampicin. Extensive Drug-Resistant Tuberculosis (XDRTB) development was noticed in patients resistant to isoniazid, rifampicin, fluoroquinolones and second-line injectable drugs accounted for 4-20% of infections[3,4]. Favourable outcomes with treatment in MDRTB were found to be 48% and mortality was between 1-30%[5].

In a study conducted utilizing radiological signs for assessing pulmonary MDRTB, it was observed that Multidrug-Resistant Pulmonary Tuberculosis (MDRPTB) cases had extensive involvement and were likely to be bilateral. The same study noticed pleural involvement, bronchiectasis and loss of lung volume. Thick-walled multiple cavity lesions appear to be noteworthy findings during radiological examination assisting MDRPTB diagnosis[6]. Drug-sensitive TB radiological evidence revealed lesions and interstitial infiltrations, mostly compared to drug-resistant TB[7].

Haematological disorders with tuberculosis treatment were noticed as serious side effects. During the treatment period, abnormalities of red cells, white cells, platelets and clotting factors are considered blood picture abnormalities. Researchers cautioned about continuous monitoring of haematological abnormalities throughout the therapy[8]. The risk scores classify the patients on the disease progression or for a confined outcome by adjusting the covariates[9]. Clinical scoring tools are drawn systematically using several statistical methods to help in the clinical management of patients and predicting an outcome. These tools aid in decision-making for improved efficiency or outcome[10]. A specific context is required in developing the clinical scores and for its application[11]. The clinical score developed in this study predicts and defines the severity of lung infection in MDRPTB patients.

In the present study, haematological findings in contrast to the radiological examination of the chest were used to classify chest involvement as mild, moderate and severe. Along with chest X-ray, we utilized resistance to various anti-TB drugs. The purpose of the current study is to describe the radiological examination of MDRPTB and a few extensively drug-resistant pulmonary tuberculosis patients who had a history of TB. Different reports have suggested haematological changes during TB treatment. Despite several observations, no comprehensive study has appraised radiological examinations with haematological findings among MDRPTB patients.

MATERIALS AND METHODS

Study area: The study was conducted in District Nodal MDRTB Centre, Tuberculosis and Chest Hospital, Hanumakonda, Warangal, Telangana, India from February, 2018 to December, 2020.

Informed consent: The protocol of the prospective observational study was approved by the Jayamukhi College of Pharmacy, Institutional Review Board (JCPN: 112/2018). Informed consent was obtained from the enrolled patients.

Criteria: The inclusion criteria for the subjects included a confirmative diagnosis of drug-resistant mycobacterium infecting the pulmonary system. Positive reports proven by rapid molecular tests, such as the Cartridge-Based Nucleic Acid Amplification Test (CBNAAT), First-Line Probe Assay (FL-LPA) and Second-Line Probe Assay (SL-LPA), were used to identify resistance among the patients. The subjects included patients with or without comorbid conditions above 18 years and not on the drugs affecting the hemogram. Pregnant women and cachexic and terminally ill patients were excluded from this study. A total of 273 confirmed MDRPTB-diagnosed patients, (197 of 273) males and (77 of 273) females, were enrolled in this study.

The data set involves demographic and clinical investigations and hemograms. Radiologic imaging techniques are used to classify the severity of the disease into mild, moderate and severe and are incorporated as a clinical prediction model. The concept of categorization based on the involvement of one lobe with interstitial infiltrations is mild, unilateral lung with cavitations, more interstitial infiltrations, pleural involvement as moderate while bilateral lung involvement, more alveolar infiltrates, cavitations, fibrosis, loss of lung volume considered severe and investigated. The obtained chest radiograph was interpreted by the chest physician to grade the severity of the lung infection.

Methodology: The data set involves demography, clinical investigations and hemograms. Radiologic imaging was used to classify the severity of the disease into mild, moderate and severe and incorporated as a clinical prediction model. The concept of categorization based on the involvement of one lobe with interstitial infiltrations is mild, unilateral lung with cavitations, more interstitial infiltrations, pleural involvement as moderate while bilateral lung involvement, more alveolar infiltrates, cavitations, fibrosis, loss of lung volume considered severe and investigated. The obtained chest radiograph was interpreted by the chest physician to grade the severity of the lung infection.

Four millilitres of blood was collected from venipuncture to investigate the haematological changes, performed on the same day of withdrawal. The 'Mindray BC 2800 Automated Hematology Analyzer' (Shenzhen Mindray, Bio-Medical Electronics Co., Ltd.) was used.

Statistical analysis: The demography and clinical findings are mentioned in number and percentage. The binary logistic regression model was first performed using the severity of the chest radiograph as a dependent variable coding mild and moderate as 0 and severe as 1. The independent variables included the hemogram parameters and categorical variables. The abnormality in the parameters of the hemogram was coded as 1 and normal as 0. The categorical variables gender grouped into a male as 1 and female as 0, resistance to one anti-TB drug as 0 and more than one as 1, no previous episodes of MDRPTB as 0 and with history of MDRPTB as 1, weight band 16-30 kg as 1, 31-45 kg as 2 and 46-70 kg as 0, new diagnosis as 0 and reoccurrence of MDRPTB as 1 with $p<0.2$.

In the second step, the dependent variable was coded into mild 0, moderate 1 and severe 2 radiological grading to utilize multinomial logistic regression and to select independent variable predictors with $p<0.05$. The significant independent variables and the evaluated regression coefficient (β) in the multinomial logistic regression analysis were utilized to develop the score for the severe manifestations of lung involvement. The scoring system was developed according to the previous literature[12]. The derivation of the points was performed considering the regression coefficient (β) of multinomial logistic regression and the reference values of the predictors. The lowest β value in the model was applied to calculate the score for the variable. The continuous predictor variables were subcategorized for their equal class interval according to the reference ranges. The mid values of the reference and subcategories of continuous variables were determined to be substituted in the formula. The constant (B) was calculated by choosing the lowest β value multiplied by 5. The constant in our study was based on the study of Han *et al.*[12] and calibrated with the lowest β value of B = 1.257*5 = 6.285. The risk scoring system for MDRPTB patients was developed using a formula applying the derived factors: Platelets, Red Blood Cell Distribution Width Standard Deviation (RDWSD), lymphocytes, monocytes, resistance to more than one anti-TB drug and history of MDRPTB confirmed in the second step by applying multinomial logistic regression analysis. The reference values of each risk factor are coded as zero and the points allotted are calculated based on the formula. Decimal points of the final score rounded to the nearest unit and designated the points that would best predict the factors for severe grading of radiological manifestations. The aggregate of the score for every individual patient was obtained and categorized the subjects into

mild, moderate and severe risk. The evaluated scoring system in MDRPTB patients was used to distinguish the patients with prognosis and the extent of lung involvement. The risk score determined by the total sum of points has a range of -10 to 7 points and when the values for risk factors are in the normal reference value, we award -10 to -5 points. Based on the total points, risk categories are assigned. In our study, the maximum total points are 7. The categorization of subjects into groups helps in simple interpretation in a clinical setting. The patients were classified into three categories: -10 to -5 had mild risk, -4 to 0 points had moderate risk and 1 to 7 points had severe risk. All inferential statistical analyses were performed using IBM SPSS statistics version 26.

RESULTS

Demography and radiological grading of lung involvement

Demography: Based on the radiographic features, patients were categorized into mild, moderate and severe lung infections. Patient hemogram, resistance and history of MDRPTB infection were noted. Male outnumbered female patients. Social habits were noticed in maximum patients (139 of 273). The allied clinical conditions were assessed (72 of 273) in subjects.

Radiological grading of lung involvement: The chest X-ray findings included multiple cavitations, tracheal deviation, loss of lung volume, lobar atelectasis, elevated diaphragm dome, homogenous opacity and interstitial and alveolar infiltrates. The chest X-ray screening based on the aforementioned characteristics assorted the MDRPTB patients into mild (71 of 273), moderate (102 of 273) and severe (100 of 273) extents of lung involvement. Resistance to more than one anti-TB drug was observed in (83 of 273) subjects and intense lung infection was observed in half of the patients (43 of 83). Relapse (5 of 273) and reinfection was reported in a few (98 of 273) patients. Most of the patients attended the hospital for reinitiation of treatment, being defaulters or for a change in anti-TB therapy for adverse reaction to the anti-tubercular therapy (Table 1).

Haematological findings in radiological grading: The investigated peripheral blood parameters, observed normocytosis, hypochromic anaemia, neutrophilia, lymphocytopenia and an elevated erythrocyte sedimentation rate in MDRPTB patients. A few of the haematological parameters, lymphocytes, haemoglobin and hematocrit values were lower than the reference range (Table 2).

We performed binary and multinomial logistic regression analyses to identify the predictors of severe lung infection. The first step of binary logistic regression was used to obtain odds ratios and helps in determining how well the model fits the data. The outcome in the logistic regression analysis showed platelets (OR = 1.816, p = 0.115), mean corpuscular hemoglobin concentration (OR = 0.544, p = 0.185), RDWSD (OR = 1.894, p = 0.05), monocytes (OR = 0.372, p = 0.021), red cell count (OR = 0.490, p = 0.05), resistance to more than one drug (OR = 0.026, p = 2.110) and history of MDRPTB (OR = 3.212, p = 0.0001) as predictors (Table 3). Among these independent variables, platelet count (OR = 0.213, p = 0.001), lymphocyte (OR = 0.377, p = 0.005) significant between mild vs. moderate while platelet count (OR = 0.153, p = 0.0001), lymphocyte (OR = 0.234, p = 0.0001), RDWSD (OR = 0.457, p = 0.047), monocytes (OR = 3.516, p = 0.009), acquisition of resistance (OR = 0.426, p = 0.040) and history of MDRPTB (OR = 0.355, p = 0.010) were significant for intense lung involvement in mild vs severe according to multinomial logistic regression analysis (Table 4). The multinomial predictor variable's β regression, reference and mid values and constant value were applied in the formula to obtain the score (Table 5). The patients were allotted a number and summed up. The aggregate number categorized the patients into mild-risk, moderate-risk and severe-risk. The maximum number of patients (146 of 273) was observed in the moderate-risk group, followed by severe-risk (118 of 273) and mild-risk (9 of 273) categories (Table 6). The scores of -10 to -5 in the mild category denoted an increase in the platelet count and RDWSD. The categorized moderate group scored between -4-0 implying an increase in the platelet

count, abnormal RDWSD, reduced lymphocyte count and involvement of an increase in the monocyte count in a few patients. The scores of 1-7 indicated reduced platelet number, lymphocyte count, aberrant RDWSD and an increase in monocyte count in maximum patients (Table 7).

Table 1: Clinical characteristics of multidrug-resistant tuberculosis patients

Variables	Subcategory	Total (%)	X^2 value	p-value
Gender	Male	196 (71.79)	51.87	0.0001
	Female	077 (28.21)		
Resistance	One drug	190 (69.59)	41.93	0.0001
	Two drugs	083 (30.40)		
Reoccurrence	Yes	103 (37.73)	16.44	0.0001
	No	170 (62.27)		
History of MDRTB	Yes	100 (36.63)	19.52	0.0001
	No	173 (63.34)		
Chest X-ray	Mild	71 (26.00)	6.61	0.03
	Moderate	102 (37.36)		
	Severe	100 (36.64)		
Weight band	16-30	013 (4.76)	223.91	0.0001
	31-45	205 (75.09)		
	46-70	055 (20.14)		

Table 2: Frequency of haematological abnormalities in multidrug-resistant tuberculosis patients

Variables	Subcategory	Total (%)	X^2 value	p-value
White blood count	Normal	168 (61.5)	14.53	0.0001
	Abnormal	105 (38.5)		
Red cell count	Normal	181 (66.3)	29.01	0.0001
	Abnormal	092 (33.7)		
Haemoglobin (Hb)	Normal	027 (9.9)	175.68	0.0001
	Abnormal	246 (90.1)		
Platelet	Normal	181 (66.3)	29.01	0.0001
	Abnormal	092 (33.7)		
Hematocrit	Normal	027 (9.9)	175.68	0.0001
	Abnormal	246 (90.0)		
Mean corpuscular volume	Normal	202 (74.0)	62.86	0.0001
	Abnormal	071 (26.0)		
Mean corpuscular Hb	Normal	95 (34.8)	25.23	0.0001
	Abnormal	178 (65.2)		
Mean corpuscular Hb conc.	Normal	173 (63.4)	19.52	0.0001
	Abnormal	100 (36.6)		
RBC distribution width-SD	Normal	190 (69.6)	41.93	0.0001
	Abnormal	083 (30.4)		
RBC distribution width-CV	Normal	128 (46.9)	1.059	0.304
	Abnormal	145 (53.1)		
Platelet distribution width	Normal	254 (93.0)	202.28	0.0001
	Abnormal	019 (07.0)		
Mean platelet volume	Normal	246 (90.1)	175.68	0.0001
	Abnormal	027 (9.9)		
Platelet large cell ratio	Normal	264 (96.7)	238.18	0.0001
	Abnormal	009 (3.3)		
Plateletcrit	Normal	255 (93.4)	205.74	0.0001
	Abnormal	018 (6.6)		
Neutrophil	Normal	127 (46.5)	1.322	0.0001
	Abnormal	146 (53.5)		
Lymphocyte	Normal	094 (34.4)	26.46	0.0001
	Abnormal	179 (65.6)		
Monocyte	Normal	222 (81.3)	107.11	0.0001
	Abnormal	051 (18.7)		
Eosinophil	Normal	237 (86.8)	147.98	0.0001
	Abnormal	036 (13.2)		

Table 3: Binary logistic regression analysis of independent predictor variables in radiological grading of lung manifestations in MDRPTB subjects

Variables	B	SE	Wald	Df	Sig	Exp (B)	CI	
							LL	UL
White blood count	-0.150	0.354	0.179	1	0.672	0.861	0.430	1.723
Red cell count (RBC)	-0.714	0.375	3.636	1	0.05	0.490	0.235	1.020
Haemoglobin (Hb)	-0.056	0.695	0.007	1	0.935	0.945	0.242	3.693
Platelet	0.597	0.379	2.483	1	0.115	1.816	0.865	3.816
Hematocrit	-0.404	0.709	0.324	1	0.569	0.668	0.166	2.681
Mean corpuscular volume	0.188	0.453	0.173	1	0.677	1.207	0.497	2.934
Mean corpuscular haemoglobin	-0.138	0.386	0.127	1	0.721	0.871	0.409	1.856
Mean corpuscular Hb conc.	-0.609	0.459	1.760	1	0.185	0.544	0.221	1.338
RBC distribution width-SD	0.639	0.327	3.807	1	0.050	1.894	0.997	3.597
RBC distribution width-CV	0.327	0.376	0.757	1	0.384	1.387	0.664	2.899
Platelet distribution width	0.597	0.875	0.466	1	0.495	1.817	0.327	10.09
Mean platelet volume	-0.509	0.731	0.484	1	0.487	0.601	0.143	2.520
Platelet large cell volume	1.356	1.135	1.426	1	0.232	3.880	0.419	35.90
Plateletcrit	0.119	0.619	0.037	1	0.847	1.127	0.335	3.794
Neutrophils	0.326	0.464	0.495	1	0.482	1.386	0.558	3.441
Lymphocytes	0.799	0.490	2.666	1	0.102	2.224	0.852	5.805
Monocytes	-0.989	0.429	5.304	1	0.021	0.372	0.160	0.863
Eosinophils	0.342	0.449	0.581	1	0.446	1.408	0.584	3.397
Weight band 46-70 kg			1.492	2	0.474			
Weight band 16-30 kg	-0.632	0.713	0.786	1	0.375	0.531	0.131	2.150
Weight band 31-45 kg	-0.930	0.785	1.404	1	0.236	0.394	0.085	1.838
Gender	0.132	0.401	0.108	1	0.742	1.141	0.520	2.502
Resistant to >1 anti-TB drug	0.747	0.336	4.934	1	0.026	2.110	1.092	4.078
History of MDRPTB	1.167	0.328	12.697	1	0.0001	3.212	1.691	6.104

B: Constant, SE: Standard error, Sig: Significant, CI: Confidence interval, LL: Lower limit and UL: Upper limit

Table 4: Multinomial regression analysis of the independent predictor variables obtained in the binary logistic analysis and grading of lung involvement using chest radiographs

Variables	Sub-category	B	SE	Wald	Df	Sig	Exp (B)	CI	
								LL	UL
Moderate lung involvement									
H/o MDRPTB	No						1.00		
	Yes	0.138	0.398	0.120	1	0.729	1.148	0.526	2.505
Resistance	Single drug						1.00		
	Two drugs	-0.082	0.408	0.040	1	0.841	0.922	0.415	2.049
Monocyte	Normal						1.00		
	Abnormal	0.337	0.414	0.664	1	0.415	1.401	0.622	3.155
Lymphocyte	Normal						1.00		
	Abnormal	-0.976	0.344	8.055	1	0.005	0.377	0.192	0.739
RBC	Normal						1.00		
	Abnormal	-0.381	0.355	1.154	1	0.283	0.683	0.341	1.369
RDWSD	Normal						1.00		
	Abnormal	-0.054	0.388	0.019	1	0.890	0.948	0.443	2.028
MCHC	Normal						1.00		
	Abnormal	-0.455	0.366	1.548	1	0.213	0.634	0.310	1.299
PLT	Normal						1.00		
	Abnormal	-1.544	0.463	11.105	1	0.001	0.213	0.086	0.529
Severe lung involvement									
H/o MDRPTB	No						1.00		
	Yes	-1.037	0.401	6.688	1	0.010	0.355	0.162	0.778
Resistance	Single drug						1.00		
	Two drugs	-0.853	0.414	4.239	1	0.040	0.426	0.189	0.960
Monocyte	Normal						1.00		
	Abnormal	1.257	0.482	6.793	1	0.009	3.516	1.366	9.050
Lymphocyte	Normal								
	Abnormal	-1.454	0.380	14.650	1	0.0001	0.234	0.111	0.492

Table 4: Continue

Variables	Sub-category	B	SE	Wald	Df	Sig	Exp (B)	CI	
								LL	UL
RBC	Normal						1.00		
	Abnormal	0.470	0.397	1.404	1	0.236	1.600	0.735	3.483
RDWSD	Normal								
	Abnormal	-0.784	0.395	3.942	1	0.047	0.457	0.211	0.990
MCHC	Normal						1.00		
	Abnormal	0.135	0.409	0.108	1	0.742	1.144	0.513	2.550
PLT	Normal								
	Abnormal	-1.877	0.484	15.041	1	0.0001	0.153	0.059	0.395

Reference: Mild lung involvement, CI: Confidence interval, LL: Lower limit, MCHC: Mean corpuscular hemoglobin concentrtion, PLT: Platelet count, RBC: Red blood cells, RDWSD: Red blood cell distribution width-standard deviation and UL: Upper limit

Table 5: Developed clinical score for the severe lung involvement in MDRPTB patients using chest radiograph, hemogram parameters and other clinical variables

Variables	B	Categories	Mid value	Scoring = β (m-m_{ref})/B	Point
RDWSD	-0.784	41-55	48 (m_{ref})	0	0
		26-40	33	-0.784 (33-48)/6.28 = 1.87	1
		56-70	63	-0.784 (63-48)/6.28 = -1.87	-3
Monocyte	1.257	0-11	5.5 (m_{ref})	0	0
		12-22	17	1.257 (17-5.5)/6.28 = 2.29	2
Lymphocyte	-1.454	21-40	30.5 (m_{ref})	0	0
		01-20	10.5	-1.454 (10.5-30.5)/6.28 = 4.62	3
Platelet		-1.877	151-450	300.5 (m_{ref})	0
	0.000				
		<150	75.5	-1.877 (75.5-300.5)/6.28 = 67.19	4
		451-750	600.5	-1.877 (600.5-300.5)/6.28 = -89.59	-4
Resistance	-0.853	No	0 (m_{ref})	0	0
		Yes	1	-0.853(1-0)/6.28 = -0.13	-1
Previous MDRPTB	-1.037	No	0 (m_{ref})	0	0
		Yes	1	-1.037(1-0)/6.28 = -0.16	-2

Constant B = 1.257*5 = 6.285, m_{ref}: Mid value of the reference range, m: Mid value of the category considered and RDWSD: Red blood cell distribution width-standard deviation

Table 6: Description of the sum of the points and segregation into the categories with abnormalities in the predictor variables

Score	n	Resistance (n)	H/o MDRPTB (n)	M (n)	L (n)	Platelet (n)	RDWSD (n)
Mild risk							
-10	1	1	1	0	0	I = 1	I = 1
-7	2	2	2	0	0	I = 2	0
-6	2	1	2	0	0	I = 1	I = 1
-5	4	3	2	1	1	I = 4	I = 1/D = 1
Total	9	7	7	1	1	I = 8	I = 3/D = 1
Moderate risk							
-4	15	8	8	0	12	I = 15	I = 4
-3	31	15	29	0	20	I = 17	I = 5/D = 3
-2	19	5	14	1	12	I = 8	I = 5/D = 4
-1	33	12	11	8	22	I = 18	I = 4/D = 3
0	48	10	10	2	19	I = 6	I = 4/D = 5
Total	146	50	72	11	85	I = 64	I = 22/D = 15
Severe risk							
1	30	4	9	10	16	I = 7/D = 1	I = 1/D = 11
2	30	17	9	13	24	I = 2/D = 2	I = 3/D = 6
3	30	3	2	3	29	0	D = 4
4	13	2	0	2	12	D = 2	I = 1/D = 9
5	9	0	1	7	6	D = 3	D = 3
6	4	0	0	4	4	D = 1	I = 1/D = 3
7	2	0	0	0	2	D = 2	0
Total	118	26	21	39	93	I = 9/D = 11	I = 6/D = 36

D: Decreased count, I: Increase in the count, L: Lymphocytes (reduced count), M: Monocytes (increase in count) and RDWSD: Red blood cell distribution width-standard deviation

Table 7: Stratification of the multidrug-resistant tuberculosis patients based on the grading of lung and characteristics of predictor variables

Points	Stratification	n (%)
-10 to -5	Mild risk	009 (03.29)
-4-0	Moderate risk	146 (53.47)
1-7	Severe risk	118 (43.22)

DISCUSSION

The prognosis of MDRPTB still had a poor outcome during the study. The planning and development of effective strategies for screening MDRPTB subjects are essentially desired. Several clinical and diagnostic tests are widely employed for screening MDRPTB patients. However, risk factors focusing on progressive diseases are unavailable in monitoring patients for beneficial outcomes. Need for early prediction of poor treatment and additional support for patient care is needed. The study revealed 'poor treatment outcomes' with MDRPTB following the development of risk scores among patients.

The maximum number of subjects with severe grading of the lung was identified in the categories with a history of TB and male patients. MDRPTB treatments are difficult with second-line anti-TB drugs due to their weak sterilizing activity and are toxic. In the current study, we observed a cure rate for MDRTB similar (49.07% unpublished data from our findings) to the World Health Organization reported that 48% of MDRTB patients were cured[13]. After initiating empirical treatment of TB, based on the National Tuberculosis Elimination Programme (NTEP), relapse of the disease was noticed after successful completion of treatment, failure of the treatment and among defaulters. Reinfection (35.8%) and relapse (1.83%) patients constituted about (37.7%) of all the cases treated under NTEP. In most of the studies, the relapse rate was high. In a study following up patients, relapse rate observed a minimal difference (12.3%), with the NTEP relapse rate (10%)[14].

The study's previous history of treatment was well documented without any bias. After a systematic review of the subject register, based on the previously opted regimens of category I and II anti-TB drugs, patients were diagnostically proven to have MDRPTB. Resistance to therapy challenges is faced by global TB control programmes. Globally, in 2012, approximately 4.5 lakh new cases of MDRTB were recorded. Worldwide, 20% of patients have a history of previous treatment. In the present study, we noticed half of the subjects (62.2%) with a recent diagnosis of MDRTB and approximately the same number (36.6%) of patients had been treated previously. This confirms by a study conducted in Minsk, Belarus[15].

Our study noted the changes in the hemogram as a marker for the diagnosis, prognosis and clinical outcome of the therapy. Such haematological variations were noticed during screening and follow-up of the active TB patients[16]. The risk score was developed using both primary and secondary data from the study participants. Our study showed clinical risk factors based on the scoring system of platelets, RDWSD, monocytes, lymphocytes, history of MDRPTB and resistance to more than one anti-TB drug. In a study involving the prediction of poor outcomes among MDRPTB patients, a clinical risk score was developed from two large countries. The score predicted resistance to fluoroquinolones, history of intake of second-line anti-TB agents and positive smears after two months of therapy in MDRPTB patients[17].

The increase in platelet count was similar to that in past investigations[18]. Similar results were noticed in the current research. Anisocytosis was measured by the red blood cell volume distribution width, which contributes to reduced RBC production, malnutrition[19] iron deficiency anaemia and chronic inflammatory disorder[20]. In the current exploration, forty patients exhibited comparable results. Although the clinical score defining the progression of the infection has not yet been developed, the predictor's platelets, RDW, monocyte and lymphocyte counts were identified as contributors to prognosis. History of MDRPTB and resistance to more than one anti-TB drug showed not much influence on the clinical score.

Furthermore, the aggregate of the allotted numbers classified the patients in one the categories of mild, moderate and severe risk. Moderate- (146 of 273) and severe-risk (118 of 273) patients contributed to the risk score prediction analysis. The subjects categorized under severe risk observed an increase in monocyte count, reduced platelet count, lymphocyte count and altered RDWSD compared with their reference values. The history of MDRPTB and resistance to anti-TB drugs has not influenced risk scoring. The patients in the moderate- and severe-risk groups could potentially benefit from intensive treatment. This allows a clinician to alert the subject for better pharmaceutical care and regular follow-up. Furthermore, this investigation demonstrates the prevalence of progressive disease and interventional treatment, requiring scrupulous follow-up of the patients for better treatment outcomes. Patients at severe risk could benefit from intensive therapy, psychological attention, monetary assistance and monitoring throughout the treatment duration[21].

The progression of the lung infection investigated in the radiograph noticed an increase in the platelet count[22,23]. Reduced platelet count was also noted in other studies[24]. The clinical score determines the progression of the infection in the moderate risk category with elevated platelet count and the loss of platelet count in intense lung infection. The formation of granulomas primarily initiated by thrombocytes drives the macrophages into multinucleated giant foam cells strengthening the phagocytosis of mycobacteria[25]. An increase in the monocyte count is considered a predictor of active TB[26].

Active TB infection observed an increase in monocytes and reduced lymphocyte count and is a useful indicator for determining the response to anti-TB treatment. The monocyte and lymphocyte counts normalize during treatment[27]. The similarity is observed in the present study predicting the magnitude and prognosis of the MDRPTB grading of lung radiographs.

The categorical variables in adjunct help to identify the patients in particular for severe lung manifestations. The accuracy of this scoring system is to distinguish progressive lung infections useful in monitoring the patient. This study emphasizes that a scoring system that does not require intensive examination but can be achieved through simple statistical analysis and is useful for mass screening and identifying subjects who are at moderate and severe risk should undergo proper medical assistance.

We developed a scoring system to validate various subjective and haematological predictors and their influences on the lung using radiological parameters. The study design and statistical methods established the probability of the presence and occurrence of diagnostic outcomes in patients suffering from MDRPTB. Implementation of this clinical score in healthcare centres with limited facilities aids in predicting severe infection in MDRPTB subjects. Thus, it promotes beneficial health outcomes without any supplementary amount. The clinical score developed for MDRPTB subjects relies on the basic hemogram test predicting the severe manifestations of the lung, thereby alerting the healthcare provider to monitor the individual. This scale is derived to implement an effective TB control program. The limitations of the study include its validity being unperformed. Moreover, the sample size in two years was only 273.

CONCLUSION

The outcome of the clinical prediction model involving the radiological parameters improves both the diagnostic and prognostic settings. The developed novel clinical risk score among MDRPTB patients is useful for monitoring any progression of the infection. Platelet count, RDWSD, monocyte, lymphocyte counts, history of MDRPTB and resistance to more than one anti-TB drug could help to identify moderate- and severe-risk patients for better therapeutic outcomes. Despite this, our scoring system needs to be externally validated and yet again to improve its predictive value.

SIGNIFICANT STATEMENT

This study identifies risk variables and clinical outcomes in patients with multidrug-resistant TB. A cost-effective analysis and scoring pattern determine the severe lung involvement using radiographs. This

validated scoring system and prediction model strengthen both the diagnosis and prognostic applications and also alerts the physicians for intervention to make a clinical decision. Current research helps to uncover the critical areas of the diagnosis of TB in the presence or absence of bacteriologically susceptible tests in asymptomatic TB patients.

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