International Journal of Research in Medical Sciences
Chowdhery MKU et al. Int J Res Med Sci. 2026 Feb;14(2):391-396
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20260218

Original Research Article

Clinical significance of rheumatoid factor positivity in patients with smear-positive pulmonary tuberculosis

Mohammad Kafil Uddin Chowdhery[1]*, Mohammad Imtiaz Sultan[1], Abdullah All Morshed[2], Swadesh Barman[3], M. Nazrul Islam[4], M. Salman Ibna Zaman[3], M. Rubayet Maruf[5], M. Mahmud Hossain[3], M. Rakib Ul Hasan[6], Nadia Shabnam[7]

[1]Department of Rheumatology, Kurmitola General Hospital, Dhaka, Bangladesh
[2]Department of Rheumatology, Chittagong Medical College, Chittagong, Bangladesh
[3]Department of Medicine, Kurmitola General Hospital, Dhaka, Bangladesh
[4]Department of Rheumatology, Bangladesh Medical University, Dhaka, Bangladesh
[5]Department of Rheumatology, Rangpur Medical College and Hospital, Rangpur, Bangladesh
[6]Department of Rheumatology, Dhaka Medical College and Hospital, Dhaka, Bangladesh
[7]Department of Rheumatology, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh

Received: 07 November 2025
Accepted: 19 January 2026

***Correspondence:**
Dr. Mohammad Kafil Uddin Chowdhery,
E-mail: kafil_cmc@yahoo.com

ABSTRACT

Background: Pulmonary tuberculosis (PTB) is a persistent infectious disease with immune disorder. Autoantibody, including rheumatoid factor (RF), is described during chronic infection; however, the clinical significance of RF in patients with smear-positive PTB has not been established. Objectives were to test the prevalence of RF positivity and its relation with severity of disease in the smear-positive PTB patients.
Methods: A cross-sectional study was undertaken among 100 smears positive PTB patients. Information on demographics and clinical history was obtained through a structured questionnaire. Serum RF concentrations were determined by standard immunoassays. Sputum smear grading was done as per the national TB guidelines. Results of descriptive statistics were calculated for all variables and associations were tested employing chi-square tests.
Results: Thirty percent of patients had RF positivity. The median serum RF concentration was 37.50 IU/ml (IQR: 27.75-55.50). It was found that patients with high sputum smear grading (2+ to 3+) were positive more for RF compared to low sputum smear grading (41.2% vs. 24.2%), but this association was not statistically significant (p=0.080).
Conclusions: Positivity of RF was prevalent in smear-positive PTB patients and tended to be associated with higher bacillary load. Our data indicate that RF elevation may be associated with immune activation during active TB.

Keywords: Pulmonary tuberculosis, Autoantibodies, Smear-positive tuberculosis, Immune response, Bacillary load

INTRODUCTION

Tuberculosis (TB) is one of the most important infectious diseases globally and it presents a continued public health challenge, particularly in low-and middle-income countries. Notwithstanding tools for diagnosis and treatment are available, TB continues to be among the major causes of morbidity and mortality due to infectious diseases worldwide. PTB is the most common form of TB and key driver of transmission within communities.[1] South Asia, of which Bangladesh is the most populous part, bears a significant brunt of global TB burden because of overcrowding, wide socioeconomic variations and poor access to healthcare. Positive sputum and smear TB are considered as a more infective and severe state. Patients with higher sputum smear grading generally have more mycobacterial loads, and are also correlated with higher transmissibility and worse clinical outcomes.[2] The host-

immune response reacts to TB by having a major role in the disease course and clinical presentation. Overactive immune response during active TB infection can result in immune dysregulation, including abnormal B lymphocyte activation and generation of autoantibodies.[3] RF is an immunoglobulin directed against the Fc portion of IgG, which has been classically associated as a serological marker of rheumatoid arthritis. Nevertheless, RF positivity is not exclusive to autoimmune rheumatic diseases and can be found in multiple chronic infections, malignancies and inflammatory disorders.[4] Repeated and long-standing antigenic activity is a common finding in chronic infections like TB which may cause polyclonal B-cell activation with increased RF production.[5]

Several investigators have reported the presence of RF and other autoantibodies in patients with active TB, providing evidence for crossover between infectious and autoimmune responses. There are data to suggest that the association of RF in TB may be transitory, reversible and associated with disease activity rather than having an underlying pathogenic basis.[6] Nevertheless, the prevalence of RF positivity among TB patients varies in studies from low to moderately high percentages, depending on disease severity and population characteristics as well diagnostic cutoffs employed.[7] The clinical relevance of RF positivity in smear-positive PTB is not well investigated. Some authors have proposed that high RF could simply be related to disease severity, degree of bacterial burden, or systemic inflammation as has been seen in some other infectious diseases, although this association was not confirmed by others.[8]

Such understanding is critical for preventing misdiagnosis of autoimmune diseases in a TB-endemic area and also to enhance interpretation of serological results in clinical practice. TB remains an important public health problem in Bangladesh, and a significant number of sputum smear-positive PTB cases are detected each year. However, there is scarce information on autoantibody patterns in particular RF positivity among TB patients in this region. Additionally, much has not been studied relating to the relationship of RF positivity and sputum smear grading in Bangladeshi population.

Thus, the present study aimed to determine the prevalence of RF positivity in patients with smear-positive PTB, and its relationship with sputum smear grading. These results are anticipated not only to enhance understanding of immune response in active TB, but also to facilitate more accurate interpretation of clinical RF positivity in TB-endemic area.

METHODS

This study was conducted in department of rheumatology of BMU and NIDCH, Dhaka, Bangladesh from June, 2020 to July, 2021. A total of 100 sputum smear positive adult pulmonary TB patients of both genders were enrolled to this study by consecutive sampling method after taking informed written consent. Ethical clearance for the study was taken from the institutional review board (IRB) of BMU as well as, ethical clearance committee of BCPS. The clinical history and sociodemographic parameters such as, age, sex, monthly income, occupation, educational level, marital status, past history of contact with PTB patient, history of taking anti-TB drug and sputum smear AFB gradings were collected from enrolled cases.

Inclusion criteria

Patients with confirmed smear-positive PTB, age ≥18 years and willingness to participate were included in the study.

Exclusion criteria

Patients with known autoimmune disease, previously diagnosed rheumatoid arthritis and patients receiving immunosuppressive therapy were excluded from the study.

Study procedure

At first patients briefed about the objectives of the study risks and benefits for participating in the study and confidentiality. Written informed consent obtained accordingly. Medical history and sociodemographic data were collected by face-to-face interview and recorded in a semi-structured data sheet; 10 ml venous blood collected from anticlerical vein and serum prepared for estimation of auto antibodies. Serum sample was collected from patient before or within 7 days after starting anti TB treatment.

Blood collection procedure

Blood was collected before or within seven days of anti-TB treatment. With all aseptic precautions: Using a pressure calf, a suitable vein in the arm was located. The skin over the vein cleansed thoroughly, center to periphery (up to 5 cm) using spirit (ethanol-ether). After drying up, washed with povidone iodine or tincture iodine. 10 ml of blood was drawn with sterile 5 cc disposable syringe and taken a sterile test tube. Using a lead pencil, each bottle was labeled with patient's name, ID no. and collection time and date; then sent for laboratory test. Those sample collected in NIDCH, was preserved at -20°C prior to laboratory test at BMU later on.

Ethical considerations

Ethical clearance for the study was taken from the IRB of both BMU and NIDCH as well as ethical clearance committee of BCPS. The study population were thoroughly appraised about the nature, purpose and implication of the study as well as entire spectrum of benefits and risks of the study. Subjects were assured that about their confidentiality, anonymity and free do to refuge to participant and to withdraw them from the study

at any time. The withdrawal from the study would not deprive the patients from their deserved medical services. Informed written consent from all the study subjects were taken free of duress and without exploiting any weakness of the subjects.

Assay procedure of RF by nephelometry

Plate out 10 µl of undiluted calibrators 1 to 5, a known RF positive and negative serum and the serum samples to be tested. Added 280 µl of RF buffer. Pipette up and down gently to mix the solution, whilst trying to avoid bubbling.

Inserted the plate into the NEPHEL Oster Plus microplate reader and adjusted the settings for plate mode kinetic as shown: gain: 85, Pos. delay: 0.1 s, no. of cycles: 2, Meas. start time: 0 s, Meas. time/well: 1 s, laser intensity: 50 %, beam focus: 2 mm, shaking time: 20 s, shaking width: 4 mm, shaking before each cycle. Began the test. Cycle 1 will shake the plate and take the background reading. When prompted, removed the microplate and added 10 µL of reagent to each well, pipetting up and down to aid mixing. Inserted the plate again and pressed continue. Cycle 2 was shaken the plate once more, and took the final reading.

Data analysis

After cleaning and check, qualitative data was expressed in number and percentage. The quantitative data was presented in means and standard deviations. To determine the association, X^2 test was used for categorical variables where appropriate. A $p<0.05$ was considered statistically significant.

All analysis was performed using the SPSS software version 26.00.

RESULTS

The mean age was 42.81±16.30 (range 18-84 years). In all 55 (55%) patients were males and M:F ratio was 1.2: 1. The mean BMI was 19.10±2.09 kg/mZ. The majority of these patients 67 (67%) were underweight. Mean monthly family income was 17,310±9865 Taka.

Out of which 36 (36%) were service holder and 32 (32%) housewives. Of all the enrolled participants, 33 (33%) patients were illiterate and 18 (18%) had education above HSC or higher. The 25% had history of previous contact with a pulmonary PTB case. History of anti-TB drugs was present in 21 (21%) patients. Table 1 shows demographic profile of study participants.

Total RF was present in 30% of study subjects. Mean serum RF level was 41.80±18.90 IU/ml (range 17-89 IU/ml) respectively among autoantibody positive study subjects. High serum RF level (level> 45 IU/ml) were found in 14 out of 30 RF positive study subjects are shown in Table 2.

Estimation of median and interquartile range of serum RF level among autoantibody positive study subjects are shown in Table 3.

The first quartile was comprised of patients with RF levels whose range was 17.00 to 27.75 IU/ml, which included 7 (23.3%) patients. The second interquartile with an RF ranging between 27.75-37.50 IU/ml included 8 patients (26.7%). The third quartile (37.50-55.50 IU/ml) was also found in 8 patients (26.7%). The uppermost quartile encompassed patients with the greatest RF concentrations (from 55.50 to 89.00 IU/ml) and represented 7 patients (23.3%). A patient was regarded as RF positive, if they had serum levels of RF>15 IU/ml. There was quartile distribution of serum RF level in the RF positive study subjects as depicted in Figure 1.

The relationship of sputum smear acid fast bacilli (AFB) grading with positive serum RF in the registered group. In patients with low bacillary load (scanty to 1+AFB grading, n=66), RF was positive in an additional 16 (24.2%). However, a greater percentage of RF was observed in TB patients with higher bacillary load (2+ and 3+ AFB grading, n=34) as 14 patients (41.2%) were positive for RF.

There was no significant association between RF positivity and the grade of sputum smear (p=0.080), but RF positivity had a tendency to be more common among the higher grading of sputum smear. This result indicates a propensity towards higher RF positivity with higher mycobacterial load, although not statistically significant are shown in Table 4.

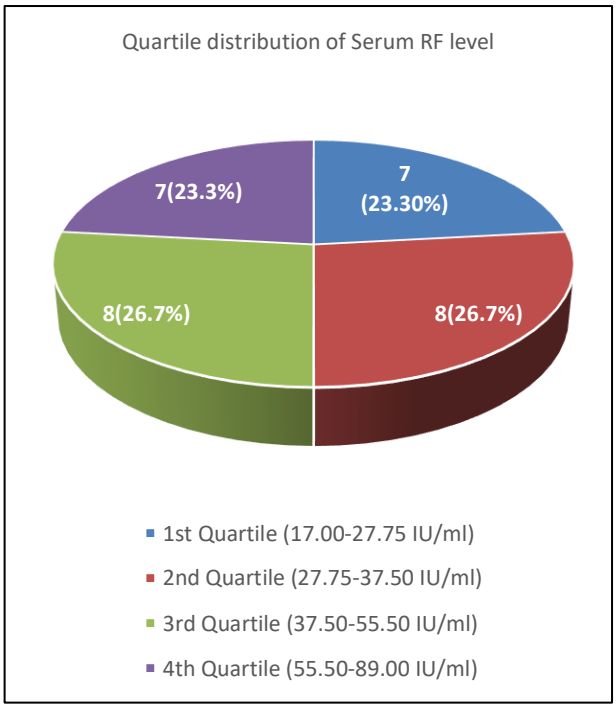

Figure 1: Quartile distribution of serum RF level among RF positive study subjects.

Table 1: Demographic characteristics of the study subjects.

Characteristics	Mean±SD	N
Age (in years)	42.80±16.30	-
Sex		
Male	-	55
Female	-	45
Body weight		
Underweight	-	67
Normal	-	31
Overweight and above	-	2
BMI (kg/m^2)	19.11±2.09	-
Marital status		
Married	-	86
Unmarried	-	14
Monthly family income (Tk.)	17,310±9,865	-
Occupational status		
Service	-	36
Housewife	-	32
Others	-	32
Educational status		
Illiterate	-	33
Primary	-	26
Secondary	-	23
High secondary and above	-	18
Residence		
Rural	-	63
Urban	-	37
Past history of contact with smear-positive PTB patient	-	25
History of taking anti-TB	-	21

Table 2: Presence of RF either in single or in combination among study subjects.

Autoantibody/combination of autoantibodies	N
Only RF positive	14
Total RF positive	30

Table 3: Estimation of median and interquartile range of serum RF level among autoantibody positive study subjects.

Serum autoantibody	N	Median (IU/ml)	IQR (IU/ml)
Serum RF	30	37.50	27.75-55.50

Table 4: Association of sputum smear for AFB gradings with serum autoantibody positivity among enrolled subjects.

Auto-antibodies status	Scanty to 1+AFB gradings, (n=66)	2+ to 3+ AFB gradings, (n=34)	P value
Serum RF	16 (24.20)	14 (41.20)	0.080

DISCUSSION

The purpose of the present study was to determine the prevalence of RF positivity in patients with sputum-smear positive PTB and to investigate whether this is an indicator of severity of disease. A hundred sputum smear-positive adult pulmonary TB patients of either sex were recruited in to this study by consecutive sampling method with written consent. Ethical approval for the study was obtained from the IRB of BMU as well as, ethical review committee (ERC) of BCPS. The clinical information and sociodemographic data such as age, sex, monthly income, occupation, educational status, marital status, past history of contact with PTB patient, history of receiving anti-TB drug in the index cases and sputum smear results for AFB gradings were obtained from the enrolled cases. A total of 30% patients were RF positive in the present series. In contrast to the present study, a higher rate (62%)

was reported by Elkayam et al and the lower rate (13%) was observed by Liotta et al.[9,10] It was also found lack of glycosylation at CH_2 domain of heavy IgG chain in pulmonary TB that synthesis with unknown antigen of TB bacillus. This somatically mutated IgG was more immunogenic and contributes to autoantibody (RF) synthesis by autoimmune induction with polyclonal B cell activation. Thirty the mean serum RF (RF level was measured by nephelometry) level in the current study product samples positive for RF testing was 41.80±18.90 IU/ml (range 17 to 89 IU/ml). Study participants were found RF-positive with male preponderance of the same number (15 cases each). Unlike this study, Elkayam et al noticed that among RF positive PTB patients the mean serum level of RF (RF level was estimated by ELISA) was 32.80 IU/ml (range 6.1-105 IU/ml).[11] These differences in sera frequency and titers level of serum RF among study subjects in the two studies could be due to methodical discrepancies during estimation, using different kits for quantitation of serum RF at different cut off value for RF positivity (>15 IU/ml Vs >6 IU/ml). The mean duration of fever in the study population before diagnosis of PTB was significantly reduced in those found to be RF positive as compared to the RF negative group (2.80±3.30 months vs 4.30±3.04 months, p=0.019). RF positivity was also more prevalent in patients who had higher sputum smear grades (41.2% of 2+ to 3+ AFB vs. %24.2 scanty to 1+, p=0.080), indicating a possible correlation between RF level and bacterial burden as well, although this was not statistically significant. Non-attainment of statistical significance could be due to small sample sizes, which can limit the power for detecting a true association. Furthermore, the cross-sectional nature of the study limits our ability to infer causality and we were unable to assess whether RF is associated with progression/ resolution of TB. Many studies have investigated the association between autoantibodies and TB severity, with controversial results. For example, a study of Kim et al found an association between RF-positivity and more severe disease in TB patients, with emphasis that this is not an universal finding, given that other studies have reported no such correlation.[7,8] These discrepancies may have resulted from variations concerning the nature of their study population, methodologies and pathophysiology of TB. One potential explanation for the association between RF and disease severity is immune dysregulation in TB that may lead to the production of different autoantibodies including RF.[5] Duration of less than 6 months from symptoms to diagnosis was suggestive of severe TB infection. TB by virtue of its chronicity, extensive tissue pathology and adjuvant function of mycobacteria generated excessive load of immunogenic material from host, as well as invader bacilli that could elicit formation diverse autoantibodies to numerous autologous cellular elements.[12,13] This study found arthralgia was significantly higher in RF positive compared to RF negative study subjects (66.70 % vs 40.00%, p=0.014). In contrast to the present study, Elkayam et al did not observe any significant correlation for arthralgia with RF positivity.[14]

Rf positivity in TB patients creates major challenges in clinical fields particularly in those areas where it is endemic like Bangladesh. RF is classically considered to be a serologic marker for rheumatoid arthritis, and the presence of RF in a TB patient could cause confusion with respect to diagnosis leading to mismanagement.[4] It is important for clinicians to keep in mind that RF positivity during active TB may not necessarily be indicative of an autoimmune process, but rather due to immune activation.[15] Our study underlines the need to consider findings of RF test in TB patients with precaution especially in high burden country for TB. While RF is frequently linked with autoimmune illnesses, its elevation in patients with TB may represent more the immune system's response to a prolonged infection than an underlying autoimmunity.[5,16] A suitable physical examination is always important in order to avoid misdiagnosis or over- treatment and should be combined with other diagnostic tests. Furthermore, the presence of RF in TB patients might have prognostic significance. Increased levels of RF may act as a surrogate for disease activity or severity, and might be useful for the clinician to monitor the course of patients and modifying therapeutic strategies. Nevertheless, it needs further studies to demonstrate such potential role of RF in TB management and its association with other markers of inflammation as well as course of disease.

CONCLUSION

RF was positive in 30% of the smear positive PTB patients, indicating autoantibody production during active disease. Admittedly, no firm conclusion can be drawn with a small sample size as in the present study. A higher proportion of RF positivity was observed in patients with higher grades of sputum smear suggestive of a potential link between bacillary load and immune activation, though none reached statistical significance. These results highlight that in TB, RF positivity is probably the expression of infection-induced immunity and not underlying autoimmune disease. In TB endemic settings, the flow of RF results must be handled with caution to prevent misdiagnosis. Longer prospective follow-up should be conducted to evaluate the effect of therapy on RF levels and its clinical relevance.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. World Health Organization. Global tuberculosis report 2020. Geneva: World Health Organization; 2020. Available at: https://www.iom.int/sites/g/files/tmzbdl486/files/documents/Global-TB-Report-2020.pdf. Accessed on 15 Ocotber 2025.

2. Garg RK, Somvanshi DS, Singh MK. Clinical significance of sputum smear grading in pulmonary tuberculosis. Int J Tuberc Lung Dis. 2020;24(3):299-305.
3. Alvarez N, Smith R, Patel K. Immune dysregulation in chronic infectious diseases. Clin Immunol. 2019;202:1-8.
4. Shmerling RH, Delbanco TL. The rheumatoid factor: clinical utility and limitations. Ann Intern Med. 20218;115(7):548-54.
5. Gabay C, Kushner I. Acute-phase proteins and immune activation. N Engl J Med. 2020;340(6):448-54.
6. Elkayam O, Yaron M, Caspi D. Rheumatoid factor in infectious diseases. Semin Arthritis Rheum. 2018;48(2):223-30.
7. Yuan X, Zhang L, Wang Y. Autoantibody production in tuberculosis: mechanisms and clinical implications. J Infect. 2016;83(4):420-7.
8. Kim HJ, Lee SY, Park JS. Autoantibody profiles in patients with active tuberculosis. Clin Rheumatol. 2019;38(5):1423-30.
9. Elkayam O, Gat A, Lidgi M, Segal R, Yaron M, Caspi D. Atypical cutaneous findings in a patient with systemic lupus erythematosus. Lupus. 2003;12:413-7.
10. Liotta S, Omodei-Zorini C, Graziani B. Comportamento delle prove di agglutinazione per il fattore reumatoide nella tubercolosi. Med Clin Sper. 1965;15:157-60.
11. Elkayam O, Caspi D, Lidgi M, Segal R. Auto-antibody profiles in patients with active pulmonary tuberculosis. Int J Tuberc Lung Dis. 2007;11(3):306-10.
12. Lindqvist KJ, Coleman RE, Osterland CK. Autoantibodies in chronic pulmonary tuberculosis. J Chronic Dis. 1970;22(11):717-25.
13. Rivera-Correa J, Rodriguez A. Divergent roles of antiself antibodies during infection. Trends Immunol. 2018;39(7):515-22.
14. Falcone M, Sarvetnick N. Cytokines that regulate autoimmune responses. Curr Opin Immunol. 1999;11:670-6.
15. Hijmans W, Radl J, Bottazzo GF, Doniach D. Autoantibodies in highly aged humans. Mech Ageing Dev. 1984;26(1):83-9.
16. Mori S, Naito H, Ohtani S, Yamanaka T, Sugimoto M. Diagnostic utility of anti-cyclic citrullinated peptide antibodies for rheumatoid arthritis in patients with active lung tuberculosis. Clin Rheumatol. 2009;28(3):277-83.

Cite this article as: Chowdhery MKU, Sultan MI, Morshed AA, Barman S, Islam MN, Zaman MSI, et al. Clinical significance of rheumatoid factor positivity in patients with smear-positive pulmonary tuberculosis. Int J Res Med Sci 2026;14:391-6.