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# An overview of the relation between tuberculosis and autoantibodies: a systematic review

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## Abstract

*Objective*. Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains a significant global health concern. While traditionally viewed as an infectious disease primarily affecting the lungs, accumulating evidence suggests a complex interplay between TB and the host's immune system, potentially leading to the production of autoantibodies. This systematic review aims to investigate the frequency of autoantibody positivity among active TB patients.
*Methods*. A comprehensive search of major electronic databases such as PubMed, Scopus, Google Scholar, and Web of Science was performed. The search strategy employed keywords including "tuberculosis", "autoantibodies", and specific autoantibody names such as "ANA", "Anti-dsDNA", "Anti-phospholipid", "ANCA", "RF" and "ACPA" to study the link between TB and autoantibodies. How often autoantibodies are found in TB patients and what this means for diagnosis and treatment, was analyzed.
*Results*. The results indicate a diverse spectrum of autoantibodies among patients with TB. Some of the autoantibodies, such as rheumatoid factor and anti-phospholipid antibodies, are frequently detected. This can pose diagnostic challenges by mimicking autoimmune diseases and may have implications for monitoring treatment response. Furthermore, the bidirectional relationship between TB and autoimmune diseases, where one can increase the risk of the other, underscores the need for careful clinical consideration.
*Conclusions*. Understanding this complex association is crucial for improving the management of TB, especially in individuals with or at risk of autoimmune conditions.

**Key words:** tuberculosis, autoimmunity, autoantibody, ANA, ANCA, antiphospholipid, RF, rheumatologic diseases.

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## Introduction

Tuberculosis (TB), caused by the bacterium *Mycobacterium tuberculosis* (Mtb), remains a major global health challenge. In 2022, the World Health Organization reported approximately 10.6 million new cases of TB and over a million deaths, marking an increase from previous years (1). This resurgence highlights the persistent threat posed by this infectious disease. The host's immune response to Mtb is multifaceted, involving a delicate balance between effectively controlling the bacterial infection and preventing excessive inflammation that can lead to tissue damage and complications.

Autoimmune diseases include a broad range of disorders and are increasingly acknowledged as a major cause of morbidity and mortality globally (2). An expanding body of research indicates that infections may significantly contribute to the initiation or progression of autoimmune diseases through various mechanisms (2, 3). In relation to TB, a possible connection between Mtb infection and the generation of autoantibodies has been suggested. The chronic and persistent nature of TB, marked by ongoing immune activation, offers a biologically plausible context for the emergence of autoreactive immune responses. The presence of autoantibodies in individuals with active TB carries significant clinical implications, particularly regarding differential diagnosis and their potential role as indicators of disease activity and treatment response. One of the key difficulties in clinical practice is distinguishing between TB and autoimmune diseases, as the presence of autoantibodies typical of autoimmune conditions can complicate diagnosis (4). TB can present similarly to various autoimmune diseases, such as anti-neutrophil cytoplasmic antibody (ANCA)-associated systemic vasculitis, systemic lupus erythematosus (SLE), and rheumatoid arthritis, sharing overlapping symptoms like fever, malaise, weight loss, renal issues, and lung cavity formation. The identification of autoantibodies such as anti-nuclear antibody (ANA), anti-double-stranded DNA (anti-dsDNA), and rheumatoid factor (RF) in patients with TB can further cloud the diagnostic process, possibly resulting in misdiagnosis. It is important for clinicians to recognize that a positive autoantibody test in a patient thought to have TB does not necessarily confirm an autoimmune condition, especially in areas with a high prevalence of TB. In these scenarios, attributing symptoms solely to autoimmunity and starting corticosteroid therapy could be harmful, potentially leading to the spread of Mtb and exacerbation of the infection (4, 5).

Autoantibodies have been extensively documented in correlation with SARS-CoV-2 infections, thereby reinforcing the concept that infections serve as significant environmental determinants capable of initiating *de novo* autoantibody synthesis or enhancing pre-existing autoantibody concentrations. The observations pertaining to SARS-CoV-2 and its relationship with autoantibodies

highlight the intricate and interconnected nature of infections and autoimmunity, thereby prompting further inquiry into their clinical implications and therapeutic possibilities. Autoantibodies that have been reported in COVID-19 patients include ANA, RF, anti-citrullinated protein antibodies (ACPA), antiphospholipid antibodies, and ANCA, which were mostly transient and reactive phenomena (6, 7). This review seeks to thoroughly explore the link between TB and autoantibodies. It will specifically focus on the frequency of autoantibody positivity among active TB patients and identify the various types of autoantibodies that have been documented. By reviewing the existing evidence, this article aims to clarify this intricate relationship and pinpoint areas for future research. A central question this review will address is whether the presence of autoantibodies in TB patients is transient or if it carries more profound clinical and pathological significance.

## Methods

The current systematic review was conducted according to the PRISMA 2020 statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (8) and included studies assessing the relationship between active TB and autoantibody production. The research for this review involved a comprehensive search of major electronic databases such as PubMed, Scopus, Google Scholar, and Web of Science. The search strategy employed keywords including "tuberculosis", "autoantibodies", and specific autoantibody names (*Supplementary Material*). Studies were included if they reported the prevalence of autoantibodies in patients diagnosed with active TB or investigated the clinical implications of these autoantibodies. The time frame of the search encompassed all available data from 1980 up to 2025/6/1. The process of study selection involved initially screening the titles and abstracts of the identified articles to assess their potential relevance to the topic. The following keywords were used in this search: "tuberculosis" AND "rheumatoid factor" OR "anti-citrullinated peptide" OR "antinuclear antibody" OR "anti-double stranded DNA" OR "antiphospholipid antibody" OR "anti-neutrophil cytoplasmic antibody" OR "anti-cardiolipin" OR "anti-beta 2 glycoprotein". In PubMed, keywords were searched through [MeSH] tags. Articles were required to be written in English. The reference lists of included papers were also examined to avoid missing other published data. Subsequently, the full texts of potentially eligible articles were retrieved and reviewed in detail to confirm their suitability for inclusion based on the defined criteria.

Inclusion criteria were as follows: i) studies including active pulmonary and extra-pulmonary TB patients; ii) observational studies (cohort, case-control, cross-sectional) that were conducted in adults; iii) studies investigating the prevalence of autoantibodies in TB patients, including ACPA, RF, ANA, ANCA, anti-dsDNA, anti-ribonucleoprotein (anti-RNP), antiphospholipid antibodies, anti-β2 glycoprotein, anti-cardiolipin (aCL), anti-Ro, and anti-La.

Exclusion criteria were as follows: i) studies including latent or asymptomatic TB infection; ii) case reports, *in vitro*, and preclinical studies, as well as duplicate studies, were excluded. Some of the selected studies have investigated additional autoantibodies other than those of the inclusion criteria, such as anti-mutated citrullinated vimentin, anti-RNP, and anti-Scl-70. These antibodies were briefly discussed in a separate paragraph. Figure 1 shows the PRISMA flow diagram, including detailed information on the search strategy. The quality of the included studies was examined using the Newcastle-Ottawa Scale (9). Data extraction was performed using a structured approach to collect relevant information from each included study. Data extracted from the selected studies included the first author's name, publication year, the country, patient characteristics (including the number of TB patients and controls, if any), the types of autoantibodies investigated, and the key findings related to their frequency. All steps, including searching, article screening, data extraction, and quality assessment of articles, were independently performed by two investigators. Disagreements between the two investigators were resolved by discussion to reach a consensus.

Finally, 26 articles, including 1747 TB patients, were analyzed. The extracted data were then synthesized and analyzed to provide a comprehensive overview of the current understanding of the relationship between TB and the production of autoantibodies. Descriptive statistics were used to summarize prevalence data, and thematic analysis was applied to synthesize information on clinical implications and pathological mechanisms. The key information extracted from the mentioned studies is shown in Table 1.

## Results and Discussion

### Spectrum of autoantibodies detected in tuberculosis

A wide range of autoantibodies has been detected in patients with TB, with varying frequencies and clinical associations. Despite the inconsistencies, the observation of elevated autoantibodies in a notable proportion of TB patients across various studies indicates a potential link between the infection and these antibodies (10-14).

### Antinuclear antibodies

The reported prevalence of ANA in TB patients shows considerable variation across studies. One prospective study found ANA positivity in 8.7% of active TB patients, with the coarse speckled pattern being the most common; the majority of these cases reverted to negative after 6 months of anti-TB therapy (14). This suggests that ANA positivity in some TB patients might be a transient, reactive phenomenon. Another study reported ANA in 46.7% of TB patients, a prevalence similar to that in the control group consisting of patients with acute febrile respiratory illnesses (10). Other studies have reported ANA positivity rates of 6.7% to 42% in TB patients. This heterogeneity underscores the complexity of the association between TB and ANA production, possibly influenced by factors like disease stage, patient demographics, and the sensitivity of the assays used. ANA was measured by enzyme-linked immunosorbent assay (ELISA) in some studies and by immunofluorescence (IF) in others (12, 14-18).

### Anti-double-stranded DNA

Several studies have reported increased levels of anti-dsDNA antibodies in TB patients compared to healthy controls. The prevalence of anti-dsDNA in TB patients has been reported to range from 1 to 32% across different investigations. The different methodologies and assays used for autoantibody detection might explain this variability (10-12, 16, 19, 20). One study found significantly higher mean concentrations of anti-dsDNA in TB patients (11), while another found anti-dsDNA to be absent (16). These varying findings suggest that, while some TB patients, particularly those with more severe or disseminated disease, may develop anti-dsDNA antibodies, it is not a universal feature of TB.



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## Anti-Ro and anti-La

Increased levels of anti-Ro have been observed in TB patients in some studies, with prevalence rates reaching up to 64% (11). In one study, anti-Ro was found to be numerically higher in SLE patients with latent TB compared to those without, hinting at a potential link between these autoantibodies and mycobacterial infection in the context of autoimmune predisposition (21). The prevalence of anti-La in TB patients appears to be generally low and not as consistently elevated as anti-Ro (10). The studies did not differentiate between anti-Ro52 and anti-Ro60.

## Rheumatoid factor

RF is a frequently detected autoantibody in TB patients, with reported prevalence rates ranging from 20% to 62% across various studies (10, 12, 18, 22-24). Some investigations have found signif-

**Table 1.** Summary of key studies on autoantibodies in tuberculosis.

| Authors | Publication year/country | Number of TB patients | Control group | Type(s) of autoantibodies detected and their prevalence in TB patients | Methodology | Key findings |
|---|---|---|---|---|---|---|
| Elkayam *et al.* (22) | 2005/Israel | 47 | 39 | ACPA (32%), IgM RF (62%) | ELISA | The presence of anti-CCP significantly correlated with a history of prolonged fever. No correlation was found between the presence of anti-CCP or IgM RF and any rheumatic symptom. |
| Elkayam *et al.* (26) | 2010/Israel | 134 | - | ACPA | ELISA | |
| Kakumanu *et al.* (27) | 2008/Japan | 49 | 18 | ACPA (37%) | | ACPA levels decreased after 1-2 months of treatment for TB. |
| Emami *et al.* (13) | 2017/Iran | 40 | 40 | ACPA (34%) | ELISA | In the TB group, ACPA levels were higher than in the control group. |
| Elkayam *et al* (28) | 2012/Israel | 33 | - | Anti-β2GPI (30%), aCL IgG (9%), ANCA (anti-PR3 and MPO) | ELISA | After treatment, all the patients demonstrated normalization of the levels of antibodies against β2GPI and aCL. Anti-TB treatment may induce normalization of anti-lactoferrin and anti-MPO, and *de novo* anti-PR3 and MPO formation. |
| Sherkat *et al.* (32) | 2011/Iran | 32 | 32 | c-ANCA (3.1%), p-ANCA (25%), PR3-ANCA (12.5%), MPO-ANCA (75%) | IIF was used for p-ANCA & c-ANCA; ELISA was used to detect MPO and PR3 | The positive ANCA test results significantly correlated with TB. |
| Hussein *et al.* (33) | 2014/Iraq | 70 | 20 | ANCA (71.43%) | IIF | Of the positive ANCA patients, 94% showed c-ANCA and 6% showed p-ANCA. ANCA were positive in 82.9% of the untreated group and 60% of the treated group. |
| Teixeira *et al* (34) | 2004/France | 67 | 10 | ANCA (10%), c-ANCA (4%), p-ANCA (6%) | IIF and ELISA | Controls were selected from patients known to be ANCA-positive. TB is associated with low ANCA seroprevalence and poor specificity. |
| Esquivel-Valerio *et al.* (35) | 2010/Mexico | 68 | - | ANCA (4.4%), c-ANCA (1.5%), p-ANCA (2.9%), PR3-ANCA (0%), MPO-ANCA (0%) | IIF was used for p-ANCA and c-ANCA; ELISA was used for MPO and PR3 | After treatment, c-ANCA prevalence increased to 5.8%, and p-ANCA to 23%. A positive ANCA correlated with CRP. Bactericidal/permeability-increasing protein is the main target antigen for ANCA in TB patients. |
| Lima *et al.* (37) | 2014/Brazil | 50 | | ANCA (0%) | IF and ELISA | No patient tested positive for IF ANCA, anti-MPO, or PR3. |
| Lima *et al.* (24) | 2013/Brazil | 50 | 20 | RF (60%), ACPA (4%), Anti-MCV (4%) | | |
| Faris *et al.* (12) | 2018/Iraq | 61 | 20 | IgM RF (25.7%), p-ANCA (3.2%), aCL (21.3%), ANA (9.8%), Anti-dsDNA (6.5%), Anti-Ro (8.1%), Anti-Scl-70 (3.2%) | Latex agglutination for RF; ELISA for others | RF and aCL were more prevalent among TB patients. |
| Flores-Suarez *et al.* (36) | 2003/Mexico | 45 | 47 | ANCA IF (44.4%), ANCA ELISA (40%), c-ANCA (35.5%), p-ANCA (8.8%), PR3-ANCA (33.3%), MPO-ANCA (6.6%) | IIF was used for p-ANCA and c-ANCA; ELISA was used for MPO and PR3 | ANCA positivity was more frequent in TB patients than in controls. ANCA results were not related to tuberculosis type, stage of disease, comorbidities, or pharmacotherapy. |
| Chander *et al.* (15) | 2022/India | 89 | - | ANA (6.7%), ANCA anti-elastase (96.6%), PR3-ANCA (7.8%) | IIF for ANA; ELISA for others | None were positive for anti-MPO or anti-lactoferrin. |
| Pradhan *et al.* (16) | 2004/India | 70 | 100 | ANCA (30%), c-ANCA (11.4%), p-ANCA (15.7%), PR3-ANCA (8.5%), MPO-ANCA (14.2%), Anti-LF (5.7%), ANA (24.3%), Anti-histone (21.4%) | IIF was used for ANA, p-ANCA and c-ANCA; ELISA for others | Anti-dsDNA antibodies were absent. |
| Naher *et al.* (14) | 2025/Bangladesh | 150 | - | ANA (8.7%) | IIF | 11.3 % of patients with pulmonary TB and 7.2% of patients with extrapulmonary TB were ANA positive. The most common ANA pattern was the coarse speckled pattern (69.2%). After 6 months of treatment, 92.3% of patients became ANA negative. No correlation was found between ANA positivity and TB symptoms. |
| Elkayam *et al.* (11) | 2007/Israel | 47 | 39 | Anti-dsDNA (32%), Anti-Smith (38%), Anti-RNP (15%), Anti-Ro (64%), aCL IgG (59%), aCL IgM (47%) | ELISA | |
| Huan *et al.* (38) | 2018/China | 103 | - | p-ANCA (4.8%) | IIF for ANCA; ELISA was used to detect anti MPO and PR3 antibodies | No patient had c-ANCA. Two patients were anti-MPO-positive, and both were diagnosed with ANCA-associated vasculitis. |
| Shen *et al.* (19) | 2013/Taiwan | 100 | 100 | Anti-Ro (2%), Anti-RNP (2%), Anti-Scl-70 (6%), Anti-JO1 (1%), Anti-dsDNA (1%), Anti-centromere (5%), Anti-histone (11%), aCL (17%) | ELISA | A significant proportion (32%) of patients with TB had elevated autoantibody titres. IgG aCL antibodies titre was significantly higher in TB patients than in controls. Anti-Scl70 antibodies were more frequent in TB patients compared to previous population studies. Their titre decreased after treatment. No correlation between serum titre and clinical data was observed. |
| Cheng *et al.* (10) | 2019/Bangladesh, South Africa, Peru, and Uganda | 75 | 75 | RF (56.0%), ANA (46.7%), AMA (12%), Anti-dsDNA (1.3%), Anti-β2GPI (1.3%), aCL (1.3%), Anti-Scl-70 (1.3%), Anti-Ro (5.3%), Anti-centromere (8%), ANCA (2.6%) | ELISA | No association between antibodies and active TB was observed in comparison to acute febrile respiratory illnesses. |
| Starshinova *et al.* (23) | 2023/Russia | 46 | 40 | RF (21.1%), Increased C3 (47.4%), Anti-MCV (60.7%) | ELISA | |
| Adebajo *et al.* (17) | 1993/UK | 110 | - | ANA (15%), aCL (42.7%) | IIF | |
| Isenberg *et al.* (18) | 1986/Israel | 54 | - | ANA (42%), IgM RF (20%) | ELISA and IF | |
| Goodridge *et al.* (29) | 2012/USA | 40 | - | Anti-phospholipid IgM antibodies | ELISA | Levels of IgM against all phospholipids significantly decreased by anti-TB treatment. |
| Takenam *et al.* (30) | 2018/Brazil | 37 | 48 | Anti-phospholipid IgG, aCL IgG (86.5%) | ELISA | After anti-TB treatment, the median value for all anti-phospholipid antibodies decreased significantly. |
| Shahzad *et al.* (20) | 2019/Pakistan | 80 | 80 | Anti-dsDNA (3.75%) | ELISA | Anti-dsDNA antibodies were high in TB patients as compared with healthy controls. |

ACPA, anti-citrullinated protein antibodies; RF, rheumatoid factor; ANA, anti-nuclear antibody; ANCA, anti-neutrophil cytoplasmic antibody; p-ANCA, perinuclear ANCA; c-ANCA, cytoplasmic ANCA; anti-MPO, anti-myeloperoxidase; dsDNA, double-stranded DNA; anti-RNP, anti ribonucleoprotein; anti-β2GPI, anti-β2 glycoprotein IgG; aCL, anti-cardiolipin; anti-MVC, anti-mutated citrullinated vimentin; AMA, anti-mitochondrial antibodies; anti-LF, anti-lactoferrin; TB, tuberculosis; IIF, indirect immunofluorescence; ELISA, enzyme linked immunosorbent assay.

icantly increased mean serum levels of IgM RF in TB patients compared to controls (22). Rapoport *et al*. reported a low prevalence of RF in their TB cohort when using RhcumaTec® RF latex test, although a different technique (Rheuma-Wellcotest RF test) yielded higher positivity rates (25). Therefore, the positivity of RF is dependent on the technique used. In general, the frequency of RF positivity in TB patients was relatively high.

## Anti-cyclic citrullinated peptide

The prevalence of ACPA antibodies in TB patients varies between 4% and 37% in different studies (13, 22, 24, 26, 27). Some studies have reported significantly increased mean levels of ACPA in TB patients compared to healthy controls (27). Interestingly, ACPA in TB patients may also react with unmodified arginine-containing peptides, a characteristic less common in rheumatoid arthritis (26). Furthermore, ACPA levels in TB patients decrease after anti-TB treatment (27). No relationship was found between the titer of ACPA, fever and any rheumatic symptom (13). The presence of ACPA, a highly specific marker for rheumatoid arthritis, in a subset of TB patients poses diagnostic challenges and suggests a potential overlap in the immunopathological mechanisms.

## Anti-phospholipid antibodies (including anti-cardiolipin and anti-β2-glycoprotein I)

Increased levels of aCL have been frequently reported in TB patients, with prevalence rates reaching up to 59% for IgG and 47% for IgM antibodies in some studies (11, 28). Anti-β2-glycoprotein I (anti-β2GP1) antibodies are also found in TB patients (10, 28-30). Notably, the levels of these anti-phospholipid antibodies have been shown to normalize after successful anti-TB treatment in several studies (28-30). One study found a significant association between anti-phosphatidylethanolamine antibodies and the occurrence of venous thrombosis in TB patients (31). The relatively high prevalence of anti-phospholipid antibodies in TB patients and their potential link to thrombotic events, warrant further investigation into their clinical significance in the context of TB.

## Anti-neutrophil cytoplasmic antibodies

ANCA target proteins in the cytoplasm of neutrophils. The two main types are c-ANCA, typically directed against proteinase (PR3), and p-ANCA, often directed against myeloperoxidase (MPO). Both types have been found in TB patients, with varying prevalence rates reported across studies. The p-ANCA pattern, often associated with anti-MPO antibodies, appears to be more frequently observed in TB patients compared to c-ANCA and anti-PR3 (10, 12, 15, 16, 28, 32-38). For instance, Hussein *et al*. noted ANCA in 71.4% of TB cases in Iraq (33). Similarly, a study by Flores-Suárez *et al*. reported ANCA antibodies in 44.4% of TB patients using indirect IF and 40% by ELISA (36). In contrast, studies conducted in Brazil and China found significantly lower or no ANCA positivity in their TB patient cohorts (37, 38). This variability observed in the prevalence rates might be explained by the differences in the geographical location, disease stage, and the specific methodologies employed for ANCA testing. Anti-TB treatment may induce normalization of anti-lactoferrin and anti-MPO, and *de novo* anti-PR3 and MPO formation, showing that ANCA positivity in TB patients might be transient (28, 35).

## Other relevant autoantibodies

Beyond the commonly investigated autoantibodies, other autoantibodies have also been detected in TB patients. One study reported a high prevalence (60.7%) of anti mutated citrullinated vimentin (anti-MCV) antibodies in patients with pulmonary TB (23). Elevated levels of antibodies to the C3 complement component were found in 47% of patients in the same study (23). Anti-Scl-70 and anti-histone antibodies have also been reported to be elevated in some studies. The follow-up data of anti-Scl-70 revealed decreased titres after treatment (12, 16, 19). These findings suggest that TB can trigger a broad spectrum of autoantibody production, potentially reflecting a complex interplay between the host immune system and the infecting pathogen.

## Relationship between tuberculosis infection and autoimmune rheumatologic diseases

The relationship between TB infection and autoimmune rheumatologic diseases is intricate and appears to be bidirectional. Patients with autoimmune diseases, particularly those requiring immunosuppressive medications, face an increased risk of developing TB (4, 5). The use of tumor necrosis factor-α inhibitors, a common treatment for various autoimmune conditions, is known to elevate the risk of TB reactivation (39-41). Studies have shown that patients with rheumatoid arthritis, SLE, and Sjögren's syndrome are at a higher risk of TB (42-44). This heightened susceptibility underscores the importance of TB screening and preventive measures in patients with autoimmune rheumatologic diseases.

Conversely, there is evidence suggesting that TB can potentially trigger or exacerbate autoimmune conditions in some individuals. Molecular mimicry, where similarities exist between antigens of Mtb and human autoantigens, is a proposed mechanism for this phenomenon. TB has been linked to the development or exacerba-

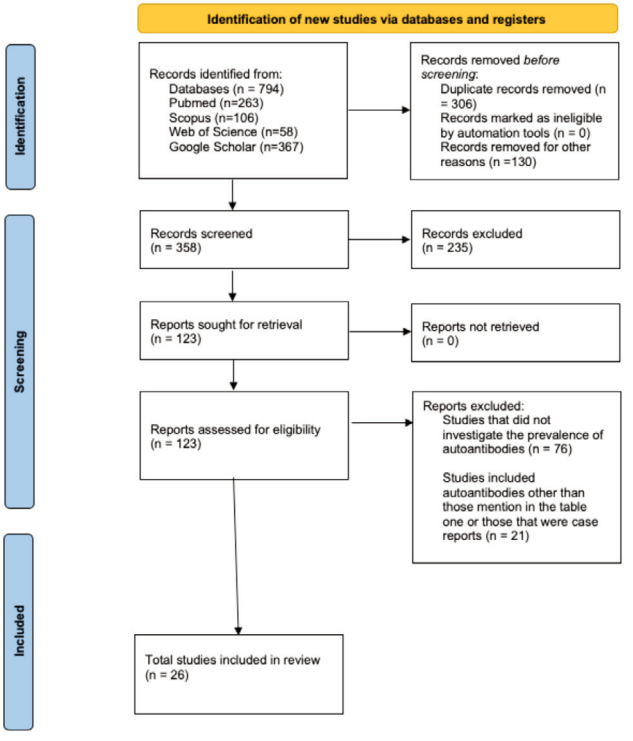



**Figure 1.** PRISMA flow diagram, including detailed information on the search strategy.



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tion of various autoimmune disorders (4, 5, 45, 46). Reactive arthritis, also known as Poncet's disease or TB rheumatism, is a well-recognized non-infectious arthropathy that can occur in the context of TB (47). Liu *et al.* reported three cases of lupus mimickers, with positive ANA and anti-ds-DNA, who exhibited atypical features of SLE, namely the absence of typical butterfly erythema, lupus hair, alopecia, or proteinuria (48). Lin *et al*. reported an increased risk of precipitating SLE among patients with TB in Taiwan from a nationwide health insurance research dataset for 9 years (49).

Several pathological mechanisms have been proposed to explain the production of autoantibodies in patients with TB, including molecular mimicry, bystander activation, release of self-antigens due to tissue damage and inflammation, impaired clearance of apoptotic debris, genetic and environmental predisposition, and neutrophil activation. The formation of autoantibodies in TB patients is likely a multifactorial process involving a combination of these mechanisms, with the relative contribution of each potentially varying depending on the individual and the specific autoantibody in question (4, 5, 50).

## Conclusions

This systematic review highlights the complex association between active TB and the presence of various autoantibodies. The prevalence of autoantibodies in TB patients is heterogeneous, with some studies reporting significant elevations in certain autoantibodies, like RF and anti-phospholipid antibodies (22, 28, 30), while others find no significant overall increase compared to control groups (19, 37). Several studies show that autoantibody positivity might be a transient and reactive phenomenon and resolves after anti-TB treatment (19, 27, 28). The variability in reported prevalence likely stems from several factors, including the specific autoantibody being investigated, the characteristics of the studied patient populations (such as age, comorbidities, and the stage and severity of TB), and the different methodologies and assays used for autoantibody detection. Some studies conducted in TB-endemic regions have reported a higher prevalence of certain autoantibodies in TB patients (12, 13, 22, 28), suggesting potential geographical influences or variations in environmental exposures that might impact the immune response to Mtb.

The presence of these autoantibodies can complicate the differential diagnosis between TB and autoimmune diseases, necessitating careful clinical interpretation. While some autoantibodies show potential as biomarkers for TB diagnosis or treatment response, further research is needed to validate these findings. The bidirectional relationship between TB and autoimmune rheumatologic diseases, where individuals with autoimmune conditions are at higher risk of TB and TB may trigger or exacerbate autoimmunity, underscores the importance of considering both conditions in patient management (48-50). Several pathological mechanisms, including molecular mimicry, bystander activation, and the release of self-antigens, have been proposed to explain autoantibody formation in TB patients, suggesting a multifactorial process (45).

### Future directions

Future research should focus on large-scale, multi-center studies employing standardized methodologies to accurately determine the prevalence of a wide range of autoantibodies in well-defined TB patient populations, considering factors such as disease stage, severity, and comorbidities. Longitudinal studies are needed to investigate the temporal dynamics of autoantibody levels throughout the course of TB and following treatment to better understand their clinical significance.

Further research into the potential utility of specific autoantibodies as diagnostic or prognostic biomarkers for TB is warranted. Studies exploring the precise mechanisms by which TB infection might trigger or exacerbate autoimmune diseases in genetically susceptible individuals are crucial. Finally, investigating the long-term clinical consequences of TB-induced autoantibodies, including their potential role in post-TB sequelae, could provide valuable insights for improving patient care.

## References


1. Bagcchi S. WHO's global tuberculosis report 2022. Lancet Microbe 2023; 4: e20.
2. Pisetsky DS. Pathogenesis of autoimmune disease. Nat Rev Nephrol 2023; 19: 509-24.
3. Nielsen PR, Kragstrup TW, Deleuran BW, Benros ME. Infections as risk factor for autoimmune diseases–a nationwide study. Journal of autoimmunity 2016; 74: 176-81.
4. Belyaeva IV, Kosova AN, Vasiliev AG. Tuberculosis and autoimmunity. Pathophysiology 2022; 29: 298-318.
5. Yablonskiy PK, Belyaeva IV, Churilov LP, Erman MV, Kudryavtsev IV, Malkova AM, et al. Tuberculosis and autoimmunity: well-coordinated duo. In: Infection and autoimmunity. Cambridge, MA, USA: Academic Press; 2024. pp. 517-41.
6. Galipeau Y, Cooper C, Langlois MA. Autoantibodies in COVID-19: implications for disease severity and clinical outcomes. Front Immunol 2025; 15: 1509289.
7. Dobrowolska K, Zarębska-Michaluk D, Poniedziałek B, Jaroszewicz J, Flisiak R, Rzymski P. Overview of autoantibodies in COVID-19 convalescents. J Med Virol 2023; 95: e28864.
8. Tugwell P, Tovey D. PRISMA 2020. J Clin Epidemiol 2021; 134: A5-6.
9. Wells G, Shea B, O'connell D, Peterson J, Welch V, Losos M, Tugwell P. Newcastle-Ottawa quality assessment scale cohort studies. University of Ottawa 2014: B-10.
10. Cheng MP, Butler-Laporte G, Parkes LO, Bold TD, Fritzler MJ, Behr MA. Prevalence of auto-antibodies in pulmonary tuberculosis. Open Forum Infect Dis 2019; 6: ofz114.
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: 306-10.
12. Faris MH, Athab AM, Fadhil RM. Evaluation of auto-antibody profiles in patients with tuberculosis. DJM 2018; 15: 50-60.
13. Emami S. Serum level of anti-CCP in patients with active pulmonary tuberculosis. Biomed J Sci Tech Res 2017; 1: 947-50.
14. Naher N, Imam H, Biswas SK, Biswas T, Azad M, Hasan MN, et al. Frequency of positive antinuclear antibody in people with active tuberculosis and its changes with antitubercular therapy. Cureus 2025; 17: e81116.
15. Chander Y, Acharya N, Naidu GS, Rathi M, Minz R, Jain S, et al. Prevalence of antineutrophil cytoplasmic antibodies and antinuclear antibodies in patients with pulmonary tuberculosis: a tertiary care center experience from north India. J Assoc Physicians India 2022; 70: 11-2.
16. Pradhan VD, Badakere SS, Ghosh K, Pawar AR. Spectrum of anti-neutrophil cytoplasmic antibodies in patients with pulmonary tuberculosis overlaps with that of Wegener's granulo-

matosis. Indian J Med Sci 2004; 58: 283-8.
17. Adebajo AO, Charles P, Maini RN, Hazleman BL. Autoantibodies in malaria, tuberculosis and hepatitis B in a west African population. Clin Exp Immunol 1993; 92: 73-6.
18. Isenberg DA, Maddison P, Swana G, Skinner RP, Swana M, Jones M, et al. Profile of autoantibodies in the serum of patients with tuberculosis, klebsiella and other gram-negative infections. Clin Exp Immunol 1987; 67: 516-23.
19. Shen CY, Hsieh SC, Yu CL, Wang JY, Lee LN, Yu CJ. Autoantibody prevalence in active tuberculosis: reactive or pathognomonic? BMJ Open 2013; 3: e002665.
20. Shahzad F, Ali A, Mushtaq A, Javaid K, Nazir A, Pervez A, et al. Raised dsDNA autoantibodies in tuberculosis patients. Egypt J Chest Dis Tuberc 2019; 68: 28-31.
21. Ms G, Narasimhan PB, Kavadichanda C, Gopal A, Bairwa D, Thabah MM, et al. AB0558 prevalence of latent tuberculosis infection and its associations with clinical and serological parameters in systemic lupus erythematosus. Ann Rheum Dis 2022; 81: 1406.
22. Elkayam O, Segal R, Lidgi M, Caspi D. Positive anti-cyclic citrullinated proteins and rheumatoid factor during active lung tuberculosis. Ann Rheum Dis 2006; 65: 1110-2.
23. Starshinova A, Malkova A, Zinchenko Y, Kudryavtsev I, Serebriakova M, Akisheva T, et al. Identification of autoimmune markers in pulmonary tuberculosis. Front Immunol 2023; 13: 1059714.
24. Lima I, Oliveira RC, Atta A, Marchi S, Barbosa L, Reis E, et al. Antibodies to citrullinated peptides in tuberculosis. Clin Rheumatol 2013;32:685-7.
25. Rapoport BL, Morrison RC, Sher R, Dos Santos L. A study of autoantibodies in chronic mycobacterial infections. Int J Lepr Other Mycobact Dis 1990; 58: 518-25.
26. Elkayam O, Segal R, Bendayan D, van Uitert R, Onnekink C, Pruijn GJ. The anti-cyclic citrullinated peptide response in tuberculosis patients is not citrulline-dependent and sensitive to treatment. Arthritis Res Ther 2010; 12: R12.
27. Kakumanu P, Yamagata H, Sobel ES, Reeves WH, Chan EK, Satoh M. Patients with pulmonary tuberculosis are frequently positive for anti–cyclic citrullinated peptide antibodies, but their sera also react with unmodified arginine□containing peptide. Arthritis Rheum 2008; 58: 1576-81.
28. Elkayam O, Bendayan D, Segal R, Shapira Y, Gilburd B, Reuter S, et al. The effect of anti-tuberculosis treatment on levels of anti-phospholipid and anti-neutrophil cytoplasmatic antibodies in patients with active tuberculosis. Rheumatol Int 2013; 33: 949-53.
29. Goodridge A, Cueva C, Lahiff M, Muzanye G, Johnson JL, Nahid P, Riley LW. Anti-phospholipid antibody levels as biomarker for monitoring tuberculosis treatment response. Tuberculosis 2012; 92: 243-7.
30. Takenami I, De Oliveira CC, Petrilli JD, Machado A, Riley LW, Arruda S. Serum antiphospholipid antibody levels as biomarkers for diagnosis of pulmonary tuberculosis patients. Int J Tuberc Lung Dis 2018; 22: 1063-70.
31. Bessis S, Bertin D, Million M, Meddeb L, Drancourt M, Lagier JC, et al. Thromboses in tuberculosis are linked to antiphosphatidylethanolamine antibodies levels: a cross-sectional study. J Clin Tuberc Other Mycobact Dis 2019; 15: 100092.
32. Sherkat R, Mostafavizadeh K, Zeydabadi L, Shoaei P, Rostami S. Antineutrophil cytoplasmic antibodies in patients with pulmonary tuberculosis. Iran J Immunol 2011; 8: 52-7.
33. Hussein S, Ismael M, Abdulmajeed N. Antineutrophil cytoplasmic antibodies in patients with tuberculosis. Iraqi J Sci 2014; 55: 360-6.
34. Teixeira L, Mahr A, Jaureguy F, Noel LH, Nunes H, Lefort A, et al. Low seroprevalence and poor specificity of antineutrophil cytoplasmic antibodies in tuberculosis. Rheumatology 2005; 44: 247-50.
35. Esquivel-Valerio JA, Flores-Suárez LF, Rodríguez-Amado J, Garza-Elizondo MA, Rendón A, Salinas-Carmona MC. Antineutrophil cytoplasm autoantibodies in patients with tuberculosis are directed against bactericidal/permeability increasing protein and are detected after treatment initiation. Clin Exp Rheumatol 2010; 28: 35-9.
36. Flores-Suárez LF, Cabiedes J, Villa AR, Van der Woude FJ, Alcocer-Varela J. Prevalence of antineutrophil cytoplasmic autoantibodies in patients with tuberculosis. Rheumatology 2003; 42: 223-9.
37. Lima I, Oliveira RC, Cabral MS, Atta A, Marchi S, Reis E, et al. Anti-PR3 and anti-MPO antibodies are not present in sera of patients with pulmonary tuberculosis. Rheumatol Int 2014; 34: 1231-4.
38. Huan G, Yang G, Xiao-Yu Q, Jiancheng X, Yan-Qing S. Antineutrophil cytoplasmic antibodies in Chinese patients with tuberculosis. Rev Soc Bras Med Trop 2018; 51: 475-8.
39. Xie X, Li F, Chen JW, Wang J. Risk of tuberculosis infection in anti-TNF-α biological therapy: from bench to bedside. J Microbiol Immunol Infect 2014; 47: 268-74.
40. Lorenzetti R, Zullo A, Ridola L, Diamanti AP, Lagana B, Gatta L, et al. Higher risk of tuberculosis reactivation when anti-TNF is combined with immunosuppressive agents: a systematic review of randomized controlled trials. Ann Med 2014; 46: 547-54
41. Picchianti-Diamanti A, Aiello A, De Lorenzo C, Migliori GB, Goletti D. Management of tuberculosis risk, screening and preventive therapy in patients with chronic autoimmune arthritis undergoing biotechnological and targeted immunosuppressive agents. Front Immunol 2025; 16: 1494283.
42. Lalvani A, Millington KA. Screening for tuberculosis infection prior to initiation of anti-TNF therapy. Autoimmun Rev 2008; 8: 147-52.
43. Wu Q, Liu Y, Wang W, Zhang Y, Liu K, Chen SH, Chen B. Incidence and prevalence of tuberculosis in systemic lupus erythematosus patients: a systematic review and meta-analysis. Front Immunol 2022; 13: 938406.
44. Chang YS, Liu CJ, Ou SM, Hu YW, Chen TJ, Lee HT, et al. Tuberculosis infection in primary Sjögren's syndrome: a nationwide population-based study. Clin Rheumatol 2014; 33: 377-83.
45. Starshinova A, Malkova A, Kudryavtsev I, Kudlay D, Zinchenko Y, Yablonskiy P. Tuberculosis and autoimmunity: common features. Tuberculosis 2022; 134: 102202.
46. Asherson RA, Gunter K, Daya D, Shoenfeld Y. Multiple autoimmune diseases in a young woman: tuberculosis and splenectomy as possible triggering factors? Another example of the "mosaic" of autoimmunity. J Rheumatol 2008; 35: 1224-6.
47. Rueda JC, Crepy MF, Mantilla RD. Clinical features of Poncet's disease. From the description of 198 cases found in the literature. Clin Rheumatol 2013; 32: 929-35.
48. Liu Y, Che G, Liu Y, Xu K. Tuberculosis mimicking the onset of systemic lupus erythematosus flare: case based review. Int J Rheum Dis 2023; 26: 1143-8.
49. Lin YC, Liang SJ, Liu YH, Hsu WH, Shih CM, Sung FC, Chen



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W. Tuberculosis as a risk factor for systemic lupus erythematosus: results of a nationwide study in Taiwan. Rheumatol Int 2012; 32: 1669-73.
50. Shapira Y, Agmon-Levin N, Shoenfeld Y. Mycobacterium tuberculosis, autoimmunity, and vitamin D. Clin Rev Allergy Immunol 2010; 38: 169-77.

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