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A Comprehensive Meta-Analytical Evidence on IFN-γ and TNF-α as Diagnostic and Treatment Monitoring Biomarkers in Tuberculosis

Shilpa Kishore[1] | Abraham Mainaprem[2] | Sher Rohan Paul[2*]

[1]Department of Pathology, Patil Medical College, Pune, India | [2]Department of Medicine, Patil Medical College, Pune, India

***Correspondence:** Sher Rohan Paul (sherrohanpaul@gmail.com)

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ABSTRACT

Background: The accurate diagnosis and effective surveillance of tuberculosis (TB) is a global health issue. The responsible cytokines in host immune response against Mycobacterium tuberculosis were interferon-gamma (IFN-γ) and tumor necrosis factor -alpha (TNF-α). This study was aimed at synthesizing the existing evidence on diagnostic accuracy of IFN-γ and TNF-α levels in TB, and to evaluate their role in monitoring treatment response. **Methods:** This review followed PRISMA 2020 guidelines for its synthesis. Relevant published articles from in PubMed, Scopus, Web of Science, and Google Scholar from 2016 to 2025 were analyzed. The included studies were those that compared circulating IFN-γ and/or TNF-α levels in patients with TB, with or without treatment. Review-based studies, and studies without comparable biomarker data were excluded. For risk of bias assessment, Newcastle-Ottawa Scale was utilized, and the certainty of evidence was measured through GRADE framework. **Results:** The analysis of 12 included studies demonstrated that high levels of IFN-γ were a uniform biomarker of diagnosis for latent and active TB infection, whereas higher levels of TNF-α level were associated with active pulmonary TB. Longitudinal data showed that reduction in both cytokine levels was associated with successful treatment outcomes, while their persistent elevated levels suggested poor outcomes or relapse. Risk of bias among studies was low to moderate, and certainty of evidence was found to be moderate. **Conclusion:** IFN-γ was a good diagnostic biomarker throughout the TB spectrum, TNF-α was promising in the detection of active disease and assessment of therapeutic response.

Keywords: Tuberculosis; Interferon-gamma; Tumor Necrosis Factor-alpha; Biological Markers; Diagnosis; Treatment; Monitoring; Systematic Reviews as Topic; Meta-Analysis as Topic

Tuberculosis (TB) remained a significant global health problem, with clinical manifestations ranging from latent TB infection (LTBI) to active disease [1,2]. The accurate diagnosis and monitoring of TB treatment were critical for effective disease management and control. Interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α) were among the key mediators activated in response to *Mycobacterium tuberculosis* infection [3,4]. Their importance in the TB diagnosis and differentiation between latent and active TB, as well in the monitoring treatment response, had been extensively investigated [5,6].

The current diagnostic methods including sputum smear microscopy, culture and molecular tests were suitable for the diagnosis of TB, but had some limitations such as limited sensitivity and specificity [7,8]. Strategies based on biomarkers offered an alternative approach. LTBI diagnosis had already been tested using IFN-γ release assays (IGRAs) [9]. However, the diagnostic and prognostic value of circulating IFN-γ and TNF-α levels, especially in active TB and for monitoring treatment response, were not well-defined and had inconsistent findings in different populations and disease conditions [10]. Although multiple studies had investigated IFN-γ and TNF-α in TB, there were limited evidences with higher heterogeneity on these biomarkers, which resulted in inconsistent findings. Further studies are needed to evaluate the findings on the diagnostic, prognostic, and therapeutic relevance of these critical biomarkers in TB. Due to the heterogeneity and the lack of methodological consistency in the published literature, additional rigorous studies are required to support the reported findings for clinical translation

This study was aimed at synthesizing the existing evidence on diagnostic accuracy of IFN-γ and TNF-α levels in TB, and to estimate their possible applicability in monitoring anti-tubercular treatment response. In particular, it was focused to compare cytokine levels in TB (latent versus active) and non-TB patients, to evaluate their discriminatory potential and association with treatment outcomes.

Methodology

This study was conducted by following PRISMA guidelines, to ensure reproducibility of study findings [11]. The primary outcome of this review was to evaluate the diagnostic accuracy of IFN-γ and TNF-α levels in TB, and to evaluate their role in monitoring anti-tubercular treatment response.

Databases and Search String Used: Research reported from 2016 to October 2025 was searched by using different databases including PubMed, Scopus, Web of Science, and Google Scholar. The search was made by using study relevant MeSH terms as well as free-text keywords i.e., cytokine biomarkers, and clinical application. Core search terms included: "tuberculosis", "Mycobacterium tuberculosis", "interferon-gamma", "IFN-gamma", "tumor necrosis factor-alpha", "TNF-alpha", "biomarker", "diagnosis", "diagnostic accuracy", "sensitivity and specificity", "treatment monitoring" "treatment response", and "prognosis". Additional studies were included by screening the bibliography of relevant studies.

Eligibility Criteria: Studies examining the diagnostic utility or treatment monitoring potential of IFN-γ and/or TNF-α in human TB (latent or active) that were published in English were included. Studies were excluded, if they did not report quantitative measurements of circulating IFN-γ or TNF-α levels or focused solely on animal models or in-vitro studies.

Study Selection and Data Extraction: Two researchers independently reviewed the title and abstract of studies until proper inclusion requirement were met. The reviewers settled their selection differences either through group agreement or expert consultation. Two independent reviewers extracted data related to study design, confounding variables, outcome measured, and key results. A third person was consulted to settle any differences between their findings.

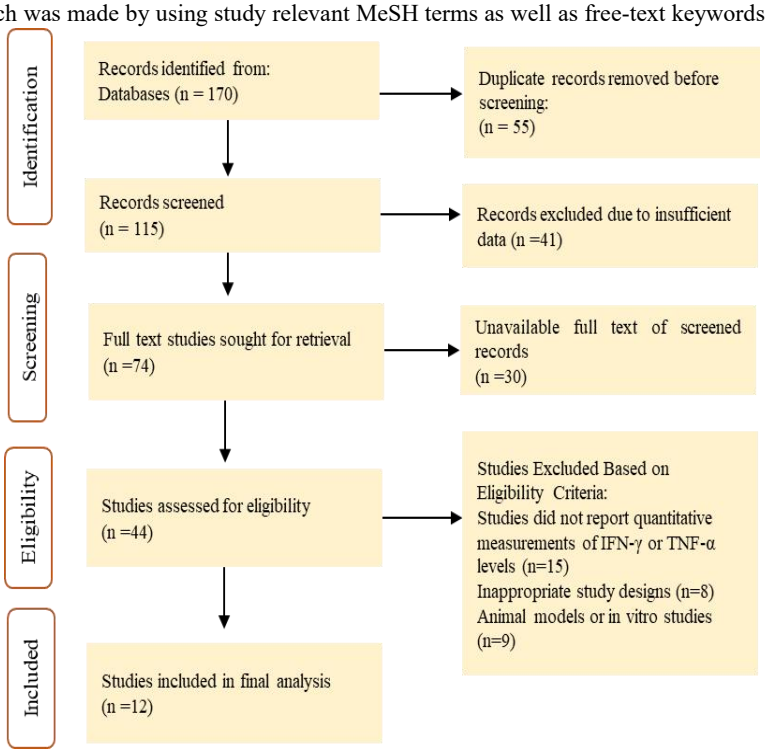

Figure 1: PRISMA Flow Diagram for Selection of Included Studies

Statistical and Quality Assessment: The statistical analysis and forest plots were generated in MetaAnalysisOnline Tool [12]. The mean and standard deviation were calculated using standard protocols where researchers had reported data in the form of medians and interquartile ranges. As a measure of heterogeneity, the I^2 value was used and considered high if its value is greater than 50. A descriptive analysis was reported in case the reported data was not comparable. The expression of cytokines (IFN-γ and TNF-α) were correlated with clinical outcome. Subgroup and sensitivity analysis were performed for eligible studies. Risks of bias among the included studies were assessed by two independent reviewers through Newcastle-Ottawa Scale (NOS) [13]. The level of evidence was determined based on the GRADE approach.

Results

The study demonstrated the role of IFN-γ and TNF-α in the progression of TB. Among the searched electronic databases and other sources, 170 research articles were initially selected. The number was reduced to 115 records after removing the duplicates. Title and abstract screening further eliminated 41 studies. From the remaining 74 articles, 30 were removed due to unavailability of access to the full-texts. Further 44 articles were screened, and 32 were eliminated due to a lack of stratified data and studies including animals, in vitro findings, reviews, case reports, or languages other than English. Ultimately, twelve studies that passed the inclusion criteria were included in this systematic review.

The PRISMA flow diagram presented in Figure 1 illustrates the selection process. A summary of major clinical studies assessing the role of IFN-γ and TNF-α as immunological biomarkers in tuberculosis in various disease conditions is provided in Table 1. It presented the differences in the levels of IFN-γ and TNF-α between latent, active, and relapse populations of tuberculosis, and study designs and demographic characteristics of patients. Moreover, the diagnostic, prognostic, and treatment-monitoring inferences of IFN- cytokine and TNF- cytokines in the treatment of tuberculosis are highlighted in Table 1.

Table 1: Characteristics of Included Studies with Cytokine (IFN-γ and TNF-α) Levels in TB cases

Author & Year	Disease Context	Key Biomolecule Investigated	Study Design & Model(s)	Sample Size / Population Characteristics	Biomolecule Levels Mean±SD (pg/mL)	Key Findings	Impact on Treatment
Priyanka et al., 2025 [14]	Latent Tuberculosis	IFN-γ (via IGRA)	Cross-sectional observational	46 young adults	IFN-γ = 533±270	IFN-γ levels used to diagnose LTBI; 30.43% IGRA was positive.	IGRA (IFN-γ-based) used for LTBI screening.
Selvavinayagam et al., 2025 [15]	Latent Tuberculosis	IFN-γ (via IGRA)	Cross-sectional observational	392 Health care workers	IFN-γ = 45 ± 25	IFN-γ detected via IGRA in 25.3% of HCWs.	IFN-γ release assay confirms LTBI status in high-risk groups.
Li et al., 2024 [16]	Tuberculosis	IFN-γ, TNF-α (via ELISA)	Retrospective cohort analysis	77 TB patients vs. 48 non-TB	TB (IFN-γ = 17.5 ± 19.6; TNF-α = 2.79 ± 3.11) Non-TB (IFN-γ = 4.25±3.19; TNF-α = 1.80±1.73)	IFN-γ significantly higher in TB patients; TNF-α not significantly elevated.	IFN-γ supports TB diagnosis; TNF-α not a strong biomarker.
Manna et al., 2018 [17]	Active Tuberculosis vs. Latent Tuberculosis vs. non-Tuberculosis	IFN-γ, TNF-α (via BD Cytometric bead array)	Case-control study	27 active TB, 32 LTBI, 20 non-TB	IFN-γ = (Active TB = 85 ± 40; LTBI = 90 ± 45; Non-TB = 30 ± 20) TNF- α = 52 ± 23 (for all cohorts)	IFN-γ elevated in TB/LTBI; TNF-α levels not discriminatory between groups.	IFN-γ is a reliable biomarker for TB infection; TNF-α less useful.
Huaman et al., 2016 [18]	Latent Tuberculosis Infection	IFN-γ (via ELISA)	Cross-sectional Study	430 LTBI vs. 430 non-LTBI	IFN-γ (LTBI = 1.25 ± 0.87 Non-LTBI = 0.96 ± 0.72)	LTBI is associated with significantly higher circulating IFN-γ levels compared to non-LTBI.	Elevated IFN-γ in LTBI suggests ongoing immune activation, which may indicate subclinical inflammation and could influence adjunctive immunomodulatory strategies in high-risk LTBI patients.
Walles et al., 2020 [19]	Latent Tuberculosis	IFN-γ (via QFT plus +ELISA)	Cross-sectional diagnostic study	n=1834 pregnant women	IFN-γ = 60 ± 25	IFN-γ positivity increased with age and HIV co-infection.	IFN-γ-based assay detects LTBI in high-risk populations.
Chen et al., 2025 [20]	Active Tuberculosis	IFN-γ (via ELISA)	Retrospective cohort	n=1080 (904 TB, 176 non-TB)	IFN-γ in TB = 376.8 ± 125.6; IFN-γ in non-TB = 68.1 ± 22.7	IFN-γ levels were higher in TB vs. non-TB	IFN-γ aids in distinguishing active TB from non-TB disease.

Indrati et al., 2024 [21]	HIV-TB co-infection	TNF-α, IFN-γ (via BD Cytometric bead array)	Cross-sectional study	n=70 (HIV-ATB=19, HIV-LTB=21, HIV=30)	TNF-α = (HIV-ATB = 3.1 ± 4.5 HIV-LTB = 1.2 ± 1.8 HIV = 0.8 ± 3.0) IFN-γ = (HIV-ATB = 4.5 ± 6.2 HIV-LTB = 0.6 ± 0.5 HIV = 0.8 ± 1.1)	TNF-α and IFN-γ levels were higher in HIV-ATB vs. HIV-LTB and HIV alone.	Elevated TNF-α and IFN-γ are associated with active TB in HIV co-infection.
Nie et al., 2020 [22]	Active Tuberculosis	TNF-α, IFN-γ (via ELISA)	Prospective cohort study	67 active TB patients	TNF-α = (Pre-treatment = 814 ± 233; 1–2 months treatment = 692 ± 216; 6 months post-treatment = 484 ± 196); IFN- γ = (pre-treatment = 484 ± 66; 1–2 months treatment = 358 ± 33; 6 months post-treatment = 410 ± 55)	TNF-α and IFN-γ Pretreatment higher in smear-positive cases; it decreased after 6 months treatment.	TNF-α (cut-off 845 pg/ml) and IFN-γ (cut-off 393 pg/ml) may serve as biomarkers for monitoring anti-TB treatment.
Al-Zubaidi et al., 2024 [23]	Active pulmonary Tuberculosis	TNF-α (via ELISA)	Cross-sectional observational	90 ATB patients, 90 healthy controls	TNF-α in Active ATB = 18.7 ± 9.4 TNF-α in Healthy controls = 6.1 ± 2.8	TNF-α levels significantly higher in ATB vs. controls.	TNF-α levels and ratios may help assess TB severity and early treatment response.
Jumaar et al., 2025 [24]	Active pulmonary Tuberculosis	TNF-α (via ELISA)	Observational cross-sectional study	Post-TB: n=22; Active TB: n=21	Post-TB = 92,680 ± 46,430 Active TB (in treatment) = 86,930 ± 50,810	TNF-α remained elevated post-treatment and during active TB above normal range.	Persistent TNF-α elevation suggests ongoing inflammation; may indicate need for anti-inflammatory therapy post-TB.
Waghmare et al., 2019 [25]	Pulmonary & Extrapulmonary Tuberculosis	TNF-α, IFN-γ (via BD Cytometric bead array)	Case-control study	100 subjects (25 per group: relapse, fresh TB, healthy)	TNF-α = (Freshly Diagnosed TB = 43.87 ± 23.90; Relapse TB = 85.59 ± 10.68; HC = 4.78 ± 9.57) IFN-γ = (Freshly Diagnosed TB = 36.06 ± 18.38; Relapse TB = 83.62 ± 23.23; HC = 10.28 ± 3.70)	TNF-α & IFN-γ levels significantly high in relapse group.	High TNF-α & IFN-γ may indicate poor response/relapse. Low levels suggest treatment effectiveness.

TB = Tuberculosis; LTB = Latent Tuberculosis; IGRA = Interferon-Gamma Release Assay; HCWs = Healthcare Workers; PM = Particulate Matter; HIV = Human Immunodeficiency Virus; ATB = Active Tuberculosis; ATT = Anti-Tubercular Therapy/Therapy; HC = Healthy Controls; TNF-α = Tumor Necrosis Factor-Alpha; IFN-γ = Interferon-Gamma.; ELISA = Enzyme Linked Immunosorbent assay; QFT plus = QuantiFERON-TB Gold Plus

The analysis of the twelve incorporated studies indicated some major trends in the expression levels of cytokines in the spectrum of TB. The IFN-γ levels in the cohort of those with latent and active TB were consistently higher, as compared to those with no infection, which proved that

the IFN-γ is an important core biomarker of immune recognition. The levels of TNF-α exhibited a more selective pattern with significant higher levels being reported in active pulmonary TB studies. Crucially, longitudinal data of various studies showed that the concentrations of both cytokines significantly declined when patients were put on anti-tubercular treatment, especially those with good clinical prognoses. In contrast, results with relapse cases or post-treatment follow-up showed consistently high levels, suggesting a link between sustained cytokine elevation and unresolved infection or inflammation. This cumulative review demonstrated the diagnostic and prognostic capability of these biomarkers. Only studies with comparable disease state, independent groups, and consistent comparator definitions were included in quantitative synthesis. Studies assessing treatment response, relapse TB, HIV-TB co-infection, or single-arm cytokine levels were excluded from meta-analysis and synthesized narratively due to clinical and methodological heterogeneity.

For diagnostic point of view, comparison was made for IFN-γ levels between patients with active tuberculosis and non-TB controls. The pooled effect size of all 3 studies a total of 1008 subjects in the experimental cohort and 256 subjects in the control cohort were analyzed using random effects model with Inverse variance method to compare the standardized mean difference (SMD), and no statistical difference between the two cohorts were observed (SMD: 1.15, 95% CI: -0.46 to 2.76). Significant heterogeneity ($p<0.01$) was detected, suggesting inconsistent effects in magnitude and/or direction. The I^2 value indicated that 99% of the variability among studies arises from heterogeneity rather than random chance.

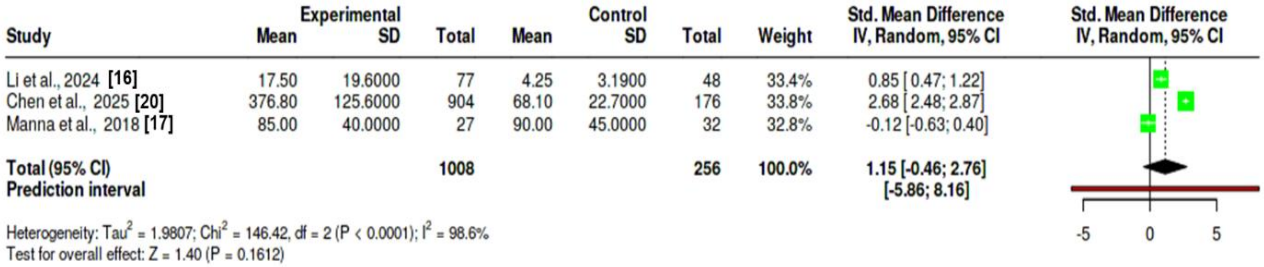

Figure 2: Forest plot analyzing IFN-γ levels between patients with active tuberculosis and non-TB controls

For comparing the levels of IFN-γ between individuals with latent tuberculosis infection (LTBI) and non-infected controls, two eligible studies were analyzed with a total of 462 subjects in the experimental cohort and 450 subjects in the control cohort. Based on the analysis performed using random effects model with Inverse variance method to compare the standardized mean difference (SMD), there was no statistical difference between the two cohorts (SMD: 0.93, 95% CI: -0.26 to 2.11). A significant heterogeneity was detected ($p<0.01$), suggesting inconsistent effects in magnitude and/or direction. The I^2 value indicated that 92% of the variability among studies arises from heterogeneity rather than random chance.

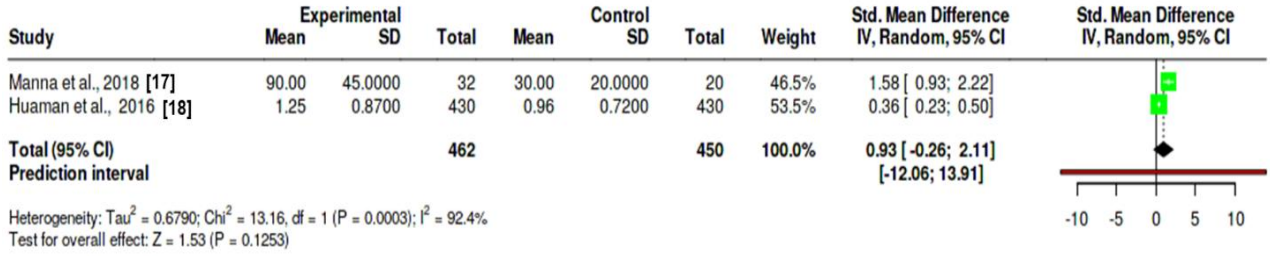

Figure 3: Forest plot analyzing IFN-γ levels between individuals with latent tuberculosis infection (LTBI) and non-infected controls

For comparing TNF-α levels between patients with active tuberculosis and healthy controls, 2 eligible studies were analyzed with a total of 115 subjects in the experimental cohort and 115 subjects in the control cohort. Based on the analysis performed using random effects model with inverse variance method to compare the standardized mean difference (SMD), no statistical difference between the two cohorts was observed (SMD: 4.77, 95% CI: -1.15 to 10.68). A significant heterogeneity was detected ($p<0.01$), suggesting inconsistent effects in magnitude and/or direction. The I^2 value indicated that 98% of the variability among studies arises from heterogeneity rather than random chance.

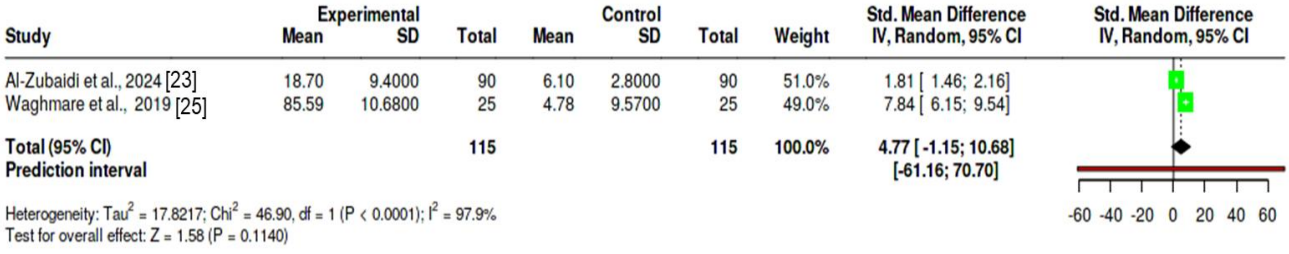

Figure 4: Forest plot analyzing TNF-α levels between patients with active tuberculosis and healthy controls

Substantial heterogeneity was observed across all pooled analyses (I^2 = 92–99%), indicating that variability within the selected studies was driven by true differences rather than random error. To explore potential sources of heterogeneity, subgroup analysis was conceptually performed. IFN-γ and TNF-α were highly context-dependent biomarkers which were greatly affected by the disease context, individual's immune status, assay used for measuring their levels, and treatment phase. Overall, although pooled estimates did not reach statistical significance, the direction and magnitude of effects varied systematically across clinically meaningful subgroups. These findings support cautious interpretation of pooled effect sizes and underscore the importance of stratified analyses when evaluating cytokines as diagnostic or prognostic biomarkers in tuberculosis. The impact of individual studies on the aggregated effect size was evaluated using the leave-one-out sensitivity analysis. The robustness of reported findings was confirmed by the fact that eliminating any one study did not substantially change the overall results. Risk of bias assessment is shown in Figure 5, 6, 7.

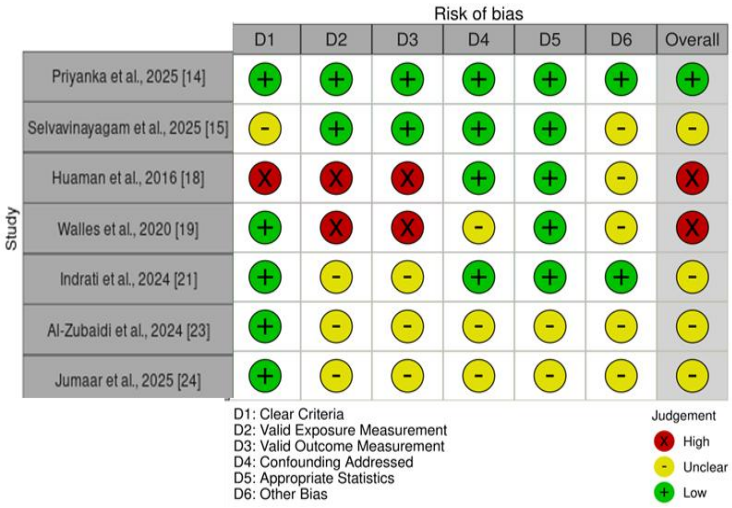

Figure 5: Risk of Bias Traffic Light Plot for Cross-sectional Studies using JBI-checklist

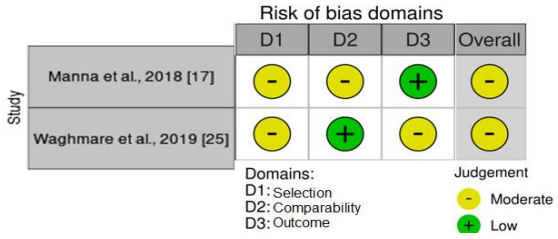

Figure 6: Risk of Bias Traffic Light Plot for Case-Control Studies using Newcastle Ottawa Scale

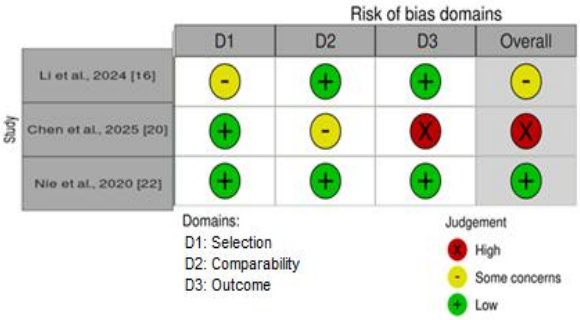

Figure 7: Risk of Bias Traffic Light Plot for Cohort Studies using Newcastle Ottawa Scale

Traffic plots reflecting risk of bias in each study as shown in above Figures . Overall, the risk of bias among studies was low to moderate. The overall GRADE certainty of the evidence was moderate. The quality of the included studies was evaluated with risk-of-bias traffic light plots. The cross-sectional studies were rated with moderate to high risks of bias when appraised with the Joanna Briggs Institute checklist for cross-sectional studies. The case-control studies assessed with the NOS for cohort studies revealed a moderate risk of bias. The cohort studies (retrospective/prospective) showed a moderate risk of bias (according to NOS assessment). The certainty of evidence, based on GRADE, was found moderate, which reflected consistency of results between studies.

Discussion

The findings of this study revealed that high levels of IFN-γ could be exploited as diagnostic biomarker for the identification of both latent and active TB infection when compared to non-infected controls. It showed the central relevance of cell-mediated immunity in *Mycobacterium tuberculosis* infection [26]. Experimental studies have also demonstrated that dysregulated cytokine signaling and associated cellular alterations play a critical role in immune-mediated disease processes [27,28]. The level of TNF-α was considerably high in active TB, demonstrated its importance in the formation of granuloma, and the inflammatory pathology of symptomatic disease [29,30]. Moreover, longitudinal data indicated that a quantifiable decrease in the levels of both IFN-γ and TNF-α, especially TNF-α, was correlated with successful treatment outcome [31], whereas persistently high or fluctuating levels were associated with treatment failure, relapse, or a persistent inflammatory state [32].

The associations between persistent molecular alterations and disease progression had been reported in experimental and clinical models of chronic disorders [33,34]. The data supported that along with the utility of IFN-γ and TNF-α as TB biomarkers, they could also be used to measure the inflammatory load and intensity of bacterial activity [35]. The findings aligned with the existing pathophysiological data, where role of IFN-γ in the macrophage mediated killing of *Mycobacterium tuberculosis* had been reported, supporting its central role in immune-based diagnostics such as IGRA [36,37]. Similarly, higher levels of TNF-α in active TB patients reaffirmed its involvement in the formation of granuloma and inflammation [38,39]. This review elucidated that although expression levels of both cytokines were upregulated, their discriminatory abilities were different; IFN-γ was valuable across the entire TB spectrum, whereas TNF-α showed more pronounced response in the evaluation of disease activity and inflammatory load during active infection [40,41]. The results suggested that serial TNF-α measurement, in combination with IFN-γ, could be considered as a complementary tool for monitoring treatment response in active TB.

The main limitations of the included studies were their methodological heterogeneity. Variations in assay techniques (ELISA, cytometric bead array), sample types, and units of measurement complicated direct comparisons. Also, there was a wide range of patient populations (TB patients with HIV), types of TB (pulmonary vs. extrapulmonary), and treatment stages. The sample sizes of some studies were also relatively small and this could had impacted the accuracy and generalizability of the individual results. Despite comprehensive searches, publication bias for smaller studies might be present, and the exclusion of non-English literature might have introduced a selection bias. Standardized and large-scale future studies with prospective designs to define clinically validated cut-off values are needed. The incorporation of these biomarkers could facilitate clinicians in managing algorithms, especially in the determination of treatment efficacy and relapse.

Conclusion

This meta-analysis and systematic review demonstrated that IFN-γ was a good diagnostic biomarker throughout the TB spectrum, whereas TNF-α was promising in the detection of active disease and assessment of therapeutic response. The quality of the conclusions was weak because of considerable heterogeneity and variability in methods. Future prospective studies employing standardized assays are required to validate the utility of these cytokines in guiding therapeutic decisions and improving TB management outcomes.

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Authors' Contribution: All authors contributed equally as per ICMJE.

Ethical Statement: Not Applicable

References

1. Hange N, Somagutta MR, Sharma A, Agadi K, Ngaba NN, Paikkattil N, et al. Latent tuberculosis: challenges and opportunities for diagnosis and treatment. Discov Med. 2022;5(1):e27. https://doi.org/10.15190/drep.2022.1
2. Palanivel J, Sounderrajan V, Thangam T, Rao SS, Harshavardhan S, Parthasarathy K. Latent tuberculosis: challenges in diagnosis and treatment, perspectives, and the crucial role of biomarkers. Curr Microbiol. 2023;80(12):392. https://doi.org/10.1007/s00284-023-03491-x
3. Yuk J-M, Kim JK, Kim IS, Jo E-K. TNF in human tuberculosis: a double-edged sword. Immune Netw. 2024;24(1):e4. https://doi.org/10.4110/in.2024.24.e4
4. Shanmuganathan G, Orujyan D, Narinyan W, Poladian N, Dhama S, Parthasarathy A, et al. Role of interferons in Mycobacterium tuberculosis infection. Clin Pract. 2022;12(5):788-96. https://doi.org/10.3390/clinpract12050082
5. Arias AA, Neehus A-L, Ogishi M, Meynier V, Krebs A, Lazarov T, et al. Tuberculosis in otherwise healthy adults with inherited TNF deficiency. Nature. 2024;633(8029):417-25. https://doi.org/10.1038/s41586-024-07866-3
6. Yilmaz E, Pasin Ö, Pasin T. Screening potential of tuberculin skin and interferon gamma release tests for latent tuberculosis prior to anti-tumor necrosis factor (TNF)-α therapy in patients with rheumatoid arthritis and spondyloarthritis. Egypt Rheumatol. 2025;47(1):31-5. https://doi.org/10.1016/j.ejr.2024.11.003
7. Zachariou M, Arandjelović O, Sloan DJ. Automated methods for tuberculosis detection/diagnosis: a literature review. BioMedInformatics. 2023;3(3):724-51. https://doi.org/10.3390/biomedinformatics3030047
8. Kontsevaya I, Cabibbe AM, Cirillo DM, DiNardo AR, Frahm N, Gillespie SH, et al. Update on the diagnosis of tuberculosis. Clin Microbiol Infect. 2024;30(9):1115-22. https://doi.org/10.1016/j.cmi.2023.07.014
9. Datta K, LaRue R, Permpalung N, Das S, Zhang S, Mehta Steinke S, et al. Development of an interferon-gamma release assay (IGRA) to aid diagnosis of histoplasmosis. J Clin Microbiol. 2022;60(10):e01128-22. https://doi.org/10.1128/jcm.01128-22
10. Yang Y, Wang H-J, Hu W-L, Bai G-N, Hua C-Z. Diagnostic value of interferon-gamma release assays for tuberculosis in the immunocompromised population. Diagnostics. 2022;12(2):453. https://doi.org/10.3390/diagnostics12020453
11. Parums DV. Review articles, systematic reviews, meta-analysis, and the updated preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 guidelines. Med Sci Monit. 2021;27:e934475-1. https://doi.org/10.12659/MSM.934475
12. Fekete JT, Győrffy B. MetaAnalysisOnline. com: web-based tool for the rapid meta-analysis of clinical and epidemiological studies. J Med Internet Res. 2025;27:e64016. https://preprints.jmir.org/preprint/64016
13. Carra MC, Romandini P, Romandini M. Risk of bias evaluation of cross-sectional studies: Adaptation of the Newcastle–Ottawa Scale. J Periodontal Res. 2025 Apr;60(2):e13405. https://doi.org/10.1111/jre.13405
14. Priyanka, Bhatt P, Bedi AK, Basil MV, Sharma M, Sharma S. Association of latent tuberculosis and Vitamin D levels in young individuals: An exploratory study. Int J Mycobacteriol. 2025;14(1):66-72. https://doi.org/10.4103/ijmy.ijmy_6_25
15. Selvavinayagam ST, Sankar G, Yong YK, Sankar S, Zhang Y, Tan HY, et al. Association of clinical laboratory parameters with latent tuberculosis infection among healthcare workers of primary health centers—A cross-sectional observational study. PLOS Glob Public Health. 2025;5(6):e0004873. https://doi.org/10.1371/journal.pgph.0004873
16. Li X, Zhao W, Han H, Yang Z, Bi F, He Y. Retrospective analysis of the clinical utility of multi-cytokine profiles in smear-negative pulmonary tuberculosis. Saudi Med J. 2024;45(7):658. https://doi.org/10.15537/smj.2024.45.7.20240310
17. Manna MP, Orlando V, Li Donni P, Sireci G, Di Carlo P, Cascio A, et al. Identification of plasma biomarkers for discrimination between tuberculosis infection/disease and pulmonary non tuberculosis disease. PLoS One. 2018;13(3):e0192664. https://doi.org/10.1371/journal.pone.0192664
18. Huaman MA, Deepe Jr GS, Fichtenbaum CJ. Elevated circulating concentrations of interferon-gamma in latent tuberculosis infection. Pathog Immun. 2016;1(2):291. https://doi.org/10.20411/pai.v1i2.149

19. Walles J, Tesfaye F, Jansson M, Balcha TT, Sturegård E, Kefeni M, et al. Tuberculosis infection in women of reproductive age: a cross-sectional study at antenatal care clinics in an Ethiopian city. Clin Infect Dis. 2021;73(2):203-10. https://doi.org/10.1093/cid/ciaa561
20. Chen J, Deng B, Li M, Huang Y, Han J, Li Q, et al. Analysis of the clinical value and influencing factors of combined detection of tuberculosis-specific cytokines IFN-γ and IL-2 in the diagnosis of active tuberculosis in children and adolescents. Eur J Med Res. 2025;30(1):732. https://doi.org/10.1186/s40001-025-02895-8
21. Indrati AR, Sumarpo A, Haryanto J, Rosmiati NMD, Munaya S, Turbawaty DK, et al. Identification of cytokine signatures in HIV-infected individuals with and without Mycobacterium tuberculosis co-infection. Biomed Rep. 2024;21(3):131. https://doi.org/10.3892/br.2024.1819
22. Nie W, Wang J, Jing W, Shi W, Wang Q, Huang X, et al. Value of serum cytokine biomarkers TNF-α, IL-4, sIL-2R and IFN-γ for use in monitoring bacterial load and anti-tuberculosis treatment progress. Cytokine: X. 2020;2(2):100028. https://doi.org/10.1016/j.cytox.2020.100028
23. Al-Zubaidi MI, Lafi SA, Abdulateef YM. Cytokine Dysregulation in pulmonary Tuberculosis: The role of TNF-α/IL-10 and TNF-α/TGF-β ratios as severity indicators. Hum Immunol. 2025;86(2):111256. https://doi.org/10.1016/j.humimm.2025.111256
24. Jumaar C, Malefane L, Jacobs S, Sanni O, Louw E, Baines N, et al. Delineating the Significance of Several Inflammatory Markers in a Lung Tuberculosis Cohort During the Active and Post-Tuberculosis Stages of the Disease: An Observational Study in Cape Town, South Africa (2019 to 2024). Infect Dis Rep. 2025;17(3):52. https://doi.org/10.3390/idr17030052
25. Waghmare PJ, Lende T, Goswami K, Gupta A, Gupta A, Gangane N, et al. Immunological host responses as surveillance and prognostic markers in tubercular infections. Int J Mycobacteriol. 2019;8(2):190-5. https://doi.org/10.4103/ijmy.ijmy_48_19
26. Khanna H, Gupta S, Sheikh Y. Cell-Mediated Immune Response Against Mycobacterium tuberculosis and Its Potential Therapeutic Impact. J Interferon Cytokine Res. 2024;44(6):244-59. https://doi.org/10.1089/jir.2024.0030
27. Singha SP, Memon S, Kazi SAF, Nizamani GS. Gamma aminobutyric acid signaling disturbances and altered astrocytic morphology associated with Bisphenol A induced cognitive impairments in rat offspring. Birth Defects Res. 2021;113(12):911–24. https://doi.org/10.1002/bdr2.1886
28. Singha SP, Memon S, Bano U, Isaac AD, Shahani MY. Evaluation of p21 expression and related autism-like behavior in Bisphenol-A exposed offspring of Wistar albino rats. Birth Defects Res. 2022;114(11):536–50. https://doi.org/10.1002/bdr2.2022
29. Arbues A, Brees D, Chibout S-D, Fox T, Kammüller M, Portevin D. TNF-α antagonists differentially induce TGF-β1-dependent resuscitation of dormant-like Mycobacterium tuberculosis. PloS pathogens. 2020;16(2):e1008312. https://doi.org/10.1371/journal.ppat.1008312
30. Conrad A, Neven B, Mahlaoui N, Suarez F, Sokol H, Ruemmele FM, et al. Infections in patients with chronic granulomatous disease treated with tumor necrosis factor alpha blockers for inflammatory complications. J Clin Immunol. 2021;41(1):185-93. https://doi.org/10.1007/s10875-020-00901-8
31. Lopetuso LR, Cuomo C, Mignini I, Gasbarrini A, Papa A. Focus on anti-tumour necrosis factor (TNF)-α-related autoimmune diseases. Int J Mol Sci. 2023;24(9):8187. https://doi.org/10.3390/ijms24098187
32. Wadee R, Wadee AA. The pathology of lymphocytes, histiocytes, and immune mechanisms in Mycobacterium tuberculosis granulomas. Am J Trop Med Hyg. 2021;104(5):1796. https://doi.org/10.4269/ajtmh.20-1372
33. Shaikh P, Bano U, Memon S, Bano S, Gul S, Pirya. Neuroanatomical study of in-vivo brainstem abnormalities in autism spectrum disorder and their clinical correlations. Pak J Med Dent. 2025;14(3). https://doi.org/10.36283/ziun-pjmd14-3/039
34. Ghafoor A, Kashif S, Ali SMS, Memon S, Memon SS, Mehmood A, et al. Evaluating neurotherapeutic potential of naringenin by true experiments: insights into in-vivo psychiatry care models. Pak J Med Dent. 2025;14(3). https://doi.org/10.36283/ziun-pjmd14-3/043
35. Kim HW, Kim EH, Lee M, Jung I, Ahn SS. Risk of cancer, tuberculosis and serious infections in patients with ankylosing spondylitis, psoriatic arthritis and psoriasis treated with IL-17 and TNF-α inhibitors: a nationwide nested case-control analysis. Clin Exp Rheumatol. 2023;41(7):1491-9. https://doi.org/10.55563/clinexprheumatol/qkiorp
36. Mundra A, Yegiazaryan A, Karsian H, Alsaigh D, Bonavida V, Frame M, et al. Pathogenicity of type I interferons in mycobacterium tuberculosis. Int J Mol Sci. 2023;24(4):3919. https://doi.org/10.3390/ijms24043919
37. Petruccioli E, Farroni C, Cuzzi G, Vanini V, Palmieri F, Vittozzi P, et al. VIDAS® TB-IGRA reagents induce a CD4+ and CD8+ T-cell IFN-γ response for both TB infection and active TB. Int J Tuberc Lung Dis. 2022;26(1):65-8. https://doi.org/10.5588/ijtld.21.0478
38. Beig H, Singh A. Neutrophils from Protection to Pathogenesis in Tuberculosis. ACS Infect Dis. 2025;11(11):2926-50. https://doi.org/10.1021/acsinfecdis.5c00096
39. Park E-J, Kim I, Jo E-K. Host Immune Pathways to Mycobacterium Tuberculosis Infection. J Bacteriol Virol. 2024;54(3):167-90. https://doi.org/10.4167/jbv.2024.54.3.167
40. Madrid-Paulino E, Mata-Espinosa D, León-Contreras JC, Serrano-Fujarte I, Díaz de León-Guerrero S, Villaseñor T, et al. Klf10 favors Mycobacterium tuberculosis survival by impairing IFN-γ production and preventing macrophages reprograming to macropinocytosis. J Leukoc Biol. 2022;112(3):475-90. https://doi.org/10.1002/JLB.4MA0422-288R
41. Akter S, Chauhan KS, Dunlap MD, Choreño-Parra JA, Lu L, Esaulova E, et al. Mycobacterium tuberculosis infection drives a type I IFN signature in lung lymphocytes. Cell Rep. 2022;39(12):110983. https://doi.org/10.1016/j.celrep.2022.110983