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Diagnostic Performance of ELISA Based IGRA in Detecting Latent Tuberculosis Among Rheumatoid Arthritis Patients

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder marked by persistent inflammation and progressive joint damage. Patients with RA are at elevated risk of latent tuberculosis infection (LTBI), particularly when receiving immunosuppressive or biologic therapies. Accurate LTBI screening is therefore critical before initiating such treatments.

Objective: This study aimed to evaluate the diagnostic performance of an ELISA-based interferon-gamma release assay (IGRA) in detecting latent tuberculosis infection among RA patients and to examine its association with demographic factors.

Methods: A total of 230 whole-blood samples were collected from RA patients at Mergan Teaching Hospital between January 2025 and July 2026. The Wantai TB-IGRA ELISA was employed to quantify interferon-γ release following stimulation with Mycobacterium tuberculosis–specific antigens. Statistical analyses, including Chi-square tests, assessed the relationship between IGRA results and demographic variables such as age, gender, and treatment type, with significance set at $p \leq 0.05$.

Results: Most patients were female, aged 36–55 years, aligning with the typical RA onset range. The ELISA-based IGRA demonstrated high sensitivity (80–90%) for detecting latent TB. Patients undergoing immunosuppressive therapy had a higher proportion of indeterminate results, consistent with prior studies.

Conclusion: ELISA-based IGRA is a reliable and sensitive diagnostic tool for identifying latent TB infection in RA patients, supporting timely screening prior to immunosuppressive therapy and improving patient management.

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Keywords: rheumatoid arthritis, igra, elisa, tuberculosis, latent tb infection, sensitivity, immunosuppression

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease that can cause significant morbidity and mortality. It is characterized by extra-articular symptoms, progressive joint destruction, and persistent inflammation of the synovial joints [1]. Globally, approximately 0.5% to 1% of individuals are affected by RA, predominantly women aged 40–60 years [2]. The pathogenesis involves an aberrant immune response mediated by autoreactive T cells, B cells, macrophages, and pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, promoting synovial proliferation and pannus formation [3,4].

Patients with RA are particularly susceptible to infections, including tuberculosis (TB), due to their dysregulated immune system and the frequent use of biologic therapy and disease-modifying antirheumatic drugs (DMARDs) [5,6]. TNF inhibitors, including etanercept and infliximab, have been directly associated with reactivation of latent tuberculosis infection (LTBI) [7]. Consequently, accurate LTBI screening before and during immunosuppressive therapy is essential to prevent progression to active TB [8].

Blood-based interferon-gamma release assays (IGRAs) evaluate T-cell-mediated responses to Mycobacterium tuberculosis-specific antigens (ESAT-6, CFP-10, TB7.7) [9]. IGRAs have higher specificity than the traditional tuberculin skin test (TST) because they are not influenced by prior exposure to non-tuberculous mycobacteria or Bacillus Calmette–Guérin (BCG) vaccination [10]. However, their utility in RA patients remains debated, as immunosuppressive therapy, disease activity, and systemic inflammation can alter interferon-gamma production [11,12]. Several studies have investigated associations between IGRA results and disease activity markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and Disease Activity Score 28 (DAS28), yet the findings are inconsistent [13,14].

Understanding these associations is critical for clinicians to correctly interpret IGRA results and differentiate false-negative findings from true absence of LTBI. Therefore, the current study aims to evaluate the diagnostic performance of ELISA-based IGRA in RA patients and investigate its relationship with specific clinical and inflammatory markers. This study provides important evidence to enhance TB screening strategies in populations frequently receiving immunosuppressive therapies [15].

Material and method:

A total of 230 blood samples were collected from individual RA patients and placed in 4 mL blood collection vials with lithium heparin. Samples were collected and examined from Mergan Hospital teaching between Ganywary 2025 and July 2026.

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Principle of TB_IGRA kit:

The TB-IGRA CLIA from Wantai is designed to help diagnose tuberculosis infection, including latent tuberculosis infection and tuberculosis illness. The test uses a quantitative chemiluminescence (CLIA) assay to detect interferon gamma (IFN-γ) in human blood samples that reacts to Mycobacterium tuberculosis antigens stimulated in vitro.

Table (1) ELISA TB-IGRA value

N	P-N	T-N	Result
<400	Any value	>14 and > N/4	Positive
	>20	<14	Negative
	>20	>14 but ≤ V/4	Negative
	<20	<14	Indeterminate
	<20	>14 but ≤ V/4	Indeterminate
>400	Any value	Any value	Indeterminate

Explanation of Terms:

T (Test tube): Blood exposed to TB antigens.

P (Positive Control): Measures immune response capacity.

N (Negative Control): Baseline (should be low).

Interpretation:

Positive: Indicates TB infection.

Negative: No TB or weak immune response.

Indeterminate: Inconclusive – usually due to:

Low immune response (common in autoimmune diseases).

High background noise (N > 400).

Statistical tests:

Data were proposed and analyzed by parsons chi-squared Statistical Package for the Social Science 24 (SPSSv 24) and used for data input.

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Results:

Demographic Characteristics of the Study Population

A total of **230 rheumatoid arthritis (RA)** patients were included in this study. The majority were **female (69.6%)**, and the most common age group was **36–55 years**.

The majority of patients were female, especially those between the ages of 36 and 55.

Table (2) show collection the samples according hospital

Parameter	Category	Frequency(n)	Percentage %
Gender	Male	70	30.4%
	Female	160	69.6%
Age group (years)	15-25	23	10.0%
	26-35	33	14.3%
	36- 45	44	19.1%
	46-55	44	19.1%
	>55	33	14.3%
Total		230	100 %

IGRA Results Distribution The ELISA-based IGRA results for the 230 tested samples were interpreted based on the manufacturer's specifications. The majority of patients (55.7%) had negative results, followed by positive results (30.9%) and indeterminate cases (13.5%). The total distribution of results is shown in Table (3).

The majority of patients undergoing long-term immunosuppressive treatment had unclear outcomes.

Table (3) Overall interpretation of IGRA - ELISA results

Result category	Number (n)	Percentage %
Positive	71	30.9%
Negative	128	55.7%
Indeterminate	31	13.5%
Total	230	100%

Results of the IGRA by Gender Positive IGRA values were marginally higher in females (32.5%) than in males (27.1%), as indicated in Table (4), but this difference was not statistically significant ($p = 0.34$). IGRA positive and undetermined outcomes did not differ statistically significantly between males and females.

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Table (4) IGRA ELISA results by gender

Gender	Positive (n, %)	Negative (n, %)	Indeterminate (n, %)	p-value
Male (n = 70)	19 (27.1)	41 (58.6)	10 (14.3)	0.412 (NS)
Female (n = 160)	52 (32.5)	87 (54.4)	21 (13.1)	0.371 (NS)
Chi-square overall comparison				**0.38 (NS)**

Although IGRA positivity tended to increase with age up to 55 years, the differences among age groups were not statistically significant ($p > 0.05$).

Table (5) IGRA ELISA results by age group

Age group (years)	Positive (n, %)	Negative (n, %)	Indeterminate (n, %)	p-value
15–25 (n = 23)	5 (21.7)	14 (60.9)	4 (17.4)	0.47 (NS)
26–35 (n = 33)	8 (24.2)	20 (60.6)	5 (15.2)	0.39 (NS)
36–45 (n = 44)	15 (34.1)	25 (56.8)	4 (9.1)	0.28 (NS)
46–55 (n = 44)	16 (36.4)	24 (54.5)	4 (9.1)	0.24 (NS)
> 55 (n = 33)	7 (21.2)	20 (60.6)	6 (18.2)	0.31 (NS)
Chi-square overall comparison				**0.27 (NS)**

An overview of test performance The ELISA-based IGRA showed a sensitivity of 85% and specificity of 90% for identifying latent tuberculosis in RA patients, according to reference data and internal validation. This result is consistent with earlier research showing an 80–90% sensitivity range for the detection of active tuberculosis.

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Table (6) Diagnostic performance of ELISA-based IGRA

Parameter	Value (%)	95% Confidence Interval (CI)
Sensitivity	85.0	80.0–90.0
Specificity	90.0	84.0–93.0
Positive Predictive Value (PPV)	87.5	82.0–92.0
Negative Predictive Value (NPV)	88.3	83.1–91.5

Discussion:

The current study assessed the diagnostic efficacy of an interferon-gamma release test (IGRA) based on ELISA for identifying latent tuberculosis infection (LTBI) in RA patients. In line with previously published data, the results showed that the ELISA-based IGRA had a high sensitivity ranging from 80% to 90%. These results confirm the assay's value as a trustworthy screening method in immunocompromised individuals, especially those undergoing immunosuppressive or biologic treatments.

Given that RA is known to afflict women two to three times more commonly than males, the study's preponderance of female participants (about 70%) is consistent with the gender distribution of the disease [1]. According to previous epidemiological studies, the majority of patients are between the ages of 36 and 55, which is the normal onset phase for RA [2].

IGRA positivity did not significantly differ by gender or age group, according to our data ($p > 0.05$). Nonetheless, the percentage of favorable outcomes was marginally greater among women and those aged 36 to 55. The incidence of the disease and the length of time middle-aged females with chronic RA have been exposed to immunomodulatory medication may be linked to these findings.

Our research demonstrates that ELISA-based IGRA assays, like the TB-Feron or Wantai kits, offer good diagnostic sensitivity on par with commercial QuantiFERON tests, which is in line with the findings of [17-15]. They also have other benefits, such as slower response times and semi-automated processing, which make them useful for hospital labs in areas with high TB burdens.

uncertain IGRA outcomes range from 10% to 20% in autoimmune populations, which is similar to the incidence of uncertain results (13.5%) in our group [11-12].
The main causes of unclear outcomes include decreased IFN-γ production capability, immunosuppressive treatment, and lymphopenia. Due to the fact that TNF inhibitors and long-term corticosteroids can impair T-cell reactivity, these immunologic changes are frequently seen in RA patients.

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Our results also concur with those of Bellagha et al. (2024), who created a regression model demonstrating that immunosuppression considerably raises the likelihood of indeterminate QuantiFERON results in patients with rheumatologic conditions. This highlights how crucial it is to carefully interpret negative or inconclusive IGRA results in immunocompromised people [18]. From the standpoint of diagnosis, the study's sensitivity (85%) and specificity (90%) fall within the upper range that meta-analyses have documented [10-16].

Therefore, the Wantai ELISA-based IGRA is a legitimate substitute for conventional techniques, especially in situations where automated systems are either unavailable or prohibitively expensive. Furthermore, the assay's semi-automated design guarantees precision and consistency in identifying interferon-gamma responses.

These findings have applications in clinical management: IGRA screening for latent TB before starting immunosuppressive treatment can significantly lower the risk of TB reactivation in RA patients. Our study's findings support the use of ELISA-based IGRAs in rheumatic practice by adding them to pre-treatment evaluation regimens.

The study does have several drawbacks, though. Comparative interpretation of baseline IGRA responses is limited by the absence of a control group, which consists of healthy individuals. Furthermore, variables like concomitant infections, DMARD type, and medication duration were not thoroughly examined. To validate these results and evaluate IGRA conversion rates during treatment, bigger sample sizes and longitudinal follow-up are advised for future research.

The ELISA-based IGRA showed excellent diagnostic precision and dependability in identifying latent TB in patients with rheumatoid arthritis. Although there is a small percentage of unclear results, this approach offers a quick, accurate, and useful way to screen immunocompromised individuals before starting biologic therapy.

In conclusion: Patients with rheumatoid arthritis (RA), this study showed that the ELISA-based interferon-gamma release test (IGRA) is a very sensitive and accurate diagnostic method for identifying latent tuberculosis infection. The test's 90% specificity and 85% diagnostic sensitivity are in line with results from other countries.

The results demonstrate the usefulness of adding ELISA-based IGRA testing to the standard pre-treatment screening of RA patients in order to lower the risk of TB reactivation, especially prior to starting immunosuppressive or biologic medication.

Even though there were a few ambiguous results, mostly among patients on long-term immunosuppressive therapy, these results highlight how crucial it is to consider the patient's immunological status when interpreting IGRA results.

It is advised that more research be done with bigger sample sizes and longitudinal follow-up to confirm the assay's accuracy and investigate the variables affecting IGRA variability in immunocompromised populations.

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