Research Article / Araştırma Makalesi

Reliability of PCR Testing Versus Culture Testing in Tuberculosis Diagnosis: A Six-Year Retrospective Study

PCR ve Kültür Testlerinin Tüberküloz Tanısındaki Güvenilirliği: Altı Yıllık Geriye Dönük Çalışma

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Abstract

Background: Tuberculosis (TB) remains a global health challenge, particularly in regions with high migration rates like Şanlıurfa, Türkiye. Rapid and accurate diagnosis is essential to improve treatment outcomes and reduce transmission. This study evaluated the reliability of Polymerase Chain Reaction (PCR) testing compared to culture testing, the gold standard, in pulmonary TB diagnosis.
Materials and Methods: This retrospective study analyzed the records of 1,231 patients diagnosed with pulmonary TB at the Şanlıurfa Tuberculosis Dispensary between January 2018 and June 2022. Patient demographics, clinical findings, and diagnostic test results were collected. Sensitivity and specificity of PCR and acid-fast bacilli (ARB) smear tests were calculated using culture results as the reference standard. Statistical significance was set at p<0.05.
Results: The majority of patients were male (60.3%) and over 18 years old (94.5%). PCR showed a sensitivity of 97% and a specificity of 88%, while ARB had a sensitivity of 77% and a specificity of 99%. PCR and culture concordance was statistically significant across ethnic groups (p=0.001). Common clinical findings included pleural effusion (18.14%) and atelectasis (15.02%).
Conclusions: PCR demonstrates high sensitivity and acceptable specificity, supporting its use as a rapid diagnostic tool for pulmonary TB, particularly in resource-limited settings. However, culture testing remains indispensable for definitive diagnosis.

Keywords: Tuberculosis, PCR Testing, Culture Testing, Diagnostic Reliability

Öz

Amaç: Tüberküloz (TB), özellikle yüksek göç oranlarına sahip bölgelerde küresel bir sağlık sorunu olmaya devam etmektedir. Tedavi sonuçlarını iyileştirmek ve bulaşmayı azaltmak için hızlı ve doğru tanı şarttır. Bu çalışmada, akciğer tüberkülozu tanısında altın standart olan kültür testiyle karşılaştırıldığında PCR testinin güvenilirliği değerlendirilmiştir.
Materyal ve Metod: Bu retrospektif çalışmada, Ocak 2018 ile Haziran 2022 tarihleri arasında Şanlıurfa Verem Savaş Dispanseri'nde akciğer tüberkülozu tanısı alan 1.231 hastanın kayıtları analiz edilmiştir. Hasta demografik özellikleri, klinik bulgular ve tanı test sonuçları toplanmıştır. PCR ve aside dirençli basil (ARB) yayma testlerinin duyarlılığı ve özgüllüğü, kültür sonuçları referans standart olarak kullanılarak hesaplanmıştır. İstatistiksel anlamlılık p<0,05 olarak belirlenmiştir.
Bulgular: Hastaların çoğunluğu erkek (%60,3) ve 18 yaşın üzerinde (%94,5) idi. PCR %97 duyarlılık ve %88 özgüllük gösterirken, ARB %77 duyarlılık ve %99 özgüllük göstermiştir. PCR ve kültür uyumu etnik gruplar arasında istatistiksel olarak anlamlı bulunmuştur (p=0,001). Yaygın klinik bulgular arasında plevral efüzyon (%18,14) ve atelektazi (%15,02) yer almaktadır.
Sonuç: PCR yüksek duyarlılık ve kabul edilebilir özgüllük göstermekte olup, özellikle kaynakların kısıtlı olduğu durumlarda akciğer tüberkülozu için hızlı bir tanı aracı olarak kullanımını desteklemektedir. Bununla birlikte, kültür testi kesin tanı için vazgeçilmez olmaya devam etmektedir.

Anahtar Kelimeler: Tüberküloz, PCR Testi, Kültür Testi, Tanı Güvenilirliği

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Introduction

Tuberculosis (TB) remains one of the most significant global health challenges, contributing to high morbidity and mortality rates worldwide. Accurate and timely diagnosis is pivotal in reducing TB transmission and improving patient outcomes (1). Among the diagnostic methods, culture testing has long been regarded as the gold standard due to its high sensitivity and specificity in identifying Mycobacterium tuberculosis. However, culture testing is inherently time-consuming, often requiring several weeks for definitive results. This delay in diagnosis can hinder the timely initiation of treatment, thereby prolonging patient suffering and increasing the risk of disease transmission (2, 3)

In recent years, molecular techniques such as polymerase chain reaction (PCR) testing have emerged as promising alternatives, offering faster results with comparable sensitivity in certain contexts. PCR's ability to detect TB directly from clinical samples within hours has positioned it as a potential game-changer in TB diagnostics. Despite its advantages, concerns remain regarding the reliability and consistency of PCR in diverse clinical settings, particularly when compared to the well-established accuracy of culture testing (2, 4, 5).

This study aims to address this critical gap by retrospectively analyzing six years of clinical data to compare the diagnostic reliability of PCR and culture testing for TB. By examining the sensitivity, specificity, and overall diagnostic accuracy of these methods, we seek to evaluate whether PCR testing can serve as a dependable alternative to culture testing. Additionally, we aim to explore the potential of PCR to expedite the diagnostic process and improve TB management in routine clinical practice.

Materials and Methods

This study was a retrospective review of patients diagnosed with pulmonary tuberculosis at the Şanlıurfa Tuberculosis Dispensary between January 2018 and June 2022. Located in southeastern Turkey, bordering Syria, Şanlıurfa has experienced a significant influx of Syrian migrants due to ongoing regional conflicts. All patients diagnosed with pulmonary tuberculosis by specialists were included in the study. Patients were eligible for inclusion if they had complete medical records and either completed their treatment or defaulted during the study period. Patients with incomplete clinical information or cases where a confirmed diagnosis of tuberculosis was unavailable were excluded.

The study was approved by the Harran University Clinical Research Ethics Committee (date: 20.02.2025; decision number: 2025-021).

Patient demographics, clinical characteristics, and laboratory test results were extracted from hospital logbooks and patient charts maintained at the Şanlıurfa Tuberculosis Dispensary. The data collected included age, gender, smoking status, ethnicity (Turkish or Syrian), and clinical symptoms and signs. Diagnostic test results from culture, PCR, and ARB (acid-fast bacilli smear) tests were compared. PCR and culture test agreement was evaluated in both Turkish and Syrian participants. Sensitivity and specificity were calculated for PCR and ARB tests using culture results as the gold standard.

All analyses were performed using IBM SPSS Statistics. Categorical variables were summarized as counts and percentages (n, %). The diagnostic performance of PCR was evaluated against culture (reference standard) using 2×2 contingency tables. Sensitivity and specificity were calculated. The association between PCR and culture results was assessed using the chi-square test. In addition, receiver operating characteristic (ROC) curve analysis was performed, and the area under the curve (AUC) with 95% confidence intervals was reported to evaluate the discriminative ability of PCR. A p value <0.05 was considered statistically significant.

As inclusion and exclusion criteria for the study:

Inclusion And Exclusion Criteria

Inclusion Criteria

1. Patients with clinical and/or radiological suspectation of Tuberculosis
2. Patients whose body fluid samples (Sphemma, Bronchial Lavage, Urine, Etc.) were tested simultaneously for Arb, Arb Culture, And Pcr

Exclusion Criteria

1. Cases for which body fluid samples could not be obtained
2. Patients whose concurrent Arb culture and Pcr were not tested
3. Patients whose laboratory records are unavailable

Results

A total of 1231 participants participated in the study, of which 60.3% (742) were male and 39.7% (489) were female. The majority of participants were over 18 years old (94.5%, n=1163), while 4.6% (n=57) were between 2 and 18 years old and 0.9% (n=9) were ≤2 years old. Most participants were Turkish (88.5%, n=1090) and 11.5% (n=141) Syrian. 45.8% (n=564) reported smoking, while 54.2% (n=667) were non-smokers (Table 1), by PCR (Table 2).

Table 1. Demographic characteristics of participants

Variable	n	%
Age		
≤2 years	9	0.9
2-18 years	57	4.6
>18 years	1163	94.5
Gender		
Male	742	60.3
Female	489	39.7
Ethnicity		
Turkish	1090	88.5
Syrian	141	11.5
Smoking		
Yes	564	45.8
No	667	54.2

Table 2. Diagnostic Comparison of PCR and Culture Tests in Tuberculosis

		Culture Test		
		Positive n (%)	**Negative n (%)**	**p**
PCR	**Positive**	97 (%97)	140 (%12,4)	0.0
	Negative	3 (%3)	991 (%87,6)	0.1

A total of 237 patients were found to have positive cultures. Ethnic differences in PCR-culture test agreement showed that in Turkish participants, 80 positive and 1 negative case were detected by PCR in culture-positive individuals, while 114 positive and 895 negative cases were detected in culture-negative individuals. In Syrian participants, 17 positive and 2 negative cases were detected by PCR in culture-positive individuals, while 26 positive and 96 negative cases were detected in culture-negative individuals. Both comparisons were statistically significant (p=0.001) (Table 3).

When comparing PCR and culture tests for tuberculosis diagnosis, PCR identified 97 positive and 3 negative cases among those confirmed positive by culture, with a significant difference (p=0.001). In the culture-negative group, 140 positive and 991 negative cases were detected The PCR test showed a sensitivity of 97% and a specificity of 88%. The sensitivity of the ARB test was 77%, and its specificity was 99%.

Table 3. PCR and Culture Test Concordance in Tuberculosis Patients: Ethnic Variations

			Culture Test			
			Positive n (%)	**Negative n (%)**	**n**	**p**
PCR	***Turkish***	+	80 (%98.8)	114 (%11.3)	194	0.001
		-	1 (%1.2)	895 (%88.7)		
	Syrian	+	17 (%89.5)	26 (%21.3)	43	0.001
		-	2 (%10.5)	96 (%78.7)		

Table 4. Radiological and Clinical Findings Associated with Pulmonary Tuberculosis

	Frequency (n)	**Percentage (%)**
Pleural Effusion	244	18.14
Lymphadenopathy (LAP)	138	10.26
Atelectasis	202	15.02
Nodule	180	13.38
Miliary Infiltration	34	2.53
Mass	174	12.94
Elevated Diaphragm	24	1.78
Bronchiectasis	67	4.98
Volume Loss	67	4.98
Plaque	8	0.59
Increased Airing (Hyperinflation)	121	9.00
Bronchial Prominence	45	3.35
Cyst	15	1.12
Abscess	4	0.30
Cardiomegaly	10	0.74
Destroyed Lung	3	0.22
Pneumothorax (PNX)	9	0.67

Regarding symptoms and clinical signs, pleural effusion was observed in 18.14% (n=244) of cases, lymphadenopathy in 10.26% (n=138), and atelectasis in 15.02% (n=202). Other common findings included nodules (13.38%, n = 180), masses (12.94%, n = 174), and hyperinflation (9.00%, n = 121). Less common findings included cysts (1.12%, n = 15), abscesses (0.30%, n = 4), and destroyed lungs (0.22%, n = 3) (Table 4).

Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of the PCR test using culture results as the reference standard. The analysis revealed an area under the curve (AUC) of 0.920 (95% CI: 0.897–0.944; p < 0.001), indicating excellent discriminative ability of PCR in detecting pulmonary tuberculosis (Figure 1).

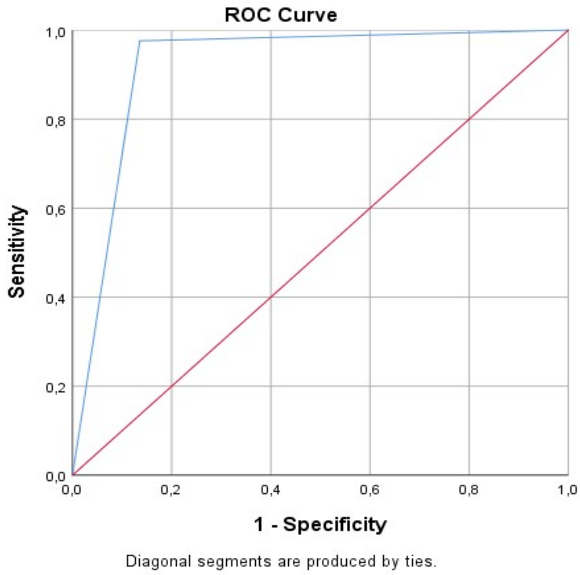

Figure 1. PCR in detecting pulmonary tuberculosis

Discussion

Tuberculosis (TB) remains a significant global health challenge, where early and accurate diagnosis is pivotal for controlling disease transmission and improving patient outcomes. Despite advancements in diagnostic tools, conventional culture testing is still regarded as the gold standard; however, it is a time-intensive and resource-demanding method.. Our findings demonstrate that PCR testing offers high diagnostic accuracy, with notable sensitivity (97%) and reasonable specificity (88%), enabling rapid detection.

In a study conducted by Abdulmajed et al. (6), the sensitivity and specificity of the Ehrlich Ziehl Neelsen (Acid-Resistant Dyeing =EZN) staining method were reported as 32% and 66%, respectively, with a low level of agreement observed between EZN staining and culture methods. In our study, the sensitivity and specificity of the EZN method were found to be 77% and 99%, respectively. Additionally, a high level of agreement between EZN staining and culture was observed in our findings. Despite the EZN staining method's advantages, including the ability to produce results within 24 hours and its cost-effectiveness, its sensitivity is subject to several factors. These include the quality of the microscope used, the type of specimen, the thickness of the smear, the duration of decolorization during staining, the speed of centrifugation, the experience of the evaluator, and the prevalence of tuberculosis in the population being tested (7).

Our findings on the sensitivity and specificity of PCR testing align with previous studies. For instance, a meta-analysis reported pooled sensitivity and specificity estimates of 96% and 92%, respectively, for in-house real-time PCR assays in diagnosing tuberculosis (8). Additionally, a study evaluating the performance of microbiological tests for TB diagnosis found that PCR displayed higher sensitivity and specificity than microscopy for all respiratory specimens, supporting a smear-independent PCR-based approach (9). These findings corroborate the high diagnostic accuracy observed in our study.

The findings of the ROC curve analysis further reinforce the diagnostic value of PCR testing in tuberculosis detection. With an area under the curve (AUC) of 0.920, PCR demonstrated excellent discriminative ability in distinguishing TB-positive from TB-negative cases when compared to culture testing. This level of diagnostic performance aligns with prior research supporting PCR as a reliable and rapid diagnostic tool, particularly in regions with high disease burden or limited access to culture facilities. The narrow confidence interval observed in the ROC analysis also indicates the consistency of PCR test accuracy across the study population. These results emphasize the potential of PCR to serve not only as a complementary method but also as a frontline diagnostic strategy in appropriate clinical settings.

PCR testing proves to be a critical diagnostic tool in cases where culture results are negative (10, 11). Initiating treatment and implementing preventive measures based on a positive PCR result in clinically suspected patients, without awaiting culture confirmation, can facilitate early infection control (12). Furthermore, PCR is highlighted as highly beneficial in differentiating TB from non-TB cases and in diagnosing patients with incomplete or inadequate TB treatment histories (13, 14). In our study, we compared culture, PCR, and microscopic examination methods for TB diagnosis in our laboratory. The sensitivity of PCR was 97% and its specificity was 88%. Variables such as the type of PCR method used, the sample type, and the bacterial load in the sample significantly influenced sensitivity results. In theory, even a few bacilli in a sample are sufficient for PCR positivity. However, in practice, many studies have shown that the sensitivity of PCR for TB is not always as high. Failure to detect Mycobacterium tuberculosis DNA may result from bacilli loss during processing or the presence of inhibitory substances in the sample (15, 16).

Our study found a significant correlation between PCR positivity and culture positivity. Rapid PCR results are crucial for identifying positive TB cases. However, false-negative results in PCR-negative but culture-positive cases could limit the routine use of PCR testing. Similar studies in the literature also emphasize the need for further research to enhance the sensitivity and specificity of PCR tests. Cho, Smith, and colleagues underscored that while PCR can provide a quick preliminary diagnosis, it must be corroborated by culture testing (17).

The lower sensitivity of PCR among migrant populations, such as Syrian participants in our study, underscores the importance of addressing disparities in healthcare access and the potential influence of social determinants of health. Tailored diagnostic and public health strategies are needed to ensure equitable care for migrant populations. A review on tuberculosis and COVID-19 interaction suggests that immunosuppression, including steroids used to treat COVID-19, may result in TB reactivation, highlighting the need for vigilant TB screening in vulnerable groups (18). Such differences could stem from limited healthcare access, social determinants of health, or clinical variations. Although various screening strategies exist, approaches tied to immigration enforcement or legal residency requirements tend to reach a larger proportion of migrants. (19, 20). However, these strategies, even when not overtly discriminatory, may carry questionable public health implications and require ethical scrutiny. However, even when such strategies are not explicitly discriminatory, they can carry questionable public health implications (21) and require ethical scrutiny (20). Entry-point screening, based primarily on country of origin as a risk factor, often excludes undocumented migrants and those who appear healthy at entry. Furthermore, lack of health insurance coverage can hinder effective screening for diseases like tuberculosis (19).

The COVID-19 pandemic exacerbated challenges in accessing healthcare, causing delays in TB diagnosis and treatment. While the rapid turnaround time of PCR testing was beneficial, increased laboratory workload and diagnostic delays highlight the need for optimization. WHO's 2014 policy update on automated nucleic acid amplification technologies emphasized biopsy material over pleural fluid for diagnosing pleural TB (20, 22). In this study, clinical findings such as pleural effusion, lymphadenopathy, and nodules were crucial for diagnosis, with PCR testing serving as a valuable complementary tool to expedite treatment. The pandemic's disruptions in TB diagnostic services led to reduced TB notifications and treatment access (23). Furthermore, studies have reported increased mortality among TB patients during the pandemic, underscoring the need for resilient TB healthcare services (24). These disruptions emphasize the critical need for rapid diagnostic tools like PCR testing to mitigate delays in TB diagnosis and treatment during global health crises.

The speed advantage of PCR testing presents a critical opportunity for the early diagnosis and prompt treatment of TB. However, based on the data obtained in this study, some strategic adjustments are necessary for the routine implementation of PCR testing. Developing protocols to minimize false-negative rates and increasing access to healthcare for vulnerable populations, such as migrants, are crucial public health priorities. Investments in technology to improve the accuracy of TB diagnostic tests are also essential.

Conclusion

In conclusion, PCR testing emerges as a rapid and effective alternative for TB diagnosis. However, due to its false-negative and false-positive rates, it must be complemented by culture testing. Future research should focus on improving the accuracy of PCR tests and fostering the widespread adoption of standardized practices through technological advancements. Additionally, improving healthcare access for vulnerable populations, such as migrants, represents a critical step in TB control efforts.

Ethical Approval: *This study was approved by the Harran University Clinical Research Ethics Committee (date: 20.02.2025; decision number: 2025-021).*

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