Vol.20, No.5, Page 831- 839, 2026 http://dx.doi.org/10.59628/jchm.v20i5.3283 ISSN 2958-7476 JMCH

Sana'a University Journal of Medical and Health Sciences

The impact of the rs1861494 interferon-gamma gene polymorphism on susceptibility to pulmonary tuberculosis in the Yemeni population: a case-control study

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Abstract

Background and aims: Pulmonary tuberculosis remains a major public health challenge. This study investigated the association between the interferon-gamma rs1861494 Cytosine/Thymine polymorphism and pulmonary tuberculosis susceptibility among Yemeni individuals and evaluated environmental and socioeconomic risk factors.

Methods: A matched case–control study included 200 patients with newly diagnosed Pulmonary tuberculosis and 200 age- and sex-matched healthy controls. Pulmonary tuberculosis was confirmed using GeneXpert, and interferon-gamma rs1861494 genotyping was performed by TaqMan real-time Polymerase Chain Reaction.

Results: No significant association was observed between the interferon-gamma rs1861494 polymorphism and Pulmonary tuberculosis susceptibility under any genetic model (all $p > 0.05$). However, illiteracy (OR = 63.60, 95% CI: 24.23–166.96, $p < 0.001$), low income (OR = 15.09, 95% CI: 6.08–37.41, $p < 0.001$), close contact with TB patients (OR = 13.40, 95% CI: 4.69–52.20, $p < 0.001$), family history of TB (OR = 7.72, 95% CI: 3.92–15.20, $p < 0.001$), poor household ventilation (OR = 5.14, 95% CI: 1.72–21.10, $p = 0.001$), smoking (OR = 2.00, 95% CI: 1.34–2.98, $p = 0.0006$), and absence of Bacillus Calmette–Guérin vaccination (OR = 1.70, 95% CI: 1.09–2.50, $p = 0.020$) were significantly associated with increased Pulmonary tuberculosis risk.

Conclusion: The interferon-gamma rs1861494 polymorphism was not associated with Pulmonary tuberculosis susceptibility in this population. In contrast, environmental and socioeconomic determinants were major contributors to Pulmonary tuberculosis risk, highlighting the importance of targeted public health interventions and further genetic studies.

Article Info

Keywords:
Pulmonary tuberculosis, IFN-γ, rs1861494, Genetic polymorphism, Risk factors; Yemen.

Article History:
Received: 18-June-2026,
Revised: 14-August-2026,
Accepted: 17-September-2026,
Published: 28-October-2026

1. INTRODUCTION

Tuberculosis (TB) remains a major global public health challenge and continues to rank among the leading causes of mortality from infectious diseases worldwide. According to the 2024 World Health Organization (WHO) Global Tuberculosis Report, an estimated 10.8 million people developed active TB in 2023, resulting in approximately 1.25 million deaths [1]. The burden of TB is unevenly distributed across geographic regions. The South-East Asia Region accounts for 46% of newly reported cases, followed by the African Region (24%) and the Western Pacific Region (17%). Notably, approxi-

mately 87% of incident TB cases occur in 30 high-burden countries, including Bangladesh, China, the Democratic Republic of the Congo, India, Indonesia, Nigeria, Pakistan, and the Philippines [2].

Despite widespread exposure to *Mycobacterium tuberculosis* (*M*TB), only 5–10% of infected individuals progress to active disease. This progression is influenced by a complex interplay of environmental and host-related factors, including nutritional status, Bacillus Calmette–Guérin (BCG) vaccination, socioeconomic conditions, co-infections, and genetic susceptibility [3]. Epidemiological data indicate that adults account for nearly 90% of annual TB cases, with men consistently exhibiting higher incidence rates than women [1].

Accumulating evidence suggests that host genetic factors may play a critical role in determining susceptibility to TB, with heritability estimates ranging from 39% to 71% [4, 5].

Such genetic variability may contribute to population-specific differences, including innate and adaptive immune responses to *M*TB infection [6].

Among the key mediators of anti-mycobacterial immunity is interferon-gamma (IFN-Υ), a pleiotropic cytokine predominantly produced by CD4+ T-helper 1 (Th1) cells, CD8+ T lymphocytes, and natural killer (NK) cells [7]. IFN-Υ exerts multiple immunoregulatory functions, including enhancement of leukocyte–endothelium interactions, activation of macrophages, promotion of phagocytosis, and augmentation of antimicrobial and antiviral responses [8, 9]. Importantly, IFN-γ serves as a central component of host defense against *M*TB by activating macrophages and inducing the production of reactive nitrogen intermediates, particularly nitric oxide (NO), which restricts intracellular mycobacterial replication[10]. Activated macrophages subsequently produce interleukin-12 (IL-12), which stimulates Th1 cells to secrete IFN-Υ, thereby enhancing macrophage activation and antimicrobial activity [11].

In turn, IFN-Υ-stimulated macrophages sustain IL-12 production, promoting further Th1-cell expansion and continued IFN-Υ secretion while suppressing Th2-mediated responses that may attenuate pro-inflammatory cytokine production [12].

Furthermore, pathogenic mycobacteria possess mechanisms that facilitate their intracellular survival by inhibiting phagolysosomal maturation within macrophages. IFN-Υ-activated macrophages can overcome this immune evasion strategy by restoring phagolysosomal function and inducing apoptosis, thereby limiting mycobacterial persistence and replication [13]. The protective role of IFN-Υ in TB immunity is supported by substantial clinical and genetic evidence [14]. Consequently, genetic polymorphisms in the IFN-Υ gene may alter cytokine expression or function, thereby influencing individual susceptibility to TB [15]. In Yemen, TB remains a significant public health problem, with a reported incidence of 48 cases per 100,000 individuals in 2021 [16]. Regional epidemiological data from Al-Mukalla documented an incidence rate of 26.1 cases per 100,000 individuals between 2011 and 2018 [17]. Despite the ongoing tuberculosis burden, few genetic studies have addressed susceptibility in the Yemeni community. Therefore, this study investigated the relationship between the IFN-Υ rs1861494 polymorphism and PTB, as well as analyzed certain important environmental and demographic risk factors.

2. MATERIALS AND METHODS

2.1. Study Design and Subjects

This case–control study was conducted between 2022 and 2025. It included 400 Yemeni participants, comprising 200 newly diagnosed patients with active PTB and 200 healthy controls matched for age and sex. The control group consisted of asymptomatic community volunteers and blood donors with no prior clinical history of tuberculosis. Pulmonary tuberculosis (PTB) cases were recruited through the National Tuberculosis Program (NTP) from eight governorates across Yemen, including Sana'a, Ibb, Taizz, Dhamar, Hajjah, Al Hudaydah, Raymah, and Lahj. The diagnosis of PTB was rigorously established through sputum smear microscopy for acid-fast bacilli (AFB), mycobacterial culture positivity, and polymerase chain reaction (PCR) confirmation. Stringent exclusion criteria were applied to both study groups. Individuals younger than 18 years of age, pregnant women, and participants with diabetes mellitus, chronic inflammatory diseases, or a history of immunosuppressive therapy were excluded.

2.2. Specimen Collection

Early morning sputum specimens were collected from each participant using sterile, leak-proof containers. Two containers were provided for each participant to enable independent microbiological and molecular analysis. All specimens were labeled with a unique sample identification code, participant name, and date and time of collection.

In addition, 3 mL of peripheral venous blood was obtained from each participant and placed into a labeled K2EDTA tube for genomic DNA extraction. Genomic DNA extraction was performed within 4 hours of collection, and the extracted DNA was stored at -80℃ until genotyping analysis.

2.3. Microbiological and Molecular Techniques

For each suspected PTB patient, two sputum samples were collected. The first sample underwent Ziehl–Neelsen staining for AFB detection. Smears were

prepared, heat-fixed, stained with carbol-fuchsin, decolorized with acid-alcohol, and counterstained with methylene blue. Slides were examined under oil immersion at 100× magnification. Presence of red acid-fast bacilli was considered AFB positive and suggestive of active tuberculosis.

The second sputum sample was analyzed using the GeneXpert MTB system (Cepheid Inc., USA) to simultaneously detect *Mycobacterium tuberculosis* DNA. Sputum samples were mixed with GeneXpert buffer reagent at a 2:1 ratio, incubated for 15 minutes, and 2 mL aliquot of the processed mixture was transferred into a cartridge for automated DNA extraction and real-time PCR analysis. Test results were generated within approximately 2 h.

For more confirmation, for decontaminated sputum specimens, an equal volume of 4% NaOH was added to each sputum specimen. The container was tightly capped, thoroughly shaken to facilitate digestion and decontamination, and then allowed to stand at room temperature for 15 minutes. Then inoculated onto Modified Ogawa medium and incubated at 37℃ for up to eight weeks. Rough, tough, buff-colored colonies were considered characteristic of *M. tuberculosis* . To definitively exclude active PTB among controls, sputum samples from all control participants were tested using the GeneXpert MTB assay and confirmed negative. Healthy controls reported no medical history or exposure to tuberculosis. All microbiological and molecular procedures were performed at the National Tuberculosis Program.

2.4. Genomic DNA Extraction, Single-Nucleotide Polymorphism Selection, and Genotyping

Genomic DNA was extracted from whole blood using the salt precipitation method adapted from the Puregene protocol. Briefly, 3 mL of whole blood was mixed with 9 mL of red blood cell (RBC) lysis solution in a sterile 15 mL polypropylene centrifuge tube and gently agitated at room temperature for 10 min to ensure complete RBC lysis. The hemolysate was centrifuged at 2000 × g (3300 rpm) for 10 min using a swing-out rotor centrifuge (Centrifuge R-8C PLUS, REMI Elektrotechnik Ltd - India). The supernatant was discarded, leaving approximately 200 μL of residual pellet. The pellet was resuspended in 3 mL of white blood cell (WBC) lysis solution, inverted several times, and incubated at 37℃ for 30 min to achieve complete lysis. After cooling on ice for 5 min, 1 mL of protein precipitation solution was added, vortexed for 20 s, and centrifuged at 2000 × g for 10 min to remove proteins. The supernatant was transferred to a fresh sterile tube, and DNA was precipitated by adding 3 mL of isopropanol and gently inverting, followed by centrifugation at 2000 × g for 10 min. The DNA pellet was washed with 3 mL of 70% ethanol, gently inverted twice, and centrifuged again at 2000 × g for 10 min. The ethanol was carefully removed, and the tube was air-dried inverted in a fume cupboard for approximately 30 min. Finally, the DNA pellet was dissolved in 200 μL of ultrapure sterile deionized water and left overnight at room temperature. DNA concentration and purity were assessed using a NanoDrop spectrophotometer (Genova Nano, JENWAY, United Kingdom), with quantification based on absorbance at 260 nm and purity determined by A260/A280 and A260/A230 ratios.

One single-nucleotide polymorphism (rs1861494) was selected based on previous studies that reported an association with tuberculosis [15, 18, 19] rs1861494 (C/T in IFN-Υ). Genotyping was performed using a QuantStudio 5 real-time PCR instrument (Applied Biosystems, USA) with the TaqMan® SNP Genotyping Assay with predesigned primers and probes (Thermo Fisher Scientific).

The thermal cycling protocol consisted of initial Taq polymerase activation at 95℃ for 10 minutes, followed by 40 cycles of denaturation at 95℃ for 15 seconds and annealing/extension at 60℃ for 1 minute. Genotyping data were analyzed using the TaqMan® Genotyper Software, with allelic discrimination visualized via cluster plots based on VIC and FAM fluorescence signals [20].

2.5. Statistical analysis

Data were analyzed using SPSS Statistics version 27.0 (IBM, USA). Descriptive statistics were summarized as mean ± standard deviation for continuous variables and frequencies (percentages) for categorical variables. Normality was assessed using the Shapiro–Wilk test. Group comparisons were performed using the chi-square test for categorical variables.

Genotype frequencies were compared between cases and controls using chi-square tests. Hardy–Weinberg equilibrium (HWE) was evaluated in the control group. Associations between SNPs and PTB were examined using binary logistic regression, with results expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Dominant, recessive, and log-additive genetic models were applied. All p-values were two-tailed, and $p < 0.05$ was considered statistically significant.

2.6. Ethics approval and consent to participate

The study protocol was approved by the Ethical Research Committee of the Faculty of Medicine and Health Sciences, Sana'a University. In accordance with ethical guidelines, written informed consent was obtained from all participants before their inclusion in the study. The study procedures, potential risks, and anticipated benefits were clearly explained, and participants provided signed consent before participating in the research.

3. RESULTS

3.1. Demographic Characteristics of the Study population

A total of 200 patients with PTB (125 males and 75 females) and 200 healthy controls (126 males and 74 females) aged 18–65 years were enrolled in this study. The participants were matched for age and sex. The demographic characteristics are summarized in Table 1. No statistically significant differences were observed between the cases and controls in terms of age, sex, or place of residence ($p > 0.05$).

3.2. Risk Factors Associated with Pulmonary Tuberculosis Infection

Table 2 outlines several key environmental and behavioral factors significantly associated with an increased risk of developing TB in this population. Most patients showed clear risk factors compared with relatively few individuals in the control group. Smoking was significantly more common among patients with TB than among controls [108(54.0%) vs. 74 (37.0%)], and smokers had approximately twofold higher odds of developing PTB (OR = 2.0, 95% CI: 1.34–2.98, $p = 0.0006$), indicating that smoking is an important independent risk factor for TB susceptibility. Individuals without BCG vaccination exhibited significantly increased odds of PTB compared to vaccinated participants (OR 1.7, 95% CI: 1.09–2.50, $p = 0.020$). In contrast, participants with unknown vaccination status showed no significant association with PTB risk (OR 0.9 [95% CI 0.5–1.9], $p = 0.900$).

A previous history of tuberculosis was observed exclusively among TB cases (17.5%) and was absent in controls, yielding an undefined or infinite odds ratio with a highly significant association ($p < 0.001$). This finding indicates that a prior history of TB strongly predisposes individuals to recurrent or reactivated disease. Similarly, having relatives with TB was significantly associated with PTB susceptibility. Participants who reported a family history of TB had approximately 7.7-fold higher odds of disease than those without affected relatives (OR = 7.72, 95% CI: 3.92–15.2, $p < 0.001$). Moreover, compared with university-educated participants, individuals with secondary education had significantly increased odds of PTB (OR = 12.53, 95% CI: 6.44–24.38, $p < 0.001$). The risk further increased among participants with primary education (OR = 37.2, 95% CI: 17.13–80.76, $p < 0.001$), those who could only read and write (OR = 11.78, 95% CI: 4.87–28.52, $p < 0.001$), and illiterate individuals, who exhibited the highest risk (OR = 63.6, 95% CI: 24.23–166.96, $p < 0.001$). Participants with low income had markedly increased odds of PTB compared with those with high income (OR = 15.09, 95% CI: 6.09–37.41, $p < 0.001$), whereas medium income was not significantly associated with PTB risk (OR = 0.539, 95% CI: 0.219–1.327, $p = 0.174$). Lack of household ventilation was significantly associated with PTB, with poorly ventilated households showing approximately fivefold increased odds of disease (OR = 5.14, 95% CI: 1.72–21.10, $p = 0.001$).

3.3. Association of the Studied Single-Nucleotide Polymorphism (rs1861494) with Pulmonary Tuberculosis

Table 3 shows that the single-nucleotide polymorphism IFN-Y rs1861494 was in Hardy–Weinberg equilibrium in the control group ($p > 0.05$).

Analysis of the IFN-Y rs1861494 (C/T) polymorphism revealed no statistically significant association with susceptibility to PTB in the study group under any of the evaluated genetic models (Table 4).

At the allelic level, the frequency of the T allele was higher among PTB patients than in the controls (40.75% vs. 35.0%); however, this difference did not reach statistical significance (OR = 1.30, 95% CI: 0.96–1.70, $p = 0.094$). Similarly, the dominant model (TT + CT vs. CC) showed a non-significant trend toward increased PTB risk among carriers of the T allele (OR = 0.72, 95% CI: 0.48–1.10, $p = 0.100$).

Under the recessive model, individuals carrying the TT genotype exhibited a modest but non-significant increase in PTB susceptibility compared with carriers of the CC and CT genotypes combined (OR = 1.30, 95% CI: 0.80–2.20, $p = 0.300$). Likewise, the additive model analysis demonstrated no significant differences in genotype distribution between cases and controls. Compared with the CC genotype, neither the CT genotype (OR = 1.40, 95% CI: 0.90–2.10, $p = 0.168$) nor the TT genotype (OR = 1.50, 95% CI: 0.80–2.70, $p = 0.160$) were significantly associated with PTB risk.

4. DISCUSSION

No statistically significant differences were observed between the cases and controls in terms of mean age, sex distribution, or residential status, indicating appropriate matching between the study groups. Despite the absence of statistical differences between the cases and controls for these variables, PTB occurred more frequently among males and predominantly affected young adults, with a mean age of approximately 32 years. These findings are consistent with those of previous regional studies that reported a higher burden of PTB among males and economically productive age groups. For instance, Abuabat *et al.* (2023) reported a male predominance of 63.6% among Saudi patients with disseminated TB, closely comparable to the 62.5% observed in our cohort [21]. Similarly, Alsharani *et al.* . Alshahrani et al.(2021) documented a mean patient

age of 38.04 ± 9.66 years in the Asir region of Saudi Arabia, supporting the observation that TB disproportionately affects young and middle-aged adults in the Arabian Peninsula [22]. Comparable findings were also reported by Ghermi *et al.* . (2021) in Algeria, where pulmonary TB cases were predominantly men [23]. Yezli et al. (2023) confirmed a similar demographic pattern among Hajj pilgrims [24]. The predominance of males in TB epidemiology may be attributable to several interacting factors, including sex-related differences in immune responses, higher prevalence of smoking and occupational exposure among men, and socio-behavioral factors influencing healthcare access and transmission dynamics.

In contrast, Al-Shehari *et al.* . In a large national analysis of more than 92,000 Yemeni TB cases, Al-Sharqi et al. (2022) reported a nearly equal male-to-female ratio of 1.03:1 [17]. This discrepancy may reflect methodological differences, as their study included all forms of TB across all age groups, whereas the present study specifically focused on adult patients with PTB. Likewise, Abuabat *et al.* (2023) reported a substantially higher median age of 64 years, likely reflecting the tertiary care setting of their study, which may preferentially receive older patients with severe or complicated disease presentations [21]. Furthermore, Kia *et al.* . (2020) reported a female predominance and a greater proportion of elderly patients in Iran [25] underscoring the influence of geographic, demographic, and healthcare-related factors on TB epidemiology across populations.

Smoking was significantly more prevalent among patients with PTB than among controls [108(54.0%) vs. 74 (37.0%)], and was associated with an approximately twofold increase in disease risk (OR = 2.0, 95% CI: 1.34–2.98, $p = 0.0006$). This finding is consistent with studies from Ethiopia (OR = 3.55, 95% CI: 1.1.09-11.61, $p = 0.036$ and other settings, demonstrating that smoking contributes to TB susceptibility through multiple mechanisms, including impaired alveolar macrophage function, reduced mucociliary clearance, and suppression of cell-mediated immunity, particularly CD4+ T-cell responses [26]. In contrast, Alsharani et al. (2021) and Andarge *et al.* (2021) did not observe a significant association between smoking and TB risk in their cohorts [22, 27]. Such discrepancies may reflect differences in sample size, statistical power, smoking patterns, or variations in tobacco control policies among countries.

Poor household ventilation was also significantly more common among TB patients than controls (9.5% vs. 2%, OR = 5.14, 95% CI: 1.72–21.1, $p = 0.001$), supporting the established role of confined and inadequately ventilated environments in facilitating airborne transmission of *M. tuberculosis*. In addition, socioeconomic disadvantage emerged as a prominent determinant of disease susceptibility. Most PTB patients reported low income (OR = 15.09, 95% CI: 6.09–37.41, $p < 0.001$), and limited educational attainment (OR = 63.6, 95% CI: 24.23–166.96, $p < 0.001$), findings that are consistent with previous studies from Iran, Ethiopia, and Pacific Island populations linking poverty, overcrowding, malnutrition, and reduced health literacy with increased TB burden [25, 26, 28]. These observations reinforce the multifactorial nature of TB transmission and progression, particularly in resource-limited settings.

A positive family history of TB (OR = 7.72, 95% CI: 3.92–15.2, $p < 0.001$) was the strongest predictor of PTB in the present study. In addition, our findings revealed that the absence of BCG vaccination significantly increased the risk of PTB among Yemeni adults (OR = 1.7, 95% CI: 1.09–2.50, $p = 0.020$). This is consistent with a recent global individual participant data meta-analysis by Martinez *et al.* (2022), which confirmed that infant BCG vaccination provides significant protection against pulmonary tuberculosis. However, while Martinez *et al.* highlighted that the protective efficacy of neonatal BCG tends to wane over time and becomes less effective in adolescents and adults, our study demonstrates that the history of receiving this vaccine still correlates with a lower susceptibility profile in adulthood within the Yemeni population, underscoring the long-term relative benefit or perhaps the impact of early-life protection in high-burden, low-income settings [29].

In contrast to the strong associations observed for environmental and socioeconomic determinants, the present study did not identify a statistically significant association between the IFN-Υ rs1861494 C/T polymorphism and susceptibility to PTB in the Yemeni population. The rs1861494 variant is located within the third intron of the IFN-Υ gene and has been suggested to function as an intronic enhancer involved in the regulation of IFN-Υ [30]. This polymorphic region contains a T-box binding element that may influence transcriptional activity, while the C allele has been reported to demonstrate greater affinity for several putative nuclear transcription factors, including zinc-finger proteins such as RU49, zinc-finger proliferation 1, and myeloid zinc-finger 1 factor [31]. These molecular characteristics provide biological plausibility for the potential role of rs1861494 in modulating host immune responses against Mycobacterium tuberculosis through altered IFN-Υ production.

Despite this functional relevance, the current findings revealed only a modest and statistically non-significant trend toward increased PTB susceptibility among carriers of the T allele across the examined genetic models. This observation is consistent with the findings of a recent meta-analysis that reported no definitive association between the rs1861494 polymorphism and TB susceptibility in both Asian and non-Asian populations, suggesting that the effect of this variant, if present, may be limited or population-dependent[32].

Previous studies investigating this polymorphism have produced inconsistent results across different ethnic and

geographic populations. For instance, a protective association was reported in an Argentine population (OR = 0.235, $p = 0.012$) [18],whereas studies conducted in Indian cohorts demonstrated a significant increase in TB susceptibility among variant carriers (OR = 2.18, 95% CI = 1.57–3.03; $p < 0.001$). [15]. Such discrepancies may reflect interpopulation differences in genetic architecture, linkage disequilibrium patterns, environmental exposures, and population stratification. In addition, variations in study design, sample size, and statistical power may further contribute to the heterogeneity of reported associations. The influence of gene–environment interactions should also be considered, particularly in high-burden settings where socioeconomic and environmental determinants may exert stronger effects on disease susceptibility than individual genetic variants.

In the present study, the substantial impact of established environmental and socioeconomic risk factors may have obscured the more subtle genetic effects associated with IFN-Υ rs1861494. Given the multifactorial nature of TB pathogenesis, this polymorphism may only modestly contribute to disease susceptibility and may require interaction with additional host genetic or environmental factors to exert a measurable effect.

Overall, the findings of this study do not support a major independent role for the IFN-Υ rs1861494 polymorphism in PTB susceptibility in the Yemeni population. Nevertheless, further investigations involving larger sample sizes, ethnically diverse populations, functional genomic approaches, and integrated gene–environment interaction analyses are warranted to clarify the precise contribution of this variant to host susceptibility to tuberculosis.

5. CONCLUSION

This study demonstrated that susceptibility to PTB among Yemeni adults is strongly associated with environmental, behavioral, and socioeconomic determinants, particularly low educational attainment, poverty, household exposure to tuberculosis, poor ventilation, smoking, and lack of BCG vaccination. In contrast, no significant association was detected between the IFN-Υ rs1861494 polymorphism and PTB susceptibility under any of the genetic models examined. Future investigations involving larger sample sizes and additional immune-related genetic markers are recommended to better elucidate the genetic basis of tuberculosis susceptibility among the Yemeni population.

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Table 1. Demographic characteristics of cases and controls

Variables	TB cases $n = 200$	Controls $n = 200$	OR (95% CI)	χ^2	*p* value
Mean ± SD age (years)	32.0±12.6	31.9±11.7	–	–	0.93
Gender					
Female (%)	75 (37.5%)	74 (37%)	1.02	0.01	0.92
Male (%)	125 (62.5%)	126 (63%)			
Place of Residence (%)					
Urban (%)	115 (57.5%)	114 (57.0%)	1.02	0.01	0.92
Rural (%)	85 (42.5%)	86 (43%)			

χ^2 = chi-square test; *p* value = probability value; OR = odds ratio.

Table 2. Risk factors associated with tuberculosis infection in Yemeni patients.

Risk factors		TB cases $n = 200$	Controls $n = 200$	OR (95% CI)	χ^2	*p* value
Smoking (%)	Yes	108 (54.0%)	74 (37.0%)	2.00 (1.34–2.98)	11.65	0.0006
	No	92 (46.0%)	126 (63.0%)			
BCG vaccine (%)	Yes	90 (45.0%)	110 (55.0%)	Ref		
	No	93 (46.5%)	68 (34.0%)	1.70 (1.09–2.50)	5.80	0.020
	Unknown	17 (8.5%)	22 (11.0%)	0.90 (0.50–1.90)	0.03	0.900
History of tuberculosis (%)	Yes	35 (17.5%)	0 (0.0%)	∞ or N/A*	38.26	< 0.001
	No	165 (82.5%)	200 (100%)			
Relatives (%)	Yes	62 (31.0%)	11 (5.5%)	7.72 (3.92–15.20)	43.85	< 0.001
	No	138 (69.0%)	189 (94.5%)			
Educational level (%)	University	20 (10.0%)	144 (72.0%)	Ref		
	Secondary	47 (23.5%)	27 (13.5%)	12.53 (6.44–24.38)	66.39	< 0.001
	Primary	62 (31.0%)	12 (6.0%)	37.20 (17.13–80.76)	115.70	< 0.001
	Read and write	18 (9.0%)	11 (5.5%)	11.78 (4.87–28.52)	38.76	< 0.001
	Illiterate	53 (26.5%)	6 (3.0%)	63.60 (24.23–166.96)	118.77	< 0.001
Income level (%)	High	8 (4.0%)	21 (10.5%)	Ref		
	Medium	31 (15.5%)	151 (75.5%)	0.539 (0.219–1.327)	1.85	0.174
	Low	161 (80.5%)	28 (14.0%)	15.09 (6.08–37.41)	47.87	< 0.001
Ventilation (%)	Yes	181 (90.5%)	196 (98.0%)	5.14 (1.72–21.10)	9.00	0.001
	No	19 (9.5%)	4 (2.0%)			

χ^2 = chi-square test; *p* value = probability value; OR = odds ratio.

*OR not calculable due to zero value in the control group; *p* value determined by Fisher's exact test.

Table 3. Frequencies of genotype under Hardy–Weinberg equilibrium.

SNPs	Genotype	Observed value	Expected value	χ^2	*p*
rs1861494 C/T (IFN-γ)	CC	89	84.5	1.96	0.162
	CT	82	91.0		
	TT	29	24.5		

χ^2 = chi-square test; *p* value = probability value.

Table 4. Association of IFN-γ polymorphisms with PTB susceptibility.

SNP / Genetic model	Genotype/Allele	Case ($n = 200$)		Control ($n = 200$)		OR	95% CI	χ^2	*P*
		No.	%	No.	%				
IFN-γ rs1861494 C/T									
Allele	C	237	59.25	260	65.0	Ref			
	T	163	40.75	140	35.0	1.30	0.96–1.70	2.8	0.094
Dominant	CC	73	36.50	89	44.5	Ref			
	TT+CT	127	63.50	111	55.5	0.72	0.48–1.10	2.7	0.100
Recessive	CT+CC	164	82.00	171	85.5	Ref			
	TT	36	18.00	29	14.5	1.30	0.80–2.20	0.9	0.300
Additive	CC	73	36.50	89	44.5	Ref			
	CT	91	45.50	82	41.0	1.40	0.90–2.10	1.9	0.168
	TT	36	18.00	29	14.5	1.50	0.80–2.70	2.0	0.160

χ^2 = chi-square test; *P* value = probability value; OR = odds ratio.