

Dynamic Challenges of Active Tuberculosis: Prevalence and Risk Factors of Co-Infection in Clinical and Microbiological Characteristics at King Abdulaziz University Hospital, Jeddah, Saudi Arabia

Jawahir A Mokhtar ¹⁻³, Dalya M Attallah ², Asif Ahmad Jiman-Fatani ^{1,2}, Mohammed W Al-Rabia¹, Mona Abdulrahman Alqarni¹, Bandar Hasan Saleh ^{1,2}, Maysaa Mohammed Amboon⁴, Tarfa A Altorki ^{3,4}, Khalil K Alkuwaity^{3,4}, Turki Abujamel^{3,4}, Reham Kaki^{5,6}, Taghreed Nassir Albarakati⁷, Hussam Daghistani^{8,9}, Mazen A Ismail¹⁰, Ohood Alharbi ¹¹, Ibrahim Ismail Mohammed Abu ¹², Abdelbagi Alfadil ^{1,13}, Karem Ibrahim ^{1,2}, Mohammed Mufrrih ^{4,14}, Ahmad M Sait^{4,9}

¹Department of Clinical Microbiology and Immunology, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia; ²Department of Clinical Microbiology Laboratory, King Abdulaziz University Hospital, Jeddah, 21589, Saudi Arabia; ³Vaccines and Immunotherapy Unit, King Fahd Medical Research Center, King Abdulaziz University, Jeddah, 21589, Saudi Arabia; ⁴Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, 21589, Saudi Arabia; ⁵Department of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia; ⁶Department of Infectious Disease & Infection Control and Environmental Health, King Abdulaziz University Hospital, Jeddah, Saudi Arabia; ⁷Microbiology Unite in King Fahd General hospital Jeddah (KFHJ), Jeddah, Saudi Arabia; ⁸Department of Clinical Biochemistry, Faculty of Medicine, King Abdulaziz University Jeddah, Jeddah, 21589, Saudi Arabia; ⁹Regenerative Medicine Unit, King Fahd Medical Research Center, King Abdulaziz University, Jeddah, 21589, Saudi Arabia; ¹⁰Department of Medical Education, Faculty of Medicine, King Abdulaziz University, Jeddah, 21589, Saudi Arabia; ¹¹Department of Microbiology and Parasitology, Faculty of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia; ¹²Department of Community Medicine, Faculty of medicine, King Abdulaziz University, Jeddah, 21589, Saudi Arabia; ¹³Centre of Research Excellence for Drug Research and Pharmaceutical Industries, King Abdulaziz University, Jeddah, Saudi Arabia; ¹⁴Special Infectious Agents Unit BSL-3, King Fahd Medical Research Center, King Abdulaziz University, Jeddah, Saudi Arabia

Correspondence: Karem Ibrahim, Department of Clinical Microbiology and Immunology, Faculty of Medicine, King Abdulaziz University, P.O. Box 80205, Jeddah, 21589, Saudi Arabia, Email kaibrahem@kau.edu.sa

Background: Tuberculosis (TB) is a major public health issue in Saudi Arabia, particularly impacting the elderly. Immunocompromising conditions, including comorbidities, malignancies, and the use of immunosuppressive agents, are major risk factors for active TB (ATB).

Objective: To analyze clinical factors and estimate mortality in TB and drug-resistant cases.

Methods: This retrospective study analyzed medical records of 12,494 patients at KAUH (2019–2021), identifying 131 confirmed TB cases with comprehensive data on demographics, clinical features, comorbidities, diagnostics, and outcomes. Data were analyzed using SPSS, with chi-square and logistic regression identifying risk factors. Statistical significance was determined at a threshold of $p < 0.05$. In our study, logistic regression was employed to identify significant predictors of mortality among TB patients. The results were presented using beta coefficients (B) to quantify the relationship between predictors and the outcome, along with the adjusted odds ratio (AOR) to provide an interpretable measure of the strength of these associations.

Results: Of the 131 TB patients involved in this paper, a higher incidence of pulmonary TB was observed among men under 30 years old. This group also showed a higher mortality rate due to comorbidities such as renal failure, human immunodeficiency virus (HIV), and autoimmune disease. The risk of mortality was heightened by 69.47% with drug susceptibility. Additionally, 19.85% of the patients had multidrug-resistant TB (MDR-TB), and 10.69% had extensively drug-resistant TB (XDR-TB). Patients undergoing hemodialysis, and those with respiratory comorbidities, cancer, diabetes, and smoking were found to have a higher mortality hazard, indicating these as significant risk factors for TB.

Conclusion: This study highlights TB's prevalence and drug resistance at KAUH, emphasizing high-risk groups, including males and young adults. Effective strategies, targeted interventions, and future research are vital for reducing mortality.

This study examines the stability of tuberculosis (TB) disease presentation using dynamic models among patients treated at King Abdulaziz University Hospital (KAUH) in Jeddah, Saudi Arabia.

Key findings include:

- This is the first study to analyze TB disease stability across different demographic groups.
- Males, elderly individuals, cancer patients, and those with pulmonary disease or other comorbidities were found to have a higher risk of death from TB.
- The results emphasize the need for healthcare practices to adopt the “equilibrium state” method for hazard assessment. Incorporating this gold-standard approach into treatment plans can help identify high-risk cases and improve control measures to reduce TB-related mortality.

This study provides valuable insights for improving TB patient care and treatment outcomes, particularly for vulnerable groups.

Keywords: Tuberculosis, Pulmonary, Risk Factor, Prevalence, Drug Resistance

Background

Tuberculosis (TB) remains a major global health problem. In Saudi Arabia, the incidence and impact of TB, particularly among vulnerable populations such as the elderly and immunocompromised, necessitate ongoing research and intervention. This emphasis is evident at pivotal institutions like King Abdulaziz University Hospital, where TB research is prioritized. A recent study conducted in a Saudi tertiary care unit reviewed 58,141 records and reported that tuberculosis (TB) remains a significant public health concern, affecting individuals of all genders and age groups, with a particular risk to the elderly.¹ Previous research has demonstrated that TB can be caused by infection with members of the *Mycobacterium tuberculosis* complex (MTBC), which are slow-growing, aerobic, acid-fast bacilli capable of surviving in the environment for extended periods. *Mycobacterium tuberculosis* is the most commonly isolated subspecies in human TB cases.² However, molecular identification has shown that many human isolates belong to non-*M. tuberculosis* members of the MTBC. These include *M. bovis*, *M. africanum*, *M. microti*, *M. canetti*, *M. caprae*, *M. orygis*, *M. pinnipedii* (a non-tuberculous mycobacterium, NTM), and *M. mungi*.³ Numerous studies have investigated the transmission of TB through the mucosa of the oropharynx or the gastrointestinal tract,⁴ with pulmonary TB being the most infectious form. Scientists have now established that TB can spread through infectious aerosols. When infected individuals sneeze, cough, or expectorate, they release droplets and contaminated dust particles into the air, which can be inhaled by susceptible individuals.⁵ The bacteria have a remarkable ability to attack the lungs but also have the potential to affect other parts of the body, including the lymph nodes, pleura, and osteoarticular system.⁴ Recent arguments have shown that the ingestion of unpasteurized milk or inadequately cooked meat from infected cattle is a significant source of infection if bovine tuberculosis is not well controlled.⁴ The infection can remain inactive for years, potentially reactivating in some individuals. The evidence supports the idea that primary TB can occur when the immune system fails to protect against the infection, leading to a stage known as latent tuberculosis, caused by the bacteria *Mycobacterium tuberculosis* (MTB).⁵ A notable example of first-line drugs used for treating active tuberculosis is the common regimen that starts with an intensive phase and follows with an extension phase. In the intensive phase, a four-drug combination of isoniazid, rifampin, ethambutol, and pyrazinamide is administered for two months. This is followed by an extension phase where isoniazid and rifampin are used for an additional 4-7 months.⁶ The development of antimycobacterial resistance during the first line of therapy has been highlighted in the Global Tuberculosis Report by the World Health Organization (WHO; 2013). When resistance occurs, patients are usually switched to second-line drugs, which include streptomycin, amikacin, kanamycin, viomycin, capreomycin, levofloxacin, gemifloxacin, ofloxacin, and moxifloxacin.⁶ TB bacteria can quickly develop resistance to the two most powerful first-line drugs, rifampicin and isoniazid.⁶ This condition is known as multidrug-resistant TB (MDR-TB).⁶ In more severe cases, resistance extends to several powerful drugs, leading to extensively drug-resistant TB (XDR-TB).⁶ Studies have demonstrated the importance of evaluating second-line anti-TB treatments to identify the most effective drugs for achieving optimal clinical outcomes

in DR-TB patients with HIV. Comparative analyses of multiple chemotherapy regimens provide a foundation for evidence-based practices in managing these complex cases. Notably, bedaquiline and linezolid have been shown to significantly enhance treatment outcomes in drug-resistant TB patients with HIV, as highlighted in a systematic review and meta-analysis.⁷ The WHO's Global Tuberculosis Report emphasized the need for screening to detect MDR-TB and XDR-TB, recommending traditional phenotypic (or culture-based) techniques using systems like Versa TREK and Cepheid GeneXpert[®] system.⁶ It is essential to consider that strains causing multidrug-resistant TB (MDR-TB) are typically resistant to both isoniazid and rifampin. Extensively drug-resistant TB (XDR-TB) strains are resistant to fluoroquinolones and most second-line injectable drugs.⁶ In 2019, approximately 10 million people worldwide developed tuberculosis (TB), with 1.2 million HIV-negative and 208,000 HIV-positive individuals dying from the disease.^{8,9} This raises several questions regarding the situation in Saudi Arabia. According to WHO statistics, the number of new TB cases increased from 5.7–5.8 million per year in 2009–2012 to 10 million in 2019.¹⁰ This increase, despite being attributed to improved reporting of detected cases in countries like India and Indonesia, could also be due to a higher prevalence of TB-HIV co-infection, diabetes, and COVID-19, as these diseases may reactivate or exacerbate active TB.¹¹ A retrospective study in 2021 on the prevalence of tuberculosis among patients at a tertiary hospital in Riyadh highlighted that TB is endemic in Saudi Arabia. The incidence rate decreased from 18 cases per 100,000 people in 2002 to 10 cases per 100,000 in 2017.¹ Despite the implementation of WHO-recommended directly observed therapy short (DOTS) course TB control strategies, the reduction in TB incidence in Saudi Arabia has been minimal. The incidence is significantly higher among non-nationals residing in Saudi Arabia than among national citizens, with rates of 10.9 versus 7.4 per 100,000 population in 2019. Additionally, males account for approximately 71.2% of all notified cases, and young adults (aged less than 45 years) account for approximately 68.6% of all notified TB cases, regardless of gender. Pulmonary tuberculosis accounts for nearly 86% of newly reported TB cases in Saudi Arabia.¹² Moreover, The study, conducted in 2024, examined the global incidence of tuberculosis and its spatial autocorrelation. It revealed a general decline in tuberculosis incidence over this period, while spatial autocorrelation trends remained significant. Additionally, the study found that the risk factors for tuberculosis incidence vary by geography, with low literacy rate emerging as the most widespread and significant risk factor.¹³

Assessing the prevalence of TB risk factors and their impact on the mortality rate is crucial for TB mitigation. This study aims, for the first time, to identify the prevalence of various TB risk factors, anti-TB drug resistance associated with higher mortality rates per person-years (PY), and TB disease presentation among different age groups of TB patients treated at KAUH in Jeddah, Saudi Arabia. This is a crucial step in improving TB control and treatment outcomes.

Material and Methods

Data Collection and Procedures

This retrospective study reviewed the medical records of 12,494 patients at King Abdulaziz University Hospital, identifying 131 confirmed TB cases diagnosed between January 2019 and December 2021. Data were collected from microbiology lab databases and patient medical files, including demographic information, clinical features, comorbidities, and outcomes. Full medical records for all the patients were thoroughly reviewed, including physician notes, physical examinations, radiology (scans and imaging), laboratory tests, and follow-up notes. All newly diagnosed TB cases during the study timeframe, confirmed based on microbiological features (positive acid-fast stain and TB culture), were included. Both pulmonary and extra-pulmonary TB cases were considered, and only those patients with complete information recorded in the TB notification register were included for analysis. Data was collected from medical records using a structured data collection form. Five age groups were designated for this investigation: 0–14, 15–29, 30–43, 44–60, and over 60 years old. Demographic data included age, gender, nationality, smoking status, marital status, and residence. Clinical data included information on diabetes mellitus, renal disease, cancer, chemotherapy, COVID-19, organ transplantation, immunosuppressive drugs/steroids use, HIV status, BCG vaccination, and contact with TB patients. Additionally, data on drug susceptibility were collected for both pulmonary tuberculosis (PTB) and extra-pulmonary tuberculosis (EPTB) groups. Ethical approval for the study (approval number HA-02 J-008) was obtained from the Research Committee of the Unit of Biomedical Ethics at King Abdulaziz University's Faculty of Medicine, part

of the Kingdom of Saudi Arabia's Ministry of Education. As is usual in hospitals, patient isolates used for infection diagnosis are handled in accordance with stringent ethical guidelines. As ethical approval has been received, inclusion of these data in our manuscript is permissible with no further patient consent. It is important to clarify that the Local Research Ethics Committee at KAUH has granted a waiver for patient consent to access and review their medical records for this study. This decision was based on the retrospective design of the study, which involved the use of anonymized data and posed minimal risk to patient privacy and confidentiality. We are committed to upholding the highest ethical standards, ensuring full compliance with the Declaration of Helsinki, and safeguarding patient confidentiality. All data utilized in this research was managed with the utmost care to maintain privacy and adhere to ethical guidelines.

Laboratory Methods

Isolation and identification of *Mycobacterium tuberculosis* were performed following laboratory standard operating procedures in several stages. The process included decontamination and digestion of non-sterile samples, followed by culturing concentrated samples in a liquid-based medium (Myco Broth, culture bottles containing 7H9 broth and cellulose sponges) optimized for the recovery of all types of mycobacteria. The incubation of the cultures was conducted using the Versa TREK (ESP Culture System II) (Trek Diagnostic Systems, Inc., Westlake, Ohio) for the isolation of mycobacteria from clinical specimens. Smears were also prepared and examined for the presence of acid-fast bacilli using the conventional AFB stain (Kinyoun stain). PCR was performed using the GeneXpert MTB/RIF assay (Cepheid, USA) to identify *Mycobacterium tuberculosis* complex and simultaneously detect rifampicin resistance.

Sample Preparation

Non-sterile clinical samples, such as sputum, were initially subjected to a decontamination process to eliminate contaminants and competing microorganisms. This step involved using reagents such as N-acetyl-L-cysteine (NALC) and sodium hydroxide (NaOH) to both digest the mucus and decontaminate the sample. The processed samples were then centrifuged at high speed to concentrate the mycobacteria, ensuring their adequate recovery. The concentrated pellet obtained after centrifugation was used for culturing and microscopic analysis.

Culture and Isolation

The concentrated samples were inoculated into Myco Broth, a liquid-based culture medium consisting of Middlebrook 7H9 broth enriched with necessary nutrients and cellulose sponges to enhance bacterial growth. This medium is optimized to support the recovery of all types of mycobacteria, including slow-growing strains. Culture bottles containing the medium were incubated using the Versa TREK ESP Culture System II. This automated system continuously monitored the cultures for signs of microbial growth, such as changes in gas pressure within the bottles, which indicate metabolic activity.

Microscopic Examination

From the concentrated samples, smears were prepared on clean, grease-free glass slides. These smears were stained using the Kinyoun method, a cold acid-fast stain specifically designed for detecting acid-fast bacilli (AFB). Stained slides were examined under a light microscope using high-power magnification (oil immersion) to identify the presence of red-colored bacilli against a blue background, characteristic of *Mycobacterium tuberculosis*. This step provided preliminary evidence of infection.

Molecular Identification and Drug Resistance Testing

For precise identification and drug resistance testing, molecular analysis was performed using the GeneXpert MTB/RIF assay (Cepheid, USA). This real-time PCR-based diagnostic tool identifies the *Mycobacterium tuberculosis* complex with high specificity and sensitivity. The assay also simultaneously detects mutations in the *rpoB* gene, which confer resistance to rifampicin, a key first-line anti-TB drug. The entire process, from DNA extraction to result generation, is automated and takes approximately two hours, making it a rapid and reliable diagnostic tool for TB and rifampicin-resistant TB detection.

Statistical Analysis

Data were analyzed using SPSS for Windows, release 23.0 (SPSS Inc., Chicago, IL, USA). Frequencies described the data, and the chi-square test was used for testing qualitative data. Logistic regression analysis identified diabetes and smoking as significant risk factors for TB, with a significance level set at $p < 0.05$.

Results

Basic Demographics

In this paper, 131 patients were identified as TB cases at KAUH during January 2019 to December 2021. Most patients were male and aged between 15 and 29 years, with this age group having the highest survival rate. When categorized by age, the highest number of TB cases were found among those aged 15–29 years and the highest positive rate was found among Saudis. Additionally, 41.2% of the patients were single, and 71% were living in Jeddah (Table 1).

Risk Factors and Drug Resistance

A total of 110 (84%) patients were newly infected, while 21 patients were reinfected. The main risk factors for TB identified were diabetes and smoking. Patients with HIV, autoimmune diseases, and renal conditions had a higher mortality rate. In our study, 69.47% of patients were susceptible to anti-TB drugs, 19.85% had MDR-TB, and 10.69% had XDR-TB (Figure 1). When comparing treatment response according to medical history among TB patients, all variables showed non-significant differences except for patients undergoing dialysis, where 75% had resistance to at least

Table 1 Displays the Demographic Profiles of the TB Patients. Males Accounted for 55.7% of Cases, and the Highest Incidence Was Among Those Aged 15–29 years

		N	%
Age groups in years	0–14	5	3.8%
	15–29	40	30.8%
	30–43	32	24.6%
	44–60	26	20.0%
	Over 60	27	20.8%
Sex	Female	58	44.3%
	Male	73	55.7%
Nationality	Unknown	2	1.5%
	Saudi	65	49.6%
	Non-Saudi	64	48.9%
Marital Status	Unknown	35	26.7%
	Single	54	41.2%
	Married	42	32.1%
Residence	Unknown	35	26.7%
	Jeddah	93	71.0%
	Makkah	2	1.5%
	Egypt	1	0.8%

Abbreviations: N, number of cases; %, percentage.

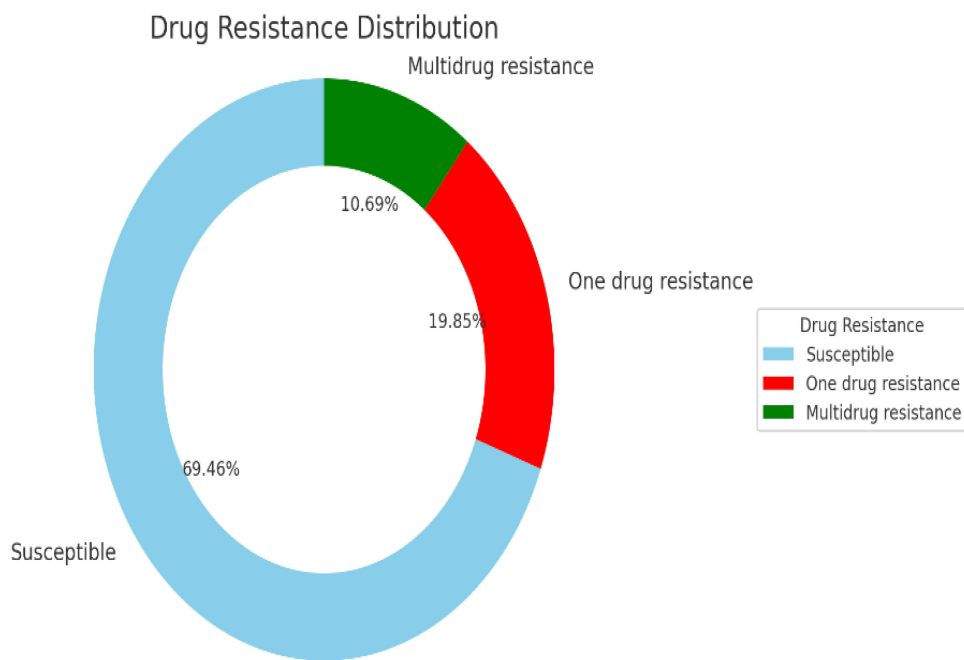


Figure 1 The distribution of drug resistance among patients in our study. Blue represents patients who were susceptible to anti-tuberculosis (TB) drugs, comprising 69.47% of the study population. Red indicates patients with resistance to one drug, accounting for 19.85% of the cases classified as multidrug-resistant TB (MDR-TB). Green denotes patients with extensive drug resistance, with 10.69% identified as having extensively drug-resistant TB (XDR-TB). The color distinctions visually highlight the varying levels of resistance observed in the patient cohort.

one drug ($P=0.019$). Treatment response according to medical history among (Table 2) summarizes the TB patients treated at KAUH. Additionally, 38.9% had deep vein thrombosis (DVT), 19.8% were diabetic, and 18.3% were smokers. Only 48.1% had received the BCG vaccination (Table 3). Among TB patients, the types of TB according to medical history showed non-significant differences for all variables except for those undergoing dialysis, where 75% had extrapulmonary TB ($P=0.023$) (Table 4). The prevalence of TB was higher in 2020 compared to 2019 and 2021, with rates of 14.07, 10.27, and 7.09 per 1000, respectively, though the differences were not statistically significant. Prevalence

Table 2 Treatment Response According to Medical History Among TB Patient's Treated at KAUH

	Sensitive		MDR		XDR		p-value
	N	%	N	%	N	%	
Infection cases							
New	80	72.7%	20	18.2%	10	9.1%	0.162
Reinfection	11	52.4%	6	28.6%	4	19.0%	
Family history of TB	7	77.8%	1	11.1%	1	11.1%	0.791
Smoking	14	58.3%	6	25.0%	4	16.7%	0.387
Diabetes Miletus	17	65.4%	5	19.2%	4	15.4%	0.686
HIV	6	60.0%	3	30.0%	1	10.0%	0.702
Autoimmune disease	3	75.0%	1	25.0%	0	0.0%	0.773
IV drug user	1	100.0%	0	0.0%	0	0.0%	0.801
Kidney disease	11	73.3%	3	20.0%	1	6.7%	0.864

(Continued)

Table 2 (Continued).

	Sensitive		MDR		XDR		p-value
	N	%	N	%	N	%	
Dialysis	1	25.0%	3	75.0%	0	0.0%	0.019
Organ transplant	1	50.0%	0	0.0%	1	50.0%	0.178
Cancer and chemotherapy	6	85.7%	1	14.3%	0	0.0%	0.552
COVID 19	7	58.3%	5	41.7%	0	0.0%	0.090
Travel history (immigration)	2	100.0%	0	0.0%	0	0.0%	0.640
DVT	38	74.5%	8	15.7%	5	9.8%	0.578
BCG vaccination	42	66.7%	15	23.8%	6	9.5%	0.535

Note: p-value indicates statistical significance ($p < 0.05$).

Abbreviations: N, number of cases; %, percentage; HIV, Human Immunodeficiency Virus; DVT, Deep Vein Thrombosis; IV drug user, Intravenous Drug User; MDR, Multidrug-resistant tuberculosis; XDR, Extensively drug-resistant tuberculosis.

Table 3 Medical History of TB Patients Treated at KAUH

	N	%
Infection cases		
New	110	84.0%
Reinfection	21	16.0%
Family history of TB	9	6.9%
Smoking	24	18.3%
Diabetes	26	19.8%
HIV	10	7.6%
Autoimmune disease	4	3.1%
IV drug user	1	0.8%
Kidney disease	15	11.5%
Dialysis	4	3.1%
Organ transplant	2	1.5%
Cancer and chemotherapy	7	5.3%
Covid 19	12	9.2%
Travel history (immigration)	2	1.5%
DVT	51	38.9%
BCG vaccination	63	48.1%

Abbreviations: N, number of cases; %, percentage; TB, Tuberculosis; HIV, Human Immunodeficiency Virus; DVT, Deep Vein Thrombosis; IV drug user, Intravenous Drug User.

Table 4 TB Types According to Medical History Among TB Patients Treated at KAUH (n=131)

	TB				p-value
	PTB		EPTB		
	N	%	N	%	
Infection cases					
New	80	72.7%	30	27.3%	0.431
Reinfection	17	81.0%	4	19.0%	
Family history of TB	6	66.7%	3	33.3%	0.601
Smoking	18	75.0%	6	25.0%	0.906
Diabetes Miletus	19	73.1%	7	26.9%	0.900
HIV	7	70.0%	3	30.0%	0.761
Autoimmune disease	2	50.0%	2	50.0%	0.265
IV drug user	1	100.0%	0	0.0%	0.552
Kidney disease	9	60.0%	6	40.0%	0.187
Dialysis	1	25.0%	3	75.0%	0.023
Organ transplant	2	100.0%	0	0.0%	0.399
Cancer and chemotherapy	4	57.1%	3	42.9%	0.294
COVID 19	10	83.3%	2	16.7%	0.441
Travel history (immigration)	2	100.0%	0	0.0%	0.399
DVT	36	70.6%	15	29.4%	0.471

Note: p-value indicates statistical significance ($p < 0.05$).

Abbreviations: N, number of cases; %, percent, TB, Tuberculosis, HIV, Human Immunodeficiency Virus, DVT, Deep Vein Thrombosis, IV drug user, Intravenous Drug User, PTB, Pulmonary Tuberculosis, EPTB, Extrapulmonary Tuberculosis.

was calculated as the number of cases per 1000 individuals examined (Table 5). Out of 131 tuberculosis (TB) patients, 19.8% had resistance to one drug, while 10.7% had multidrug resistance. Additionally, 16% of the patients died. Furthermore, approximately 75.6% of the patients exhibited pulmonary TB (Table 6).

Treatment Response and Survival Rates and TB Types

When comparing TB types according to demographic characteristics among TB patients, no significant differences were observed across all variables (Table 7). The survival rates according to demographic characteristics among TB patients

Table 5 Prevalence of Tuberculosis During the Period From January 2019 to December 2021

Year	Number of Cases	Total Examined for Tuberculosis	Prevalence per 1000 Among the Examined	p-value
2019 (r)	47	4572	10.27	
2020	56	3980	14.07	0.113
2021	28	3942	7.09	0.120
Total	131	12,494	10.48	

Note: p-value indicates statistical significance ($p < 0.05$).

Table 6 Prevalence of Drug Resistance to TB Treatment, and TB Types Among TB Patients Treated at KAUH (n=131)

Item	N	%
Drug susceptibility Susceptible	91	69.5%
One drug resistance (MDR)	26	19.8%
Multidrug resistance (XDR)	14	10.7%
Types of TB _lung	99	75.6%
Tb-meningitis	9	6.9%
TB- LN	19	14.5%
TB- intestinal	2	1.5%
TB -organ	4	3.1%

Abbreviations: N, number of cases; %, percentage; TB; Tuberculosis.

showed non-significant differences for all variables except age groups. The highest survival rate (95%, $P=0.047$) was found among patients in the younger age group (Table 8).

Mortality Predictors

Survival among TB patients showed non-significant differences for most variables except for HIV (where survival was 50%, $P=0.002$), autoimmune disease (where survival was 25%, $P=0.001$), and kidney disease (where survival was 60%, $P=0.007$) (Table 9). Following a logistic regression analysis to identify mortality predictors among TB patients, significant predictors were identified: patients aged 15–29 years (AOR = 0.115, $p = 0.016$) and HIV patients (AOR = 9.653, $p = 0.006$) (Table 10).

Table 7 TB Types According to Demographic Characteristics Among TB Patients Treated at KAUH

		TB				p-value
		PTB		EPTB		
		N	%	N	%	
Age	0–14	4	80.0%	1	20.0%	0.777
	15–29	27	67.5%	13	32.5%	
	30–43	24	75.0%	8	25.0%	
	44–60	19	73.1%	7	26.9%	
	Over 60	22	81.5%	5	18.5%	
Sex (gender)	Female	44	75.9%	14	24.1%	0.673
	Male	53	72.6%	20	27.4%	
Nationality	Unknown	1	50.0%	1	50.0%	0.294
	Saudi	45	69.2%	20	30.8%	
	Non-Saudi	51	79.7%	13	20.3%	

(Continued)

Table 7 (Continued).

		TB				p-value
		PTB		EPTB		
		N	%	N	%	
Marital Status	Unknown	26	74.3%	9	25.7%	0.661
	Single	38	70.4%	16	29.6%	
	Married	33	78.6%	9	21.4%	
Residence	Unknown	26	74.3%	9	25.7%	0.105
	Jeddah	70	75.3%	23	24.7%	
	Makkah	0	0.0%	2	100.0%	
	Egypt	1	100.0%	0	0.0%	

Abbreviations: N, number of cases; %, percentage; PTB, Pulmonary Tuberculosis; EPTB, Extrapulmonary Tuberculosis.

Table 8 Survival Rate According to Demographic Characteristics Among TB Patients Treated at KAUH

		Survival				p-value
		Survived n =110		Non survived n =21		
		N	%	N	%	
Age	0–14	4	80.0%	1	20.0%	0.047
	15–29	38	95.0%	2	5.0%	0.047
	30–43	27	84.4%	5	15.6%	
	44–60	22	84.6%	4	15.4%	
	Over 60	18	66.7%	9	33.3%	0.019
Sex (gender)	Female	50	86.2%	8	13.8%	0.534
	Male	60	82.2%	13	17.8%	
Nationality	Unknown	2	100.0%	0	0.0%	0.382
	Saudi	57	87.7%	8	12.3%	
	Non-Saudi	51	79.7%	13	20.3%	
Marital Status	Unknown	31	88.6%	4	11.4%	0.245
	Single	47	87.0%	7	13.0%	
	Married	32	76.2%	10	23.8%	
Residence	Unknown	30	85.7%	5	14.3%	0.862
	Jeddah	77	82.8%	16	17.2%	
	Makkah	2	100.0%	0	0.0%	
	Egypt	1	100.0%	0	0.0%	

Note: p-value indicates statistical significance ($p < 0.05$).

Abbreviations: N, number of cases; %, percentage.

Table 9 Comparison of Survival According to Medical History Among TB Patients Treated at KAUH

	Survival				p-value
	Survived N =110		Non Survived N=21		
	N	%	N	%	
Infection cases					
New	94	85.5%	16	14.5%	0.289
Reinfection	16	76.2%	5	23.8%	
Family history of TB	6	66.7%	3	33.3%	0.143
Smoking	17	70.8%	7	29.2%	0.052
Diabetes Miletus	20	76.9%	6	23.1%	0.274
HIV	5	50.0%	5	50.0%	0.002
Autoimmune disease	1	25.0%	3	75.0%	0.001
IV drug user	1	100.0%	0	0.0%	0.661
Kidney disease	9	60.0%	6	40.0%	0.007
Dialysis	3	75.0%	1	25.0%	0.619
Organ transplant	1	50.0%	1	50.0%	0.187
Cancer and chemotherapy	6	85.7%	1	14.3%	0.897
Covid 19	9	75.0%	3	25.0%	0.374
Travel history (immigration)	1	50.0%	1	50.0%	0.187
DVT	42	82.4%	9	17.6%	0.687
BCG vaccination	55	87.3%	8	12.7%	0.317

Note: p-value indicates statistical significance ($p < 0.05$).

Abbreviations: N, number of cases; %, percentage; TB, Tuberculosis; HIV, Human Immunodeficiency Virus; DVT, Deep Vein Thrombosis; IV drug user, Intravenous Drug User; PTB, Pulmonary Tuberculosis; EPTB, Extrapulmonary Tuberculosis.

Table 10 Logistic Regression Analysis for Predictors of Mortality Among TB Patients Treated at KAUH. B: Beta Coefficient, AOE: Adjusted Odd Ratio

	B	p-value	AOR	95% C.I. for AOR	
				Lower	Upper
Age groups in years					
0–14 vs Over 60	1.134	0.395	0.322	0.024	4.383
15–29 vs Over 60	0.164	0.016	0.115	0.020	0.670
30–43 vs Over 60	1.498	0.060	0.224	0.047	1.064
44–60 vs Over 60	1.040	0.168	0.353	0.081	1.549
HIV	2.267	0.006	9.653	1.909	48.794

(Continued)

Table 10 (Continued).

	B	p-value	AOR	95% C.I. for AOR	
				Lower	Upper
Autoimmune disease	2.440	0.105	11.475	0.602	218.851
Kidney disease	0.913	0.200	2.492	0.617	10.072

Notes: p-value indicates statistical significance ($p < 0.05$). Constant: -1.114. Model χ^2 : 24.749, $P=0.001$. Overall Percent predicted: 86.9%.

Abbreviations: %, percentage; TB, Tuberculosis; HIV, Human Immunodeficiency Virus; B, Regression coefficient; AOR, Adjusted Odds Ratio; C.I., Confidence Interval.

Discussion

This study presents the findings of a retrospective study conducted at KAUH to determine the prevalence of TB and correlated co-infection risk factors among active tuberculosis cases. Our findings revealed a high prevalence of drug-resistant TB among patients with comorbid conditions such as renal failure and HIV, consistent with previous studies highlighting the vulnerability of immunocompromised individuals to TB. Overall, the prevalence of TB was relatively low during the study period, with the highest TB positive rate observed in the year 2020. Although there was a slightly higher percentage of TB-positive cases among Saudis (49.6%) compared to non-Saudis (48.9%), the difference was not statistically significant. These findings suggest that TB may be endemic to Saudi Arabia. It is consistent with previous research.^{12,14} While focusing on the relationship between TB and nationality, it's essential to acknowledge the limitations of this approach, and further studies are needed to provide more comprehensive explanations. In recent years, there has been a challenge concerning the age group of TB patients, with those aged between 15 and 29 years being at a 31% higher risk of TB compared to other age groups. Additionally, a higher proportion of TB isolates were found among males (55.7%), consistent with other studies conducted in Saudi Arabia.¹⁵ Evidence shows TB affects individuals under 40, with males more affected than females.¹⁶ Similarly, our study, using standardized methods, found that males are at a higher risk of TB (55.7%) compared to females. The association between gender and tuberculosis risk may be attributed to a combination of biological, behavioral, and social factors, including smoking, which significantly contributes to increased exposure and susceptibility to TB among males. Indeed, WHO annual reports have consistently highlighted smoking as one of the main risk factors for TB-related illness, with smokers having a 20% higher risk of developing tuberculosis compared to non-smokers.⁹

A systematic review of studies examining the association between diabetes and tuberculosis suggested that individuals with diabetes were three times more likely to develop tuberculosis compared to others.⁹ Our study findings align with this, advocating previous research based on the rate of cases (19.8%). Furthermore, it has been shown that the increased risk of tuberculosis in diabetic patients may be influenced by factors such as a decrease in the number and function of T lymphocytes⁹ and impaired respiratory burst in expelling pathogens due to hyperglycemia. However, while Yorke et al (2017) claimed that diabetes was associated with a 2- to 3-fold increased risk of developing tuberculosis, there was no clear evidence of an increased risk of developing diabetes leading to tuberculosis.¹⁷

Regarding human immunodeficiency virus (HIV) infection, although extensive research has been conducted, our study demonstrated that individuals with HIV/AIDS are more susceptible to tuberculosis compared to individuals who are not infected with HIV.¹⁸ Ogyiri et al (2019) also supported this evidence, emphasizing that HIV-positive TB patients had a significantly higher risk of mortality compared to HIV-negative TB patients.¹⁸ Selection bias is a potential concern, as our study showed a mortality rate of exactly 50% in patients affected by both TB and HIV/AIDS. Autoimmune diseases, such as rheumatoid arthritis, lupus, and multiple sclerosis, affect the immune system, resulting in inflammation and damage to various organs and tissues. Our data suggested a mortality rate of 25% for patients with autoimmune diseases (p -value=0.001). Additionally, Jung et al (2010) found a positive association between HIV and autoimmune diseases, leading to a higher hazard of mortality. However, our study did not delve into treating these cases in detail, noting a discrepancy in results, possibly due to changes in autoimmunity over recent years.¹⁸

Acute kidney disease significantly impacts tuberculosis-related mortality, while chronic kidney disease may exacerbate future tuberculosis-related mortality.¹⁹ Our data revealed a 60% mortality rate for kidney disease in TB patients (p value=0.007). This result indicates that several factors influence TB-related mortality, including disease severity, timing and effectiveness of treatment, and the overall health status of the patient. Research conducted by Vikrant et al (2019) identified that dialysis patients are more likely to develop extrapulmonary tuberculosis (EPTB), aligning with our findings indicating a 75% of extrapulmonary TB infection among dialysis patients compared to pulmonary TB.²⁰ A recently published article by Ali et al (2022) observed that pulmonary tuberculosis is the most common type of tuberculosis,²¹ aligning with our data where 75.6% of our patients were infected with pulmonary tuberculosis. Several studies have investigated the prevalence of TB drug resistance in different regions of the Kingdom of Saudi Arabia. Our research, along with other relevant studies and the World Health Organization's annual reports, indicates a wide variation in the rate of drug-resistant tuberculosis (TB) in Saudi Arabia.^{22,23} While most studies have reported a low incidence of multidrug-resistant tuberculosis (MDR-TB) in Saudi Arabia, likely due to enhanced compliance with directly observed treatment strategies and advancements in tuberculosis diagnosis and resistance detection, our study highlights a significant prevalence of drug-resistant TB. Specifically, we found that 19.85% of patients were classified as having MDR-TB, and 10.69% were identified as having extensively drug-resistant TB (XDR-TB). These findings underscore the pressing need to further strengthen diagnostic and treatment approaches to address this growing challenge in high-risk groups.

The BCG vaccine remains the sole approved vaccine for tuberculosis (TB), offering protection against the disease. Despite its century-long existence and widespread adoption in TB-endemic regions, TB remains a significant global health challenge. Our statistical analysis confirms this, revealing a 48% tuberculosis incidence rate among vaccinated individuals.²⁴ Our study also highlights a notable increase in tuberculosis cases in 2020 compared to 2019 and 2021. This surge could be attributed to various factors, including the implementation of quarantine measures during the COVID-19 pandemic in 2020. The increased availability of free time may have led to higher smoking rates among smokers, considering smoking's strong association with TB. Moreover, COVID-19's impact on the immune system could have rendered individuals more susceptible to TB infection, especially those with pre-existing conditions like diabetes or HIV/AIDS. Additionally, challenges posed by the COVID-19 pandemic, such as disruptions in healthcare services and interruptions in TB treatment, may have contributed to the rise in TB cases and the emergence of drug-resistant strains. Addressing TB effectively requires a multifaceted approach, including improving healthcare access, early diagnosis and treatment, addressing social determinants of health, and enhancing living conditions in high-risk settings.²²

Conclusion

This study underscores the significant prevalence of TB and drug-resistant TB among specific high-risk groups at King Abdulaziz University Hospital. To mitigate this, effective TB control strategies must prioritize these vulnerable populations to reduce mortality and improve treatment outcomes. The study identified 131 TB cases, with a higher prevalence among males and young adults aged 15–29 years. Most *M. tuberculosis* clinic isolates (69.47%) were susceptible to anti-TB drugs, while 19.85% were resistant to at least one drug. These results enforce the need for targeted policy and practice recommendations for public health departments. Strategies should include focused screening and awareness campaigns for high-risk groups, such as individuals under 40 years of age and males, who are disproportionately affected by TB. Additionally, prioritizing the monitoring and control of key risk factors, including smoking, diabetes, and HIV, is essential to reduce TB incidence and mortality rates. Further research is crucial to enhance our understanding of TB risk factors. Future studies should investigate the roles of socioeconomic and environmental variables, as well as conduct longitudinal analyses to better predict TB trends and patterns of drug resistance. Additionally, the evaluation of TB, including the development of active TB diseases and drug resistance, along with associated risk factors, globally requires more support and attention.

Strengths and Limitations

This study has several notable strengths. First, it is one of the few studies conducted in Saudi Arabia that provides a detailed and comprehensive analysis of TB and drug-resistant TB within a large and diverse patient population at

a major tertiary care center. The inclusion of 131 confirmed TB cases over a three-year period allows for an in-depth assessment of the epidemiology, clinical characteristics, and risk factors associated with TB in this region. Second, the study utilized rigorous laboratory methods, including the GeneXpert MTB/RIF assay, which is a reliable and widely accepted diagnostic tool for TB and rifampicin resistance, thereby enhancing the accuracy and reliability of the findings. Additionally, the use of logistic regression analysis to identify significant predictors of mortality adds a valuable statistical dimension to the study, offering insights into the factors that most strongly influence TB outcomes.

This study has several limitations that should be considered when interpreting the findings. First, the data were collected from a single tertiary care center in Jeddah, Saudi Arabia, which may not fully represent the national epidemiology of tuberculosis (TB) or its associated risk factors. The dataset lacked granular details, particularly regarding specific autoimmune diseases and their potential impact on TB outcomes, as well as adherence monitoring for TB treatment regimens, which could have influenced treatment efficacy. Furthermore, mortality rates were not stratified by comorbidities such as HIV or kidney disease, limiting the ability to analyze their specific contributions to patient outcomes. The small sample size in certain subgroups, such as patients undergoing dialysis, constrained the ability to draw definitive conclusions. Additionally, challenges during the COVID-19 pandemic, including potential interruptions in healthcare access, may have impacted the study's findings. The relatively small sample size for certain subgroups, such as HIV-positive patients and those undergoing dialysis, may have limited the statistical power to detect significant associations. Moreover, potential confounding factors, such as socioeconomic status and treatment adherence, were not accounted for in this analysis, which could influence the study's outcomes. Lastly, the study period overlapped with the onset of the COVID-19 pandemic, which may have affected TB diagnosis, treatment, and outcomes in ways that were not fully captured in the analysis. Moreover, a key limitation of this study is the absence of whole genome sequencing (WGS) to determine if the infections were linked to specific strains of *Mycobacterium tuberculosis*. Incorporating WGS in future research could provide valuable insights into strain-specific transmission dynamics, resistance patterns, and clustering of cases, enhancing the epidemiological understanding of tuberculosis in the studied population.

These limitations highlight the need for more comprehensive, multi-center studies with detailed data collection to enhance the understanding of TB epidemiology and outcomes.

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