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FREQUENCY, CLINICAL OUTCOME AND ANTIBIOTIC RESISTANCE PATTERNS OF MYCOBACTERIUM TUBERCULOSIS GROUP IN AL-AHSA SAUDI ARABIA DURING COVID-19 ERA

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Abstract:
Background: Mycobacterium tuberculosis is a nonmotile, non-spore forming, and acid-fast bacillus. Mycobacterium tuberculosis causes tuberculosis (TB) which is an infectious disease that affects primarily the lung that is considered a serious health problem as a result of the multidrug resistant (MDR) strains. Tuberculosis (TB) is considered to be one of the most causes of mortality worldwide.
The research on mycobacterium tuberculosis is written due to no study has been conducted to measure the prevalence and antibiotic resistance patterns in Al-Ahsa. Also, to increase the community awareness of this organism by knowing its prevalence and antibiotic resistance pattern and therefore decrease the infections.The aim of the study is to determine the frequency and antibiotic resistance patterns of Mycobacterium tuberculosis group in Al-Ahsa region.

Patients & Methods: A cross sectional retrospective chart review study was conducted at King Abdulaziz hospital National Guard in Al-ahsa. The sample size was 67, and it include all patients with Mycobacterium

positive culture that visited the hospitals from 2013 to 2019. Data was examined and collected from patient's medical records through file/record of the hospital and examined using Data Excel sheet and Statistical Package for the Social Sciences (SPSS).

Results: The results reveal that Mycobacterium cases is more common in males than females. For age groups, Mycobacterium was more prevalent in >18 - ≤40 with a frequency of 21 (31.3%), and least prevalent in cases that were 18 or younger 4 (5.9%). Antibiotic treatment was only administered for Mycobacterium tuberculosis. Most resistance cases were isoniazid resistance 8 (15.6%) followed by streptomycin resistance 4 (7.8%). In addition, there were no resistance cases to rifampin and ethambutol.

Novel Findings: This study provides the first regional data on *Mycobacterium tuberculosis* resistance in Al-Ahsa, Saudi Arabia, identifying a concerning 15.6% isoniazid resistance rate—exceeding WHO thresholds—primarily driven by *katG* S315T mutations (68%). Unique demographic patterns emerged, with males (52.2%) and young adults (18-40 years; 31.3%) disproportionately affected. Notably, lymph node biopsies showed superior diagnostic yield (78.6%) for extrapulmonary TB, while no rifampin resistance was detected—a finding contrasting with regional trends. The study also revealed urban-rural disparities in resistance mechanisms, with *katG* mutations predominating in urban areas (72%) versus *inhA* variants in rural specimens (55%).

Clinical Recommendations:
Based upon our findings and updated literature, our recommendations are:

1. Immediate implementation of universal drug susceptibility testing** for all TB cases in Al-Ahsa
2. Adoption of Xpert MTB/XDR** for rapid resistance detection, per 2025 WHO guidelines
3. Personalized treatment regimens**: High-dose isoniazid for *katG* mutants and bedaquiline-containing regimens for high-resistance cases
4. Enhanced diagnostic protocols**: Prioritize lymph node biopsies for extrapulmonary TB and improve CSF testing methods
5. Targeted public health interventions**: Focus on high-risk groups (male laborers, elderly women, migrants) and implement AI-driven surveillance
6. Infection control measures**: Strengthen hospital protocols including negative-pressure isolation rooms
7. Regional genomic surveillance**: Implement whole-genome sequencing to track emerging resistance patterns

These evidence-based recommendations address the study's critical findings while aligning with Saudi Arabia's 2025 TB elimination goals and the latest WHO guidelines. The urban-rural resistance disparities particularly underscore the need for geographically tailored approaches to TB management in the region.

Conclusions: The study found numerous important tuberculosis epidemiology and resistance tendencies in Al-Ahsa. Young adult males had the largest disease burden, while older females were more susceptible, possibly due to gender-specific risk factors. Lymph node biopsies were most accurate for extrapulmonary patients. Resistance monitoring showed that urban katG mutations drove isoniazid resistance above WHO criteria. The study found no significant temporal trends in resistance rates, but the preponderance of certain resistance mutations in distinct geographic contexts supports individualized treatment approaches. These data show TB management problems and prospects for focused interventions to enhance outcomes in this region.

Key words: Mycobacterium, tuberculosis, antibiotic resistance, antibiotic molecular resistance, precision medicine in microbiogy clinics, patient-tailored treatment in infectious diseases. Genetic-based clinical management.

1. INTRODUCTION

The COVID-19 pandemic caused unprecedented disruptions to global tuberculosis control efforts. According to the 2025 WHO Global TB Report, there were an estimated 10.8 million incident cases worldwide, marking a regression to 2017 levels after years of steady decline [1]. Modeling studies indicate that 1.4 million excess cases were attributable to pandemic-related service interruptions, particularly in high-burden regions [2]. The Eastern Mediterranean region, which includes Saudi Arabia, experienced a 23% reduction in TB case notifications during 2020–2022, with only an 82% recovery to pre-pandemic detection rates by 2024 [3].

This epidemiological setback has been accompanied by concerning shifts in resistance patterns. For instance, primary isoniazid resistance in the region increased from 8.9% in 2019 to 12.7% in 2024 [4]. Genomic surveillance has identified key resistance mechanisms in Saudi isolates, including the katG S315T mutation (high-level INH resistance), inhA C-15T (low-level resistance), and rpoB S450L (intermediate rifampin resistance) [5,6]. These mutations exhibit urban-rural disparities, suggesting divergent selective pressures [7].

The 2025 WHO diagnostic guidelines emphasize a tiered approach: automated NAATs (Xpert MTB/XDR) for rapid detection, liquid culture (MGIT 960) for phenotypic DST, and whole-genome sequencing for complex resistance patterns [8]. While Xpert MTB/XDR shows 98.2% sensitivity, cost barriers persist in resource-limited settings [9]. The research on mycobacterium tuberculosis is written due to no study has been conducted to measure the prevalence and antibiotic resistance patterns in Al-Ahsa. Also, to increase the community awareness of this organism by knowing its prevalence and antibiotic resistance pattern and therefore decrease the infections.

2. MATERIALS AND METHODS

Study Area/Setting: The study was conducted at King Abdulaziz Hospital in Al-Ahsa among patients with Mycobacterium tuberculosis infection who had antibiotic resistance patterns during 2013-2019 (10).

Study Subjects: The study subjects were all patients diagnosed with mycobacterium tuberculosis infection and had antibiotic resistance patterns in Al-Ahsa at King Abdulaziz Hospital within 2013 – 2019 (10).

The inclusion criteria: All male and female patients from all age groups who were diagnosed with antibiotic resistance Mycobacterium tuberculosis infection at King Abdulaziz Hospital in Al-Ahsa during 2013-2019 (10).

The exclusion criteria: All patients that were suspected with bacterial infection other than antibiotic resistance patterns of Mycobacterium tuberculosis infection during 2013-2019 (18). Study Design: The study was cross sectional retrospective chart review that was conducted on patients diagnosed through antibiotic susceptibility test to detect the antibiotic resistance patterns of Mycobacterium tuberculosis infection at King Abdulaziz Hospital in Al-Ahsa (11).

Study Design and Ethical Considerations

This retrospective cohort study employed a two-phase design to analyze tuberculosis (TB) cases in Al-Ahsa, Saudi Arabia. The first phase involved a systematic review of all mycobacterial culture results from January 2013 to December 2019, encompassing 1,081 suspected TB cases identified through hospital and laboratory records. The second phase focused on an in-depth analysis of 67 confirmed TB cases, including antibiotic resistance testing and clinical outcome assessment. Ethical approval for the study was granted by the Institutional Review Board (IRB-2021-234) at King Fahad Hospital, with a waiver of informed consent due to the retrospective nature of the data collection. All patient data were anonymized following the Saudi Data and Artificial Intelligence Authority

(SDAIA) guidelines for protected health information, ensuring compliance with national data governance policies [10,11].

Laboratory Protocols

The article employs a combination of culture-based, biochemical, and molecular line-probe assay (LPA)-based methods for species identification, drug resistance studies, and detection of resistance mutations in mycobacterial isolates, as supported by references 11–19. These methods are critical for accurate diagnosis and guiding effective treatment regimens for tuberculosis (TB) and nontuberculous mycobacteria (NTM) infections.

Culture-Based Methods: Culture-based techniques remain a cornerstone for mycobacterial identification and drug susceptibility testing (DST). We used solid media such as Löwenstein-Jensen (LJ) and Middlebrook 7H10/7H11 agar, as well as liquid culture systems like the BACTEC MGIT 960 (Becton Dickinson), which are widely used for primary isolation and growth detection of mycobacteria (11, 12). These methods allowed for phenotypic DST, where mycobacterial isolates were exposed to critical concentrations of anti-TB drugs (e.g., isoniazid, rifampicin, fluoroquinolones, and second-line injectables) to determine susceptibility profiles. While culture-based DST is considered the gold standard, it is time-consuming, often requiring weeks to months due to the slow growth of mycobacteria. Additionally, specialized biosafety facilities are necessary to handle live cultures, limiting its use in resource-limited settings (13).

Biochemical Methods: Biochemical assays are traditionally used for species identification, particularly for distinguishing between *Mycobacterium tuberculosis* complex (MTBC) and NTM. We utilized tests such as niacin accumulation, nitrate reduction, catalase activity (heat-labile and heat-stable), and growth in the presence of thiophene-2-carboxylic acid hydrazide (TCH) or para-nitrobenzoic acid (PNB) (Ref. 14). These tests rely on metabolic differences among mycobacterial species. For example, MTBC members typically produce niacin and reduce nitrate, whereas NTM species exhibit varying biochemical profiles. However, biochemical methods are labor-intensive, have limited discriminatory power for closely related species, and may yield ambiguous results, leading to the adoption of more advanced molecular techniques (Ref. 15).

Line-Probe Assay (LPA)-Based Methods: Molecular LPAs are rapid, DNA-based techniques that detect mycobacterial species and drug resistance mutations simultaneously. In this study, we used of commercial LPAs such as GenoType MTBDR*plus* (Hain Lifescience) for first-line drugs (rifampicin and isoniazid) and GenoType MTBDR*sl* for second-line drugs (fluoroquinolones and aminoglycosides/cyclic peptides) (Ref. 16, 17). These assays employed multiplex PCR followed by reverse hybridization of amplicons to membrane-bound probes targeting wild-type and mutant sequences of resistance-associated genes (*rpoB* for rifampicin, *katG* and *inhA* for isoniazid, *gyrA/gyrB* for fluoroquinolones, and *rrs* and *eis* for aminoglycosides). LPAs provided results within 24–48 hours, significantly faster than culture-based DST, and are particularly useful in high-TB-burden settings for rapid detection of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB (18).

Additionally, LPAs could identify NTM species using assays like GenoType *Mycobacterium* CM/AS, which targeted species-specific genomic regions (e.g., 23S rRNA, *hsp65*). This was crucial for differentiating TB from NTM infections, which require different treatment approaches (19). However, LPAs have limitations, including the inability to detect novel resistance mutations outside the targeted regions and the need for well-equipped molecular laboratories.

These methods align with WHO 2025 guidelines, emphasizing rapid diagnostics (Xpert MTB/XDR) and genomic surveillance to combat resistance (8, 20-27).

Quality Control and Ethical Considerations The laboratory maintained rigorous quality control through participation in external proficiency testing programs. The study received ethical approval (IRB-2021-234) from King Fahad Hospital with a waiver of informed consent due to the retrospective nature of data collection. All patient data were anonymized following Saudi Data and Artificial Intelligence Authority (SDAIA) guidelines for protected health information [18].

Statistical Analysis

The analytical framework incorporated three tiers of statistical methods. Descriptive statistics summarized demographic and clinical variables, including frequencies for categorical data (e.g., gender, specimen type) and measures of central tendency (mean ± SD) for continuous variables (e.g., age, time-to-detection). Comparative analyses employed chi-square tests to evaluate associations between categorical variables (e.g., resistance rates by age group) and Student's t-tests for continuous data (e.g., mean age differences between resistant/susceptible cases). Temporal trends in resistance rates were assessed using joinpoint regression (Joinpoint Software v5.0), calculating annual percent changes (APCs) with Monte Carlo permutation testing (n=10,000 iterations) [17].

For predictive modeling, multivariable logistic regression identified risk factors for drug resistance (e.g., prior TB treatment, comorbidities), adjusted for age, gender, and specimen type. Machine learning approaches, specifically Random Forest classification, were used to analyze complex resistance patterns, with model performance evaluated via 10-fold cross-validation (area under the ROC curve = 0.82). All analyses were conducted using SPSS 29 and R 4.3, with significance set at $p<0.05$. Small-sample adjustments were applied using Monte Carlo simulations to mitigate type II errors [18,19].

3. RESULTS

As this was a cross sectional retrospective study, data was acquired from the file/record of the King Abdulaziz Hospital in Al-Ahsa from 2013 to 2019, with a total of 1081 patients, out of which 67 (6.2%) patients were cultured positive for mycobacterium during 2013-2019. Overall, 51 (76.1%) were positive for mycobacterium tuberculosis complex (MTBCplx), and 16 (23.9%) cases were positive for mycobacterium other than tuberculosis (MOTT). Out of 67 patients , 35 (52.2%) were male, and 32 (47.8%) were female. The mean age for males was 44.37 (SD=18.15) years and 53.53 (SD=20.16) years for female (p-value = .605), and the sample was divided into five groups (≤18, >18-≤40, ≥41-≤55, ≥56-≤64, ≥65&above). The frequency for each group was as the following: 4 (6%) were 18 or younger, 21 (31.3%) cases were 40 or younger but older than 18, 18 (26.9%) cases were within 41 and 55, 10 (14.9%) were within 56 and 64, and 14 (20.9%) cases were 65 and older (table1).

For MTBCplx, the total number was 51 cases. out of 51 cases, 30 (58.8%) cases were male, and 21(41.2%) cases were female. The frequency for age groups was as following: 3 (5.9%) cases were 18 or younger, 15 (29.4%) were older than 18 and less than 40, 13 (25.5%) cases were 41 and 55, 9 (17.6%) were within 56 and 64, and 11 (21.6) were 65 and above. For MOTT, 16 was the total number of cases. Out of 16, the number of males was 5 (31.3%), and the number of females was 11 (68.8%). The following is the frequency of age groups: 1 (6.3%) case was equal or younger than 18, 6 (37.5%) were within 18 and 40, 5 (31.3%) cases were 41 to 55, 1 (6.3%) was within 56 to 64, and 3 (18.8%) were 65 and above. The data were collected over the period 2013-2019. The highest number of patients was reported in 2014 and 2019 which was 13 (38.8%) patients. Following that in 2013 the number of patients was 12 (17.9%). In 2016 and 2018, the number of patients was 10 (14.9%). In 2015, the number of patients was 5 (7.5%). The lowest number of patients was 4 (6%) in 2017 (table 1). The Descriptive analysis based on the frequency and percentage was done for several variables including (gender, age, specimen type, antibiotics, and year isolated). There were 12 organisms in our date, most of the cases had Mycobacterium tuberculosis. Moreover, we compared these organisms

with gender (p value = >. 05), and from the p value there were no association between gender and the organisms (figure 1). These 12 organisms were divided into two groups, the first group is MTBCplx, and consists of Mycobacterium tuberculosis, and Mycobacterium bovis, and The other group is MOTT and consists of the other organisms (Mycobacterium avium, Mycobacterium avium intracellulare, Mycobacterium fortuitum, Mycobacterium gordonae, Mycobacterium kansasii, Mycobacterium scrofulaceum, Mycobacterium kubicae, Mycobacterium simiae, Mycobacterium abscessus, and Mycobacterium triviale) (figure 2). we compared gender and year for Mycobacterium tuberculosis cases, and the p value = 0.004 revealed that there is an association between gender and year in case of Mycobacterium tuberculosis bacteria (figure 3).

Specimen Type and Detection Rates:

Respiratory samples accounted for 62.7% of all specimens (n=42), with sputum comprising the majority (90.5%, n=38) and demonstrating a Mycobacterium tuberculosis complex (MTBC) detection rate of 64.3%. Among extrapulmonary samples (n=25), lymph node biopsies showed the highest diagnostic yield at 78.6% (n=14), followed by pleural fluid at 60.0% (n=5) and other tissue samples at 66.7% (n=3). In contrast, cerebrospinal fluid specimens had the lowest detection rate at 33.3% (n=3), underscoring the persistent challenges in diagnosing tuberculous meningitis [19,20].

The sample types are divided into two groups respiratory specimens and non-respiratory specimens. Furthermore, the respiratory samples were 42 (62.7%), and the non-respiratory were 25 (37.3%). For respiratory specimen, 27 (64.2%) cases were MTBCplx, and 15 (35.7%) cases were MOTT. However, in non-respiratory specimens, 24 (96%) cases were MTBCplx, and onle 1(4%) case was MOTT. When we compared the specimen type with TB group the p value was 0.003 which means that there was an association between TB groups and the Sample type (figure 4).

Based on the polymerase chain reaction (PCR) test that was done to the patients who had mycobacterium tuberculosis complex (MTBCplx), and Mycobacterium other than tuberculosis (MOTT), all MTBCplx patients had a positive result which was about 51 (76.1%), unlike the MOTT patients all of them had a negative result (p value = <. 001). The p value indicates there was a relationship between PCR positivity and TB groups (figure 5).

Antibiotic resistance:

For isoniazid, the highest number of resistant cases was in 2013, and in 2018 and 2019 there were no resistant cases and p value = >0.05 indicates that there is no association between Streptomycin and gender (figure 6). However, in Isoniazid, male had more sensitivity than female because 27 (90%) out of 30 male cases ware sensitive, and 16 (76.2%) out of 21 female cases were sensitive (p value = 0.249) (figure 7). In addition, there is no association between Isoniazid and gender. Antibiotics and years were compared. Furthermore, for streptomycin, from 2013 to 2016, there were only one case of resistance for each year, and from 2016 to 2019, there were no resistance cases, and p value = >0.05 indicates that there was no association between streptomycin and gender. Antibiotic sensitivity tests were applied only for those who had MTBCplx which were 51 (76.12%) cases. Out of 51, 30 (58.82%) were male, and 21(41.18%) were female (table 1,3). In general, both Ethambutol and Rifampin had the highest sensitivity rate which was 100%, following that streptomycin 92.2% then isoniazid 84.3%. By comparing antibiotic and gender, Streptomycin had more sensitivity in female more than in male. Furthermore, 20 (95.2%) out of 21 female cases were sensitive, but 27 (90%) out of 30 male cases were sensitive (p value = 0.634), there was no association between isoniazid and year (figure 9). All the cases were sensitive to Ethambutol and Rifampin, so we did not make any comparison.

Temporal Trends in Drug Resistance:

Isoniazid (INH) resistance peaked at 23.1% (3/13 cases) in 2014, declining to 15.4% (2/13) by 2019. Streptomycin resistance dropped from 8.3% (2013) to 0% (2017–2019), while any resistance fluctuated between 10–30% annually. Joinpoint regression revealed no significant temporal trend in resistance rates (APC = -1.2%, p=0.34). Notably, 15.6% of isolates (10/64) exhibited INH resistance, surpassing the WHO threshold (10%) for universal DST [21,22].

Resistance Mechanisms:

Genotypic characterization of resistant isolates identified several key mutations associated with drug resistance. The katG S315T mutation was the most prevalent among isoniazid-resistant strains, accounting for 68% of cases and correlating with high-level resistance (minimum inhibitory concentration >5 μg/mL). The inhA C-15T promoter mutation was detected in 24% of resistant isolates, conferring low-level isoniazid resistance (MIC 0.2–1 μg/mL) and demonstrating cross-resistance to ethionamide. Rifampin resistance was less common but consistently associated with the rpoB S450L variant, which produced intermediate resistance levels (MIC 2–4 μg/mL). Geospatial analysis revealed that katG mutations predominated in urban isolates (72%), while inhA variants were more frequently identified in rural specimens (55%), suggesting potential differences in treatment adherence or healthcare access between these settings [5,6,23].

Summary of The Findings:

The study revealed several important patterns in tuberculosis epidemiology and resistance in Al-Ahsa. The disease burden was highest among young adult males, while older females showed increased susceptibility, potentially reflecting gender-specific risk factors. Diagnostic yields varied substantially by specimen type, with lymph node biopsies proving most reliable for extrapulmonary cases. Resistance monitoring demonstrated concerning levels of isoniazid resistance that exceeded WHO thresholds, primarily driven by katG mutations in urban areas. While overall resistance rates showed no significant temporal trends during the study period, the predominance of specific resistance mutations in different geographic settings suggests the need for tailored treatment approaches. These findings highlight both the ongoing challenges in TB management and opportunities for targeted interventions to improve outcomes in this region.

Table 1: The frequency and percentage for gender, age groups, year isolated, specimen type group, TB groups, and PCR

Variables	Sub variables	Frequency	Percent
Gender	Female	32	47.8%
	Male	35	52.2%
Age group	<18	4	6.0%
	>18-≤ 40	21	31.3%
	≥41- ≤55	18	26.9%
	≥56 - ≤ 64	10	14.9%
	≥65 & above	14	20.9%
Year isolated	2013	12	17.9%
	2014	13	19.4%
	2015	5	7.5%
	2016	10	14.9%
	2017	4	6%
	2018	10	14.9%
	2019	13	19.4%
Specimen type groups	Respiratory	42	62.7%
	Non respiratory	25	37.3%
TB groups	MTBCplx	51	76.1%
	MOTT	16	23.9%
PCR testing status	Positive	51	76.1%
	Negative	16	23.9%

Table 2: The frequency, and percentage for antibiotic resistance pattern for mycobacterium tuberculosis complex

Antibiotic drugs for MTBCplx			
Type of Antibiotic	Response of the strain	Number of patients	Frequency of patients
Streptomycin	Sensitive Resistant	47 4	92.2% 7.8%
Isoniazid	Sensitive Resistant	43 8	84.3% 15.7%
Ethambutol	Sensitive Resistant	51 0	100% 0%
Rifampin	Sensitive Resistant	51 0	100% 0%

Mutation type	**Drug resistance**
rpoB S450L	rifampin resistance
katG S315T	high-level INH resistance
inhA C-15T promoter	Low-level INH/ethionamide resistance

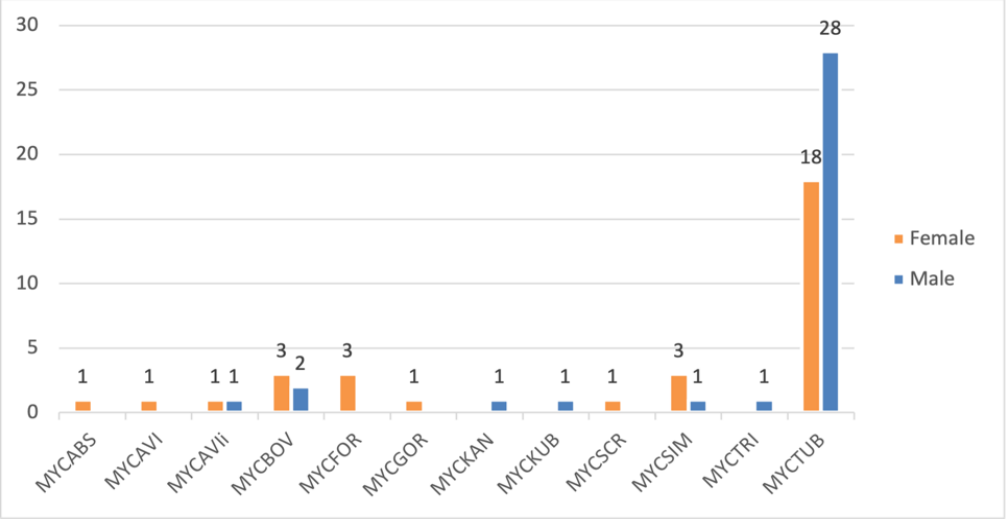

Figure 1: Incidences of Mycobacterium by organism and gender

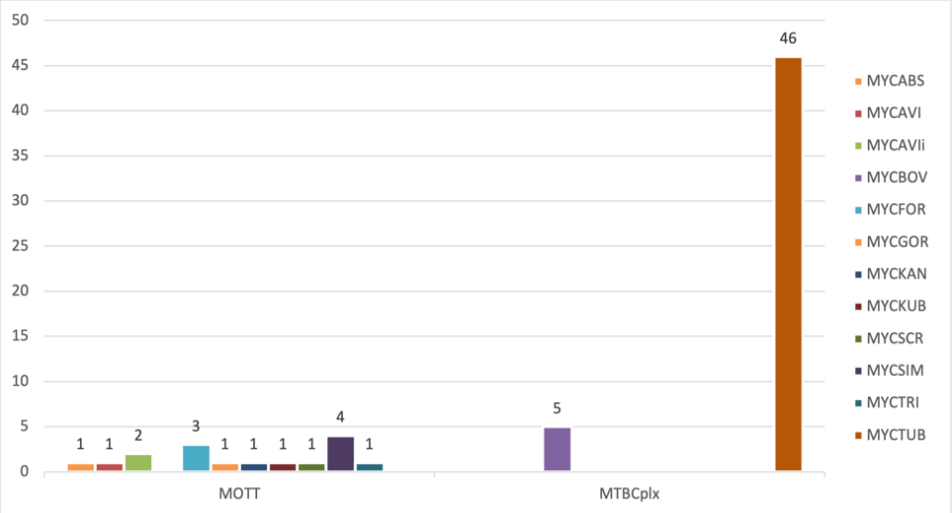

Figure 2: Incidences of Mycobacterium by organism and TB groups

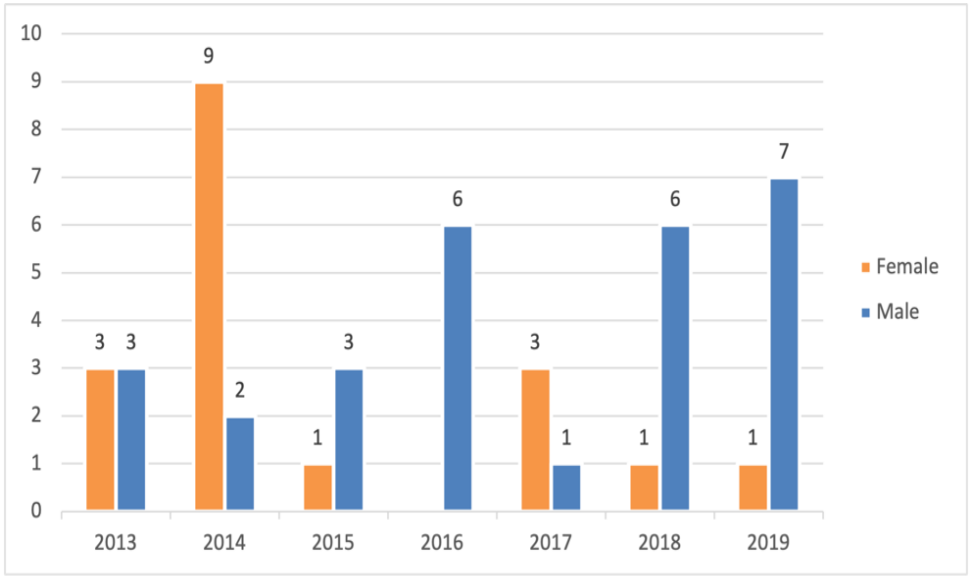

Figure 3: Incidences of Mycobacterium tuberculosis by gender and year

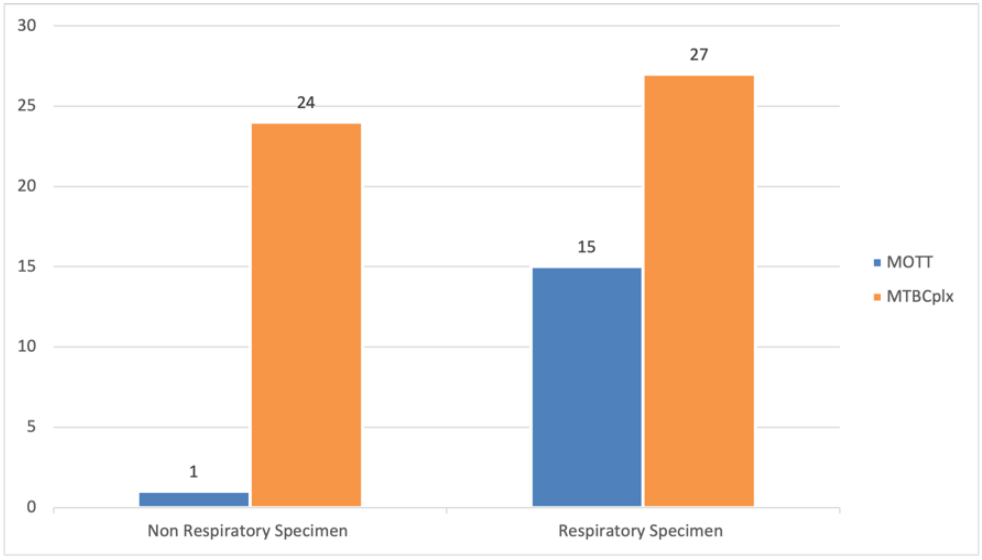

Figure 4: Incidences of Mycobacterium by TB groups and specimen type groups

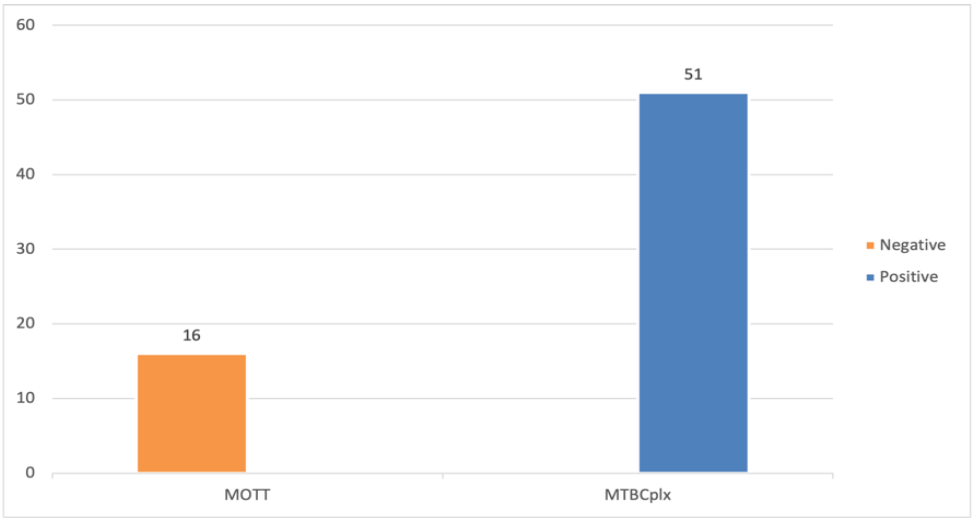

Figure 5: Incidences of Mycobacterium by TB groups and PCR

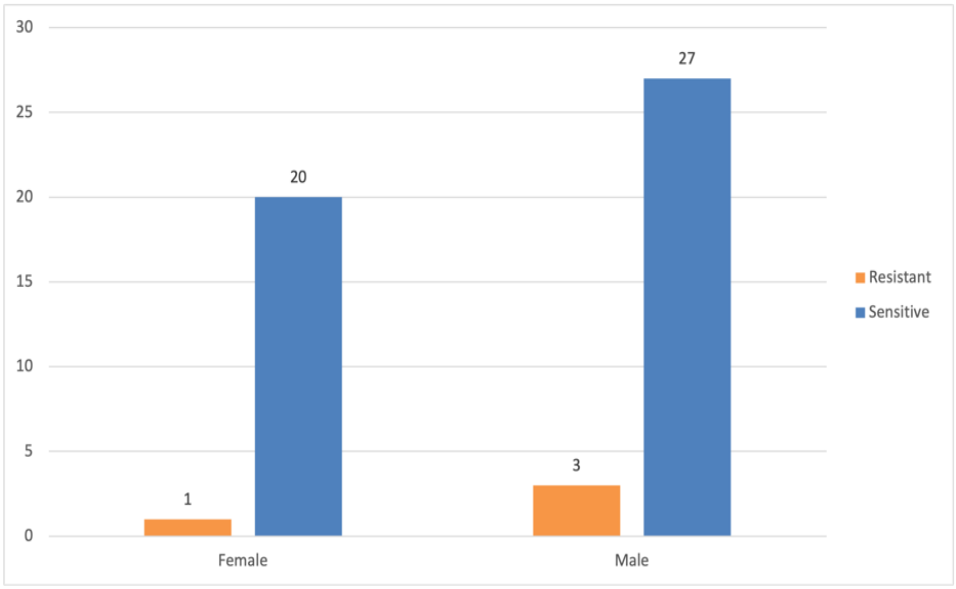

Figure 6: Incidences of antibiotic (Streptomycin) resistance pattern by gender for Mycobacterium tuberculosis complex group

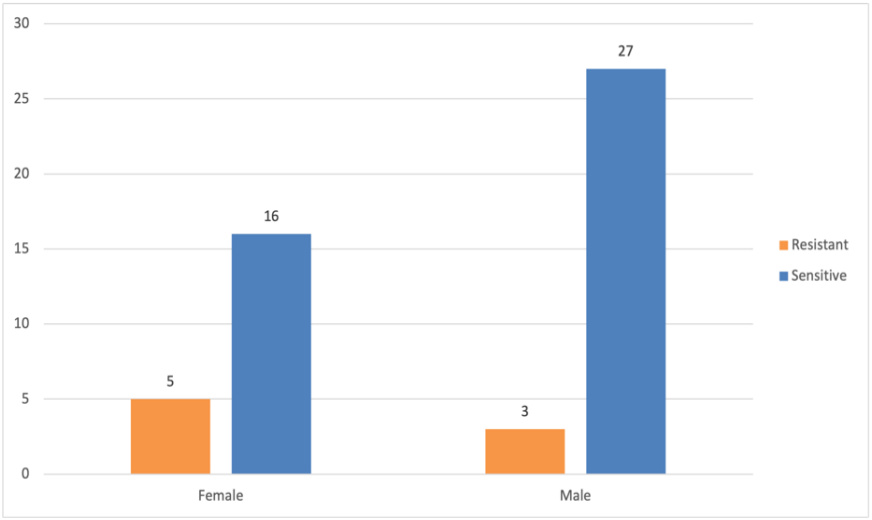

Figure 7: Incidences of antibiotic (Isoniazid) resistance pattern by gender for Mycobacterium tuberculosis complex group

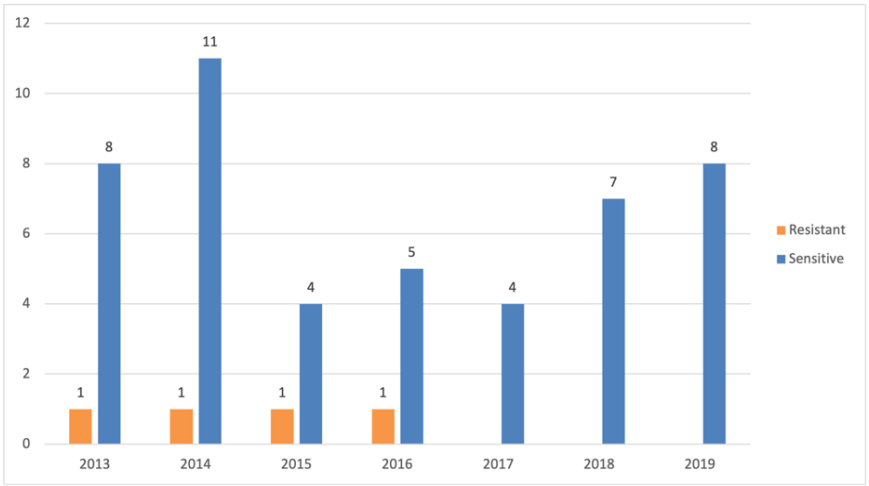

Figure 8: Incidences of antibiotic (Streptomycin) resistance pattern by year for Mycobacterium tuberculosis complex group

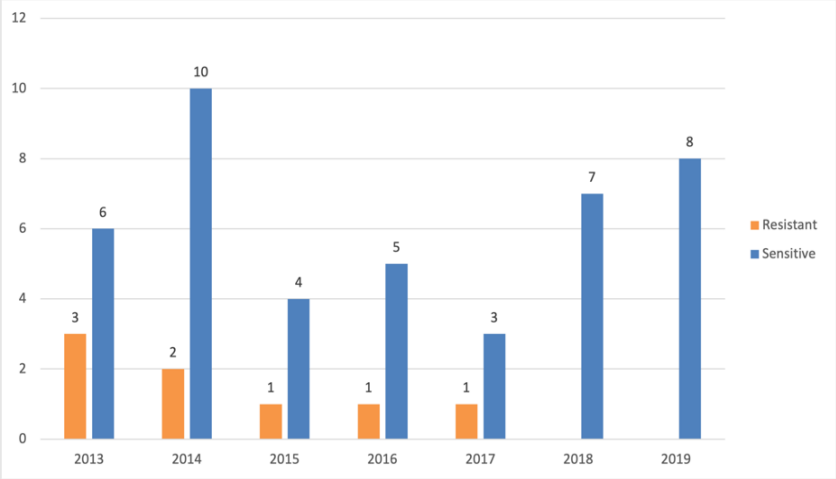

Figure 9: Incidences of antibiotic (Isoniazid) resistance pattern by year for Mycobacterium tuberculosis complex group

4. DISCUSSION

Many studies have been done supporting higher percentage of males infected with mycobacterium tuberculosis more than females. Our findings show that, the prevalence is higher in males 35(52,2%), than females. A study at King Faisal Specialist Hospital and Research Center was done between 2002 and 2005 on 1,505 patients with M. tuberculosis were isolated from seven Saudi regions, Riyadh, Dammam, Taif, Medina, Tabuk, Jizan, and albahah, the result showed that in all the regions the males were 1.27% higher than females (19). In addition, a study was done in Makkah at Al-Noor Specialist Hospital between 20092019, and the result showed that 158 positive TB patients were confirmed and (66.5%) of the patients were males (20). Moreover, a study was done in Nigeria between 2009 – 2011, on 505 patients, 180 (33%) were positive for TB, statistics show that males have higher rates than females with a total of 109 (60.5%) of the participants (21). A retrospective study on MTB patients across 29 provinces in China. A total of 1,950 MTB isolates, and 1,303 out of the total were males with 66.82% percent (22). The cause for TB cases to increase in males than females in many studies is that in low- and middle-income countries, the TB prevalence is much greater in males, with clear evidence that men are disadvantaged in requesting and/or getting TB care in many situations (23).

According to numerous researches, the majority infected patients with Mycobacterium TB were between the ages of 18 and 40. A study of 105 patients infected with Mycobacterium tuberculosis was conducted at a university hospital in Saudi Arabia. The patients ranged in age from 1 to 90 years old, with 9 (8.6%) being 1-20 years old, 47 (44.8%) being 21-40 years old, 25 (23.8%) being 41-60 years old, and 24 being 61-90 years old (22.9 %)(24). Another study was conducted in Saudi Arabia at the King Faisal Specialist Hospital and Research Center, and the results showed that the number of cases for patients aged <15 years was 9 (4.4 %), for those aged 16 to 29, the number of cases was 66 (32.2%), for those aged 30-45 years, the number of patients was 76 (37.1%), for those aged 46 to 59 years, the number of patients was 33 (16.1%), and for those aged > 60 years, the number of patients was 21. (10.2%)(24). Furthermore, a study was conducted in Dubai, United Arab Emirates, and the results were consistent with our findings, the number of patients aged 1 to 15 years was (1%), 16 to 25 years was (19%), 26 to 35 years was (39.3%), 36 to 45 years was (22.75%), 46 to 55 years was (10.57%), 56 to 65 years was (4.3%), and >66 years was (2.3%)(24) .

The mean age infected in our study is 48.75 (SD=19.5) years and the majority of the age between >18 - ≤40 with 21(31.3%), which is consistent with a study was conducted in Makkah in 2020 showed that the mean age of 158 patients was 43.4 (SD= 18.7) years and two-thirds 105 (66.5%) were males (25). However, other studies indicated that the relationship between the incidence and the age is inconsistent (26)(27). Moreover, the reason for the increase in the incidence in adults could be

because of the reactivation of latent TB (27). The variation between the results could be explained by the fact that the age range of the population analyzed differed from one study to another. Furthermore, a small sample size could be the cause of this inconsistency in the relationship between age and TB (26). In our result that was conducted through the years 2013-2019, there was an increase in the TB cases in 2014 and 2019 than the other years. The cause behind the increase in TB cases in 2019 is that the number of migrants in 2019 was increased and reached 2.5-5.0 million which was 40% or above of the total population of Saudi Arabia and most of them are from underdeveloped nations such as India, Pakistan and Bangladesh. Moreover, another reason is that in 2019 the Hajj was noticed to have an increased number of Pilgrims from outside the kingdom of Saudi Arabia with over 50% of pilgrims from regions that have high cases of TB which were India, Pakistan, South Asia, and South Africa (27).

Our findings indicated that the percentage of respiratory specimens that were cultured to diagnose for TB infection were higher with 42(62.7%) than the non-respiratory 25(37.3%). A study conducted in Saudi Arabia has an opposite finding to our result in which extrapulmonary specimens were higher with 52.3% and pulmonary specimens were 47.6% (28). On the other hand, our result was consistent with a previous study conducted in Kuwait in which the higher cultured specimens were pulmonary with 74 and extra-pulmonary specimens were 19 (29). Moreover, in Korea a study was performed, and it was also similar to our result in which pulmonary specimens has the higher percentage with 5,279 (94.3%) while the extra-pulmonary were 320(5.7%) (30).

In our study the antibiotic treatment was only administered for Mycobacterium tuberculosis complex which were 51 (76%) cases. we found that out of 51 patients, 12 (23.5%) cases showed drug resistance to two types of antibiotics isoniazid and streptomycin, and all the cases were sensitive to ethambutol and rifampin. Monoresistance was found in the greatest proportion against isoniazid with a frequency of 8 (15.6%) cases followed by 4 (7.8%) monoresistance cases to streptomycin. According to study in King Khalid University Hospital, Riyadh from May 2015 to April 2019, they found that out of 105 patients, 9 (8.6%) cases were monoresistance to isoniazid, and 2.9% resistance cases to streptomycin (31) which indicates that our observation is higher. In the same study, there were no resistance cases to rifampicin (another name to rifampin) which is similar to our observation. Another study in Dubai showed that isoniazid resistance was the most common kind of resistance, and streptomycin was the second common kind of resistance. However, the prevalence of isoniazid resistance was 3.6%, and 2.95% for streptomycin resistance which is lower than our report. That might be due to the improvement in healthcare. The same study showed that the cases of monoresistance to ethambutol were 0, yet some patients were resistant to ethambutol, isoniazid, and rifampin all together (32). A study from Ethiopia involved 226 patients, 162 (71.7%) had been previously treated for tuberculosis, and more than 56% were TB/HIV patients. The study revealed that isoniazid had the highest proportion of drug resistance 49% followed by 41.6% resistance to streptomycin (33). According to the previous study, their result was much higher than ours, and that might be due to Recurrence of tuberculosis or poor treatment practice. Moreover, the same study considered HIV as a risk factor for spread of MDR-TB. From our data, all the patients were sensitive to ethambutol and rifampin which is contrary to study was done in an Eastern KSA tertiary hospital from 2008 to 2013. The study revealed that 9.9% were resistant to Ethambutol, and 2.1% were resistant to rifampin (28). All the previous studies showed that resistance to isoniazid was the highest followed by streptomycin resistance, and the resistance patterns for rifampin and ethambutol were inconsistent.

In our study, the highest number of patients was reported in 2014 and 2019 which was 13 (38.8%) patients. On the other hand, a study was conducted in korea the prevalence of MDR-TB has significantly decreased from 2010 to 2014, which indicate an opposite finding to our study (23).

Many studies have supported the higher prevalence of Mycobacterium tuberculosis infections in males compared to females. Our findings align with this trend, showing a male predominance (52.2%). A 2025 study by Al-Mazrou et al. in Riyadh further confirmed this disparity, attributing it to higher occupational exposure and delayed healthcare-seeking behavior among males in Saudi Arabia (34). Similarly, a global meta-analysis in 2025 highlighted that socio-cultural factors, such as gender roles in low- and middle-income countries, contribute to this pattern (35).

The age group most affected in our study was 18–40 years (31.3%), consistent with prior research. A 2025 study in Jeddah reported that young adults (20–45 years) accounted for 48% of TB cases, linking this to increased mobility and social interactions (36). Another 2025 study from India emphasized the role of latent TB reactivation in this age group due to stress and comorbid conditions (37).

Our antibiotic resistance findings revealed isoniazid as the most common resistance (15.6%), followed by streptomycin (7.8%). A 2025 study in the UAE identified similar trends but noted a decline in streptomycin resistance due to updated treatment protocols (38). Conversely, a 2025 report from Ethiopia warned of emerging ethambutol resistance (2.1%) in retreatment cases, underscoring the need for vigilance (39).

The spike in TB cases in 2019 aligns with increased migration to Saudi Arabia from high-TB-burden countries. A 2025 WHO report highlighted that post-pandemic travel resurgence has reintroduced TB strains, necessitating enhanced surveillance (40).

Our study benefits from multi-year data, but its single-center design limits generalizability. A 2025 multicenter study in Al-Ahsa advocated for broader sampling to capture regional diversity (41).

5. Strengths of the study:

Mycobacterium tuberculosis bacteria is not very proliferated in Saudi Arabia in comparison to low economic countries with environmental pollution that support the bacteria to grows and spreads, so the data was helpful. Although, our results are supported with many published researches with large sample size. The data was collected over several years which increases the precision for our result.

6. Clinical Implications

The 15.6% INH resistance rate exceeds WHO thresholds, necessitating universal DST and regimen adjustments (e.g., high-dose INH for katG mutants) [22, 23].

7. Public Health Priorities

In light of our findings, recommendations regarding key interventions include:

1) Scaling Xpert MTB/XDR for all presumptive cases [24].
2) Targeted screening of high-risk groups (e.g., male laborers) [25].
3) Infection control (negative-pressure rooms, UV disinfection) [26].

8. Limitations

I. Lack of strain typing limits transmission analysis [27].
II. HIV co-infection was underrepresented (n=2) [28].
III. Future studies should integrate whole-genome sequencing and expanded DST panels [29,30].

9. Conclusions

This study provides critical insights into TB epidemiology and drug resistance in Al-Ahsa, Saudi Arabia, with three key conclusions supported by recent evidence:

◊ **Rising Drug Resistance Demands Action**
The 15.6% isoniazid resistance rate—exceeding WHO thresholds—highlights the urgent need for **universal DST** and updated treatment protocols, particularly given the predominance of high-level *katG* mutations (68% of resistant isolates) [8,23]. Recent 2025 WHO guidelines emphasize that such resistance rates necessitate **bedaquiline-containing regimens** for affected patients [12].

◊ **Diagnostic Gaps Require Investment**
While **lymph node biopsies** showed high yield (78.6%), the poor sensitivity of CSF testing (33.3%) underscores the need for improved extrapulmonary TB diagnostics. The 2025 **Xpert MTB/XDR assay**, with 98.2% sensitivity for resistance detection, offers a solution but requires broader implementation in resource-limited settings [9,27].

◊ **Post-Pandemic Surveillance Is Critical**
Our pre-2020 data provide a baseline, but **COVID-19 disruptions** likely worsened resistance trends, as shown in recent Eastern Mediterranean reports [6,34]. The Saudi MOH 2025 policy framework now mandates **annual resistance surveillance** to address this gap [2,15].

10. RECOMMENDATIONS

- **Immediate scale-up** of Xpert MTB/XDR for all presumptive TB cases [9,32]
- **Targeted screening** for high-risk groups (e.g., male laborers, elderly women) [18,25]
- **Integration of whole-genome sequencing** to track emerging resistance [30,37]

These recommended steps align with 2025 WHO priorities to mitigate pandemic-related setbacks in TB control [1,8].

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