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Demographic Characteristics and Tuberculosis Drug-Resistance Patterns in Yemen: A 10-Year Retrospective Study of 482 Patients (2014–2023)

Nuha Abdul Aziz Al-Yousfi[1], Ibrahim Mohammed Amed Nahshal[2], Sami Mohammed Abdo Hassan[3], Emad Hassan Al-Shamahi[4], Khaled Abdul Karim Al-Moyed[2], Sami Sultan Ahmed Abdu[2], Nawal Mohammed Al-Hababi[3], Hassan Abdulwahab Al-Shamahy[2] and Abdulhafeedh Al-Habeet[5*]

[1]Department of Internal Medicine, Faculty of Medicine and Health Sciences, Sana'a University, Yemen

[2]Department of Medical Microbiology and Clinical Immunology, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a City, Yemen

[3]Department of Medical Microbiology and Clinical Immunology, Faculty of Medical Sciences, Al-Nasser University, Sana'a City, Yemen

[4]Department of Ophthalmology, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a City, Yemen

[5]Department of Epidemiology and Biostatistics, Faculty of Medical Sciences, Al-Razi University, Sana'a City, Yemen

ABSTRACT

Background: Drug-resistant tuberculosis (TB) remains a major public health challenge, particularly in resource-limited settings. This study aimed to characterize TB drug-resistance patterns and examine their associations with age and sex among patients in Yemen.

Methods: This retrospective cross-sectional study included 482 culture-confirmed TB patients who underwent drug susceptibility testing (DST) at the National Tuberculosis Institute in Sana'a, Yemen, between 2014 and 2023. Patients were classified as having non-multidrug-resistant TB (non-MDR-TB), multidrug-resistant TB (MDR-TB), or extensively drug-resistant TB (XDR-TB) according to recorded laboratory classifications. Resistance patterns were compared across age and sex groups.

Results: Of 482 patients, 308 (63.9%) were male and 174 (36.1%) were female. Overall, 393 (81.5%) were classified as non-MDR-TB, 83 (17.2%) as MDR-TB, and 6 (1.2%) as XDR-TB. Patients aged 21–30 years constituted the largest age group (46.9%), whereas the highest within-group MDR-TB proportion occurred among those aged 31–40 years (23.5%). MDR-TB proportions were similar in males (16.9%) and females (17.8%). Neither age ($p = 0.0718$) nor sex ($p = 0.177$) showed a statistically significant association with resistance classification.

Conclusions: MDR-TB represented a substantial proportion of patients undergoing DST, without statistically significant differences across age or sex groups. These findings highlight the need for strengthened drug-resistance surveillance and diagnostic services in Yemen.

***Corresponding author**
Abdulhafeedh Al-Habeet, Department of Epidemiology and Biostatistics, Faculty of Medical Sciences, Al-Razi University, Sana'a City, Yemen.

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Introduction

Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains a major global public health challenge, particularly in low- and middle-income countries with limited diagnostic and healthcare resources. Despite substantial progress in TB prevention, diagnosis, and treatment, the emergence and transmission of drug-resistant strains continue to threaten global TB control efforts. According to the World Health Organization (WHO), approximately 10.7 million people developed TB worldwide in 2024, resulting in an estimated 1.23 million deaths. Of particular concern, approximately 390,000 people developed multidrug-resistant or rifampicin-resistant tuberculosis (MDR/RR-TB), yet only 42% accessed appropriate treatment [1].

Drug-resistant TB presents substantial clinical and public health challenges because of its complex treatment requirements, potential for adverse drug reactions, and increased demands on healthcare systems. Multidrug-resistant tuberculosis (MDR-TB) is defined as TB caused by strains resistant to at least isoniazid and rifampicin, the two principal first-line anti-TB medications. More

advanced resistance patterns include pre-extensively drug-resistant TB (pre-XDR-TB), characterized by additional resistance to a fluoroquinolone, and extensively drug-resistant TB (XDR-TB), which additionally involves resistance to bedaquiline or linezolid [2]. Timely and accurate drug susceptibility testing (DST) is therefore essential for identifying resistance patterns, guiding appropriate treatment, and strengthening surveillance. Recent WHO recommendations emphasize expanding access to rapid molecular diagnostics and comprehensive testing for resistance to first- and second-line anti-TB drugs [3].

The distribution of drug-resistant TB varies considerably across populations and geographical settings. Previous TB treatment, inadequate treatment adherence, interruptions in drug availability, and weaknesses in TB control programmes have been associated with the emergence or detection of resistant disease. A worldwide systematic review and meta-analysis identified previous TB disease and a history of anti-TB treatment as important factors associated with MDR-TB [4]. Furthermore, a 2026 systematic review and meta-analysis from the Middle East and North Africa (MENA) region demonstrated substantial variation in MDR-TB prevalence across the included studies, highlighting the importance of locally generated epidemiological evidence [5]. Although demographic characteristics such as age and sex may be associated with differences in resistance patterns, these relationships require careful interpretation because they may be influenced by treatment history, healthcare access, and population characteristics.

In Yemen, TB control faces additional challenges associated with prolonged armed conflict, population displacement, economic instability, and disruptions to healthcare services. The ongoing humanitarian crisis has severely affected healthcare infrastructure, potentially compromising timely diagnosis, continuity of treatment, and disease surveillance [6]. Previous epidemiological research involving 92,482 registered TB cases across Yemen between 2006 and 2018 documented substantial geographical and demographic variation in TB occurrence [7]. Earlier national drug-resistance surveillance reported MDR-TB in 3.0% of newly diagnosed patients and 9.4% of previously treated patients [8]. Additionally, a multicenter Yemeni study conducted between 2014 and 2016 described the clinical characteristics, resistance patterns, and treatment outcomes of patients with MDR-TB, highlighting the continuing challenges of managing resistant disease in the country [9].

Although these studies have contributed valuable information, further characterization of drug-resistance patterns among patients undergoing DST is important, particularly over extended periods of healthcare disruption. Describing the distribution of resistant and non-multidrug-resistant isolates across demographic groups may help identify variations within tested populations and support improvements in diagnostic surveillance and TB control services. However, findings derived from patients selected for DST must be distinguished from population-level estimates of drug-resistance prevalence.

Therefore, this study aimed to characterize the distribution of M. tuberculosis drug-resistance patterns and examine their associations with age and sex among 482 culture-confirmed TB patients who underwent DST at the National Tuberculosis Institute in Sana'a, Yemen, between January 2014 and December 2023. By examining data collected over a 10-year period, the study seeks to provide additional laboratory-based epidemiological evidence relevant to drug-resistant TB surveillance and control in Yemen.

Patients and Methods

Study Design and Setting

This retrospective, record-based cross-sectional study was conducted using TB laboratory and clinical registry records from the National Tuberculosis Institute (NTI), Sana'a, Yemen. The study covered cases recorded between 1 January 2014 and 31 December 2023. The NTI serves as a facility for TB diagnosis and DST within the national TB control system.

Study Population and Eligibility Criteria

The study population comprised Yemeni patients with culture-confirmed TB whose isolates underwent DST during the study period. Records of non-Yemeni patients, cases with incomplete data, and specimens with contaminated cultures were excluded. All eligible records were included, yielding a study sample of 482 patient records.

Data Collection and Study Variables

Data were extracted retrospectively from laboratory records and the TB case registry. Recorded information included age, sex, place of residence, TB treatment history (new or previously treated cases), and DST findings. The demographic comparisons reported in this analysis were based on age and sex.

Age was classified into five groups (≤20, 21–30, 31–40, 41–50, and >50 years), and sex was recorded as male or female. Drug-resistance status was the categorical outcome for the demographic comparisons.

Specimen Processing, Culture and Identification

Sputum specimens were processed with 4% sodium hydroxide (NaOH) and homogenized by vigorous stirring. A 0.1-mL aliquot of the processed material was inoculated into each of two tubes containing 2% Kudoh medium. Cultures were incubated at 37 °C. They were examined in the first week and at four weeks, followed by weekly inspection for up to eight weeks before cultures without growth were reported as negative [10].

Mycobacterial isolates were identified on the basis of growth characteristics and colony morphology, together with niacin testing and susceptibility testing using p-nitrobenzoic acid.

Drug Susceptibility Testing

Phenotypic DST was performed using the proportion method on solid culture media. Löwenstein–Jensen (LJ) medium was used at the NTI, whereas Ogawa medium was used at another laboratory. Resistance was determined by comparing the proportion of colonies growing on drug-containing media with growth on drug-free control media. A critical proportion of 1% was used to classify resistance [8,11].

The reported critical concentrations were 0.2 µg/mL for isoniazid and 40 µg/mL for rifampicin; for streptomycin, 4.0 µg/mL on LJ medium and 10 µg/mL on Ogawa medium; and for ethambutol, 2.0 µg/mL on LJ medium and 2.5 µg/mL on Ogawa medium. Preliminary DST readings were obtained at weeks 2, 3, and 4.

Definitions and Classification of Drug Resistance

MDR-TB was defined as TB caused by M. tuberculosis isolates resistant to at least isoniazid and rifampicin, with or without resistance to other anti-TB drugs. For the analysis, isolates were assigned to three reported categories: XDR-TB, MDR-TB, and non-MDR-TB. The three categories were treated as mutually exclusive.

Statistical Analysis

Data were coded and analysed using IBM SPSS Statistics, version 27.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages. The distribution of TB drug-resistance categories was tabulated by age group and sex. Pearson's chi-square test was used to assess associations between categorical variables. All tests were two-sided, with statistical significance defined as $p < 0.05$.

Ethical Considerations

The study was approved by the Ethics Committee of the Faculty of Medicine and Health Sciences, Sana'a University. Patient information was extracted without personal identifiers to maintain confidentiality. An official request for permission to conduct the study was submitted to the NTI.

Results

Patient Characteristics and Overall Resistance Classification

Among 482 patients with culture-confirmed TB who underwent DST, 393 (81.5%) were classified as non-multidrug-resistant tuberculosis (non-MDR-TB), 83 (17.2%) as MDR-TB, and 6 (1.2%) as XDR-TB (Figure 1).

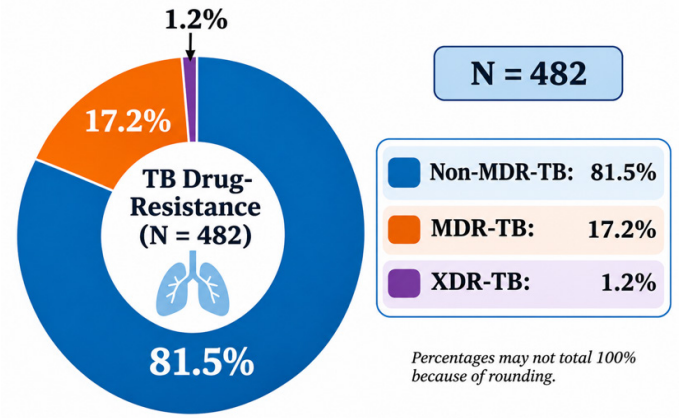


Figure 1: Percentage Distribution of Tuberculosis Drug-Resistance Classifications in the Overall Study Sample (N = 482)

Resistance Classifications by Age

Patients aged 21–30 years constituted the largest age group (46.9%; Figure 2). Within-group MDR-TB proportions were 23.5% at ages 31–40 years and 22.4% at ages 41–50 years, compared with 14.6% at ages 21–30 years. All six recorded XDR-TB cases occurred among patients aged 21–50 years. The overall association between age group and resistance classification did not reach statistical significance ($p = 0.0718$; Table 1).

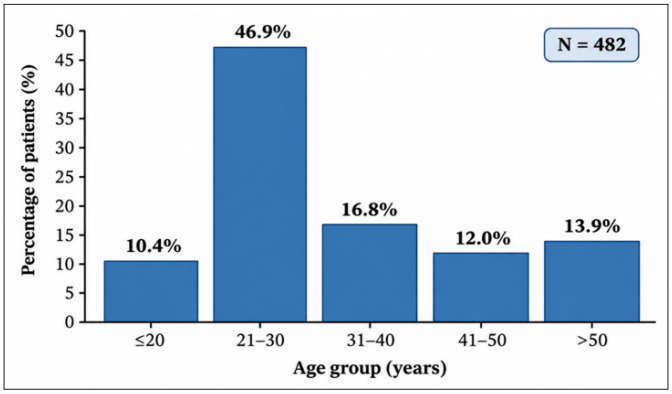


Figure 2: Age Distribution of Tuberculosis Patients in the Study Sample (N = 482)

Resistance Classifications by Sex

Male patients constituted 63.9% of the cohort (Figure 3), but the MDR-TB proportion was similar in males (16.9%) and females (17.8%). All six recorded XDR-TB cases occurred in males. The overall distribution of resistance classifications by sex was not statistically significant ($p = 0.177$; Table 1).

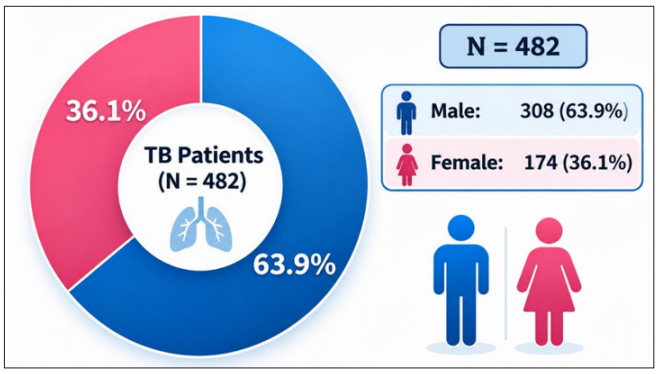


Figure 3: Sex Distribution of Tuberculosis Patients in the Study Sample (N = 482)

Table 1: Tuberculosis Drug-Resistance Classifications According to Age Group and Sex (N = 482).

Characteristic	Total n (%)	XDR-TB n (%)	XDR-TB n (%)	Non-MDR-TB n (%)	χ^2	p value
Age group (years)					14.407	0.0718
≤20	50 (10.4)	0 (0.0)	7 (14.0)	43 (86.0)		
21–30	226 (46.9)	1 (0.4)	33 (14.6)	192 (85.0)		
31–40	81 (16.8)	3 (3.7)	19 (23.5)	59 (72.8)		
41–50	58 (12.0)	2 (3.4)	13 (22.4)	43 (74.1)		
>50	67 (13.9)	0 (0.0)	11 (16.4)	56 (83.6)		
Sex					**3.46**	**0.177**
Male	308 (63.9)	6 (1.9)	52 (16.9)	250 (81.2)		
Female	174 (36.1)	0 (0.0)	31 (17.8)	143 (82.2)		
Total	482 (100.0)	6 (1.2)	83 (17.2)	393 (81.5)		

Note: Total-column percentages use N = 482 as the denominator; percentages within resistance columns use the respective age- or sex-group total. MDR-TB, multidrug-resistant tuberculosis; XDR-TB, extensively drug-resistant tuberculosis; non-MDR-TB, non-multidrug-resistant tuberculosis.

Discussion

This retrospective laboratory-based study characterized tuberculosis drug-resistance profiles among 482 culture-confirmed patients undergoing DST at the National Tuberculosis Institute in Sana'a between 2014 and 2023. Most records were categorized as non-MDR (81.5%), whereas 17.2% were categorized as MDR-TB and a further 1.2% were labelled XDR-TB. Although the distribution of resistance categories varied descriptively across age groups and sex, neither comparison reached the conventional

threshold for statistical significance. These findings describe the tested population and should not be interpreted as population-based estimates of the burden or determinants of drug-resistant TB in Yemen.

The proportion of MDR-TB observed in this selected laboratory population differs from that reported in Yemen's earlier nationwide drug-resistance survey. In the 2004 survey, Al-Akhali and colleagues reported MDR-TB in 3.0% of new TB cases and 9.4% of previously treated cases [8]. More recently, a systematic review and meta-analysis published in 2026 estimated a pooled MDR-TB prevalence of 3.54% across studies from the Middle East and North Africa, while documenting pronounced between-study heterogeneity [5]. Neither estimate is directly comparable with the present 17.2%, because the studies used different sampling frames and populations and, in the case of the earlier Yemeni survey, explicitly stratified patients by treatment history. The present data come from patients for whom culture and DST results were available; selective referral or testing of patients with suspected resistance may have increased the observed proportion of MDR-TB. Consequently, the difference cannot establish a temporal increase in MDR-TB in Yemen.

The largest share of patients in the current sample was aged 21–30 years, but this primarily reflects the age composition of the tested cohort rather than an age-specific risk of drug resistance. Within age groups, the recorded MDR-TB proportions were higher among patients aged 31–40 years and 41–50 years than among those aged 21–30 years. Nevertheless, the overall age-by-resistance comparison was not statistically significant (reported $p = 0.0718$), and the small number of records classified as XDR-TB limits the precision of comparisons across resistance categories. A worldwide meta-analysis identified previous TB and previous anti-TB treatment as prominent correlates of MDR-TB, whereas age was not consistently associated with resistance after pooling available evidence [4]. Thus, the descriptive age variation in the present cohort cannot establish an independent association, particularly without adjustment for prior treatment and other clinical factors.

Men accounted for nearly two-thirds of the included patients, yet the proportions categorized as MDR-TB were similar among men (16.9%) and women (17.8%). The reported overall comparison of resistance categories by sex was not statistically significant ($p = 0.177$). Although all six records labelled XDR-TB occurred among men, this small number is insufficient to infer a sex-related difference in advanced resistance. These observations are broadly compatible with the worldwide systematic review by Xi and colleagues, in which sex was not a consistent independent predictor of MDR-TB [4]. Moreover, differences in the numbers of male and female patients referred for testing may reflect health-service utilization and ascertainment rather than differences in biological susceptibility.

The interpretation of the XDR-TB subgroup warrants particular attention. The six records were labelled XDR-TB in the dataset, but confirmation of this designation requires documentation of relevant second-line DST and the case definition applied to each period.

The WHO revised the definition of XDR-TB in 2021 to require resistance to a fluoroquinolone and to bedaquiline or linezolid, in addition to rifampicin resistance, with or without isoniazid resistance [2]. Because the available methodological description documents testing of first-line drugs but does not specify the additional tests underpinning the XDR-TB labels, these records should not be interpreted as confirmed XDR-TB until the laboratory evidence is verified. This issue affects classification validity rather than simply the terminology used in presenting the results.

From a public health perspective, the findings underscore the value of robust and standardized DST records and the need to retain clinical and treatment-history information alongside laboratory results. Previous Yemeni research described important treatment-management challenges among patients already diagnosed with MDR-TB, and worldwide evidence consistently identifies previous TB treatment as a major correlate of resistance. However, adherence, treatment interruptions, medication supply, and comorbidities were not analyzed in the present study, so they cannot be offered as explanations for its observed resistance distribution. Future surveillance would benefit from consistent recording of new versus previously treated TB, the full DST panel, referral indications, calendar year, and key clinical characteristics, allowing more representative and adjusted comparisons [4,9].

Limitations

Several limitations should be considered. First, the retrospective, single-institution laboratory-based design is susceptible to selection and information bias. Patients who underwent culture and DST may not represent all individuals with TB in Yemen, and the proportion with MDR-TB cannot be generalized to the national TB population. Second, reliance on existing laboratory and registry records may have introduced incomplete or inaccurately recorded information, and the exclusion of incomplete records may have further affected sample composition. The non-MDR category was not further differentiated into fully drug-susceptible and other non-MDR resistance patterns. Third, important potential confounders, particularly previous TB treatment, treatment adherence, human immunodeficiency virus (HIV) infection, diabetes, referral indications, and socioeconomic characteristics, were not included in the reported analyses; therefore, independent demographic associations could not be assessed. Fourth, the six records labelled XDR-TB produced sparse cells in age- and sex-specific comparisons, potentially compromising the reliability of asymptotic chi-square tests. Finally, the available laboratory description does not document the second-line DST evidence or historical case definitions necessary to verify the XDR-TB category, and the pooled 2014–2023 data do not permit conclusions about annual trends or changes over time.

Conclusions

Among culture-confirmed TB patients undergoing DST at a national referral institution in Sana'a, MDR-TB accounted for a substantial proportion of the tested records. Resistance-category distributions differed descriptively by age and sex, but no statistically significant demographic associations were demonstrated. These findings provide laboratory-based information on the selected patient population rather than a national prevalence estimate. Improved documentation of treatment history, standardized resistance classification, and more representative DST surveillance are needed to strengthen interpretation and inform tuberculosis control in Yemen.

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