Ethiopian Journal of Health and Biomedical Sciences

Original article Open access

Common chest radiographic patterns and associated factors of among drug-resistant tuberculosis patients at the University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, 2020

***Samuel Addis Mihiretie*[1], *Temesgen Tadesse Alemayehu**[1], *Tewodros Tsegaye Ayele*[2], *Getahun Molla Kassa*[3, 4]**

[1]Department of Radiology, School of Medicine, College of Medicine and Health Science, University of Gondar, Gondar, Ethiopia, [2]Department of Internal Medicine, School of Medicine, College of Medicine and Health Science, University of Gondar, Gondar, Ethiopia, [3]Department of Epidemiology and Biostatistics, Institute of Public Health, College of Medicine and Health Science, University of Gondar, Gondar, Ethiopia, [4]Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, United Kingdom.

***Corresponding author:** email: tomtadesse@gmail.com*

Citation: Mihiretie SA, Tadesse T, Ayele TT, Kassa GM. Common chest radiographic patterns and extensive disease among adult pulmonary drug resistant tuberculosis patients at the University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. Ethiop J Health Biomed Sci 2024;14(2):3-11.

DOI: https://doi.org/10.20372/ejhbs.v14i2.855

Article History

Received: July 15, 2024

Revised: November 15, 2024

Published: December 31, 2024

Keywords: drug-resistant tuberculosis, chest radiograph, advanced tuberculosis disease

Publisher: University of Gondar

Abstract

***Background**: Drug-Resistant Tuberculosis (DR-TB) is a multifaceted public health problem. Determining the common chest radiographic patterns, degree of lung damage, and associated factors is vital in the early detection and treatment of DR-TB. Despite the availability of x ray, there are gaps in chest radiographic patterns of DR-TB disease in Ethiopia.*

***Objectives:** This study aimed to identify common radiologic patterns among pulmonary DR-TB patients.*

***Method:** A hospital-based cross-sectional study was conducted among 182 DR-TB patients who had an archive of baseline chest radiographs at the University of Gondar Comprehensive Specialized Hospital from September 2010 to October 2020. The socio-demographic and radiographic patterns were depicted using descriptive statistics. A multivariable binary logistic regression model was applied to identify associated variables with extensive DR-TB diseases at a $p < 0.05$.*

***Result:** Out of 182 DR-TB patients, 112 (61.54%) had patchy consolidation followed by focal fibrotic changes (37.91%) and focal nodular opacities (26.92%). Of all DR-TB patients, 19% had extensive pulmonary DR-TB disease. Patients' marital status was significantly associated with extensive (advanced) DR-TB disease. The odds of having advanced TB disease were 0.15 among those with single marital status (AOR: 0.15, 95% CI: 0.03, 0.68).*

***Conclusion:** This study highlighted that the most common chest radiographic feature of DR-TB was patchy consolidation followed by fibrosis and focal nodular opacities. Additionally, the study showed that close to one out of five DR-TB patients had extensive (advanced) DR-TB disease. Marital status had a significant association with extensive (advanced) DR-TB disease.*

Copyright: © 2024 at Mihiretie **et al.** This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 (CC BY NC 4.0) License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Introduction

Public health in resource-limited countries and the Tuberculosis (TB) Elimination Program are endangered by the emergence of drug-resistance tuberculosis (DR-TB). Disease management is difficult given the difficulty of diagnosis, complexity of treatment, deep adverse drug events and drug cost, high disease burden, and limited access to well-equipped health care facilities (1, 2). Tuberculosis is the leading cause of death in the world among infectious diseases (3, 4). If treatment is not initiated soon after diagnosis, a person with TB disease may infect an average of 10–15 other people every year (5).

Ethiopia is one of the 30 countries with a high burden of TB, TB/HIV, and DR-TB, with an annual estimated incidence of 177 per 100,000 carrying drug-susceptible TB (6). In addition, the burden of DR-TB reported among TB patients in Ethiopia is increasing from time to time (7, 8).

Diagnosis of DR TB relies on both laboratory studies (acid-fast staining, cultures, and different molecular tests) and imaging modalities including x-ray. Despite confirmative diagnosis of TB and DR-TB, early suspicions of DR-TB by chest imaging are highly desirable to guide the diagnostic process (9). Chest radiograph plays a major role in the detection, screening, and surveillance of DR TB as it is widely available and cheap (10). It can generally enable detection of different morphologies of lesions such as nodules, cavities, consolidation, fibrotic and bronchiectatic changes, pleural effusion, and thickening, as well as the site of involvement and number of lesions. It can also help in the follow-up of TB patients' treatment response (11). Despite the relatively low sensitivity and specificity of plain chest radiography, it is very helpful and commonly used in planning the management of complicated TB including DR-TB. Moreover, chest radiography entails reduced radiation exposure and affordable cost compared with Computer Tomography (CT) scans (18).

Radiological manifestations of pulmonary tuberculosis depend on several host factors that include prior exposure to TB, age, and underlying immune status. In people with normal immune function, radiological manifestations can be logically divided into two different forms of primary and post-primary disease that develop in individuals with and without prior TB exposure (12). Primary DR-TB chest radiographic patterns resemble those of primary drug-susceptible TB features, like consolidation and pleural effusion. On the other hand, secondary DR TB presents as an imaging feature of reactivation TB and cavitary consolidation (13, 14). In immunocompromised cases like Human Immunodeficiency Virus (HIV) positive DR-TB patients, hilar and mediastinal lymphadenopathies and miliary spread were the most common chest radiographic findings (1).

As the burden of DR- TB is high in Ethiopia, familiarity with the radiographic patterns of DR-TB can enable early detection, recognition, and treatment follow-up of the DR-TB disease. In addition, knowing the prevalence and associated factors for extensive (advanced) DR-TB disease will help the treating health care workers to quickly triage and implement patient-centered care. Despite the value of chest radiography in early detection and, follow-up, there has been no study of chest radiographic patterns of DR-TB disease in Ethiopia to date. This research aimed to explore the common radiological findings, the proportion of extensive disease, and associated factors among confirmed pulmonary DR-TB patients at the University of Gondar Comprehensive specialized hospital, Northwest Ethiopia.

Method

Study design, period, and setting

An institution-based cross-sectional study was conducted to determine common chest radiographic patterns and associated factors of drug resistant tuberculosis disease among DR-TB patients from November 01, 2020 to February 20, 2021. The study was done in the DR-TB treatment center at the University of Gondar Comprehensive Specialized Hospital with eligible patients admitted between September 2010 to October 2020. At the hospital, DR-TB treatment is based on the recommendations of the Ethiopian Federal Ministry of Health National DR-TB Guidelines, which are based on recommendations from WHO guidelines. Eligible patients should have at least bacteriological evidence of rifampicin resistance (RR-TB) confirmed by Gene Xpert/MTB-RIF, a Line Probe Assay, culture and drug sensitivity tests, the clinical judjment of the DR-TB clinical panel team based on multiple treatment failures, or a history of contact with someone having DR-TB. All the DR-TB patients in the hospital have a baseline chest x-ray film before initiating second-line anti-TB treatment. In the Department of Medical Imaging, the hospital has multimodal

imaging instruments including radiography (previously analog now replaced by digital), ultrasound, CT, and Magnetic Resonance Imaging (MRI).

Source and study population

The source population of this study was comprised of all adult (above 18 years old) DR-TB patients who registered and started second-line DR-TB treatment at the University of Gondar Comprehensive Specialized Hospital from September 2010 to October 2020. The study population consisted of those pulmonary DR-TB patients who had a documented baseline chest radiograph and started treatment at University of Gondar Comprehensive Specialized-Hospital.

Sample size and sampling procedures

All pulmonary DR-TB patients who were treated at the University of Gondar Comprehensive Specialized Hospital DR-TB clinic within the study period and have documented baseline chest radiographic films were included in this study.

Inclusion and exclusion criteria

All confirmed adult pulmonary DR-TB patients with at least one chest radiograph from their baseline evaluation were initially included in this study, but those with poor quality chest radiographs for which interpretation was difficult were ultimately excluded. The total number of DR-TB patients included in the study was 182. Data was collected by a final year radiology resident and a senior radiologist confirmed the quality of radiographs and interpretations.

Variable of the study

The dependent variable in this study was extensive (advanced) DR-TB disease measured as the presence or absence of any of the following: bilateral cavitary lung lesions, extensive parenchymal damage, diffuse chronic changes, multi-lobar consolidation, diffuse nodular opacities, or diffuse patchy consolidations and military nodules on chest radiograph (WHO operational definition) (15).

Cavity: is a gas-filled space surrounded by a complete wall that is three millimeters or greater in thickness.

Consolidation: is homogenous, ill-defined, or fluffy opacity that obscures vessels having air bronchograms with preserved lung volume and bounded by a fissure.

Pleural effusion: is homogenous increased lower lung zone opacity in the lateral costophrenic sulcus with concave interface towards the lung (meniscus sign).

Infiltrates: are reticulonodular lesions; a combination of reticular and nodular lesions.

Hilar lymphadenopathy: is considered when there is hilar enlargement, increased hilar density, lobulations of the contour, and distortion of the main bronchi.

Fibrotic changes: are old pleural and pulmonary scars, thin linear shadows with pleural thickening, and tenting of the diaphragm when these shadows extend to the pleural surface.

Bronchiectasis: refers to parallel linear shadows representing walls of cylindrically dilated bronchi seen in length and multiple peripherally located thin-walled cysts that tend to cluster in the distribution of the bronchovascular bundle. The explanatory variables in this study were sex, age, residence, occupation, religion, educational status, cigarette smoking history, alcohol drinking history, number of previous TB treatment cycles, baseline sputum smear results, baseline sputum smear grading, co-morbidities, and nutritional status.

Data collection procedures

After ethical approval, medical charts were collected from the DR-TB clinic and patient information was collected from charts. Chest radiographic findings were interpreted from the attached radiographs by a radiologist and recorded. Data completeness was verified each day.

Data processing and analysis

The collected data was entered into Epi-data 4.6.0.0 and exported to SPSS version 20 statistical software for cleaning, coding, recoding, and analysis. Descriptive statistics were derived for frequency and percent for categorical variables, means with Standard Deviation (SD) and presented in texts, tables, and graphs. COR and AOR were assessed to identify the associated factors of extensive (advanced) DR-TB at $p < 0.05$. Model fitness was assessed by using the Hosmer and Lemeshow test and reported adequate when $p > 0.05$.

Result

Socio-demographic and clinical characteristics

In this study, a total of 182 DR-TB patients were included, of which 109 were males. Age ranged from 18 - 73 years with a mean and standard deviation (SD) of 34.32 ± 0.89 years**.** All patients had been previously treated for TB at least once (all are secondary DR-TB). Of the total, 74.72% of patients had a documented positive baseline sputum smear result. A quarter of patients, 47 (25.3%) were HIV co-infected:- of these, only 28 had CD4 counts at the start of DR-TB treatment (**Table 1**).

Table 1: Socio-demographic and clinical characteristics of DR-TB patients at the University of Gondar Comprehensive Specialized Hospital (N=184), September 2010 to October 2020.

Variables	Category	Extensive (advanced) DR-TB Disease			
		Yes	No	Total	Percentage
Sex	**Male**	17	92	109	59.89%
	Female	14	59	73	40.10%
Age in years	**18-44 years**	28	114	142	78.02%
	45-64 years	7	29	36	19.78%
	≥ 65 years	0	4	4	2.19%
Residency	**Urban**	14	58	72	39.56%
	Rural	21	87	108	59.34%
Occupation	**Unemployed**	34	137	171	93.95%
	Employed	1	8	9	4.94%
Religion	**Orthodox**	33	136	169	92.85%
	Muslim	2	9	11	6.04%
Educational status	**Primary & below**	24	98	122	67.03%
	Secondary & above	9	33	42	23.07%
Marital status	**Married**	19	52	71	39.01%
	Never married	6	56	62	34.06%
	Divorced & widowed	10	39	49	26.92%
Cigarettes smoking history	**Yes**	1	13	14	7.69%
	No	34	134	168	92.30%
Alcohol drinking history	**Yes**	0	10	10	5.49%
	No	35	137	172	94.50%
History of TB treatment in number	**≤ one**	24	102	126	69.23%
	> one	11	45	56	30.79%
Anatomical site of DR-TB affected	**Only pulmonary**	26	121	147	80.76%
	Disseminated	9	26	35	19.23%
Baseline sputum smear result	**Positive**	25	111	136	74.72%
	Negative	10	32	42	23.07%
Baseline sputum smear grading	**No bacilli (0)**	10	32	42	23.07%
	Scanty +1	10	47	57	31.31%
	+2 and 3+	13	55	68	37.36%
Co-morbid conditions	**Diabetic mellitus**	0	4	4	2.19%
	CVD	0	2	2	1.09%
	HIV	10	37	47	25.82%
Have the patient started ART (N=47)	**Yes**	9	34	43	23.62%
	No	1	3	4	2.19%
CD4 count at the start of DR-TB treatment (cells/mm^3) (N=28)	**<= 50**	1	2	3	1.64%
	51-100	1	2	3	1.64%
	101-200	2	7	9	4.94%
	>200	1	12	13	7.14%

***** ***CVD*** *(Cardiovascular Disorders),* ***HIV*** *(Human Immunodeficiency Virus),* ***ART*** *(Anti-retro Viral Therapy),* ***CD4*** *(Cluster of Differentiation 4), mm (millimeter)*

Radiologic pattern and prevalence of extensive (advanced) DR-TB

Of all 182 DR-TB patients, 61.54% patients had patchy consolidation, 37. 91% had focal fibrotic changes and 26.92% of them had focal nodular opacities (**Figure 1**). In those patients with a single cavity, the mean and SD cavity diameter was 3.27 ± 0.23 cm. The smallest cavity had a diameter of 1.0 cm and the largest had 6.0 cm. Among those DR-TB patients who had multiple cavities, the mean and SD diameter size was 4.22 ± 1.47cm with the smallest and largest cavity size of 2.0 cm and 6.0 cm diameter respectively.

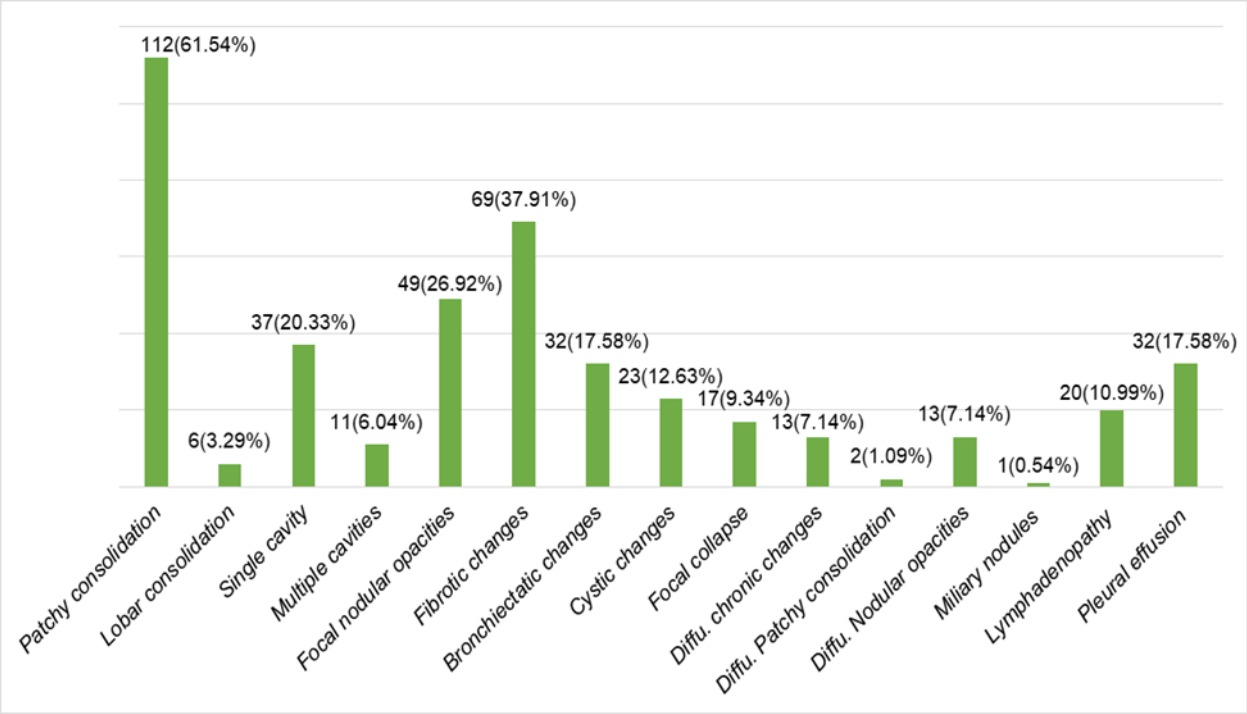

Figure 1: *Radiographic findings of DR-TB patients at the University of Gondar Comprehensive Specialized Hospital (N=184), September 2010 to October 2020.*

The prevalence of advanced DR-TB disease was 19% (95% CI: 13, 25). Of those patients with extensive (advanced) DR-TB, 13 (7.14%) had diffuse chronic changes, 13 (7.14%) had diffuse nodular opacities, 11 (6.04%) had multiple cavities, 3 (1.65%) had bilateral cavities, 2 (1.10%) had diffuse patchy consolidation and only one (0.55%) patient had miliary nodules. There was no patient with multi-lobar consolidation.

The common findings in the chest radiograph were patchy consolidation 112 (61.54%) followed by focal fibrotic chronic changes 69 (37.91%), focal nodular opacities 49 (26.92%), and single cavity 37 (20.33%) respectively. The right and left upper lung zones were the most affected anatomical sites by DR-TB (**Table 2**).

Table 2: Radiological findings of DR-TB patients at the University of Gondar Comprehensive Specialized Hospital (N=184), September 2010 to October 2020.

Findings	No. of patients	Right upper zone	Right middle zone	Right lower zone	Left upper zone	Left middle zone	Left lower zone
Patchy consolidation	112	51	26	15	45	18	14
Lobar consolidation	6	1	1	1	1	2	1
Single cavity	37	12	7	0	14	2	2
Multiple cavities	11	6	2	1	4	6	2
Focal nodular opacities	49	26	12	0	21	12	7
Focal chronic changes (fibrosis)	69	38	10	0	35	6	4
Focal chronic changes (bronchiectasis)	32	14	5	1	23	6	3
Focal chronic changes (cysts)	23	12	3	3	10	5	3
Focal chronic changes (collapse)	17	7	2	0	7	2	3

Associated factors for extensive (advanced) DR-TB disease

In this study, we have assessed the association between extensive (advanced) DR-TB disease and socio-demographic, behavioral, and clinical characteristics. From the chi-square test, sex, marital status, educational level, residency, previous TB treatment history, anatomical site of DR-TB involvement, baseline sputum smear results, baseline sputum culture results, co-morbidity, and baseline sputum grading satisfied the assumption and fitted in the multivariable binary logistic regression model. We used the backward logistic regression selection method to identify those variables that were significantly associated with extensive (advanced) DR-TB disease at a p-value of <0.05. From the multivariable binary logistic regression model, only marital status was significantly associated with extensive (advanced) DR-TB disease. (**Table 3**).

Table 3: Multivariable binary logistic regression of DR-TB patients at the University of Gondar Comprehensive Specialized Hospital (N=184), September 2010 to October 2020.

Variables	Category	Extensive (Advanced) DR-TB Disease		AOR(95% CI)	P. value
		Yes	No		
Sex	Male	17	92	0.38 (0.15, 0.98)	0.045
	Female	14	59	1	
Age in years	Mean ± SD	33.6±9.9	34.46±12.52	0.99 (0.94, 1.04)	
Marital status	Married	19	52	1	0.018
	Never married	6	56	0.96 (0.34,2.75)	
	Divorced & widowed	10	39	0.17 (0.94,0.74)	
Residency	Urban	14	58	0.62 (0.23,1.66)	0.34
	Rural	21	87	1	
Educational status	Primary & below	24	98	0.66 (0.20,2.22)	0.51
	Secondary & above	9	33	1	
Co-morbidity disease	Yes	10	45	1	0.57
	No	25	102	1.34 (0.49,3.66)	
Previous TB treatment history	≤1	24	102	2.98 (0.94,9.45)	0.064
	>1	11	45	1	
Site of TB	pulmonary only	26	121	1	0.48
	Disseminated	9	26	0.67 (0.22,2.05)	
Baseline sputum culture	Positive	19	95	1	0.45
	Negative	9	32	0.67(0.24,1.90)	
Co morbidity	Yes	10	45	1	0.57
	No	25	102	1.34(0.49,3.66)	
Smear grading	No bacilli	10	32	1	0.77
	Scanty &+1	10	47	1.19(0.37,3.84	
	+2 & +3	13	55	1.46(0.51,4.13)	

Hosmer and Lemeshow test (p-value=0.78), AOR (Adjusted Odds Ratio), CI (Confidence Interval), TB (Tuberculosis), SD (Standard Deviation)

Discussion

In this study, the four most common radiological findings were patchy consolidation (61.54%), fibrotic changes (37.91%), focal nodular opacities (26.92%), and single cavity (20.33%). Out of 182 patients included in this study, 118 patients had consolidation (either patchy or lobar), which was predominantly found on the right and left upper lung zones accounting for 52 (44.06%) and 46 (38.93%) cases respectively. Those zonal distributions, bilateralism, and preference towards the upper lung zones were noted similarly in studies done in Indonesia and Iran (11, 16). Even though consolidation was the most prevalent finding in our study, it was lower than study reports from Indonesia and Iran (11, 16). This difference might be due to the smaller

sample size or repeated TB treatments where the prevalence of fibrotic lung was higher and may lower the proportion of consolidation. Additionally, the long delay time in the diagnosis and initiation of treatment may result in ongoing chronic inflammation and as a result, causing fibrosis of the lung to be the second most common imaging feature in our cases. One can also consider the late presentation of our patients as a factor in the disease process that culminates in pulmonary fibrosis. The treatment failure rate in our country is high compared with that in other countries and several patients are subjected to repeated treatment. Moreover, cultures are done in only a few centers and most patients are subjected to repeated treatment with conventional anti- tuberculosis drugs if they do not respond to the initial treatment.

The prevalence of hilar lymphadenopathy (LAP) (10.99%) was lower than in the report from Iran (16). The reason behind this discrepancy might be the use of highly sensitive imaging like CT or digital x-ray which was not routinely taken for all of our patients.

Of all 182 adult DR-TB patients in this study, 19% had extensive (advanced) disease. Of those with extensive (advanced) DR-TB disease, diffuse chronic changes and diffuse nodular opacities were the dominant findings. This might be due to late presentations and/or due to repeated exposure to conventional anti-TB regimens before the diagnosis of DR-TB. Multiple cavities were the third main findings following diffuse chronic changes and diffuse nodular opacities. But multiple cavities were less prevalent compared with other studies which showed multiple cavities were common radiological findings (9, 17). Based on the 2020 WHO and Ministry of Health Ethiopia PMDT guideline, DR-TB patients with extensive (advanced) disease are not eligible for the shorter all-oral bedaquiline containing regimen. This implies that nearly one out of five DR-TB patients in this study were not eligible to benefit from this regimen. This short regimen is expected to reduce the duration of treatment from 18 or more months to 9-12 months, decreasing the rate of patients lost to follow-up, increase successful treatment outcomes, and improve programmatic including drug supplies and procurements than longer regimens (15, 18, 19).

In this study, the chest radiographic pattern among HIV positive and HIV negative DR-TB patients was similar. Only 28 HIV-positive patients had CD4 counts at the time of DR-TB diagnosis and we could not, therefore, evaluate imaging at different CD4 values. Lack of CD4 count was also seen in a study done in Alert hospital, Addis Ababa, Ethiopia (21).

Limitation: The inability to find an adequate number of patients, incompleteness of data, and poor quality x-ray film were the primary constraints for this study.

Conclusions and recommendation: This study highlighted that one out of five pulmonary DR-TB patients (19%) has extensive (advanced) DR-TB disease. Fibrotic changes and patchy consolidations are the most common findings on chest x-ray. Marital status had a significant association with extensive (advanced) DR-TB disease.

Hilar lymphadenopathy was not common finding in our study compared with other previous studies so additional use of routine lateral chest x-ray in addition to posterioanterior chest radiograph may increase the detection rate of lymphadenopathy.

Abbreviations: Drug-Resistant Tuberculosis (DR-TB), Tuberculosis (TB), Multidrug-Resistant Tuberculosis (MDR-TB), *Mycobacterium Tuberculosis* Rifampicin-Resistant (MTB-RIF), World Health Organization (WHO), Adjusted Odds Ratio (AOR), Confidence Interval (CI), Interquartile Range (IQR), Standard Deviation (SD), Acquired Immune-Deficiency Syndrome (AIDS), Human Immunodeficiency Virus (HIV), Computer Tomography (CT), and Magnetic Resonance Imaging (MRI), Rifampicin Resistance (RR-TB).

Competing interests: The authors have declared that there is no conflict of interest in this study.

Data availability: The data used for the current study was available based on a reasonable request from the lead author.

Ethical considerations: Ethical approval was obtained from the Institutional Review committee of the University of Gondar. A letter granting permission to conduct the study was secured from the Chief Clinical Director of the University of Gondar Comprehensive Specialized Hospital and the head of the DR-TB clinic. Confidentiality was ensured by omitting personal identifiers.

Consent for publication: Not applicable.

Funding: This study had funding for the data collection from the University of Gondar to compensate the post-graduate student.

Authors' contributions: All authors: selected the title, analyzed the data, conceptualizing the discussion, prepared and

approved the manuscript. SAM and TTA: developed the proposal. SAM, GMK, and TTA: followed the data quality. SAM and GMK: wrote the methods section of the manuscript.

Acknowledgment

We would like to express our thanks to the University of Gondar Comprehensive Specialized Hospital for permitting us to conduct this research. We especially thank the DR-TB treatment center staff and data collectors for their contributions to the success of this research article.

Author information: Samuel Addis Mihiretie (MD, Radiologist at the University of Gondar), Temesgen Tadesse Alemayehu (MD, Assistance Professor of Radiology at the University of Gondar), Tewodros Tsegaye Ayele (Assistance professor of Medicine, MPH, MD), and Getahun Molla Kassa (Lecturer at the University of Gondar, MPH in Epidemiology and Biostatistics, MSc in Clinical Tropical Infectious Diseases and HIV Medicine).

Reference

1. Lee ES, Park CM, Goo JM, Yim J-J, Kim H-R, Lee HJ, et al. Computed tomography features of extensively drug -resistant pulmonary tuberculosis in non-HIV-infected patients. Journal of computer assisted tomography. 2010;34(4):559-63.
2. Harries AD, Kumar A. Challenges and progress with diagnosing pulmonary tuberculosis in low-and middle-income countries. Diagnostics. 2018;8(4):78.
3. World Health Organization. Global Tuberculosis Report. Geneva: World Health Organization; 2014. Contract No: WHO/HTM/TB. 2016.
4. World Health Organization. Global Tuberculosis Report. Geneva: 2020.
5. Dye C, Lönnroth K, Jaramillo E, Williams B, Raviglione M. Trends in tuberculosis incidence and their determinants in 134 countries. Bulletin of the World Health Organization. 2009;87:683-91.
6. FMoH E. Guidelines for management of TB, DR-TB and leprosy in Ethiopia. Addis Ababa, Ethiopia Federal Ministry of Health Ethiopia. 2017.
7. Sinshaw W, Kebede A, Bitew A, Tesfaye E, Tadesse M, Mehamed Z, et al. Prevalence of tuberculosis, multidrug resistant tuberculosis and associated risk factors among smear negative presumptive pulmonary tuberculosis patients in Addis Ababa, Ethiopia. BMC infectious diseases. 2019;19(1):641.
8. Girum T, Muktar E, Lentiro K, Wondiye H, Shewangizaw M. Epidemiology of multidrug-resistant tuberculosis (MDR-TB) in Ethiopia: a systematic review and meta-analysis of the prevalence, determinants and treatment outcome. Tropical diseases, travel medicine and vaccines. 2018;4(1):5.
9. Wáng YXJ, Chung MJ, Skrahin A, Rosenthal A, Gabrielian A, Tartakovsky M. Radiological signs associated with pulmonary multi-drug resistant tuberculosis: an analysis of published evidences. Quantitative imaging in medicine and surgery. 2018;8(2):161.
10. Jaeger S, Juarez-Espinosa OH, Candemir S, Poostchi M, Yang F, Kim L, et al. Detecting drug-resistant tuberculosis in chest radiographs. International journal of computer assisted radiology and surgery. 2018;13(12):1915-25.
11. Icksan AG, Napitupulu MRS, Nawas MA, Nurwidya F. Chest X-ray findings comparison between multi-drug-resistant tuberculosis and drug-sensitive tuberculosis. Journal of natural science, biology, and medicine. 2018;9(1):42.
12. Karimi M, Arvin S, Bazari RAM, editors. Computed tomography features of multidrug-resistant tuberculosis (MDR TB) in HIV+ patients2015: European Congress of Radiology 2015.
13. Fishman JE, Sais GJ, Schwartz DS, Otten J. Radiographic findings and patterns in multidrug-resistant tuberculosis. Journal of thoracic imaging. 1998;13(1):65.
14. Kahkouee S, Esmi E, Moghadam A, Karam MB, Mosadegh L, Salek S, et al. Multidrug resistant tuberculosis versus non-tuberculous mycobacterial infections: a CT-scan challenge. The Brazilian journal of infectious diseases : an official publication of the Brazilian Society of Infectious Diseases. 2013;17(2):137-42.
15. World Health Organization. WHO operational handbook on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment. Geneva2020.

16. Zahirifard S, Amiri M, Bakhshayesh KM, MIRSAEIDI SM, Ehsanpour A, Masjedi M. The radiological spectrum of pulmonary multidrug-resistant tuberculosis in HIV-negative patients. 2003.
17. Kim S, Min J, Lee J. Radiological findings of primary multidrug-resistant pulmonary tuberculosis in HIV-seronegative patients. Hong Kong J Radiol. 2014;17(1):4-8.
18. World Health Organization. WHO consolidated guidelines on drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO. . 2019.
19. Ministry of Health-Ethiopia. National Programmatic Management of Drug-resistant TB (PMDT) in Ethiopia. Addis Abeba.2019.
20. Krishnan L, Akande T, Shankar AV, McIntire KN, Gounder CR, Gupta A, et al. Gender-related barriers and delays in accessing tuberculosis diagnostic and treatment services: a systematic review of qualitative studies. Tuberculosis research and treatment. 2014;2014.
21. Legesse tK. Chest radiographic pattern of multidrug resistance (MDR) tuberculosis cases at alert hospital, Addis Ababa A retrospective cross sectional study. 2019.