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Original Article

Risk factors of MDR-TB and impacts of COVID-19 pandemic on escalating of MDR-TB incidence in lower-middle-income countries: A scoping review

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic is affecting tuberculosis (TB) treatment in many ways that might lead to increasing the prevalence of multi-drugs-resistance tuberculosis (MDR-TB), especially in lower-middle-income-countries (LMICs). This scoping review aimed to identify the risk factors of MDR-TB and to determine the impacts of the COVID-19 pandemic on MDR-TB prevalence in LMICs. This study was reported according to the preferred reporting items for systematic reviews and meta-analyses extension for scoping reviews (PRISMA-ScR) guideline. The relevant keywords were used to search studies in three databases (PubMed, ScienceDirect and SpringerLink) to identify the related articles. The English-written articles published from January 2012 to December 2022 that explored risk factors or causes of MDR-TB in LMICs were included. Out of 1,542 identified articles, 17 retrospective, prospective, case-control and cross-sectional studies from ten LMICs met were included in this scoping review. Twenty-one risk factors were discovered, with prior TB treatment (relapsed cases), diabetes, living area, living condition, smoking and low socioeconomic status were the main factors in developing MDR-TB during COVID-19 pandemic. The pandemic increased the MDR-TB prevalence through drug resistance transmission inside households, the distance between home and healthcare facilities and low socioeconomic status. This scoping review demonstrates how the COVID-19 pandemic has affected the rising incidence of MDR-TB in LMICs.

Keywords: Tuberculosis, MDR-TB, risk factor, COVID-19, scoping review

Introduction

Tuberculosis (TB) is a highly transmissible disease caused by *Mycobacterium tuberculosis* (MTB) that mainly affects the lungs and other body parts [1]. With 1.5 million or 15% of TB patients died in 2020, TB continues to be one of the leading causes of death due to infectious diseases and remains a menace to the world's public health [2]. For a drug-susceptible TB case, the preferred treatment is a 6-month regimen of four first-line drugs (isoniazid, rifampicin,

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ethambutol and pyrazinamide) with a remarkable success rate (>85%) [1,3,4]. However, inappropriate usage and administration of anti-TB drugs could evolve into anti-TB-resistant strains [5].

Resistance to at least two of the most prominent anti-TB drugs (isoniazid and rifampicin) is defined as multi-drug resistant TB (MDR-TB) [6]. Inaccurate or inefficient use of anti-TB (e.g., single drug use, poor drug quality or substandard storage environment) and early treatment discontinuation can result in drug resistance that can transmitted by person-to-person, particularly in congested settings such as healthcare facilities or prisons [7]. Other risk factors of MDR-TB are low socioeconomic status such as education, income, low nutrition, bad habits (alcoholism and smoking) and coinfection or comorbidities such as human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS), fungal infection or diabetes [7]. In 2020, approximately 500,000 TB patients were confirmed to be resistant to rifampicin and 78% of these cases were identified as MDR-TB [8].

MDR-TB continues to be a major health problem globally and it is becoming even more challenging during the coronavirus disease 2019 (COVID-19) pandemic [9]. Since the pandemic, healthcare facilities have focused primarily on treating and preventing COVID-19 infection, whereas other diseases, including TB, have been overlooked [10,11]. The pandemic has also caused significant economic disruptions worldwide, resulting in high unemployment rates and income loss that leading to a lack of nutrients, particularly in low-income households in low-middle-income countries (LMICs) [12]. These circumstances have resulted in late diagnosis and treatment, unmanageable illness, running out of medications and treatment discontinuation that might lead to MDR-TB [9].

MDR-TB has caused consternation in every country, especially in the LMICs [13]. LMICs have approximately half of WHO countries with the highest MDR-TB burden [13]. Therefore, this scoping review aimed to identify the risk factors of MDR-TB and to determine the impacts of the COVID-19 pandemic on MDR-TB prevalence in LMICs.

Methods

Study design

This study was a scoping review and reported according to preferred reporting items for systematic reviews and meta-analyses extension for scoping reviews (PRISMA-ScR) guideline. This scoping review was conducted from March to June 2023.

Search strategy and study selection

A systematic search on PubMed, ScienceDirect, and SpringerLink's databases was conducted to find articles published from January 2012 to December 2022 in the English language that explored risk factors or causes of MDR-TB (particularly isoniazid and rifampicin resistance) in LMICs. The following keywords "risk factor*", "cause*", "multidrug resistance", "tuberculosis", "isoniazid resistance", "rifampicin resistance" were used to search the related articled. The origins of articles were confirmed manually by scanning the research settings based on the World Bank list of LMICs from 2021 to 2022 [12]. Only original articles were eligible for this scoping review. Other types of articles, such as commentary, meeting abstracts, policies, book chapters, reviews, guidelines, brief communication, and case studies; and studies on drug resistance other than isoniazid and rifampicin were excluded.

Data extraction

The relevant articles were screened based on the articles' main titles, abstracts, and thorough reading of the selected materials. Any duplications between debases were excluded. After a full-text review, only articles that stated one or more risk factors of MDR-TB and originated from LMICs were included.

The following data were extracted in during data extraction process: author name, publication year, article objective, publisher, index journal, country of research, study design, number of participants, participants' characteristics, MDR-TB risk factors and main findings. By

categorizing theory and supporting data from the selected articles, this scoping review was synthesized utilizing a narrative method to achieve the study objectives.

Results

Study selection results

The initial searches yielded 1,542 articles (543 from PubMed, 612 from ScienceDirect and 387 from ScienceDirect). After the duplicates were eliminated, 1,529 articles remained. After screening the titles and abstracts, forty articles were selected for full-text assessment. The flow of the processes of selecting the articles is provided in **Figure 1**. Out of 40 articles, nine were excluded because of the different types of results and performed outside the LMICs. The remaining article then went through an assessment of inclusion criteria. Fourteen articles were excluded because the main findings did not match the study objective leaving 17 articles as the final selection for review.

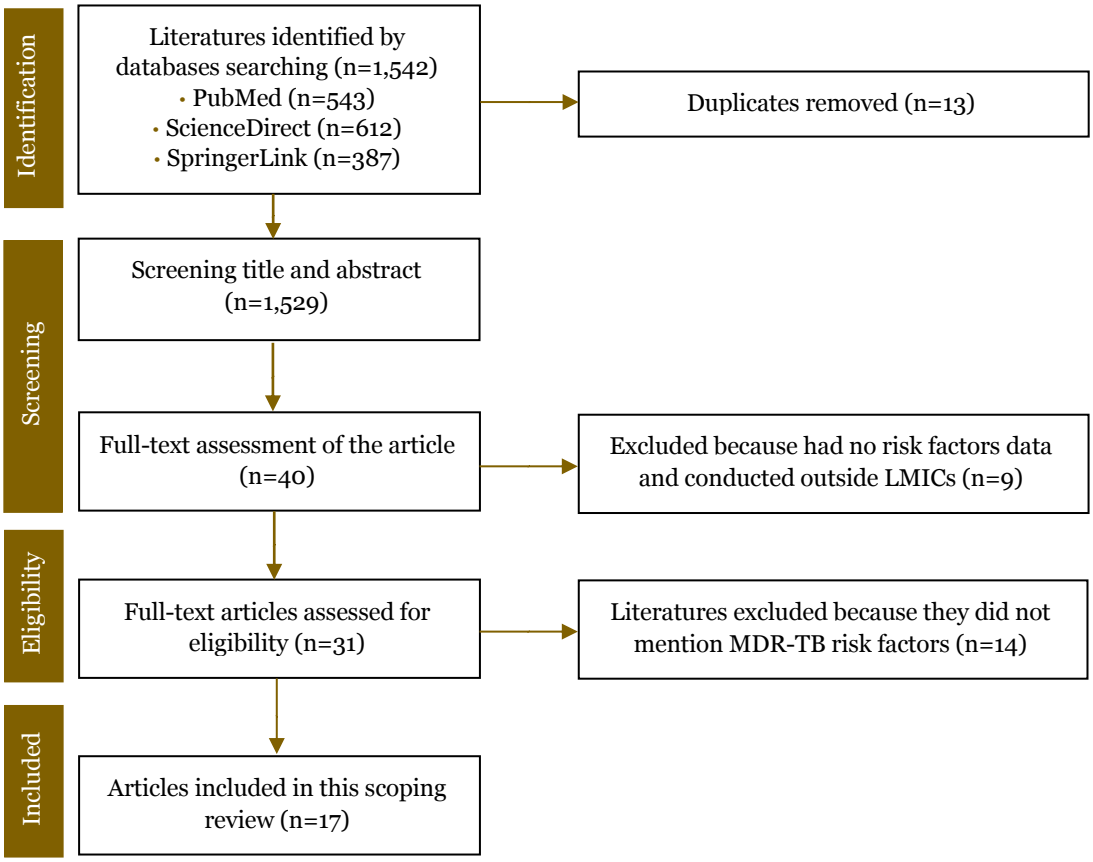

Figure 1. PRISMA-ScR flow diagram of study selection.

The 17 selected articles had ranges of characteristics such as study location, method, participants (**Table 1**). Of 17 articles, 13 were indexed in SCImago Journal & Country Rank, with three articles categorized in quartile 1 (Q1) [13-15], seven in quartile 2 (Q2) [16-22] and three in quartile 3 (Q3) [23-25] while other four articles were not indexed [26-29]. Three articles were published in 2012 [14,23,26] and 2019 [18-20] each; two in 2013 [16,24], 2015 [25,28], 2020 [13,21] and 2021 [15,22] each; one in 2014 [27], 2016 [29] and 2017 [17] each. No article published in 2018 and 2022.

India was the country where most studies were conducted (four articles) [13, 16, 19, 27], followed by Egypt (three articles) [26,28,29], Pakistan (three articles) [14,21,23], and one article each from Iran [24], Tanzania [25], Vietnam [17], Swaziland [18], Yemen [20], Ghana [15] and Cameroon [22]. Most of those articles were cohort studies which consisted of six retrospective [17,21,22,26,28,29] and five prospective studies [16,20,24,25,27], four cross-sectional studies [13-15,19] and the rest were case-control studies [18,23].

Table 1. Studies characteristics of the selected articles

Author(s)	Objective	Country	Design	Number of patients	Sex		Age ranges	MDR-TB risk factor	Main finding
					Male	Female			
Ayaz *et al.* (2012) [14]	Study the prevalence, risk factors and genotypes of drug-resistant *Mycobacterium tuberculosis* (MTB) in Karachi.	Karachi, Pakistan	Cross-sectional study	1,229	579	650	9-91	• Non-literate • Lower socioeconomic status • Living in overcrowded houses • Prior history of TB treatment	• MDR-TB patients were more likely to be female (p=0.14), married (p=0.004) and older than 27 years old(p=0.036). • MDR patients had higher rates of illiteracy (p=0.018), poorer income (p=0.006) and lower socioeconomic position (p=0.002) than non-MDR patients. • Patients with MDR-TB were more likely to report living in crowded homes (p=0.079). • After adjusting for other factors in the model, the final multivariable logistic regression model found that prior TB treatment history, being married, and belonging to the Balouchi, Sindhi and Pakhtun ethnic groups were associated with MDR-TB development
Ahmad *et al.* (2012) [23]	Evaluate risk factors for multidrug-resistant tuberculosis (MDR-TB) in an urban setting in Pakistan.	Karachi, Pakistan	Multicenter case-control study	125	62	63	≥15	• Had a TB patient in the house prior to the diagnosis of MDR-TB • Had a history of prior TB treatment • Low educational attainment • No formal schooling	• Multivariable logistic regression models revealed that cases were more likely to have a history of prior TB treatment (adjusted odds ratio (AOR) 4.2, 95%CI 1.1–15.4) or to have had a TB patient in the home prior to the diagnosis of MDR-TB (AOR 3.1, 95%CI 1.2–8.3). • Additionally, cases had higher odds of being male (AOR 3.6, 95%CI 1.4–9.7), between the ages of 15 and 25 (AOR 3.7, 95%CI 1.2–11.3), Sindhi (AOR 9.1, 95%CI 1.9–43.4), or with low educational attainment (AOR 5.5, 95%CI 1.7–17.6 for no formal schooling)
Farazi *et al.* (2013) [24]	Investigate the first-line anti-tuberculosis drug resistance rates and determine the risk	Arak, Iran	Prospective laboratory-based study	115	56	59	32-72	Prior treatment	There are significant associations between prior treatment, age <45 years, positive-smear result at the end of the second month and positive-smear result

Author(s)	Objective	Country	Design	Number of patients	Sex		Age ranges	MDR-TB risk factor	Main finding
					Male	Female			
	factors related to MDR-TB								at the end of the third month with MDR-TB.
Elmahallawy *et al.* (2012) [26]	Finding the treatment outcomes among patients with MDR-TB in Abbassia Chest Hospital	Nasr City, Cairo Governorate, Egypt	Retrospective study	200	148	52	15-76	• Lower socioeconomics • Lived in rural areas • Tobacco smokers Diabetics	• Among MDR-TB patients, 81.5% lived in rural areas, 2.5% were tobacco smokers and diabetics. • Of the patients in the study, 44.5% were defaulters, 44% had treatment failures, 4% had relapses and 7.5% had new cases. • Primary resistance was 7.5%, whereas acquired resistance was 92.5%.
Sethi *et al.* (2013) [16]	To assess the prevalence of MDR/XDR-TB in new and previously treated cases of pulmonary TB and in HIV seropositive and seronegative patients	Chandigarh, India	Prospective study	2,100	1,476	624	21-50	HIV	In 132 cases (66%) of MDR-TB, the treatment's outcome was favorable. After adjusting for prior treatment status, age and sex, there was a significantly greater correlation of MDR-TB (12/44, 27.3%) with HIV seropositive patients as compared to HIV seronegative individuals (27/175, 15.4%) (OR 2.3 (95% CI, 1.00–5.35); p=0.05).
Gaude *et al.* (2014) [27]	To evaluate the drug resistance pattern to first-line anti-TB drugs	Northern Karnataka region, India	Prospective study	66	NA	NA	20-60	• Illiteracy • Low socioeconomic status • Previous history of TB • Alcoholism	• MDR isolates were obtained in 52.2% of the cases. • Illiteracy, low socio-economic status, previous history of TB and alcoholism were found to have statistically significant associations for the development of MDR
Hoza *et al.* (2015) [25]	To determine the prevalence and risk factors associated with DR-TB at the facility-base level	Tanga, Tanzania	Prospective study	79	55	24	23-48	• Urban residence • New case	• Regarding residence, 40 were from urban and 39 from rural. • Seventy (88.6%) were new and nine (11.4%) were previously treated cases. • Regarding HIV status, 13 (16.5%) were HIV seropositive and 66 (83.5%) were seronegative. • Regarding disease type, 55 (69.4%) were both smear- and culture-positive while 24 (30.4%) were smear-negative but culture-positive. • Regarding disease type, 8.0% (n=2/25) cases with any drug

Author(s)	Objective	Country	Design	Number of patients	Sex		Age ranges	MDR-TB risk factor	Main finding
					Male	Female			
									resistance and 4.0% (n=1/25) cases of MDR-TB among smear-negative but culture-positive patients. • There was no the significant differences among all variables analyzed with the development of any drug resistance or MDR-TB.
El-Din *et al.* (2015) [28]	To assess adverse reactions of second-line TB drugs in patients treated for MDR-TB at Abbassia Chest Hospital	Nasr City, Cairo Governorate , Egypt	Retrospective study	107	78	29	37.1	• Tobacco smoking • Drug addiction • High alcohol intake • Diabetic • COPD	• The particular habits detected among the studied cases were tobacco smoking, drug addiction and alcohol intake. • Diabetes (29.9%) and COPD (11.2%) were the two most frequent comorbidities presented in the investigated MDR-TB cases.
Mohammad *et al.* (2016) [29]	To estimate the prevalence, possible risk factors, patterns of resistance and fate of MDR-TB	Alexandria, Egypt	Retrospective study	82	65	17	25-44	• Diabetic • Chronic chest disease	MDR-TB was more common in the male population, diabetic patients and those with chronic chest disease.
Mai *et al.* (2017) [17]	To examine *M. tuberculosis* isolates from TB/HIV co-infected patients	Ho Chi Minh city, Vietnam	Retrospective laboratory-based analysis	200	173	27	25-34	TB/HIV co-infection	TB/HIV co-infection was associated with high rates of TB medication resistance, although the new cases could not be distinguished from the retreatment cases.
Dlamini *et al.* (2019) [18]	The study aimed to determine risk factors associated with isoniazid-resistant TB among human immunodeficiency virus-positive patients	Swaziland	Case-control study	77	42	35	35.9	• Non-adherent to TB treatment • History of previous TB treatment	• With either isoniazid mono or poly drug-resistant tuberculosis (OR 7.91, 95%CI 4.14–15.11) or MDR-TB (OR 12.20, 95%CI 6.07–24.54), a history of prior tuberculosis therapy was positively linked. • Compared to the drug-susceptible TB group, patients with MDR-TB were more likely to not adhere to their TB therapy (OR 3.01, 95%CI 1.56–5.82).
Saldanha *et al.* (2019) [19]	To determine the prevalence of DR-TB amongst people living with HIV (PLHIV) using the line probe assay and determined risk	Pune, Western India	Cross-sectional	200	134	66	11–48	Relapsed patients	• MDR-TB prevalence was 12.5% (95%CI 7.9–17.1), isoniazid (INH) mono-resistance was 9% (6.9–11.2) and rifampicin resistance (RR) was 2.5% (1.4–3.6%). • The prevalence of MDR-TB among newly diagnosed and relapsed patients

Author(s)	Objective	Country	Design	Number of patients	Sex		Age ranges	MDR-TB risk factor	Main finding
					Male	Female			
	factors associated with the presence of MDR-TB								was 8.8% (95%CI 6.5–11.1%) and 23.1% (17.2–28.9%), respectively. • The only factor significantly linked to MDR-TB, DR-TB and INH mono-resistant TB was TB relapse.
Jaber *et al.* (2019) [20]	Evaluated the risk factors associated with MDR-TB and explored the poor TB management	Al-Hudaydah, Taiz, Aden, and Sana'a in Yemen	Prospective study	115	65	50	>18	• Body weight of ≤40 kg • Comorbidity	Multivariate logistic regression analysis showed that baseline lung cavities, comorbidity, baseline body weight ≤40 kg, and positive-culture at the end of the intensive phase were all associated with poor treatment outcomes in drug-resistant TB patients (p=0.016, 25.09, p=0.0499, AOR 4.73 and p=0.009, AOR 8.83, respectively).
Iqbal *et al.* (2020) [21]	To highlight the demographics of all MDR-TB patients recorded by NTP between 2014 and 2017	Pakistan	Retrospective study	2,145	1,105	1,040	33.4	• Occupations • Distance between patients and programmatic management of drug-resistant TB (PMDT) sites	• When considering prior treatment histories, patients with middle-level employment had a better chance of being cured than patients with lower and higher-level occupations. • Since roughly 70–80% of patients were cured after re-therapy, individuals with a prior history of anti-TB treatment had favorable treatment outcomes. • Patient treatment outcomes were significantly influenced by the distance between patients and PMDT locations. • Compared to patients who traveled more than 100 kilometers, the majority of patients who traveled less than 50 km had a much higher chance of being treated. • After correcting for any confounding factors, the probability of a successful treatment result decreased by 7.0% for every 50 km of additional distance traveled.
Shivekar *et al.* (2020) [13]	This study aims to assess the prevalence and factors associated with tuberculosis	Puducherry, India	Retrospective cross-sectional study	20,245	17,216	3,029	15-45	Treatment failure MDR-contact	• MDR contact was positively correlated with MDR-TB (AOR 3.171, 95%CI 1.747–5.754, p=0.000), treatment failure (AOR 2.175; 95%CI 1.703–2.777, p=0.000) and female gender

Author(s)	Objective	Country	Design	Number of patients	Sex		Age ranges	MDR-TB risk factor	Main finding
					Male	Female			
	drug resistance among patients from South India								(AOR 1.315, 95%CI 1.117–1.548, *p*=0.001). • There was no statistically significant positive correlation between prior TB therapy and MDR (AOR 1.113, 95%CI 0.801–1.546, *p*=0.523). • HIV seropositivity (AOR 0.580, 95%CI 0.369–0.911, *p*=0.018) and old age (AOR 0.994, 95%CI 0.990–0.999, *p*=0.023) were adversely linked with MDR-TB.
Sylverken *et al.* (2021) [15]	To investigate the level and pattern of resistance to first-line TB drugs among newly and previously treated sputum smear-positive TB cases and evaluated associations between potential risk factors and TB drug resistance	Ghana	Nation-wide cross-sectional study	927	645	282	≥ 18	Previous history of TB treatment	• MDR-TB was positively correlated with prior TB treatment experience at both univariate and multivariate analyses (OR 5.09, 95%CI 1.75–14.75, *p*=0.003; OR 5.41, 95%CI 1.69–17.30, *p*=0.004, respectively. • Regarding treatment adherence are raised by previously treated individuals' greater rates of MDR-TB and general medication resistance. Contrarily, there was no correlation between drug-resistant TB and the patients' sex, HIV status, or other characteristics (*p*>0.05).
Merker *et al.* (2021) [22]	To analyze transmission patterns and risk factors for the transmission of RR/MDR MTB strains	Cameroon	Retrospective genomic epidemiological study	261	183	78	27-43	Pre-existing resistances to short MDR-TB regimen	The likelihood of patients being newly infected increased with the number of pre-existing drug resistances to the medications employed in the brief MDR-TB regimen (high-dose isoniazid and ethambutol) (OR 1.7 per unit increment, i.e., for any extra drug resistance, 95%CI 1.3–2.3, *p*=0.001).

The largest sample size was 20,245 participants in an Indian cross-sectional study by Shivekar *et al.* [13]. A prospective study in Karnataka region, India by Gaude *et al.* had the smallest number of participants, which was 60 people only [27]. The participants' ages varied, where adult groups were the most of the participants.

Risk factors of MDR-TB in LMICs

There were 21 risk factors of MDR-TB incidence identified in this scoping review (**Table 2**). The most common risk factor identified was a prior history of TB treatment or relapsed cases (seven articles) which was followed by diabetes (three articles) lower socioeconomic level, HIV coinfection, daily habits as smokers and alcoholics, which were identified in two articles each. Chronic obstructive pulmonary disease (COPD), liver disease, treatment failure, non-adherent to TB treatment, contact with TB or MDR-TB patients, occupations, living in overcrowded houses, living in rural and urban areas, distance between patients and programmatic management of drug-resistant TB (PMDT) sites, comorbidities, chronic chest disease, drug addiction, body weight ≤40 kg and pre-existing resistances to the short MDR-TB regimen were each mentioned in one study (**Table 2**).

Table 2. MDR-TB risk factors according to the selected articles

MDR-TB risk factors	Reference(s)
Prior history of TB treatment (relapsed cases)	[14,15,18,19,23,24,27]
TB-treatment related	
Treatment failure	[13]
Pre-existing resistance	[22]
Non-adherence to treatment	[18]
Distance to programmatic management of drug-resistant TB sites	[26]
Contact with TB or MDR-TB patients	[13,18]
Individual background	
Living area & condition	[14,25,26]
Low socioeconomic status	[14,27]
Education	[14,23,27]
Occupation	[21]
Body weight	[20]
Marital status	[14]
Ethnicity	[14]
Habits	
Smoking	[26,28]
Alcoholism	[27,28]
Drug addiction	[20,28]
Comorbidities/coinfection	
Diabetes	[26,28,29]
Chronic chest disease	[29]
Liver disease	[28]
Chronic obstructive pulmonary disease (COPD)	[28]
HIV	[16,17]

Impact of COVID-19 pandemic on escalating the MDR-TB prevalence

According to the risk factors of MDR-TB, this study found several factors are directly related to the impact that the COVID-19 pandemic might influence the increasing prevalence of MDR-TB. The restrictions set out by governments (such as stay-at-home instructions) to reduce the spread of SARS-CoV-2 has altered how patient cares have been provided which are negatively affecting patients' health by delaying treatment for urgent situations, worsening chronic disease and increasing psychological distress [30]. The increasing number of MDR-TB transmissions in the household during that period cannot be prevented [23,30]. The chance of transmission within the family will increase if MDR-TB patients live in crowded homes (more than six peoples) and a threefold increased rate of developing MDR-TB persists following contact with them [13,14]. Patients also have been avoiding traveling at particular distances to reach healthcare facilities, which prevents patients from receiving the necessary follow-up treatments for TB. Most patients who travel less than 50 km had a much higher chance of being recovered from TB than patients who travel more than 100 km to reach the healthcare facilities, which possibly leading to the development of widespread drug-resistant TB (MDR-TB or XDR-TB) [21]. Moreover, patients

with low socioeconomic status are more likely to develop resistance to TB medications, especially during the COVID-19 pandemic as the generating MDR-TB may happen in this group of patients due to limited access to healthcare facilities in their residence areas [26]. The pandemic also contributed to the increasing number of unemployment, particularly in low socioeconomic groups that might lead to malnutrition, and a delayed healing process will lead to MDR-TB [11].

Discussion

There are 21 risk factors or causes of MDR-TB found in 17 studies and can be grouped into relapsed cases, matters related to TB treatment (treatment failure, non-adherence to treatment, contacts with TB or MDR-TB patients, distance to PMDT sites and pre-existing resistance), individual background (social economics status, marital status, ethnicity, education, occupations, living area and conditions), habits (smoking, alcoholism and drug addiction) and comorbidities/coinfection (diabetes, COPD, liver disease, HIV and chronic chest disease).

Prior history of TB treatment (relapsed cases) was reported to be the leading causes of MDR-TB [14,15,18,19,23,24,27]. Relapsed patients frequently comprise a diverse group that includes individuals who relapse after receiving default therapy and those who begin undergoing re-treatment after a previous round of therapy failed [27]. Resistant mutations are generated due to insufficient therapy [15]. If the poor therapy persists, mutations in a rising population will eventually result in MDR-TB [27].

Patients with a treatment failure have twice higher risk for MDR-TB than those who do not have failure experience [13]. A similar result found in Tanzania which there was about twice higher prevalence of MDR-TB in previously treated cases (22.2%) than the new cases (11.4%) [25]. This rate was even higher in Pakistan which equal to seven times riskier [14].

Moreover, the pre-existing resistance also contributes as a risk factor for MDR-TB. The probability of patients having recently acquired rifampicin resistance or MDR increased with the number of pre-existing drug resistances against those administered in the brief MDR-TB regimen, which is high-dose isoniazid and ethambutol (OR 1.7 per unit increase, i.e., for any extra drug resistance) [22].

Patients faced a range of difficulties throughout their therapy, highlighting the need for an individualized and comprehensive approach to adherence assistance [31]. Compared to the drug-susceptible TB group, patients with MDR-TB were three times more likely to not-adhere to their therapy [18]. The distance between the patient's residence and the medical facilities is one of the causes [22]. For instance, despite Pakistan having 34 operational PMDT sites, patients still must travel great distances to access healthcare [21]. Long travel distances and related costs may prevent patients from receiving the necessary follow-up treatments for MDR-TB, possibly leading to the development of widespread extensively drug-resistant TB (XDR-TB) [21].

Regarding living area and condition, previous research on contact tracing in patients with MDR-TB has demonstrated a strong correlation between prior exposure to a drug-resistant patient with infectious TB and the future development of TB with similar resistance patterns [23], with a threefold higher risk [13]. Furthermore, the MDR-TB transmission risk is even higher with the presence of TB patients in households [23] and MDR-TB patients in overcrowded houses [14]. In addition, MDR-TB patients were slightly more from urban (50.6%) than rural (49.6%) residences in Tanzania [25]. In contrast, most MDR-TB patients living in rural regions (81.5%) in Cairo [26]. This difference possibly occurred because the two studies were conducted in distinct places. Additionally, more significant numbers of MDR-TB patients came with lower socioeconomic status [26,27]. This factor may be due to limited access to healthcare facilities [26]. Moreover, a baseline body weight of 40 kg was discovered to be linked with failed treatment results in drug resistance patients (p=0.016; AOR=25.09). As a result, individuals may experience TB symptoms that last longer than usual because they have low body weight, which might indicate a weakened immune system that might induce MDR or XDR-TB [20].

Regarding habits, smoking came in first as a factor that was associated with MDR-TB patients which accounted between 25% [26] and 27.5% [28] of the total cases. Smoking has been associated with a greater risk of TB death and relapse, while passive smoking has also been identified as a risk factor for TB [32]. A history of alcohol abuse [27] and drug addiction [27, 28]

were considerably linked to induce MDR-TB as well, with seven (5.1%) and four cases (2.9%) [27], respectively.

Comorbidities, particularly diabetes, were identified as a risk factor for poor treatment results [20]. Diabetes was identified as the most frequent comorbidity affiliated with MDR-TB patients, ranged between 15% and 75.6% [26,28,29]. Low immunity caused by diabetes strengthens TB infections and makes TB medications less effective [33]. Additionally, patients' limited adherence to the program may be caused by the complicated drug schedule for TB and diabetes [33]. Other comorbidities related to MDR-TB were chronic chest illnesses (64.6%), liver disease (3.6%) and COPD (2.9%) [28]. The coinfection of TB/HIV were correlated with the high rates of TB drug resistance [17]. HIV seropositive individuals had a substantially greater incidence of MDR-TB (27.3%) than HIV-negative patients (15.4%) [16]. People with HIV are more likely to acquire MDR and XDR tuberculosis, linked to higher mortality and much shorter survival times [34].

When considering prior treatment history, patients with middle-level occupations such as physicians, attorneys, educators, entrepreneurs, or ministers had a better chance of being cured than patients with lower and higher-level occupations [21,35]. It could be that members of this group adhere to their medications better and have less work to do, which can help avoid the development of MDR-TB.

Four critical recommendations could be addressed to the community as well as stakeholders to reduce the MDR-TB prevalence and the effect of pandemic on MDR-TB cases. First, in extraordinary health events such as a pandemic, self-isolation at home or hospital isolation is essential but they need to be aware of other existing infectious diseases such as TB that could spread easily among family member or other patients in the hospital. Second, the existing long-term therapy like TB must be carried out in a disciplined manner to avoid resistance. Third, people need to change their bad behavior such as tobacco smokers, alcoholics, and drug addicts to increase their health quality in facing pandemic or other outbreak that could rise at any time. Last, all stakeholders must pay more attention to people who have low socioeconomic status to prevent drug resistance in the future.

Conclusion

The risk factors of MDR-TB in LMICs were prior TB treatment (relapsed cases), comorbidities or coinfection, low socioeconomic status, living areas, bad behavior such as tobacco smokers, alcoholics and drug addicts, non-adherence to TB treatment, and contacts to TB or MDR-TB patients. MDR-TB transmission in the household, long distances travel to healthcare facilities and low socioeconomic status were the causes of MDR-TB during the COVID-19 pandemic. This demonstrates how the COVID-19 pandemic has affected the rising incidence of MDR-TB in LMICs.

Ethics approval

Not required.

Competing interests

The authors declare that there is no conflict of interest.

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Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

How to cite

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