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FACTORS INFLUENCING THE DEVELOPMENT OF MULTI DRUG-RESISTANT TUBERCULOSIS: LITERATURE REVIEW

Faktor-Faktor yang Memengaruhi Tuberkulosis Multi Resisten Obat: Tinjauan Literatur

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ABSTRAK

Tuberkulosis resisten obat (TB-MDR) adalah tantangan besar dalam pengendalian TB global, disebabkan oleh strain Mycobacterium tuberculosis yang resisten terhadap antibiotik lini pertama, isoniazid dan rifampisin. Menurut WHO, pada tahun 2024 diperkirakan terdapat 400.000 kasus TB-MDR di dunia. Tinjauan literatur ini bertujuan menganalisis faktor-faktor sosio-demografi, komorbiditas, gaya hidup, dan kebijakan yang memengaruhi kejadian TB-MDR, dengan meninjau 20 penelitian di Afrika, Asia, Eropa, Australia, dan Amerika. Penelitian ini menggunakan pendekatan meta-analisis untuk mengidentifikasi faktor risiko, termasuk ketidakpatuhan minum obat, riwayat komorbid DM, riwayat komorbid HIV, dan usia produktif. Temuan ini menekankan pentingnya intervensi masyarakat untuk kelompok berisiko, peningkatan kepatuhan pengobatan, dan penguatan program pengendalian TB. Diperlukan kebijakan berbasis bukti untuk skrining dini dan tata laksana terpadu, serta model intervensi yang adaptif. Penelitian lanjutan disarankan untuk mengevaluasi peran pendekatan komunitas dan inovasi digital dalam meningkatkan keberhasilan pengobatan.

***Kata kunci**: Faktor risiko, PRISMA, tinjauan sistematis, tuberkulosis resisten obat, TB-MDR*

ABSTRACT

Multidrug-resistant tuberculosis (MDR-TB) poses a significant challenge in global TB control, caused by Mycobacterium tuberculosis strains resistant to first-line antibiotics isoniazid and rifampicin. According to WHO, an estimated 400,000 MDR-TB cases were reported worldwide in 2024. This literature review aims to analyze socio-demographic, comorbidity, lifestyle, and policy factors influencing MDR-TB occurrence by reviewing 20 studies conducted in Africa, Asia, Europe, Australia, and America. Employing a meta-analysis approach, the study identifies key risk factors, including medication non-adherence, history of diabetes mellitus (DM) and HIV comorbidities, and productive age. Findings highlight the importance of targeted community interventions, improved treatment adherence, and strengthened TB control programs. Evidence-based policies for early screening and integrated management, as well as adaptive intervention models, are necessary. Further research is recommended to evaluate community-based approaches and digital innovations in enhancing treatment success.

Keywords: Drug-resistance tuberculosis, MDR-TB, PRISMA, risk factors, systematic review

INTRODUCTION

Multi Drug-Resistant Tuberculosis (MDR-TB) is a form of tuberculosis that is resistant to two main drugs, Isoniazid (INH) and Rifampicin (RIF). This condition makes treatment more difficult because it requires a longer, more complex second-line drug regimen. Every year, more than 10 million people have active TB, so accelerated and concerted efforts are essential to achieve the global target of ending the TB epidemic by 2030, a commitment supported by all member states of the United Nations (UN) and the World Health Organization (WHO).[1] According to a WHO report in 2024, there are an

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estimated 400,000 cases of MDR-TB in the world, highlighting the increasing global burden of the disease. The success rate of MDR-TB treatment reaches 68%.[2] Local epidemiological data show that the incidence of MDR-TB is dominated by the productive age group under 60 years old with 140 cases (93.3%) and more in men with 177 cases (78.0%).[3]

Based on research conducted by Cecile et al in Cameroon with 304 participants, the prevalence of MDR-TB was 40.1% (122 cases). Significant risk factors include the type of occupation (informal sector workers are 61 times more at risk), income below the minimum standard, previous history of TB, alcohol consumption, self-medication, and consultation with a shaman which increases the risk by up to 155 timest.[4] MDR-TB is a serious global health challenge. Based on this background, this study aims to conduct a systematic review of the literature to explore and analyze the risk factors that influence the incidence of MDR-TB in various regions of the world.

METHODS

Search and Use Strategies for PICOS

Literature reviews are conducted with reference search strategies using databases such as PubMed, Science Direct, ProQuest, and Google Scholar. The research search used the PICOS (Population, Intervention, Comparison, Outcome, Study Design) method approach. The components of PICOS in this study are: (P) MDR-TB DISEASE, (I) influencing factors, (C) non-MDR-TB, (O) MDR-TB incidence, and (S) the research design is observational, such as cross-sectional, case-control, and cohort. Keywords were determined based on the PICOS approach to obtain relevant search results, namely: "Risk factors", "PRISMA", "systematic review", "drug-resistant tuberculosis", "MDR-TB".

Use of PRISMA and Selection Criteria

The PRISMA 2020 *(The Preferred Reporting Items for Systematic Review and Meta-Analysis)* method is used to identify and select studies in a transparent and systematic manner. The selection process was carried out through several stages, namely: initial identification of articles from various databases (n=124,989), then filtering based on titles and abstracts to evaluate relevance. Furthermore, duplicate articles that do not meet the criteria are eliminated. The remaining articles are then analyzed in full text to determine eligibility based on inclusion and exclusion criteria, i.e. articles relevant to the keyword, published in 2019–2024, and available in full text form. Articles that are not fully accessible are excluded from the review.

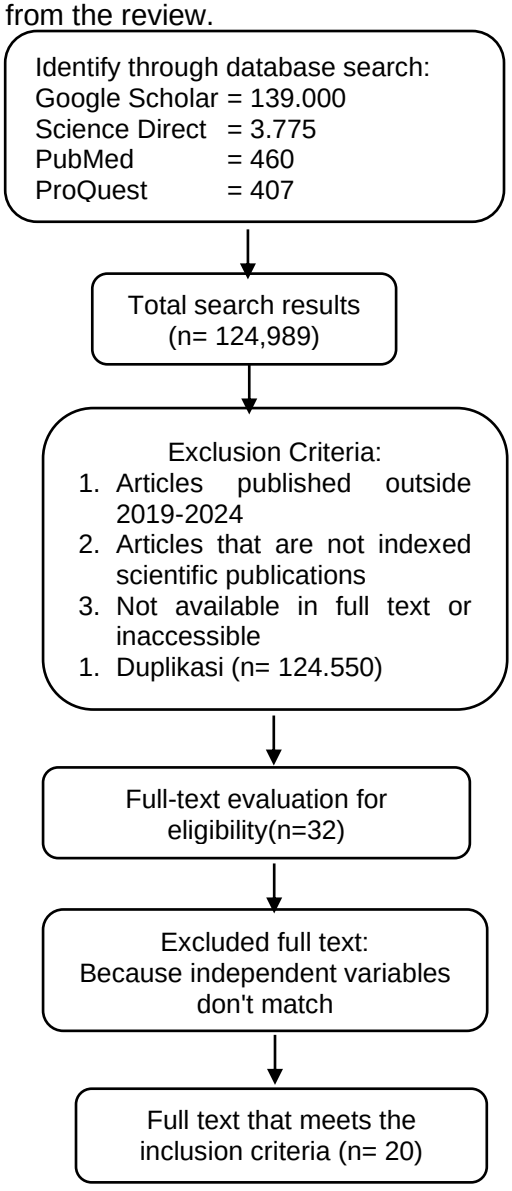

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Figure 1. Article Selection Flowchart

At the full text screening stage, as many as 12 articles were excluded because they did not meet the inclusion criteria, such as not focusing on factors that affect MDR-TB or not in accordance with the study design set. Thus, there were 20 articles that met all the criteria and were used in the preparation of the literature review (Figure 1).

RESULT

Study Selection Process Based on PRISMA

A total of 20 articles analyzed in this review came from various countries, including Central Africa, China, Ethiopia, India, Cameroon, Mali, Pakistan, Serbia, South Africa, Uganda, Sudan, Bhutan, Brazil, Canada, Indonesia, the United Kingdom (London), Liberia, Peru, and Australia. Based on the research design, there were 10 studies with a case-control design, 3 cross-sectional studies, and 7 cohort studies. These articles were used to assess the various factors that influence the incidence of MDR-TB. The following is table 1 of the characteristics of the studies reviewed:

Tabel 1. Karakteristik Studi yang Ditinjau

No	Author, Title	Country	Method	Identified Risk Factors	Result
1	Jean de Dieu Longo, et al. 2023.[5] *Risk Factors for Multidrug-resistant in The Central African Republic: A case-control study*	Central Africa	*Case-control* *Case* (n= 70) *Control* (n= 140)	Gender, type of residence, history of contact with other MDR-TB patients, smoking.	Factors significantly associated with MDR-TB: male gender, urban or suburban residence, previous TB treatment, family history with MDR-TB, and smoking.
2	Jin Bao-Ma, et al. 2022.[6] *Treatment Outcomes and Risk Factors of Multidrug-Resistant Tuberculosis Patients in Xi'an China, a Retrospective Cohort Study*	China	*Cohort* (n = 446)	Age, gender.	The main risk factors for poor treatment outcomes were age >40 years, male gender, and previous history of TB treatment.
3	Russom Mulugeta, et al. 2019.[7] *Risk Factors of Gout in MDR-TB Patients in Eritrea: A Case-Control Study*	Eritrea	*Case-control* *Case* (n = 42) *Control* (n = 42)	History of diabetes comorbidity	Frequent risk factors: patients with a history of DM
4	Ladha Nikhilesh, et al. 2022.[3] *Determinants, Risk Factors and Spatial Analysis of Multidrug Resistant Pulmonary Tuberculosis in Jodhpur, India*	India	*Case-control* *Case* (n = 150) *Control* (n = 300)	Age, gender, history of contact with other MDR-TB patients.	Risk factors for MDR-TB include age ≤60 years, male sex, high population density, use of chulha for cooking, previous history of TB, and contact with previous MDR-TB patients.
5	Cecile I Djuikoue, et al. 2022.[4] *Risk Factors Associated to Multidrug-Resistant Tuberculosis in Patients Attending the Deido*	Kameru n	*Cross sectional* (n = 304)	History with other MDR-TB patients, alcohol consumption.	Significant risk factors for MDR-TB are type of occupation, monthly income below the minimum standard, previous history of TB, alcohol consumption.

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No	Author, Title	Country	Method	Identified Risk Factors	Result
	District Hospital of Douala-Cameroon				
6	Baya Bocar, et al. 2019.[8] *Clinical Risk Factors Associated with Multidrug-resistant Tuberculosis (MDR-TB) in Mali*	Mali	*Cross sectional* (n = 214)	Age, history of contact with other MDR-TB patients	Frequently reported risk factors: age under 40 years, history of contact with TB patients, previous TB treatment failure, and bacterial load on smear microscopy. HIV was not found to be a significant risk factor for MDR-TB.
7	Saifullah Amna, et al. 2021.[9] *Evaluation of Risk Factors Associated with The Development of MDR and XDR TB in a Tertiary Care Hospital: A Retrospective Cohort Study*	Pakistan	*Cohort* (n = 580)	Age, smoking	Risk factors for MDR-TB include age ≤38 years, smoking, previous treatment history, and single marital status.
8	Kizito, Enock, et al. 2021.[10] *Risk Factors for Mortality Among Patients Diagnosed with Multidrug-resistant Tuberculosis in uganda: A Case Control Study*	Uganda	*Case-control* *Case* (n = 66) *Control* (n = 132)	History of HIV comorbidity, non-adherence to medication	Main risk factors for death in MDR-TB patients include HIV infection, non-adherence to treatment, age over 50 years, and low education level.
9	Elduma Hussein Adel, et al. 2019.[11] *Assessment of The Risk Factors Associated with Multidrug-resistant Tuberculosis in Sudan: A Case Control Study*	Sudan	*Case-control* *Case* (n = 430) *Control* (n = 860)	Smoking, history of contact with other MDR-TB patients	1. Significantly associated risk factors for MDR-TB include: 1. History of TB 2. Treatment interruption 3. Contact with MDR-TB patients 4. Smoking
10	Admassu Fantahun, et al. 2023.[12] *Risk Factors of Multidrug Resistant Tuberculosis Among Patients with Tuberculosisat Selected Multidrug Resistance Treatment Initiative Centres in Southern Ethiopia: A Case-Control Study*	Ethiopia	*Case-control* *Case* (n = 79) *Control* (n = 313)	Smoking, history of contact with MDR-TB patients	Commonly reported risk factors: direct contact with TB patients, previous TB treatment, and smoking.
11	Tenzin Chador, et al. 2019.[13] *Factors Associated with Multidrug-Resistant Tuberculosis (MDR-TB) in Bhutan: A Nationwide Case-Control Study*	Bhutan	*Case-control* *Case* (n = 79) *Control* (n = 118)	Previous treatment failure	Frequently reported risk factors: sleeping less than 8 hours per day and frequent use of public transportation.

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No	Author, Title	Country	Method	Identified Risk Factors	Result
12	Marins Soares, Valeria et al. 2019.[14] *Factors Associated with Tuberculosis and Multidrug-Resistant Tuberculosis in Patients Treated at a Tertiary Referral Hospital in The State of Minas Gerais, Brazil*	Brazil	*Cross sectional* (n = 200)	Alcohol consumption, comorbidities, previous treatment history	Commonly reported risk factors: alcohol consumption, comorbidities, and pulmonary cavitation.
13	Hirama Takashi et al. 2020[15] *Risk Factors for Drug-Resistant Tuberculosis at a Referral Centre in Toronto, Ontario, Canada: 2010–2016*	Canada	*Cohort* (n = 485)	Age, HIV comorbidity	Frequently reported risk factors: young age (under 35 years), history of previous TB treatment, recent immigration (less than 24 months), and HIV infection.
14	Yao Song, et al. 2020.[16] *Determining Mycobacterium tuberculosis Drug Resistance and Risk Factors for Multidrug-Resistant Tuberculosis in Sputum Smear-Positive Tuberculosis Outpatients in Anhui Province, China, 2015–2016*	China	*Cross sectional* (n = 3047, *stratified random sampling*)	History of previous treatment	Significant risk factors for MDR-TB include a history of previous TB treatment and more than one course of TB treatment.
15	Wang Zhenzhen, et al. 2023.[17] *Epidemiological Characteristics and Risk Factors of Multidrug-Resistant Tuberculosis in Luoyang, China*	China	*Cohort* (n = 3060)	Age, sex, type of residence	Significant risk factors for MDR-TB: history of TB treatment, age under 51 years, male gender, and urban residence.
16	S Champor Hendrik, et al. 2020.[18] *Retrospective Analysis of Multidrug-Resistant Tuberculosis Case Notifications in Australia (1999–2018)*	Australia	*Cohort* (n = 375)	Migration from other countries, HIV comorbidity	Risk factors: Migration from countries with a high TB burden, especially Papua New Guinea, is a major risk factor. HIV positivity was detected in 2.7% of cases, but HIV data were largely incomplete.
17	Carter Boye Bobby, et al. 2021.[19] *Survival Analysis of Patients with Tuberculosis Andrisk Factors for Multidrug-Resistant Tuberculosis in Monrovia, Liberia*	Liberia	*Cohort* (n = 337)	Population density, smoking, history of contact with MDR-TB patients	Risk factors for mortality: high population density, current smoking, extrapulmonary TB, family history of TB, and smoking.

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No	Author, Title	Country	Method	Identified Risk Factors	Result
18	Ovio Raul Montalvo, et al. 2020.[20] *Geographic Distribution and Risk Factors of Multidrug-Resistant Tuberculosis in Central Peru*	Peru	*Cohort* (n = 3.403)	History of treatment, age, sex	Risk factors for MDR-TB: history of previous TB treatment, previous treatment failure, household contact with MDR-TB patients, and male gender being more commonly infected.
19	Febriyanti Ratna Wulan, et al. 2021[21] *Parental Tuberculosis with Multi Drug Resistant Risk in Tertiary Referral Hospital in Java Central*	Indonesia	*Case-control* *Case (*n = 55) *Control* (n = 55)	History of treatment, smoking, nutritional status	Risk factors include a history of TB drug treatment, treatment duration ≥6 months, contact with MDR-TB patients, smoking habits, and poor nutritional status.
20	Wotale Teramaj Wongel, et al. 2024[22] *Identifying Risk Factors for Recurrent Multidrug Resistant Tuberculosis Based on Patient's Record Data ffrom 2016 to 2021: Retrospective Study*	Inggris	*Cohort* (n = 443)	Age, smoking, alcohol consumption, history of TB	Significant risk factors: age, body weight, weight gain accelerating relapse, smoking, alcohol consumption, history of TB, and education level.

An analysis of 20 studies on MDR-TB risk factors revealed several factors that consistently appear across different regions of the world. The most frequently identified risk factors include a history of previous TB treatment, male gender, and smoking habits. Age, whether over 40 years or under 51 years (productive age), is also often associated with an increased risk of MDR-TB. In addition, comorbidities such as diabetes mellitus and HIV, as well as non-adherence to treatment, are significant contributing factors

Based on regional patterns, research in Africa has highlighted more socioeconomic factors such as employment, low income, and a history of contact with MDR-TB patients. In Asia, particularly in China and India, age and previous medical history play a significant role in the incidence of MDR-TB. Meanwhile, in Europe, America, and Australia, migration factors and HIV infection are the main highlights.

From a study design perspective, many case-control studies conducted in developing countries provide an in-depth picture of specific risk factors such as contact history and lifestyle. Whereas cohort studies are more common in developed countries with greater emphasis on demographic and clinical factors such as age, comorbidities, and treatment history.

These findings underscore the need for targeted interventions for at-risk groups based on these factors and the importance of an adaptive approach appropriate to regional context and population characteristics to reduce the burden of MDR-TB globally.

DISCUSSION

MDR-TB (Multidrug-Resistant Tuberculosis) is a form of TB caused by Mycobacterium tuberculosis which is resistant to isoniazid and rifampicin, two first-line drugs for TB treatment. This resistance arises as a result of previous treatment failure, improper use of medications, or low patient adherence.[2] MDR-TB occurs as a result of previous TB treatment failure, improper use of

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drugs or poor patient adherence to treatment, which causes TB bacteria to develop resistance to commonly used drugs.[23]

MDR TB remains a global health challenge, especially in low- and middle-income countries, where the burden of TB and limited access to health services remain high. The results of this review show that risk factors for MDR-TB vary according to socio-demographic characteristics, comorbidities, and lifestyle.

Socio-Demographic Factors

Productive age <65 years was found to have a significant impact on the incidence of MDR-TB in several regions, namely Luoyang, China (ρ= <0.001), Xi'an, China (ρ= <0.001), Jodhpur, India (ρ= 0.027), Canada (ρ= 0.01), Anhui, China (ρ= 0.008), London (ρ= 0.008), and Mali (ρ= 0.001). At productive age (around 15-64 years), individuals tend to be more active in working and interacting in different social environments.[17] This increases the likelihood of exposure to *Mycobacterium tuberculosis* bacteria, especially in work or residential environments with poor sanitation and in densely populated areas.[3,6,8,15–17]

Male sex was shown to be strongly correlated with the incidence of MDR-TB in several regions, namely Luoyang, China (ρ= <0.001), Xi'an, China (ρ= <0.001), Jodhpur, India (ρ= 0.002), Liberia (ρ= 0.010), and Central African Republic (ρ= 0.001). Men are more likely to work in sectors that are at high risk of TB transmission, such as industry, construction, or jobs with dense conditions and poor ventilation. This condition makes it easier for *Mycobacterium tuberculosis* bacteria to spread, and in the event of incomplete drug exposure, the risk of MDR-TB increases.[3,5,6,17,19]

In synthesis, productive age and male sex factors consistently emerged as determinants of MDR-TB in more than half of the studies analyzed, mainly in the Asian and African regions. This pattern reflects the global demographic risks that need to be the focus of health program interventions, particularly in the active working-age group and men working in densely populated and underhealthy sectors. Gender- and age-based interventions with a promotive-preventive approach in the work environment and improved access to health services are important in the control of MDRB TB globally.

Environmental and Geospatial Factors

Factors related to population density, environmental conditions, and limited access to health services in suburban, urban, and densely populated areas affect the risk of MDR-TB events. A dense environment with limited health and social services to support TB treatment creates conditions where drug resistance can develop and spread more easily.[24] This is supported by research conducted in the Central African Republic (ρ = 0.002), London (ρ = 0.009) and Jodhpur India (ρ = <0.001), which showed that individuals living in suburban, urban and densely populated areas have a significant effect on the incidence of MDR-TB.[3,5,22]

The influence of urban and densely populated environments on MDR-TB is not only occurring in developing countries, such as India and the Central African Republic, but also in developed countries such as the United Kingdom. This indicates that population density and limited access to health services remain important factors in TB transmission and resistance, albeit in different socio-economic contexts. In developing countries, constraints usually lie in the lack of health infrastructure and treatment controls, while in developed countries, despite the availability of facilities, vulnerable groups in densely populated urban areas often face non-structural barriers such as discrimination, immigration, or administrative access to health services.

Thus, synthesize, there is a consistent pattern that residential

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locations, especially in densely populated, urban, and suburban areas, are important determinants of MDR-TB incidence across geographic contexts. These findings underscore the importance of a *place-based approach* in MDR-TB control strategies, tailoring interventions to the specific socio-environmental conditions of high-risk communities in each country.

Comorbidity and Lifestyle Factors

History of DM and HIV comorbidities, as well as alcohol consumption and smoking, was found to be a significant predictor of the incidence of MDR-TB. Studies conducted in Xi'an, China (ρ = 0.001) and Eritrea (ρ = 0.026) showed that DM comorbidities had a significant influence on the incidence of MDR-TB. Studies conducted in Uganda (ρ = 0.04) and Sudan (ρ = 0.05) showed that HIV comorbidities have a significant influence on the incidence of MDR-TB. Research conducted in Brazil (ρ= 0.001) showed that alcohol consumption has a significant influence on the incidence of MDR-TB. Meanwhile, studies in Liberia (ρ= 0.046), Indonesia (ρ= 0.029), Pakistan (ρ= 0.004) and Cameroon (ρ= 0.022) showed that smoking habits had a significant effect on the incidence of MDR TB.[4,6,7,9–11,14,19,25]

A history of direct contact with MDR TB patients increases the risk of drug-resistant TB infection due to direct exposure to bacteria that are resistant to standard treatment. This is evidenced by studies conducted in Jodhpur, India (ρ= <0.001), Indonesia (ρ= 0.004) and Mali (ρ= 0.02) which showed that a history of direct contact with other TB patients had a significant effect on the incidence of MDR TB.[3,8,25]

Malnutrition affects the risk of MDR-TB, which hinders proper TB treatment. This is supported by research in Sudan (ρ = 0.03) and Indonesia (ρ = 0.007) where malnutrition has a significant impact on the incidence of MDR-TB.[11,25]

Marital status was statistically associated with an increased risk of MDR-TB incidence due to the high intensity of contact within the household, challenges to medication adherence, and associated psychosocial and economic factors. Good support from a partner can contribute to the success of treatment, but conflict, stress or heavy financial responsibilities can increase the risk of non-compliance and lead to TB drug resistance. This is supported by research conducted in Xi'an, China (ρ= 0.023), Liberia (ρ= 0.022) and Pakistan (ρ= <0.001), which shows that marital status has a significant influence on the incidence of MDR-TB.[6,9,19]

Various studies show that the incidence of MDR-TB is influenced by clinical factors (DM, HIV), behavior (smoking, alcohol), and social factors (contact history, nutritional status, marriage). This confirms that MDR-TB is the result of a complex interaction between health, lifestyle, and social conditions. Consistent findings across countries emphasize the need for a multidimensional approach, including comorbidity screening, behavior change, and sustainable social and economic support.

Regional Differences and Health Policy

Health policies and programs implemented in different countries show significant differences in treatment outcomes and prevalence of MDR-TB. In countries with adequate health support, such as Western Europe and Australia, treatment success rates are relatively higher. This is in contrast to developing countries such as Ethiopia and Cameroon, which highlight the need for consistent implementation of surveillance and treatment support programs as well as increased laboratory capacity in resource-constrained environments. In a study conducted in Cameroon, MDR-TB is a significant health problem, mainly due to poor socioeconomic conditions and ineffective treatment management. In a study conducted in Ethiopia, the mortality rate among MDR-TB patients was quite high, including male gender,

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and patients with comorbidities. Of the 245 patients followed, the mortality rate reached 13.1%, with factors that significantly increased the risk of death being male sex (AHR= 3.7 and ρ= 0.023), older age (AHR= 14 for >41 years of age and ρ= 0.001), extrapulmonary TB type (AHR= 0.2 for pulmonary TB as protective and ρ= 0.009) and the presence of other chronic diseases (AHR= 9.2 and ρ= 0.001). These results suggest that this group of patients with risk factors requires special attention in management.[4,12]

Challenges in MDR-TB Treatment Management

MDR-TB often requires a longer, more intensive treatment regimen, which increases the risk of side effects, non-compliance, and high costs. In addition, a history of previous TB treatment failure is a factor that greatly affects MDR-TB because the process of bacterial adaptation to the drug during treatment is not optimal or incomplete. This is supported by research conducted in Pakistan (ρ= 0.001), Xi'an, China (ρ= <0.001), Jodhpur, India (ρ= <0.001), Bhutan (ρ= <0.01), Mali (ρ= 0.002), Peru (OR= 5.84), Central African Republic (ρ= <0.001).[3,5,6,8,9,13,20]

These findings consistently suggest that a history of previous TB treatment failure is a strong predictor of the incidence of MDR-TB in different countries with different income levels and health care systems. Whether in developing countries such as Pakistan, India, and Mali, as well as in countries with more established health systems such as Peru and China, patterns of resistance due to incomplete or inadequate treatment remain at the root of the problem. This underscores the importance of close monitoring of the success of first-line treatment, as well as the need for robust surveillance and follow-up systems to prevent the development of resistance. Thus, previous treatment failures can be seen as a universal indicator of MDR-TB risk that should be a key focus in global control strategies.

Integrated, Evidence-Based Interventions

From various studies, it is clear that MDR-TB control requires strategies that focus on a multidisciplinary approach, including strengthening public health education, early detection, and ongoing monitoring of TB patients, especially those with a prior treatment history. In some countries with a high MDR-TB burden, such as a study conducted in Jodhpur, India, a region-based approach using GIS technology to identify MDR-TB transmission points provides data that is critical to formulating more effective TB control policies.[3]

In addition, Peru is one of the countries that has successfully controlled MDR-TB through the implementation of a comprehensive DOTS-Plus strategy. The program includes community-based treatment, close patient monitoring, and social and economic support. Based on the research of Carole et al, this approach resulted in a treatment success rate of up to 83% in MDR-TB patients in Peru.[26]

Advantages and Limitations of the Study

The advantage of this literature review lies in its broad international coverage, thus being able to present a comprehensive and diverse perspective on the factors influencing the incidence of MDR-TB in different countries and contexts. This contributes to strengthening external validity and enriching global insights that can be used as a reference in policy formulation and further research development. However, because it is a secondary study with no primary data collection, the findings obtained are highly dependent on the quality and relevance of the reviewed study. In addition, differences in the social, economic, and health care system contexts between countries can limit the generalization of findings to local populations if not critically

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analyzed. Therefore, it is recommended that further research be conducted with a quantitative approach through the collection of primary data directly from MDR-TB patients in order to obtain more in-depth empirical evidence regarding the determinants of drug resistance.

CONCLUSION

This study shows that the incidence of MDR-TB is influenced by various factors. Socio-demographic factors such as productive age and male sex emerged as dominant determinants, particularly in Asia and Africa, reflecting global risks in the active working-age group, particularly those working in dense and unhealthy environments. Comorbidities such as DM and HIV have been shown to be significant predictors. Lifestyles such as smoking, alcohol consumption, malnutrition, marital status, and a history of TB contact are associated with MDR-TB. Environmental and geospatial factors such as population density, environmental conditions, and limited access to health services in densely populated and peripheral areas also increase the risk of MDR-TB occurrence.

Effective MDR-TB control efforts require a comprehensive approach from various aspects. First, strengthening treatment management is essential, including monitoring patient compliance, timely availability of medications, and ongoing education. The use of digital technologies such as medication consumption reminder apps and patient tracking systems can help improve adherence in undergoing treatment. Second, early detection and routine screening need to be expanded, especially in high-risk groups such as individuals with a history of TB, HIV, diabetes mellitus, or those living in densely populated environments. Drug resistance screening through Molecular Rapid Tests (TCM/GeneXpert) also needs to be widely available in primary health care. Third, improving access to health services in remote areas must be a priority, by strengthening laboratory capacity, improving the competence of health workers, and providing supporting facilities such as transportation or home visits for patients who experience access constraints. Fourth, social and economic interventions are also needed, considering that long and complex MDR-TB treatment requires support such as nutritional assistance, decent housing, and economic assistance to maintain the sustainability of patient treatment. Fifth, education and community empowerment must be improved to strengthen understanding of TB transmission, the importance of thorough treatment, and the risk of drug resistance due to non-compliance. The involvement of local health cadres can be an effective strategy in strengthening community-based approaches. Finally, follow-up research at the local level is essential to understand the determinants of MDR-TB that are appropriate to the context of local culture, geography, and health care systems. In addition, evaluation of the effectiveness of various interventions, both technology-based and community-based, is needed to support evidence-based policy formulation.

REFERENCES

1. World Health Organization WHO. *Global Tuberculosis Report*. WHO; 2023. https://www.who.int/publications/i/item/9789240083851
2. World Health Organization. Drug Resistant TB. WHO. 2024. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2024/tb-disease-burden/1-3-drug-resistant-tb?
3. Ladha N, Bhardwaj P, Chauhan NK, Naveen KHS, Nag VL, Giribabu D. Determinants, risk factors and spatial analysis of multi-drug resistant pulmonary tuberculosis in Jodhpur, India. *Monaldi Arch Chest Dis*. 2022;92(4). doi:10.4081/monaldi.2022.2026

https://doi.org/10.34011/juriskesbdg.v17i2.2902

e-ISSN: 2579-8103
p-ISSN:1979-8253

4. Abebe G, , Zegeye Bonsa WK. Treatment Outcomes and Associated Factors in Tuberculosis Patients at Jimma University Medical Center: A 5-Year Retrospective Study Gemeda. *Int J Mycobacteriology*. 2017;6(3):239-245. doi:10.4103/ijmy.ijmy
5. de Dieu Longo J, Woromogo SH, Tekpa G, et al. Risk factors for multidrug-resistant tuberculosis in the Central African Republic: A case-control study. *J Infect Public Health*. 2023;16(9):1341-1345. doi:10.1016/j.jiph.2023.06.007
6. Ma JB, Zeng LC, Ren F, et al. Treatment Outcomes and Risk Factors of Multidrug-Resistant Tuberculosis Patients in Xi'an China, a Retrospective Cohort Study. *Infect Drug Resist*. 2022;15(August):4947-4957. doi:10.2147/IDR.S376177
7. Russom M, Tesfaselassie H, Goitom R, et al. Risk Factors of Gout in MDR-TB Patients in Eritrea: A Case-Control Study. *Tuberc Res Treat*. 2019;2019:1-6. doi:10.1155/2019/9429213
8. Baya B, Achenbach CJ, Kone B, et al. Clinical risk factors associated with multidrug-resistant tuberculosis (MDR-TB) in Mali. Published online 2019:149-155. doi:10.1016/j.ijid.2019.02.004.Clinical
9. Saifullah A, Mallhi TH, Khan YH, et al. Evaluation of risk factors associated with the development of MDR-and XDR-TB in a tertiary care hospital: A retrospective cohort study. *PeerJ*. 2021;9:1-19. doi:10.7717/peerj.10826
10. Kizito E, Musaazi J, Mutesasira K, et al. Risk factors for mortality among patients diagnosed with multi-drug resistant tuberculosis in Uganda- a case-control study. *BMC Infect Dis*. 2021;21(1):1-7. doi:10.1186/s12879-021-05967-2
11. Elduma AH, Mansournia MA, Foroushani AR, et al. Assessment of the risk factors associated with multidrug-resistant tuberculosis in Sudan: A case-control study. *Epidemiol Health*. 2019;41:1-9. doi:10.4178/EPIH.E2019014
12. Admassu F, Abera E, Gizachew A, Sedoro T, Gari T. Risk factors of multidrug resistant tuberculosis among patients with tuberculosis at selected multidrug resistance treatment initiative centres in southern Ethiopia: A case-control study. *BMJ Open*. 2023;13(1):1-6. doi:10.1136/bmjopen-2022-061836
13. Tenzin C, Chansatitporn N, Dendup T, et al. Factors associated with multidrug-resistant tuberculosis (MDR-TB) in Bhutan: A nationwide case-control study. *PLoS One*. 2020;15(7 July):1-13. doi:10.1371/journal.pone.0236250
14. Soares VM, de Almeida IN, Figueredo LJ de A, et al. Factors associated with tuberculosis and multidrug-resistant tuberculosis in patients treated at a tertiary referral hospital in the state of Minas Gerais, Brazil. *J Bras Pneumol*. 2020;46(2):1-8. doi:10.36416/1806-3756/e20180386
15. Hirama T, Sabur N, Derkach P, et al. Risk factors for drug-resistant tuberculosis at a referral centre in Toronto, Ontario, Canada: 2010–2016. *Canada Commun Dis Rep*. 2020;46(04):84-92. doi:10.14745/ccdr.v46i04a05
16. Yao S, Yan J, Li L, et al. Determining mycobacterium tuberculosis drug resistance and risk factors for multidrugresistant tuberculosis in sputum smear-positive tuberculosis outpatients in Anhui province, China, 2015–2016. *Infect Drug Resist*. 2020;13:1023-1032. doi:10.2147/IDR.S244482
17. Wang Z, Hou Y, Guo T, et al. Epidemiological characteristics and risk factors of multidrug-resistant tuberculosis in Luoyang, China. *Front Public Heal*. 2023;11. doi:10.3389/fpubh.2023.1117101
18. Camphor HS, Viney K, Polkinghorne

https://doi.org/10.34011/juriskesbdg.v17i2.2902

e-ISSN: 2579-8103
p-ISSN:1979-8253

B, Pennington K. Retrospective analysis of multidrug-resistant tuberculosis case notifications in Australia (1999-2018). *Commun Dis Intell*. 2020;44. doi:10.33321/cdi.2020.44.68

19. Carter BB, Zhang Y, Zou H, et al. Survival analysis of patients with tuberculosis and risk factors for multidrug-resistant tuberculosis in Monrovia, Liberia. *PLoS One*. 2021;16(4 April):1-13. doi:10.1371/journal.pone.0249474
20. Montalvo-Otivo R, Ramírez-Breña M, Bruno-Huamán A, Damián-Mucha M, Vilchez-Bravo S, Quisurco-Cárdenas M. Distribución geográfica y factores de riesgo de tuberculosis multidrogorresistente en el centro de Perú. *Rev la Fac Med*. 2020;68(2):245-251. doi:10.15446/revfacmed.v68n2.71715
21. Aderita NI, Murti B, Suryani N. Risk Factors Affecting Multi-Drug Resistant Tuberculosis in Surakarta and Ngawi, Indonesia. *J Epidemiol Public Heal*. 2016;1(2):86-99.
22. Wotale TW, Lelisho ME, Negasa BW, Tareke SA, Gobena WE, Amesa EG. Identifying risk factors for recurrent multidrug resistant tuberculosis based on patient's record data from 2016 to 2021: retrospective study. *Sci Rep*. 2024;14(1):23912. doi:10.1038/s41598-024-73209-x
23. Chuchottaworn C, Thanachartwet V, Sangsayunh P, et al. Risk factors for multidrug-resistant tuberculosis among patients with pulmonary tuberculosis at the central chest institute of Thailand. *PLoS One*. 2015;10(10):1-17. doi:10.1371/journal.pone.0139986
24. Afrina Y. Faktor Lingkungan Dengan Kejadian Tuberculosis Paru. *J Ris Kesehat Poltekkes Depkes Bandung*. 2023;15(1):1-21. file:///C:/Users/ACER/Downloads/2105-Article Text-8372-1-10-20230204.pdf
25. Febriyanti RW, Lestari ES, Hadi P, Ciptaningtyas VR. Tuberkulosis Paru dengan Risiko Multi Drug Resistant di RS Rujukan Tertier di Jawa Tengah. *Herb-Medicine J*. 2021;4(2):61-67.
26. Shin S, Furin J, Ph D, et al. Community-Based Therapy for Multidrug-Resistant Tuberculosis in Lima, Peru. *N Engl J Med*. 2003;348(2):119-128.

https://doi.org/10.34011/juriskesbdg.v17i2.2902