Analysis of Risk Factors Affecting Survival in Tuberculosis Patients: Systematic Review

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Background: *Deaths due to TB are still a public health problem today. Monitoring tuberculosis treatment outcomes and examining factors that influence these outcomes is essential for evaluation and feedback on national TB control programs. So, this research aims to determine the risk factors that influence the survival of TB patients.*
Method: *This study used a Systematic review. The data sources used are Science Direct and PubMed databases published in 2019 – 2023. The research found 1,420 articles, filtering the abstracts according to the desired research topic and ensuring that the articles can be accessed in full-text form, resulting in 14 studies meeting the criteria.*
Results: *The results of this study showed that the factors that had the most significant influence on TB patient survival were age and HIV status in 7 of 14 studies. Meanwhile, a third of the studies reviewed found that TB classification, TB anatomical location, gender, race/ethnicity, and history of DM are factors associated with TB patient survival.*
Conclusion: *The most common variables associated with the survival of TB are age and HIV status. These conditions describe the increasing age and decreased immunity that can affect the survival of TB patients.*
Keywords: *Mortality, Risk factors, Survival, Tuberculosis*

Analisis Ketahanan Hidup Pasien Tuberkulosis: Telaah Sistematis

Latar belakang: *Kematian akibat TB masih menjadi masalah kesehatan masyarakat hingga saat ini. Pemantauan hasil pengobatan tuberkulosis dan pemeriksaan faktor-faktor yang mempengaruhi penting untuk dilakukan evaluasi dan umpan balik pada program pengendalian TB nasional. Oleh karena itu, penelitian ini bertujuan untuk mengetahui faktor-faktor risiko yang mempengaruhi kelangsungan hidup pasien TB.*
Metode: *Penelitian ini menggunakan tinjauan sistematis. Sumber data yang digunakan adalah database Science Direct dan PubMed yang diterbitkan pada tahun 2019 – 2023. Artikel penelitian ditemukan sebanyak 1.420 artikel, menyaring abstrak sesuai dengan topik penelitian yang diinginkan, dan memastikan bahwa artikel dapat diakses dalam bentuk full-text, sehingga menghasilkan 14 penelitian yang memenuhi kriteria.*
Hasil: *Hasil penelitian ini menunjukkan bahwa faktor yang paling berpengaruh terhadap ketahanan hidup pasien TB adalah usia dan status HIV, yaitu pada 7 dari 14 penelitian. Sementara itu, sepertiga dari penelitian yang direview menemukan bahwa klasifikasi TB, lokasi anatomis TB, jenis kelamin, ras/etnis, dan riwayat DM merupakan faktor yang berhubungan dengan ketahanan hidup pasien TB.*
Kesimpulan: *Variabel yang paling umum berhubungan dengan ketahanan hidup TB adalah usia dan status HIV. Kondisi ini menggambarkan semakin bertambahnya usia dan menurunnya kekebalan tubuh dapat mempengaruhi ketahanan hidup pasien TB.*
Kata kunci: *Faktor risiko, Ketahanan hidup, Mortalitas, Tuberkulosis*

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INTRODUCTION

Tuberculosis (TB) is an infectious *airborne disease* caused by *Mycobacterium tuberculosis,* which can attack the lungs and cause death. According to WHO, 10 million people are infected with TB and 1.5 million people die every year. TB is found throughout the world, but the majority of people infected with TB live in low and middle-income countries, with more than 80% of cases and deaths occurring.[1] After COVID-19, tuberculosis is ranked 2nd as an infectious killer in the world, followed by HIV/AIDS. Globally, in 2022, it is estimated that 10.6 million people will contract TB worldwide, with 1.3 million people dying.[2]

Based on WHO data for 2022, the largest number of new TB cases occurred in the Southeast Asia region (46%), followed by the Africa region (23%) and the West Pacific (18%). Approximately 87% of new TB cases occur in 30 countries with a high TB burden, with more than two-thirds of global TB cases occurring in Bangladesh, China, the Democratic Republic of Congo, India, Indonesia, Nigeria, Pakistan, and the Philippines.[1]

Globally, around 50% of TB patients and their households face total costs (medical and non-medical treatment expenses, as well as indirect costs such as loss of income), which are major problems (>20% of total household income). Many patients infected with TB have weak immune systems, such as those with HIV, malnutrition, and diabetes. Globally, in 2022, there will be 2.2 million new TB cases caused by malnutrition, 0.89 million due to HIV infection, 0.73 million due to alcohol use disorders, 0.70 million due to smoking, and 0.37 million due to diabetes.[2]

The End TB strategy aims to reduce the annual number of deaths from TB by 90% by 2030 and reduce TB incidence by 80% by 2035 compared to 2015.[3] To achieve the target of reducing TB incidence and death rates, it is necessary to reduce cases every year, make efforts to reduce the case-fatality ratio and know the risk factors for death due to TB. The global case fatality ratio needs to be reduced to 10% by 2020 and further to 6.5% by 2025.[2]

Increasing TB surveillance and rapid diagnosis needs to be emphasized by knowing the risk factors that cause death from TB. Risk factors associated with death from TB are gender, age, smoking, drug side effects, drug use, HIV, diabetes mellitus, and other comorbidities.[4] Based on research by Xie Y, et al., it was found that age, gender, HIV status, first sputum results, patient type, and delay in treatment influence patient survival.[5] Apart from that, risk factors that can influence TB mortality can be caused by other factors such as socio-economics, poor lifestyle, education, and nutritional status.

Many researchers have identified factors that cause the incidence of tuberculosis. However, there has been no comprehensive review of the risk factors that influence the survival of TB patients based on Xie, Y., et al.[5] By "comprehensive," a detailed and exhaustive review is intended, which not only identifies but also critically analyzes and synthesizes the various risk factors influencing the survival of TB patients. While previous systematic reviews may have addressed certain aspects of TB risk factors, this research aims to provide a broader, more integrative analysis that considers a wider range of variables, including emerging factors that may not have been covered in earlier studies. The goal is to fill gaps left by previous reviews and offer a more holistic understanding of the survival determinants in TB patients. This research aims to identify risk factors that can influence the survival of tuberculosis patients in the world.

METHOD

Science Direct and *PubMed* databases published in 2019 - 2023 with *the keywords* "Tuberculosis" AND ["mortality" OR "survival"] AND ["risk factors" OR "determinants"]. The search for those words in *Science Direct* and *PubMed* databases is limited to the years 2019-2023 in order to focus on the latest advances, treatment advancements, and scientific results. This time encompasses the most recent knowledge, advancements, and information on the subject, offering up-to-date and pertinent material for the research. The instrument used in this research is PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis). It uses a flow diagram based on the PRISMA checklist to sort literature according to several criteria. Articles were selected by the titles that matched keywords and obtained 1,420 articles including 934 PubMed articles and 486 Science Direct articles. After that, filter the abstracts according to the desired research topic and ensure that the articles can be accessed in full-text form, resulting in 14 studies that meet the criteria.

The inclusion criteria for this study were literature that discussed risk factors that influence the survival of tuberculosis patients and the following keywords. Researchers excluded articles based on exclusion criteria, namely articles that did not discuss risk factors that influence TB patient survival, did not have a mortality outcome, contained duplicate articles, and types of articles that did not use clinical research designs such as *cohort*, *cross-sectional*, and *case-control*. The author independently read the article and extracted information about the year and location of the research, research sample, type of research, and results obtained from the research.

RESULT

During the initial study search, 1,420 articles were found related to keywords. After assessing the title, abstract and suitability of the criteria, 14 studies were selected for assessment. All studies were published in 2019-2023 and were of international standard in English. There were articles with research designs of 11 retrospective cohorts, 2 prospective cohorts and 1 cross-sectional.

The number of samples studied was quite diverse, ranging from 111 - 283,508 people, with research sample characteristics ranging from teenagers (15-19 years), adults (20-64 years), and the elderly (65+ years). This research identified 35 factors related to TB patient survival, namely age, gender, HIV status, first sputum results, patient type, delay in treatment, education, race/ethnicity, region, TB qualifications, alcohol consumption, comorbid pneumonia, and insufficiency. Kidney, P/F ratio, intensive treatment, population density, smoking, multidrug resistance, history of Diabetes Mellitus, Acid-Fast Bacilli, hypoalbuminemia, Sequential Organ Failure Assessment score, socioeconomic, anemia, chronic liver, hypertension, TB detection, Bacillus Calmette-Guérin (a vaccine for tuberculosis) scar, malnutrition, drugs, cell increase white blood, increased urea in the body, low platelets, hospital services, and DOTS in health facilities.

The results of this study showed that the factors that had the most significant influence on TB patient survival were age and HIV status, namely in 7 out of 14 studies. Meanwhile, a third of the studies reviewed found that TB classification (5), TB anatomical location (4), gender (4), race/ethnicity (4), history of DM (4), education (3), region (3) first sputum results (2), smoking (2), alcohol consumption (2), and Hypoalbuminemia (2) are factors associated with TB patient survival.

From the review, age and HIV status showed the most consistent impact on TB patient survival, with conclusive results in 7 out of 14 studies. Other factors, such as TB classification, anatomical location, and gender, had varying levels of evidence, with some studies showing inconclusive or mixed results.

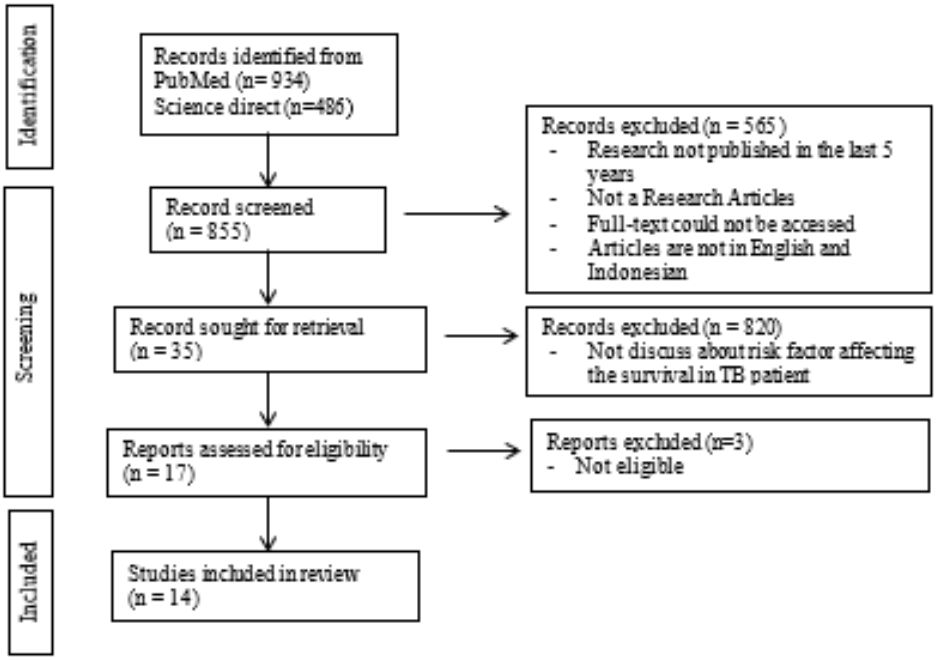

Figure 1. PRISMA Flow Chart Risk Factors for TB Patient Survival

Table 1. Factors Associated with TB Patient Survival

No	Variable	Research Articles														Total
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	
1	Age	✓	✓	✓		✓				✓	✓				✓	7
2	Gender	✓	✓					✓			✓					4
3	HIV status	✓	✓							✓	✓	✓		✓	✓	7
4	First sputum results	✓													✓	2
5	TB classification	✓				✓		✓		✓		✓				5
6	Delay in treatment	✓														1
7	Education		✓								✓	✓				3
8	Race/Ethnicity		✓								✓	✓		✓		4
9	Region		✓			✓					✓					3
10	Anatomical location of TB		✓	✓							✓			✓		4
11	Alcohol consumption		✓					✓								2
12	Comorbid pneumonia				✓											1
13	Renal insufficiency				✓											1
14	P/F Ratio				✓											1
15	Intensive treatment				✓											1
16	Population density						✓									1
17	Smoke						✓			✓						2
18	Multidrug resistant						✓									1
19	DM history								✓	✓	✓			✓		4
20	AFB								✓							1
21	Hypoalbuminemia								✓				✓			2
22	SOFA Score								✓							1
23	Socioeconomic									✓						1
24	Anemia									✓						1
25	Chronic liver									✓						1
26	Hypertension									✓						1
27	TB detection										✓					1
28	Scar BCG										✓					1
29	Malnutrition											✓				1
30	Drugs												✓			1
31	Increase in white blood cells												✓			1
32	Increase in urea in the body												✓			1
33	Low platelets												✓			1
34	Hospital Services														✓	1
35	DOTS in health facilities														✓	1
Total		6	7	2	4	4	3	3	4	9	10	5	5	4	5	71

Table 2. Overview of risk factors that influence TB patient survival

No	Author	Country	Title	Specific Condition	Design	Samples / Deaths	Variable	Results
1.	Xie, et al (2020)[5]	China	Survival Analysis of Risk Factors for Mortality in a Cohort of Patients with Tuberculosis	Age, Gender, HIV status, First sputum results, Patient type, Delay in treatment	Retrospective Cohort	7,032 / 321	Age Gender HIV status First sputum results Patient type Delay in treatment	p= 0.000; HR = 1.059 95%CI 1.051-1.067 p= 0.000; HR = 1.847 95%CI 1.387-2.459 p= 0.031; HR = 3.514 95%CI 1.122-11.00 p= 0.000; HR = 1.892 95%CI 1.495-2.395 p= 0.016; HR = 1.343 95%CI 1.057-1.706 p= 0.006; HR = 1.386 95%CI 1.096-1.753
2.	Viana, et al (2020)[6]	Brazil	Factors Associated with Death in Patients with Tuberculosis in Brazil: Competing Risks Analysis	Gender, Age, Education, Race, Region, Anatomical location, HIV status, Alcohol consumption	Retrospective Cohort	283,508 / 39,997	Gender Age Education Race Region Anatomical location HIV status Alcohol consumption	p<0.001 ; HR = 1.330 95%CI 1.26-1.40 p<0.001 ; HR = 9.29 95%CI 8.15-10.60 p<0.001 ; HR = 2.33 95%CI 2.09-2.59 p<0.001 ; HR = 1.13 95%CI 1.07-1.19 p<0.001 ; HR = 1.19 95%CI 1.10-1.28 p<0.001 ; HR = 1.91 95%CI 1.73-2.11 p<0.001 ; HR = 62.78 95%CI 55-71.63 p<0.001 ; HR = 1.90 95%CI 1.81-2.0
3.	Balaky, et al (2019)[8]	Iraq (Kurdistan)	Survival Analysis of Patients with Tuberculosis in Erbil, Iraqi Kurdistan Region	Gender, Age, Region, Anatomical location	Retrospective Cohort	728 / 50	Gender Age Region Anatomical location	p= 0.287; HR = 0.73 95%CI 0.41-1.3 p= 0.003; HR = 9.36 95%CI 2.14-40.95 p= 0.135; HR = 0.53 95%CI 0.23-1.22 p= 0.007; HR = 2.61 95%CI 1.30 – 5.27
4.	Elhidsi, et al (2021)[19]	Egypt	In-hospital mortality of pulmonary tuberculosis	Comorbid pneumonia, Renal insufficiency, P/F Ratio, Intensive treatment	Prospective Cohort	111 / 53	Comorbid pneumonia Renal insufficiency P/F Ratio Intensive treatment	p= 0.016; HR = 2.98 95%CI 1.22-7.29 p= 0.010; HR = 3.15 95%CI 1.31-7.56 p= 0.000; HR = 4.78 95%CI 2.04-11.23 p= 0.024; HR = 2.58 95%CI 1.13-5.98

5.	Liu, et al (2022)[10]	China	Survival Analysis and Associated Factors for Pulmonary Tuberculosis Death: Evidence from the Information System of Tuberculosis Disease and Mortality Surveillance in China	Gender Age Work Marital status Residence TB classification Treatment history Diabetes mellitus	Retrospective Cohort	283	Gender Age Work Marital status Residence TB classification Treatment history Diabetes mellitus	p= 0.40 ; HR = 1.26 95%CI 0.74-2.13 p= 0.05 ; HR = 1.92 95%CI 1.00-3.69 p= 0.07 ; HR = 1.53 95%CI 0.97-2.40 p= 0.08 ; HR = 0.54 95%CI 0.27-1.08 p<0.01 ; HR = 0.21 95%CI 0.08-0.52 p<0.01 ; HR = 7.59 95%CI 1.83-31.39 p<0.01 ; HR = 0.45 95%CI 0.27-0.77 p= 0.19 ; HR = 1.55 95%CI 0.8-2.98
6.	Carter, et al (2021)[17]	Liberia	Survival analysis of patients with tuberculosis and risk factors for multidrug-resistant tuberculosis in Monrovia, Liberia	Population density Smoking at the moment Former smoker TB – MDR	Retrospective Cohort	337 / 33	Population density Smoking at the moment Former smoker TB – MDR	p<0.001 ; HR = 7.942 95%CI 3.25–19.35 p= 0.023; HR = 3.546 95%CI 1.19–10.52 p= 0.002; HR = 3.773 95%CI 1.60–8.88 p= 0.001; HR = 4.632 95%CI 1.91–11.21
7.	Dos Santos, et al (2021)[14]	Brazil	Survival time among patients who were diagnosed with tuberculosis, the precocious deaths and associated factors in southern Brazil	Patient type TB HIV co-infection Alcohol consumption Gender Age Anatomical location	Retrospective Cohort	146	Patient type TB HIV co-infection Alcohol consumption Gender Age Anatomical location	p<0.01 ; HR = 0.37 95%CI 0.22-0.63 p= 0.24 ; HR = 1.54 95%CI 0.74-3.20 p= 0.03 ; HR = 1.55 95%CI 1.04-2.30 p= 0.01 ; HR = 6.49 95%CI 1.46-28.8 p= 0.08 ; HR = 1.02 95%CI 0.99-1.04 p= 0.97 ; HR = 1.01 95%CI 0.67-1.52
8.	Maranatha, et al (2021)[15]	Indonesia	The Factors Predicting Mortality in Pulmonary Tuberculosis with Accurate Respiratory Failure	Age DM Status AFB Hypoalbuminemia Pneumonia SOFA Score	Prospective Cohort	695/92	Age DM Status AFB Hypoalbuminemia Pneumonia SOFA Score	p= 0.411; HR = 0.545 95%CI 0.128-2.331 p= 0.005; HR = 8.250 95%CI 1.79-38.014 p= 0.022; HR = 11.45 95%CI 1.254-104.6 p= 0.001; HR = 12.0 95%CI 2.374-60.648 p= 0.123; HR = 3.273 95%CI 0.70-15.291 p= 0.012; HR = 7.944 95%CI 1.40-44.804

9.	Hameed, et al (2019)[9]	Pakistan	Risk factors for mortality among inpatients with smear-positive pulmonary tuberculosis	Gender Age Socioeconomic Education Anemia Chronic liver DM HIV status Hypertension History of TB Smoker	Cross-sectional	170 / 23	Gender Age Socioeconomic Education Anemia Chronic liver DM HIV status Hypertension History of TB Smoker	p= 0.8 p= 0.003 p= 0.019 p= 0.8 p= 0.03 p= 0.005 p= 0.001 p= 0.007 p= 0.006 p= 0.001 p= 0.001
10.	Keng, et al (2020)[11]	Malaysia	Determinants of unsuccessful treatment outcome and mortality among tuberculosis patients in Malaysia: A registry-based cohort study	Age Gender Nationality Residence Education TB detection Scar BCG DM Smoker TB location TB category HIV	Retrospective Cohort	97,505 / 18,805	Age Gender Nationality Residence Education TB detection Scar BCG DM Smoker TB location TB category HIV	p<0.001 ; HR = 1.042 95%CI p<0.001 ; HR = 1.12 95%CI p= 0.005; HR = 1.15 95%CI p<0.001 ; HR = 1.13 95%CI p<0.001 ; HR = 1.73 95%CI p<0.001 ; HR = 1.21 95%CI p= 0.037; HR = 1.07 95%CI p<0.001 ; HR = 1.22 95%CI p= 0.190; HR = 0.97 95%CI p<0.001 ; HR = 1.47 95%CI p= 0.271; HR = 1.08 95%CI p<0.001 ; HR = 7.47 95%CI
11.	Montes, et al (2021)[12]	USA	Risk factors for mortality and multidrug resistance in pulmonary tuberculosis in Guatemala: A retrospective analysis of mandatory reporting	Previous TB treatment HIV status Native ethnicity Malnutrition Low education level	Retrospective Cohort	3,945 / 154	Previous TB treatment HIV status Native ethnicity Malnutrition Low education level	p <0.001 ; HR = 3.57 95%CI 2.24–5.68 p <0.001 ; HR = 3.98 95%CI 2.4–6.17 p = 0.005; HR = 1.79 95%CI 1.18–2.7 p <0.001 ; HR = 7.33, 95%CI 3.24–16.59 p= 0.003 ; HR = 2.86, 95%CI 1.43–5.88

12.	Yaghi, et al (2022)[18]	Malaysia	Survival Trend of Tuberculosis Patients and Risk Factors Associated with Mortality and Developing Drug-Resistant Tuberculosis in Hospital Pulau Pinang, Malaysia: A Retrospective Study	Drugs addicted White blood cell level Urea Platelet level Albumin	Retrospective Cohort	325 / 73	Drugs addicted White blood cell level Urea Platelet level Albumin	p= 0.034 ; HR = 1,836 95%CI 1,019–3,309 p= 0.000 ; HR = 1,102 95%CI 1,057–1,148 p= 0.002 ; HR = 1.029 95%CI 1.011–1.047 p= 0.000 ; HR = 0.996 95%CI 0.995–0.998 p= 0.006 ; HR = 0.964 95%CI 0.940–0.990
13.	Nordholm, et al (2023)[13]	Denmark	Mortality, risk factors, and causes of death among people with tuberculosis in Denmark, 1990-2018	TB diagnosis Ethnicity HIV Diabetes	Retrospective Cohort	9,415 / 231	TB diagnosis Ethnicity HIV Diabetes	p< 0.0001; HR= 1.58 95% CI 0.96-2.60 p< 0.0001; HR = 3.13, 95% CI 2.84-3.45 p< 0.0001; HR = 2.41, 95% CI: 1.95-2.97 p< 0.0001; HR = 1.34, 95% CI: 1.16-1.99
14.	Bukundi, et al (2021)[7]	Tanzania	Mortality and associated factors among adult patients on tuberculosis treatment in Tanzania: A retrospective cohort study	Advanced age ≥ 45 Hospital services TB/HIV co-infection DOTS is facility-based TB results that have not been confirmed bacteriologically	Retrospective Cohort	53,753 / 1,927	Advanced age ≥ 45 Hospital services TB/HIV co-infection DOTS is facility-based TB results that have not been confirmed bacteriologically	p= 0.001; HR = 1.74, 95% CI 1.45–2.08 p<0.001; HR = 1.22, 95% CI 1.09–1.36 p<0.001; HR = 2.51, 95% CI 2.26–2.79 p<0.001; HR = 2.23, 95% CI 1.95–2.72 p<0.001; HR = 1.58, 95% CI 1.42–1.76

DISCUSSION

Based on the systematic review search carried out, 14 scientific articles met the inclusion criteria. The results of all the scientific articles analyzed explained factors related to TB patient survival. Age is a risk factor for the survival of TB sufferers. TB patients can come from all walks of life. However, the risk of death can increase in the elderly, which is influenced by low immunity, atypical symptoms, a long time to disease onset, more basic diseases, and poor health awareness in elderly patients.[5] The majority of cases occur between the ages of 20-39 years, but elderly TB patients have a 9.29 times greater risk of death than other age groups.[6] In addition, the age group >45 years has a 1.74 times risk of death compared to younger age groups.[7] The presence of other diseases associated with old age, such as cardiovascular disease, diabetes mellitus, and malignancies that often occur in elderly TB patients, and is associated with delays in TB diagnosis due to atypical clinical symptoms.[8-11] Therefore, it is necessary to strengthen TB screening at ages >45 years to achieve early detection, diagnosis, and treatment.

HIV status affects the survival of TB patients. TB-HIV coinfection can accelerate the decline in body immunity[5], delays in diagnosis, and the presence of opportunistic diseases can contribute to high mortality rates.[5, 7, 9] Patients with TB-HIV have a 62.78 times risk of death.[6] According to WHO, 1.3 million people will die from TB, including 167.000 with HIV, in 2022.[1] The double burden experienced by patients causes the occurrence of deaths in TB-HIV.[11] The higher mortality rate in clinically diagnosed TB patients suggests that People Living with HIV/AIDS (ODHA) who are severely immunosuppressed, have never used Antiretroviral Therapy (ART), and empiric treatment for tuberculosis is not superior to test-guided treatment in reducing mortality.[12] Among the comorbid diseases in the study Nordholm, et al (2023) HIV had the highest risk of death at 2.41 times. There is a need to strengthen effective management strategies for TB-HIV, increase the availability of early diagnosis, focus on vulnerable groups, and increase the availability of ARVs.[13]

TB classification consists of new and relapsed patients. Relapsed patients' success rate is lower than newly treated patients. Based on research conducted by Xie, et al it was found that relapse patients were at 1,343 higher risk of having low survival compared to new patients.[5] Apart from that, research conducted by Montes, et al (2021) also found that patients who relapse have a 3.57 times risk of contracting MDR TB and causing death.[12] The low cure rate for relapsed TB is the root of the problem of drug-resistant TB[5], longer treatment, and experiencing treatment side effects.[5, 10] However, research by dos Santos (2021) shows that the average survival from diagnosis to death in patients who died of TB was 23.5 days, namely 67.8 days in new cases and 384.4 days in case of relapse. There is a risk of death within 60 days after diagnosis due to short-term treatment caused by lack of funds and limited funds. Therefore, follow-up strategies must be systematic and rigorous to avoid potential MDR-TB epidemics in vulnerable areas. MDR-TB is a concern causing high treatment costs, toxicity, and poor outcomes.[14]

The anatomical location consists of pulmonary and extrapulmonary TB. Diagnosis of extrapulmonary TB requires a high level of clinical testing, specific diagnostic procedures, special stains, and acid-fast bacilli culture media. Delay in diagnosis will result in high rates of morbidity, mortality, and health care costs.[8] Patients with extrapulmonary disease have a 1.47 times risk of death compared to pulmonary TB patients.[11] Extrapulmonary TB can also attack the central nervous system, which has a 1.58 times risk of death.[13] In addition, there are also mixed clinical forms. The mixed clinical form has a 1.91 times higher risk of death because it is more likely to experience severe clinical severity of the case, especially in cases where treatment was started shortly before the patient died due to possible TB.[6]

One of the risk factors that can influence survival in TB patients is gender. Research conducted by Xie, et al states that men have a 1,847 times greater risk of death than women.[5] The higher risk of death in men is caused by high stress, increased participation in social activities, high labor intensity, excessive consumption of cigarettes and alcohol, and poor immune system. Apart from that, it is also caused by the tendency of low compliance with treatment regimens and malnutrition.[6] Research conducted by dos Santos (2021) also found that men are 6.49 times more likely to die than women.[14] Sociodemographic characteristics are related to the success of treatment in patients.

So, appropriate surveillance and management strategies for case detection, especially in men, are needed to control TB.[11]

The likelihood of dying from TB is higher in individuals who have black and brown skin compared to people classified as white. This is because of historical, sociological, and socioeconomic disparities and access to health services.[6] Apart from that, ethnicity also influences the survival of TB patients, this can be caused by socio-demographics and lifestyle of an ethnicity. Research by Nordholm, et al (2023) found that Danish citizens are at risk of death 3.13 times higher than migrants. This is partly due to patient characteristics and having comorbidities compared to migrants. Additionally, screening is offered voluntarily and is not offered to all groups.[13]

Diabetes Mellitus is one of the risk factors that influence the development of TB disease. The interaction between TB and DM is likely to increase the risk of developing TB, reactivate inactive TB, worsen the clinical course of TB, result in treatment failure, or require a longer duration. Meanwhile, TB also makes it difficult to control blood sugar levels. Maranatha, et al (2021) found that TB-DM patients are 8,250 times more likely to die than those who do not have comorbid DM, so TB patients who suffer from DM have a higher risk of developing TB with increased progression and mortality.[9, 11, 15] These results are also in line with research by Nordholm, et al (2023) which found that patients with TB-DM had a 1.34 times greater risk of death than ordinary TB.[13]

Diabetes that is not well managed can cause several consequences, including an increased susceptibility to infections. Diabetes increases TB susceptibility by a variety of pathways, including hyperglycemia and cellular insulinopenia, both of which have an indirect influence on macrophage and lymphocyte activity. However, TB can temporarily compromise glucose tolerance, a risk factor for developing diabetes. Transient hyperglycemia might result from the inflammation caused by TB. To establish a fresh diagnosis of diabetes mellitus, glucose levels should be checked again after 4 weeks of TB therapy, particularly once the patient is no longer feverish. TB patients with diabetes had a poorer clinical appearance and more symptoms, including weight loss, fever, dyspnea, and night sweats.[16]

Education level can be related to the risk of death from TB. Lower levels of education were associated with treatment failure and death. This depends on individual knowledge, attitudes and behavior towards TB. Research by Keng, et al (2020) found that people who have a low level of knowledge have a 1.73 times higher risk of dying than people with proper education.[11] This is in line with the research of Viana, et al (2020), which states that illiterate patients have the highest risk of death. The neglected and illiterate school categories are strongly associated with mortality regardless of cause, creating a risk gradient as education levels decrease.[6]

Alcoholism is the inability to control drinking due to physical and emotional dependence on alcohol. Addiction to drinking alcohol can worsen the condition of TB patients. Based on research by Viana, et al (2020) alcohol misuse affects not just the prevalence of TB, but also its clinical progression and prognosis.[6] Individuals with AUD are regarded as more infectious since AUD has been connected with the discovery of cavitary illness on chest X-rays and hence with smear-positive.[16] TB patients with alcohol addiction are at risk of dying 1.90 times compared to controls. Alcohol use can interfere with the immune response and increase susceptibility to respiratory diseases. Alcoholism can also cause loss of income, interpersonal violence, family disruption, low self-esteem, and stigmatization, as well as aspects commonly found among TB patients. Alcoholism can interfere with access to treatment, increase the risk of health problems, and increase poverty.[14]

Current and former smokers experience respiratory symptoms that can lead to lung cancer, coronary artery disease, or chronic bronchitis. Smoking can increase the risk of death in TB patients. Currently, there are more than 1 billion tobacco users, nearly 80% of whom live in low- and middle-income countries and limited health resources are available to treat costly diseases including TB.[17] Cigarette smoke's role in TB pathogenesis is linked to ciliary dysfunction, decreased immunological response, and macrophage immune response deficiencies, with or without a drop in CD-4 count, increasing susceptibility to TB infection. A history of parental smoking is already being

investigated in the context of childhood respiratory infections. A recent study also showed that the risk of infection with TB was increased in children living in a TB-endemic region and parental smoking was significantly associated with the risk of active TB, even after being adjusted for associated factors.[16]

Albumin is a plasma protein incorporated by the liver and catabolized by several organs at a balanced synthesis and breakdown pace. Albumin is essential for maintaining fluid balance and transport function and has antioxidant, anticoagulant, and anti-inflammatory properties. Albumin's physiologic function changes in specific settings, particularly when oxidative stress occurs, such as sepsis. Hypoalbuminemia is characterized by an albumin serum level of less than 3.0 g/dL. It is frequent in severely unwell patients, including bleeding, increased capillary permeability, and malnutrition. Hypoalbuminemia is associated with poor clinical outcomes in critically sick patients, including more comorbidities and a shorter survival rate. Based on Maranatha, et al (2021) TB-hypoalbuminemia has 12 times as the risk factors for mortality than control.[15] Similar results were also obtained by Yaghi, et al (2022), patients with hypoalbuminemia had a 28 times higher risk of death than controls.[18] The study's weaknesses include potential biases in the selection of articles, which may affect the generalizability of the findings. The reliance on data from various sources without standardized methodologies can lead to inconsistencies in results. Additionally, the study may not account for all confounding variables or changes in TB management practices over time, limiting the applicability of conclusions to current clinical settings. Furthermore, the inclusion criteria might exclude relevant studies, impacting comprehensiveness.

CONCLUSION

The results of this study showed that the factors that had the greatest influence on TB patient survival were age and HIV status, in 7 of 14 studies. Meanwhile, a third of the studies reviewed found that TB classification, TB anatomical location, gender, race/ethnicity, and history of DM are factors associated with TB patient survival. The most common variables associated with the survival of TB are age and HIV status. These conditions describe the increasing age and decreased immunity that can affect the survival of TB patients. In conclusion, it is possible to understand the factors associated with mortality in patients receiving TB treatment as useful contribution to the End TB strategy, especially in efforts to achieve targets to reduce deaths from TB by 95%, between 2015 and 2035. It can also help to organize local health services to provide optimal patients support and prevent avoidable deaths.

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