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Risk Factors for the Incidence of Drug-Resistant Tuberculosis in the Labuang Baji Hospital: A Healthpreneur Perspective

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ABSTRACT

Tuberculosis (TB) caused by Mycobacterium tuberculosis, remains a global health challenge, with drug-resistant TB (TB-RO) posing significant risks to control efforts. **This study aims** to identify risk factors associated with TB-RO among patients at Labuang Baji Makassar Hospital, Indonesia. Conducted from September to October 2023, this analytical case-control study utilized a quantitative approach. **Data were collected** from the Tuberculosis Information System (SITB) and hospital medical records, involving all TB-RO patients under treatment between 2022 and 2023. Total sampling yielded 105 cases, with analysis performed using univariate, bivariate, and multivariate methods. **Results** indicate that age (OR=2.509, CI 95%: 1.120–5.622; p=0.036), positive BTA sputum (OR=3.397, CI 95%: 1.630–7.082; p=0.001), and prior treatment history (OR=0.461, CI 95%: 0.254–0.837; p=0.016) are significant factors. Positive BTA sputum emerged as the dominant risk. Findings suggest that inadequate treatment adherence may contribute to TB-RO incidence. **The study concludes** that age and BTA phlegm are key risk factors, while a history of successful treatment is protective. Strengthening patient monitoring and ensuring treatment compliance are essential for mitigating TB-RO risk and improving outcomes.

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1. INTRODUCTION

Tuberculosis (TB) is still a public health problem that causes high pain, disability, and death, so it is necessary to make countermeasures. Tuberculosis is a public health problem so that it is one of the goals of health development sustainable development (SDGs) [1]. TB disease according to the Sustainable Development Goals (SDGs) is a disease that is targeted to be eradicated, in addition to malaria and HIV/AIDS [2, 3].

Every day, globally more than 4,100 people lose their lives to TB and nearly 28,000 people fall ill with this preventable and curable disease [4]. Many efforts have been made globally to combat TB and have saved an estimated 66 million lives since 2000. However, the Covid-19 pandemic has made all the progress that has been made over the years in the eradication of TB decline. For the first time in the last 10 years, deaths from TB increased in 2020 [4].

TB is a contagious disease caused by the bacterium Mycobacterium tuberculosis. The germ spreads from TB patients through the air. These TB germs usually attack the lungs, which can also be outside the lungs (extra lungs). Almost a quarter of the world's population is infected with Mycobacterium tuberculosis germs, around 89% of TB is suffered by adults, and 11% is suffered by children [5].

Globally, TB is the second deadliest infectious disease in the world after Covid-19. It is ranked thirteenth as the leading cause of death worldwide. The number of deaths due to TB globally in 2021 was 1.6 million, this has increased compared to 2020, which was 1.3 million. Of the 1.6 million deaths due to TB, 187,000 of them died from TB and HIV. The death rate due to TB in Indonesia reached 150,000 cases, an increase of 60% from 2020 as many as 93,000 cases of death due to TB. The TB mortality rate in 2021 increased by 56 per 100,000 population when compared to the TB mortality rate in 2020, which was 34 per 100,000 population [5]. Based on data from the South Sulawesi Provincial Health Office, the number of TB patients per district/city in 2020 was 12,444 cases or around 40%. The highest TB incidence rate in South Selawesi Province is in the city of Makassar which has the most TB patients with 3,421 patients or around 51% while the lowest TB incidence rate is in Tana Toraja Regency with 161 cases or around 21.41% [6, 7].

In 2021, the number of TB patients in South Sulawesi Province was 15,154 cases or around 48.84%. The highest incidence rate is in Takalar Regency with 640 cases or around 66.32%, while the lowest incidence rate is still in Tana Toraja Regency with 171 cases or around 22.47% and in 2022, the number of TB patients in South Sulawesi Province increased to 21,183 cases or around 60.16%. The highest incidence rate is again held by Makassar City with the number of patients 6,097 cases or around 80.14% and the lowest is still held by Tana Toraja Regency which is 275 cases or around 31.71%.

Drug-Resistant Tuberculosis (TB-RO) is still a threat in TB control and is one of the major public health problems in many countries around the world. TB-RO is a term used to describe a strain of Mycobacterium tuberculosis that is resistant to the first line of Anti-Tuberculosis Drugs (OAT), namely Rifampicin (Rif) and Isoniazid (INH) which are very effective in killing Mycobacterium tuberculosis germs. TB-RO becomes a new challenge in the program TB control due to difficult diagnosis enforcement, high rates of therapy failure and mortality.

Based on WHO data, in 2015-2020 the estimate of TB-RO cases globally is relatively stable. In 2021, the proportion of TB-RO cases is estimated at 3.6% (450,000 cases). This figure increased when compared to 2020 there was 3.1% (437,000 cases). This is thought to be related to the COVID-19 pandemic which causes obstacles to early detection of tuberculosis [4, 8].

In 2021, WHO reported that the estimated proportion of people with TB-RO globally is 3.6%. Of the 3.6% of MDR-TB patients, it is a new case and 18% are TB patients who have had a history of previous treatment. Based on the Southeast Asian region, in 2020 there were 164,000 cases of MDR-TB while in 2021 there was an increase of 172,000 cases.

WHO said there are 30 countries with the highest TB cases accounting for 87% of total global cases. Meanwhile, there are 8 countries among them accounting for more than two-thirds of the total global cases. The first country is occupied by India with a proportion of 28% of total global cases. Second is Indonesia with a contribution of 9.2%. WHO explained, India can be estimated to reach 2 million cases in 2021. Meanwhile, Indonesia had 1 million cases in the same period. Third, China with an achievement of 7.4%. Fourth is the Philippines with a proportion of 7%. Next are Pakistan 5.8%, Nigeria 4.4%, Bangladesh 3.6% and the Democratic Republic of the Congo 2.9%.

In 2021, Indonesia ranked fifth among the 30 countries with the heaviest TB-RO burden in the world. In 2020, the estimated incidence of TB-RO cases was 2.4% of all new TB patients and 13% of TB patients who had been treated with a total estimated incidence of TB-RO cases of 24,000 cases (8.8/100,000 population) [9] while in 2021 there was an increase of 28,000 cases related to the impact of the COVID-19 pandemic on the detection of tuberculosis.

Every year, TB-RO cases in South Sulawesi Province have increased. Based on data from the South Sulawesi Provincial Health Office, in 2021 there were 391 new cases of TB-RO and increased in 2022 to 492 cases. The proportion of TB-RO cases in Makassar is 42.5%, ranking first among all cities/regencies in South Sulawesi Province while Tana Toraja Regency has the smallest proportion of 0.2% among cities/regencies in South Sulawesi Province [6]. Labuang Baji Hospital is one of the TB-RO referral hospitals in South Sulawesi. Based on data from the Tuberculosis Information System (SITB) of Labuang Baji Hospital, it is recorded that TB-RO sufferers have experienced ups and downs in the last three years. In 2020 there were 86 cases, then decreased in 2021 to 38 cases and in 2022 increased again to 105 cases.

TB-RO is a heavy burden on the health care system because it is a complication in the cure, hindering TB control programs and requiring treatment costs that are more valuable than TB that is resistant to treatment. TB-RO is associated with higher rates of therapy failure and case mortality than TB in general. The sample in this study predominantly consists of patients from a single geographic location, which may limit the generalizability of the findings to other populations. While this provides important insights into the specific factors influencing TB-RO in the South Sulawesi region, future research should consider incorporating a more demographically diverse sample. This would ensure a broader application of the results and improve the external validity of the findings [10, 11].

Identification of risk factors is essential as a foundation for the development of disease prevention and control strategy programs. According to [12] have 5 (five) drug resistance factors in TB-RO patients, namely sociodemographic factors, lifestyle factors, health factors, environmental factors, and knowledge and stigma factors. Sociodemographic factors include age, gender, marital status, education level, employment status, family income history [13]. Lifestyle factors include smoking history, number of cigarettes/day, alcohol consumption, sleep duration, travel history and type of transportation used. Health factors include previous TB treatment history, drug side effects, contact history of TB cases, BCG vaccine status, and access to health services [14, 15]. Environmental factors include the history of the residential area, the frequency of crossing the border, the residential environment, the type of house, the number of rooms, and the frequency of visiting crowded areas [16].

Research conducted by [17] in Ternate showed that TB-RO was significantly related to respondents who had undergone previous TB treatment and had a history of comorbid diseases of Diabetes Mellitus. However, health service facilities in Poso Regency are not so adequate that they cannot guarantee the regularity of taking medication for TB-RO patients, and health workers do not carry out early detection in special conditions such as the presence of complicated DM in TB patients so that they cannot prevent comorbidities with the occurrence of TB-RO [18].

A study conducted by [19] in Sudan stated that patients who had a history of contact with MDR-TB patients had a 5 times greater chance of developing MDR-TB compared to patients who did not have a history of contact with MDR-TB patients. The results of a study conducted by [20] in Pakistan show that cavitation on x-ray examination is a risk factor for MDR-TB. Patients who had pulmonary cavities were 30 times more likely to develop MDR-TB compared to patients who did not have lung cavities on x-rays. Research by [21] in Mali showed that BTA 3+ phlegm also had an effect on the incidence of MDR-TB. Patients with BTA 3+ sputum test results have a 2 times greater risk of MDR-TB events. According to [12], patients who have a previous treatment history have a 5 times more chance of developing MDR-TB than patients who do not have a previous treatment history. MDR-TB patients who have comorbid DM have a 3 times greater chance of developing MDR-TB compared to MDR-TB patients without comorbidities [22, 23].

Research conducted by [22] in Makassar using a cross-sectional study design with a total of 77 case samples consisting of 46 patients with Rifampicin Resistant/RR, 20 patients with Multi Drug Resistant/MDR and 11 patients with pre-extensive drug resistant/pre-XDR. The results showed that there was a significant relationship between the previous history of TB treatment and the classification of TB-RO at Labuang Baji Hospital. There have been many studies that discuss the risk factors for TB-RO. Identifying risk factors associated with TB-RO has important benefits to help guide treatment, develop follow-up strategies in at-risk populations and primarily modify these risk factors to prevent the development of TB-RO [24].

Unfortunately, based on several studies on TB-RO, inconsistencies were found related to the factors that affect the incidence of TB-RO in different regions, this is influenced by the geographical location of each research location which distinguishes the background where the disease occurs so that the natural history of the disease and risk factors also vary. Therefore, identification of risk factors must be carried out regionally in order to develop the most effective strategies in efforts to control TB-RO [10, 25].

2. LITERATURE REVIEW

TB is a significant global public health problem caused by the bacterium Mycobacterium tuberculosis. It primarily affects the lungs but can also impact other parts of the body (extrapulmonary TB). Despite being a preventable and curable disease, TB remains one of the leading causes of death worldwide, especially in low- and middle-income countries [26]. The World Health Organization (WHO) reports that TB is the second most deadly infectious disease globally, following COVID-19, with approximately 1.6 million deaths in 2021 alone.

The COVID-19 pandemic has further exacerbated TB control efforts, leading to an increase in TB deaths for the first time in a decade [27].

TB-RO poses an additional challenge to TB control. DR-TB includes Multidrug-Resistant TB (MDR-TB), resistant to at least isoniazid and rifampicin, and extensively drug-resistant TB (XDR-TB), which is also resistant to fluoroquinolones and second-line injectable drugs [28]. The emergence of DR-TB is attributed to various factors, including inadequate treatment regimens, poor patient adherence to treatment, and incomplete TB control programs [29].

Healthpreneurship offers a potential solution to these challenges. Healthpreneurs, by merging entrepreneurial strategies with healthcare innovations, can drive the creation and implementation of new models for tackling diseases like TB and DR-TB [30]. These professionals bring business efficiency, technological advancements, and innovative care models into the healthcare sector, ensuring that more patients receive timely diagnosis and treatment. In the context of TB and DR-TB, healthpreneurs can introduce initiatives such as mobile diagnostic clinics, telemedicine services for remote patients, and personalized medication tracking systems that improve treatment adherence [31].

Through healthpreneurship, healthcare institutions can address critical issues such as poor patient adherence to TB treatment by deploying innovative patient management systems that monitor medication intake and remind patients about their schedules. Moreover, healthpreneurs can improve healthcare accessibility by introducing low-cost diagnostic tools and health education programs aimed at reducing TB-related stigma, which often hinders timely treatment-seeking behavior.

Incorporating healthpreneurship into TB control programs, especially in high-burden regions like Indonesia, where DR-TB incidence is rising, could significantly strengthen the healthcare infrastructure. Healthpreneurs can help healthcare providers at facilities such as Labuang Baji Hospital streamline patient management and reduce the incidence of DR-TB by offering solutions that are tailored to local healthcare challenges [32].

2.1. Epidemiology of Drug-Resistant Tuberculosis

Indonesia ranks among the top countries with the highest burden of DR-TB. In 2021, Indonesia was estimated to have 24,000 DR-TB cases, representing 2.4% of all new TB cases and 13% of previously treated cases. The South Sulawesi Province, particularly Makassar City, reports a high incidence of DR-TB. The Labuang Baji Regional Hospital in Makassar has seen fluctuating numbers of DR-TB cases over recent years, highlighting the ongoing challenge of managing and controlling this disease.

2.2. Risk Factors for Drug-Resistant Tuberculosis

Identifying and understanding the risk factors associated with DR-TB are crucial for developing effective prevention and control strategies. Several studies have highlighted various risk factors contributing to the incidence of DR-TB. Sociodemographic factors such as age and gender play a significant role. Studies have shown that individuals in the productive age group (15-58 years) are at a higher risk of developing DR-TB, possibly due to increased exposure and transmission dynamics within this age group. While some studies indicate no significant difference in DR-TB risk between males and females, others suggest that males may have slightly higher odds of developing DR-TB. Clinical factors, particularly a history of prior TB treatment, are significant risk factors for DR-TB. Incomplete or improper treatment regimens can lead to the development of drug resistance, making patients who have previously received TB treatment more susceptible to developing MDR-TB [33]. Additionally, the presence of a high bacillary load, indicated by sputum smear positivity, especially with high grades (e.g., 3+), is associated with an increased risk of DR-TB.

Comorbid conditions such as Diabetes Mellitus (DM) are also known risk factors for TB and DR-TB. Patients with DM have compromised immune systems, making them more susceptible to TB infection and progression to DR-TB [34]. Studies have shown that DR-TB patients with DM have a higher likelihood of poor treatment outcomes. Behavioral and environmental factors further contribute to the risk of TB and DR-TB. Lifestyle factors such as smoking and alcohol consumption can impair the immune response, increasing susceptibility to TB and DR-TB, and are also linked to poorer adherence to TB treatment regimens [35, 36]. Moreover, socioeconomic status, including low income and poor living conditions, contributes to the risk of TB and DR-TB. Crowded living environments and limited access to healthcare services facilitate the transmission and hinder the management of TB and DR-TB. Addressing these multifaceted risk factors is essential for effective TB control programs [37].

3. RESEARCH METHOD

This research used a case-control study design conducted at Labuang Baji Hospital, Makassar. The case group consists of TB-RO sufferers who have been and are currently undergoing treatment and the control group consists of TB sufferers who have undergone treatment and were not diagnosed with TB-RO. A total of 105 cases of TB-RO were recorded in 2022. The Lemeshow formula is applied to determine the number of samples as follows:

$$n = \frac{\{Z1-\alpha/2\sqrt{[2P^*(1-P^*)]} + Z1-b\sqrt{[2P^*(1-P1)+P2^*(1-P2^*)]}\}^2}{(P1^*-P2^*)^2} \quad (1)$$

where:

n = Minimum number of samples required

$Z1-\alpha/2$ = The normal standard deviation used is 1.96 according to the degree of significance of 95% ($\alpha = 0.05$)

$Z1-\beta = \beta = 0.10$ used 1.282

OR = 3

$P1$ = The probability of an event occurring in the case group

$P2$ = Probability of an event occurring in the control group = 0.05

The case group sample obtained using the formula was 76 patients. For the control group, we used a ratio of 1:2 for cases to controls. Therefore, the control group obtained 152 patients and the total samples collected were 228 patients. The sampling technique uses purposive sampling. For the control group, inclusion criteria included those who had or were undergoing outpatient treatment. The exclusion criteria are TB patients with HIV and TB patients whose data is incomplete in the medical record.

3.1. Instruments and procedures

Procedures and interviews were carried out at the Labuang Baji Makassar District Hospital, involving TB-RO, TB-RO patients who had and were undergoing treatment and were recorded in SITB as a case group and TB patients who had undergone treatment and were recorded in SITB and not diagnosed with TB-RO as a control group who regularly visit the Hospital Pulmonary TB Polyclinic (regular patients) or are first/new patients [38].

Researchers took 5-10 minutes to conduct face-to-face interviews with each patient. The interview questionnaire collected information about socio-demographic factors (age, gender, highest level of education, occupation, income, and marital status). Research variables consisted of BTA sputum, nutritional status, previous treatment history, drug side effects and comorbidities. All independent variables are then categorized into low risk and high risk. Low risk means all variables have positive results, while high risk means they have negative results.

This research was carried out after obtaining written consent from each patient/respondent. This research has been approved by the Health Research Ethics Committee, Hasanuddin University (Approval Letter Number: 5865/UN4.14.1/TP.01.02/2023 to the Faculty of Public Health, Hasanuddin University and Labuang Baji Regional Hospital).

3.2. Data analysis

Data analysis was carried out using the SPSS version 25 software and the STATA program. Univariate analysis was applied to examine the sociodemographic characteristics of the participants. Multivariate analysis was conducted using a logistic regression model to determine the relationship between various risk factors and the incidence of TB-RO. The analysis focused on identifying significant predictors of DR-TB among the patients at Labuang Baji Regional Hospital, considering factors such as age, gender, previous TB treatment, bacteriological factors, comorbid conditions, and behavioral and environmental influences.

4. RESULT AND DISCUSSION

The highest number of TB-RO cases were female, namely 50.6% (41 people), while the majority of controls were also female, namely 52.8% (64 people). age group, it was found that the majority of TB-RO

cases were in the 15-58 year age group, namely 88.6% (64 people), while the majority of controls were also in the 15-58 year age group, namely 75.6% (99 people). The highest number of TB-RO cases with the latest education were those who had a final education of SMA/SMK/MA, namely 30.4% (25 people), and likewise, the highest number of controls were those who had a final education of SMA/SMK/MA, namely 31 .7% (38 people). Employment status showed that the largest group of TB-RO cases and controls were in the working group, namely 55.7% (43 people) and 54.5% (68 people). Type of work found that the TB-RO case group was mostly found in the Housewife group, namely 20.3% (12 people), the self-employed group 15.2% (11 people), and the private sector employee group 15.2% (9 people), while the majority of controls were in the student group, namely 17.1% (20 people), the non-working group was 16.3% (17 people), and the self-employed group was 13.0% (17 people). It was found that the income of the TB-RO case and control group was the largest in the group without income, namely 44.3% (36 people) and 45.5% (55 people). Marital status found that the largest group of TB-RO cases and controls were in the married group, namely 62.0% (45 people) and 54.5% (71 people).

Based on the table 1, it was found that the most TB-RO case and control groups were in the productive age group, which was 88.6% (64 people) and 75.6% (99 people). Based on the gender variable, there were more cases and control of TB-RO obtained by female respondents, namely 50.6% (41 people) and 52.8% (64 people). Based on the knowledge variable, it was found that the TB-RO case and control groups obtained more respondents who had good knowledge, namely 72.2% (58 people) and 52.8% (64 people). Based on the variable of employment status, it was found that the TB-RO case and control groups obtained more working respondents, namely 55.7% (43 people) and 54.5% (68 people). Based on the income variable, it was found that the TB-RO case group and control group obtained more respondents who did not have any income, 44.3% (36 people) and 45.5% (55 people). Based on the BTA phlegm variable, it was found that the TB-RO case and control groups obtained more respondents who suffered from TB-RO with BTA $< 3+$ or negative sputum, which was 69.6% (64 people) and 88.6% (100 people). Based on the nutritional status variable, it was found that the TB-RO case group and control group obtained more respondents who had BMI ≥ 18.5, namely 81.0% (63 people) and 78.9% (98 people). Based on the variables of previous treatment history, it was found that the TB-RO case and control groups obtained more respondents who had just started treatment and respondents who were treated after discontinuing treatment (negligence), which were 55.7% (52 people) and 73.2% (82 people). Although the sample size used in this study is statistically adequate for the analysis, it may still not be large enough to generalize the findings to a broader population. The relatively small sample from a single hospital limits the ability to extend the conclusions to other regions or populations with different characteristics. Future research should consider expanding the sample size and incorporating multiple hospitals or regions to improve the generalizability of the findings and capture a more comprehensive range of risk factors for TB-RO. Based on the variables of drug side effects, it was found that the TB-RO case group and control group obtained more respondents who felt side effects from mild category drugs, namely 55.7% (46 people) and 60.2% (72 people). Based on the variables of comorbidity factors, it was found that the TB-RO case and control groups obtained more respondents who did not have comorbidities such as hypertension, diabetes mellitus, and/or HIV, which were 54.4% (42 people) and 52.8% (66 people).

Table 1. Characteristics of Respondents

Characteristics Respondents	**TB-RO Incident**		**Control**		**Sum**	
	N	%	n	%	n	%
1. Age						
15-58 years old	64	88,6%	99	75,6%	163	80,7%
>58 years old	15	11,4%	24	24,4%	39	19,3%
2. Gender						
Man	38	49,4%	59	47,2%	97	48,0%
Woman	41	50,6%	64	52,8%	105	52,0%

3. Last Education						
No School	3	3,8%	5	4,1%	8	4,0%
SD	7	3,8%	12	13,0%	19	9,4%
Junior High School/MTs	20	30,4%	30	21,1%	50	24,8%
High School/Vocational School/MA	25	30,4%	38	31,7%	63	31,2%
Sarjana	23	31,6%	35	26,8%	58	28,7%
Postgraduate	2	0,0%	2	3,3%	4	2,0%
4. Employment Status						
Not Working	36	44,3%	55	45,5%	91	45,0%
Work	43	55,7%	68	54,5%	111	55,0%
5. Job Type						
Not Working	11	10,1%	17	16,3%	28	13,9%
PNS/TNI/POLRI/BUMN/BUMD	9	10,1%	15	13,0%	24	11,9%
Self-employed	11	15,2%	17	13,0%	28	13,9%
Farmers/Fishermen/Workers	9	8,9%	13	12,2%	22	10,9%
Pensioner	6	6,3%	9	8,1%	15	7,4%
Students/Students	12	13,9%	20	17,1%	32	15,8%
Housewives	12	20,3%	19	12,2%	31	15,3%
6. Income						
None	36	44,3%	55	45,5%	91	45,0%
Less than UMR	12	15,2%	18	14,6%	30	14,9%
More than UMR	32	40,5%	49	39,8%	81	40,1%
7. Marital Status						
Married	45	62,0%	71	54,5%	116	57,4%
Divorced (for life/for death)	9	10,1%	15	13,0%	24	11,9%
Unmarried	24	27,8%	38	32,5%	62	30,7%

Table 2 provides a summary of various factors associated with TB-RO in both cases and controls. It covers demographic, socioeconomic, and clinical variables influencing TB-RO occurrence. Key findings include the following a higher proportion of cases (88.6%) fall within the productive age group compared to controls (75.6%). Gender distribution shows a slight female predominance in both groups. Knowledge levels were generally good, reported by 72.2% of cases and 74.8% of controls. Employment status reveals over half of both cases (55.7%) and controls (54.5%) were employed. However, a larger share of cases (44.3%) than controls (45.5%) had no income, suggesting a possible socioeconomic influence.

Nutritional status, sputum smear (Dahak BTA) results, and treatment history further illustrate associations with TB-RO. Cases were more likely to have poor nutritional status (19%) compared to controls (41%). The majority in both groups had low sputum smear risk, but cases (69.6%) showed higher susceptibility. Previous treatment history and drug side effects highlight significant differences in risk profiles, emphasizing their relevance to TB-RO prevalence. This overview underscores the multifactorial nature of TB-RO risk.

Table 2. Research Variables

Research Variables	**TB-RO Incident**		**Control**		**Sum**	
	N	%	N	%	N	%
1. Age						
Productive	64	88.6%	99	75.6%	163	80.7%
Non-Productive	15	11.4%	24	24.4%	39	19.3%
2. Gender						
Male	38	49.4%	59	47.2%	97	48.0%
Female	41	50.6%	64	52.8%	105	52.0%

3. Knowledge						
Poor	21	27.8%	32	25.2%	53	53%
Good	58	72.2%	91	74.8%	149	73.8%
4. Employment Status						
Not Working	36	44.3%	55	45.5%	91	45.0%
Working	43	55.7%	68	54.5%	111	55.0%
5. Income						
None	36	44.3%	55	45.5%	91	45.0%
Below UMR	12	15.2%	18	14.6%	30	14.9%
Above UMR	32	40.5%	49	39.8%	81	40.1%
6. BTA Sputum						
High Risk	15	30.4%	23	11.4%	38	13.9%
Low Risk	64	69.6%	100	88.6%	164	86.1%
7. Nutritional Status						
Poor	16	19.0%	25	41%	41	20.3%
Good	63	81.0%	98	78.9%	161	79.7%
8. Previous Treatment History						
Low Risk	52	55.7%	82	73.2%	134	66.3%
High Risk	27	44.3%	41	26.8%	68	33.7%
9. Drug Side Effects						
Low Risk	46	55.7%	72	60.2%	118	58.4%
High Risk	33	44.3%	51	39.8%	84	41.6%
10. Comorbidity Factors						
High Risk	37	45.6%	57	47.2%	94	46.5%
Low Risk	42	54.4%	66	52.8%	108	53.5%

Table 3 shows the results of bivariate analysis, it is known that the age variable in this study obtained the results of a statistical test with a value of OR = 2.509 (Cl 95%: 1.120-5.622). This shows that age is a risk factor for TB-RO by 2.509 times, and statistically significant with the Lower limit and Upper limit (LL-UL) values above the value of 1. The gender variable was obtained from the statistical test with an OR = 1.093 value (Cl 95%: 0.621-1.924). This shows that gender in this study is not a risk factor for TB-RO, and is statistically meaningless with the Lower limit and Upper limit (LL-UL) values including a value of 1. The knowledge variable was obtained from the results of the statistical test with the value of OR = 1.145 (Cl 95%: 0.605-2.169). This shows that knowledge is not a protective factor for the occurrence of TB-RO, and is statistically meaningless with the Lower limit and Upper limit (LL-UL) values including the value of 1. To make the key findings more accessible and easily understandable, we have added graphical representations of the significant and non-significant results. These include bar charts for the distribution of TB-RO incidence by gender, employment status, and income level, as well as a graphical comparison of the odds ratios for significant risk factors such as age, BTA phlegm, and previous treatment history. These visual aids allow readers to quickly grasp the trends in the data and understand the relationship between different variables and TB-RO incidence.

The variable of employment status obtained the results of the statistical test with the value of OR = 0.952 (Cl 95%: 0.539-1.680). This shows that the employment status is a protective factor for the occurrence of TB-RO, and is statistically meaningless with the Lower limit and Upper limit (LL-UL) values including the value of 1. The income variable was obtained from the statistical test with an OR value = 0.973 (Cl 95%: 0.547-1.731). This shows that income is a protective factor for the occurrence of TB-RO, and is statistically meaningless with the Lower limit and Upper limit (LL-UL) covering a value of 1. The BTA phlegm variable in this study was obtained from the results of a statistical test with an OR value = 3.397 (Cl 95%: 1.630-7.082). This shows that BTA phlegm is a risk factor for TB-RO by 3.397 times, and statistically significant with Lower limit and Upper limit (LL-UL) values above 1.

The nutritional status variable in this study was obtained from the results of a statistical test with a value of OR = 0.874 (Cl 95%: 0.430-1.778). This shows that nutritional status is a protective factor for the occurrence of TB-RO, and is statistically meaningless with the Lower limit and Upper limit (LL-UL) values including a value of 1. The variables of previous treatment history in this study were obtained from statistical

test results with OR = 0.461 (Cl 95%: 0.254-0.837). This shows that the previous treatment history is a protective factor for the occurrence of TB-RO, and is statistically meaningless with the Lower limit and Upper limit (LL-UL) values including a value of 1. The drug side effect variables in this study were obtained from statistical test results with an OR value = 0.832 (Cl 95%: 0.470-1.745). This shows that drug side effects are a protective factor for the occurrence of TB-RO, and are statistically meaningless with the Lower limit and Upper limit (LL-UL) values including a value of 1. The non-significant results, such as gender, employment status, and income, suggest that these factors may not have a strong or direct influence on the occurrence of TB-RO within the studied population. This finding highlights the complexity of TB-RO risk factors and the potential for regional or contextual variability. It is essential to interpret these non-significant results with caution, as they could reflect the limits of certain variables in this specific population rather than a universal lack of association. Future studies might benefit from larger, more diverse samples to further explore these variables and clarify their role in TB-RO development. The comorbidity factor variable in this study was obtained from the results of a statistical test with an OR value = 0.938 (Cl 95%: 0.532-1.654). This shows that comorbidity is a protective factor for the occurrence of TB-RO, and is statistically meaningless with the Lower limit and Upper limit (LL-UL) values including a value of 1.

Table 3. Risk of Research Variables on TB-RO Incidence

Variable	**TB-RO Incident**				**OR**	**P value**
	Case		**Control**		**(Cl 95%, LL-UL)**	
	n	%	N	%	N	%
1. Age						
Productive	64	88.6%	99	75.6%	2.509	0.036
Unproductive	15	11.4%	24	24.4%	(1.120-5.622)	
2. Gender						
Man	38	49.4%	59	47.2%	1.093	0.871
Woman	41	50.6%	64	52.8%	(0.621-1.924)	
3. Knowledge						
Less	21	27.8%	32	25.2%	1.145	0.800
Good	58	72.2%	91	74.8%	(0.605-2.169)	
4. Employment Status						
Not Working	36	44.3%	55	45.5%	0.952	0.979
Working	43	55.7%	68	54.5%	(0.539-1.680)	
5. Income						
None	36	44.3%	55	45.5%	0.973	1.000
Less than UMR	12	15.2%	18	14.6%	(0.547-1.731)	
More than UMR	32	40.5%	49	39.8%		
6. BTA Sputum						
High Risk	15	30.4%	23	11.4%	3.397	0.001
Ease of Risk	64	69.6%	100	88.6%	(1.630-7.082)	
7. Nutritional Status						
Bad	16	19.0%	25	41%	0.874	0.848
Good	63	81.0%	98	78.9%	(0.430-1.778)	
8. Previous Treatment History						
Low Risk	52	55.7%	82	73.2%	0.461	0.016
High Risk	27	44.3%	41	26.8%	(0.254-0.837)	
9. Side Effects Medicine						
Light	46	55.7%	72	60.2%	0.832	0.630
Heavy	33	44.3%	51	39.8%	(0.470-1.745)	
10. Comorbidities						
High Risk	37	45.6%	57	47.2%	0.938	0.940
Low Risk	42	54.4%	66	52.8%	(0.532-1.654)	

Table 4 shows that from the results of the analysis, it can be seen that the most risky variable for TB-RO incidence is the BTA phlegm variable with a value of OR = 3.495 (95% Cl; 1.618-7.548). The statistical test value showed that the BTA phlegm variable was significantly at risk of TB-RO incidence by 3.495 times.

Based on the results of the analysis, a logistical equation for TB-RO events can be made as follows:

$$\text{TB-RO incidence logit} = -2.007 + 1.049\,(\text{age}) + 1.251\,(\text{BTA sputum}) + 0.769\,(\text{prior treatment history})$$

$$\text{and} \quad = a + \beta^1 x^1 + \beta^2 x^2 + \cdots + \beta^i x^i$$

$$\text{and} \quad = -2.007 + 1.049 + 1.251 + 0.769$$

$$= 1.062$$

The interpretation of the logistical equation of TB-RO events is that in a condition where there is no influence from age, BTA phlegm, and previous treatment history, by paying attention to negative constant values, the risk of developing TB-RO will decrease by 2.007 times. However, if the constant value is taken into account with the influence of the addition of these risk factors, the risk of being exposed to TB-RO will also increase.

Table 4. Results of Multivariate Analysis of TB-RO Risk Factors

Research Variables	**B**	**S.E**	**Forest**	**Mr**	**OR**	**95% CI**	
						LL	**HIVE**
Age	1.049	0.431	5.924	0.015	2.85	1.22	6.641
Dahak BTA	1.251	0.393	10.147	0.001	3.49	1.61	7.548
Previous Medical History	0.769	0.320	5.765	0.016	0.46	0.24	0.868
Constant	-2.007	1.005	3.987	0.046	0.13	-	-

The results of these values, if summed with constant values, will show a direct comparison, namely the greater the value of the independent variable, the greater the risk of suffering from TB-RO. The value generated from the equation of 1.062 shows that the more risk factors a person has, such as age, BTA sputum, and previous treatment history, the greater the risk of developing TB-RO.

The probability value of a person getting TB-RO if they have age, BTA phlegm, and previous treatment history at visitors at Labuang Baji Makassar Hospital is as follows:

$$P = \frac{1}{1 + e^{-y}} \tag{2}$$

Where:
P = probability for the occurrence of an event y
e = natural number (2.72)
$y = a + \beta^1 x^1 + \beta^2 x^2 + \cdots + \beta^i x^i$

Substitute the values:

$$P = \frac{1}{1 + e^{-1.062}} \tag{3}$$

$$P = \frac{1}{1 + 2.72^{-1.062}} \tag{4}$$

$$P = \frac{1}{1 + 0.346} \tag{5}$$

$$P = \frac{1}{1.346} \tag{6}$$

$$P = 0.74 \text{ or } 74\% \tag{7}$$

This means that if a person has age, BTA sputum, and previous treatment history, then the probability of developing TB-RO is 74%.

5. CONCLUSION

The study concludes that age and BTA phlegm are significant risk factors for the incidence of TB-RO in patients at Labuang Baji Hospital. The findings indicate that individuals in the productive age group are more susceptible to developing TB-RO, while BTA phlegm, particularly with a high bacterial load, serves as the dominant risk factor. Additionally, previous treatment history is identified as a protective factor, suggesting that patients with no prior treatment failures or treatment interruptions are less likely to develop drug-resistant tuberculosis. These insights emphasize the importance of managing treatment adherence to mitigate the risk of developing TB-RO.

To further enhance tuberculosis control programs, the study highlights the need for a more robust monitoring system for patients who have discontinued or failed treatment. The failure to adhere to treatment plans has been shown to contribute to the development of drug resistance, underlining the need for closer surveillance and follow-up care for these patients. By improving monitoring and support for at-risk individuals, healthcare systems can reduce the rates of TB-RO and improve patient outcomes.

One limitation of the study is the lack of longitudinal data, which restricts the ability to observe how risk factors for drug-resistant tuberculosis may evolve over time. A longitudinal study design that tracks changes in patient health and risk factors could provide deeper insights into the progression of TB-RO, allowing for earlier detection and intervention. Future research should focus on this approach to better understand the dynamics of TB-RO development and to create more effective strategies for controlling and preventing drug-resistant tuberculosis.

6. DECLARATIONS

6.1. About Authors

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6.2. Author Contributions

Conceptualization: AM; Methodology: NN; Software: IL; Validation: AM and NN; Formal Analysis: IL and AM; Investigation: NN; Resources: IL; Data Curation: AM; Writing Original Draft Preparation: NN and AM; Writing Review and Editing: IL, AM, and GD; Visualization: NN; All authors, AM, NN, IL, and GD, have read and agreed to the published version of the manuscript.

6.3. Data Availability Statement

The data presented in this study are available on request from the corresponding author.

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6.5. Declaration of Conflicting Interest

The authors declare that they have no conflicts of interest, known competing financial interests, or personal relationships that could have influenced the work reported in this paper.

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