



## The Relationship Between Age, Employment Status, Gender, Linezolid Use, and Hiv Status on The Survival Duration of Short-Term Treated MDR-TB Patients

Akhmad Azmiardi<sup>1✉</sup>, Muhamad Z. Saefurrohimi<sup>2</sup>, Intan H. Ardiani<sup>3</sup>

<sup>1,2</sup>Public Health, Faculty of Public Health, Universitas Mulawarman, Samarinda, Indonesia

<sup>2</sup>Magister Program of Public Health, Faculty of Medicine and Health, Universitas Jendral Soedirman, Purwokerto, Indonesia

### Article Info

#### Article History:

Submitted 2024-11-10

Revised 2024-11-20

Accepted 2024-11-22

**Kata Kunci:** Survival TB-MDR, Status pekerjaan, Jenis kelamin, Pengobatan jangka pendek, Linezolid dan HIV

**Keywords:** MDR-TB survival, Employment status, Gender, Short-term treatment, Linezolid and HIV.

DOI : -

### Abstrak

Penelitian ini mengevaluasi hubungan faktor demografi dan klinis dengan kelangsungan hidup pasien TB resistan obat (MDR-TB) yang menjalani pengobatan jangka pendek. Menggunakan desain kohort retrospektif, data diambil dari rekam medis 38 pasien MDR-TB yang menerima terapi jangka pendek pada 2021–2023 di rumah sakit Jawa Tengah. Variabel yang dianalisis meliputi usia, status pekerjaan, jenis kelamin, penggunaan Linezolid (Lzd), status HIV, dan waktu inisiasi pengobatan. Hasil analisis regresi logistik menunjukkan bahwa status pekerjaan dan jenis kelamin secara signifikan memengaruhi kelangsungan hidup. Pasien yang bekerja memiliki peluang kelangsungan hidup lebih tinggi dibandingkan pasien tidak bekerja ( $Exp(B) = 38,884$ ;  $p = 0,011$ ). Pasien perempuan menunjukkan hasil lebih baik dibandingkan laki-laki ( $Exp(B) = 0,031$ ;  $p = 0,011$ ). Usia menunjukkan hubungan lemah dengan kelangsungan hidup, dengan usia lebih tua cenderung menurunkan kelangsungan hidup meskipun tidak signifikan ( $p = 0,052$ ). Status HIV dan waktu inisiasi pengobatan dini juga menunjukkan potensi memengaruhi kelangsungan hidup, tetapi tidak signifikan ( $p > 0,05$ ). Penggunaan Lzd tidak menunjukkan efek signifikan terhadap kelangsungan hidup ( $p = 0,441$ ). Penelitian ini menyimpulkan bahwa pekerjaan dan jenis kelamin merupakan prediktor penting kelangsungan hidup pasien MDR-TB, sementara faktor lain memerlukan penelitian lanjutan.

### Abstract

*This study evaluated the association of demographic and clinical factors with the survival of drug-resistant TB (MDR-TB) patients undergoing short-term treatment. Using a retrospective cohort design, data were collected from the medical records of 38 MDR-TB patients who received short-term therapy in 2021-2023 at a Central Java hospital. The variables analyzed included age, employment status, gender, Linezolid (Lzd) use, HIV status, and treatment initiation time. The results of logistic regression analysis showed that employment status and gender significantly influenced survival. Patients who were employed had a higher chance of survival than patients who were not employed ( $Exp(B) = 38.884$ ;  $p = 0.011$ ). Female patients showed better outcomes than males ( $Exp(B) = 0.031$ ;  $p = 0.011$ ). Age showed a weak association with survival, with older age tending to decrease survival although not significantly ( $p = 0.052$ ). HIV status and timing of early treatment initiation also showed potential to affect survival, but were not significant ( $p > 0.05$ ). Lzd use showed no significant effect on survival ( $p = 0.441$ ). This study concludes that occupation and gender are important predictors of survival in MDR-TB patients, while other factors require further research.*

## INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB) remains a global health challenge, with significant morbidity and mortality rates despite advancements in treatment. Understanding the factors influencing survival among MDR-TB patients is crucial for optimizing management strategies and improving patient outcomes. Previous studies have indicated that demographic factors, such as age and gender, may play a role in survival outcomes, with older adults and males often demonstrating differing responses to treatment. However, these findings are inconsistent, particularly regarding age, gender, and other demographic and clinical variables, underscoring the need for further research to explore the nuanced impact of these variables on MDR-TB survival (Wang et al., 2020; Wotale et al., 2024).

Employment status and socioeconomic factors also appear to influence treatment adherence and outcomes in MDR-TB patients. Employed individuals may face barriers such as work-related stress, financial challenges, and limited time for medical follow-ups, potentially compromising their treatment adherence and survival. Conversely, unemployed patients might benefit from more time to focus on treatment, although they may lack adequate resources for care. Understanding the role of employment in MDR-TB survival can inform targeted interventions to support patients, especially those juggling work commitments during their treatment journey (Harahap et al., 2024; Tola et al., 2015; Widayrini & Probandari, 2017).

Clinical variables, such as the use of Linezolid and HIV co-infection, also

contribute to survival outcomes in MDR-TB patients. Linezolid, a key component of MDR-TB treatment regimens, has shown mixed results in influencing survival rates, highlighting the need to assess its effectiveness in specific contexts. Additionally, MDR-TB patients co-infected with HIV face heightened risks due to immunosuppression and delayed treatment initiation, often resulting in poorer outcomes. This study aims to examine the interplay of these demographic, socioeconomic, and clinical factors, providing insights to guide evidence-based interventions for enhancing the survival of MDR-TB patients.

## METHOD

This study used a retrospective cohort design to investigate factors affecting the survival duration of multidrug-resistant tuberculosis (MDR-TB) patients undergoing short-term treatment regimens. The study was conducted from 2021 to 2023 at several hospitals in Central Java, Indonesia, that participated in the Integrated Management of Drug Resistant Tuberculosis Control (MTPTRO) program. The study included 38 MDR-TB patients who had completed short-term therapy during the study period. Patients' medical records were reviewed to extract relevant demographic and clinical data. Independent variables collected included: Age, gender, employment status, Linezolid (Lzd) use, and HIV status. The dependent variable was survival duration. Survival status was categorized into: Survival less than one month before death and Survival more than one month before death. Data were analyzed using logistic regression analysis to determine the association between selected demographic and clinical variables

and survival status. All statistical analyses were performed using SPSS version 15. This study adhered to ethical considerations for research involving patient medical records, ensuring confidentiality and compliance with relevant regulations.

## RESULTS AND DISCUSSION

**Table 1.** Characteristics of Study Participants

Variable	Category	N	%
Age	≤ 50 years	18	47.4
	> 50 years	20	52.6
Gender	Male	26	68.4
	Female	12	31.6
Employment	Employed	13	34.2
	Unemployed	25	65.8
Linezolid Usage	Without Linezolid (Lzd)	32	84.2
	With Linezolid (Lzd)	6	15.8
HIV Status	Positive	1	2.6
	Negative	20	52.6
	Unknown	17	44.7
Survival Duration	≤ 1 month	13	34.2
	> 1 month	25	65.8

The table above shows that of the total 38 MDR-TB patients analyzed, the majority were over 50 years old (52.6%), while the rest were 50 years old and below (47.4%). Most of the patients were male (68.4%), while females only accounted for 31.6%. Based on employment status, the majority of patients did not work (65.8%), and only 34.2% were employed. Most patients (84.2%) were not receiving Linezolid (Lzd) therapy, with only 15.8% of patients using Linezolid in their treatment. Based on HIV status, the majority of patients were found to be HIV negative (52.6%), while only 2.6% were positive. However, there was a sizable proportion (44.7%) with unknown HIV status. Regarding duration of survival, most patients survived for more than one month (65.8%), while the rest (34.2%) died within one month of starting therapy. These data provide an important insight into the demographic and clinical characteristics of the MDR-TB patient population undergoing short regimen treatment.

**Table 2.** Association Between Participant Characteristics and Survival Duration

Variable	≤ 1 Month		> 1 Month		95% CI (Low)	95% CI (Up)	OR	P Value
	n	%	n	%				
Age								
≤ 50 years	8	44.40%	10	55.60%	0.6	9.486	2.4	0.207
> 50 years	5	25.00%	15	75.00%				
Gender								
Male	6	23.10%	20	76.90%	0.049	0.928	0.21	0.033
Female	7	58.30%	5	41.70%				
Employment								
Employed	6	46.20%	7	53.80%	0.545	8.91	2.2	0.263
Unemployed	7	28.00%	18	72.00%				
Linezolid Usage								
Without Linezolid (Lzd)	11	34.40%	21	65.60%	0.165	6.646	1.048	0.961
With Linezolid (Lzd)	2	33.30%	4	66.70%				
HIV Status								
Positive	1	100.00%	0	0.00%	-	-	-	0.349
Negative	7	35.00%	13	65.00%				
Unknown	5	29.40%	12	70.60%				

The results of chi square analysis showed that several demographic and clinical variables were associated with the survival duration of MDR-TB patients. Patients aged over 50 years had a greater proportion surviving more than one month (75.0%) than patients aged 50 years and below (55.6%), although this association was not statistically significant (OR: 2.40; 95% CI: 0.60-9.486;  $p=0.207$ ). Gender showed a significant association with survival duration. Male patients tended to survive longer (>1 month) with a proportion of 76.9%, compared to females (41.7%), and this difference was statistically significant (OR: 0.21; 95% CI: 0.049-0.928;  $p=0.033$ ).

Employment status also showed that patients who did not work had a higher chance of surviving more than one month (72.0%) than patients who worked (53.8%), but this difference was not statistically significant (OR: 2.20; 95% CI: 0.545-8.910;  $p=0.263$ ). The use of Linezolid (Lzd) showed no significant difference in survival duration. Patients who received Linezolid had a proportion of survival of more than one month of 66.7%, slightly higher than patients who did not use Linezolid (65.6%), but the difference was not significant (OR: 1.048; 95% CI: 0.165-6.646;  $p=0.961$ ). Based on HIV status, all HIV-positive patients died in less than one month, but the numbers were so small that statistical analysis was not possible. Patients with HIV-negative status survived more than one month (65.0%), while patients with unknown HIV status also had a sizable proportion surviving longer (70.6%), although this association was not significant ( $p=0.349$ ).

**Table 3.** Logistic Regression Analysis Results

Variable	B	SE	OR	P
Age > 50 years	1.457	0.924	4.29	0.115
Female Gender	2.918	1.207	0.05	0.016
Employment Status:				
Unemployed	2.673	1.241	14.4	0.031

Variable	B	SE	OR	P
HIV Status:				
Unknown	0.99	0.812	2.69	0.223
Use of Linezolid OAT	0.489	1.348	0.61	0.717

The results of logistic regression analysis showed that some variables had a significant association with the survival duration of MDR-TB patients, while others showed no significant association. Female patients were significantly less likely to survive more than one month than males, with OR: 0.05 (95% CI not available), and this association was statistically significant ( $p=0.016$ ). Employment status was also significantly associated, with non-employed patients having 14.4 times greater odds of surviving more than one month than employed patients (OR: 14.4;  $p=0.031$ ).

Age above 50 years showed a positive association with survival beyond one month (OR: 4.29), but this association was not statistically significant ( $p=0.115$ ). Patients with unknown HIV status had a greater chance of survival longer than patients with HIV negative status (OR: 2.69), but this association was also not significant ( $p=0.223$ ). Linezolid use showed a negative association with odds of survival longer than one month (OR: 0.61), but this result was not statistically significant ( $p=0.717$ ). Gender and employment status showed a significant association with patient survival duration, with females and employed patients having a lower chance of survival beyond one month.

The findings of this study highlight the complex interplay between demographic, clinical, and treatment-related factors in influencing the survival duration of patients with multidrug-resistant tuberculosis (MDR-TB). Age was found to have a positive, though not statistically significant, association with longer survival. Older patients (aged >50 years) showed a higher proportion of survival beyond one month compared to younger patients. This could reflect the

resilience of older adults who might better adhere to treatment protocols or have more access to supportive care. However, the lack of statistical significance suggests the need for larger sample sizes or additional variables to clarify this relationship (Ayuningsih & Wahyono, 2019; Hase et al., 2021; Machmud et al., 2021; Wotale et al., 2024).

Gender emerged as a significant determinant of survival duration. Male patients were more likely to survive beyond one month than females. This finding aligns with previous research that suggests gender-related disparities in access to healthcare, biological responses to MDR-TB treatment, or adherence to therapy could influence outcomes. Notably, logistic regression confirmed the strong association of gender with survival, indicating the necessity for gender-sensitive approaches in MDR-TB management. Programs should aim to understand and address the barriers faced by female patients to improve survival rates (Baluku et al., 2021; Kosgei et al., 2020; McQuaid et al., 2020).

Employment status was another important factor. Non-employed patients were significantly more likely to survive beyond one month compared to employed patients. This counterintuitive finding might be related to employment-related stress, less time for treatment adherence, or financial barriers among employed individuals (Baluku et al., 2021; Kosgei et al., 2020; Przybylski et al., 2014). These results underscore the importance of integrating occupational considerations into MDR-TB treatment strategies. Tailored interventions such as workplace health programs or financial support could enhance treatment adherence and outcomes.

Interestingly, the use of Linezolid, a key drug in MDR-TB treatment regimens, did not show a significant association with survival. This result might be due to the small sample size or the confounding effects of other variables like disease severity or drug resistance patterns (Singh et al., 2019; Sotgiu et al., 2012). The

absence of a clear benefit in this study should not diminish the importance of Linezolid, as previous research has demonstrated its effectiveness in treating MDR-TB under certain conditions. Future studies should explore the contextual factors influencing the efficacy of Linezolid.

HIV status also played a notable role, although the small sample size of HIV-positive patients limited the statistical power of the analysis. The lack of survival among HIV-positive patients emphasizes the critical need for integrated TB-HIV management programs to improve outcomes in co-infected individuals (Dlatu, Longo-Mbenza, & Apalata, 2023; Dlatu, Longo-Mbenza, Oladimeji, et al., 2023; Kosgei et al., 2020). For patients with unknown HIV status, the higher survival proportion might reflect differences in clinical profiles or unmeasured confounders. Expanding HIV testing and ensuring timely antiretroviral therapy could significantly impact survival rates among MDR-TB patients. The study underscores the multifaceted nature of survival outcomes in MDR-TB patients, highlighting the importance of addressing gender and employment-related disparities. Future research should involve larger and more diverse populations to confirm these findings and explore potential interventions to optimize survival outcomes.

## CONCLUSION

This study highlights the significant influence of gender and employment status on the survival duration of MDR-TB patients, with male and non-employed patients demonstrating better outcomes. Although age, Linezolid use, and HIV status showed associations with survival, these were not statistically significant, indicating the need for further investigation with larger sample sizes and more robust methodologies. The findings emphasize the importance of gender-sensitive approaches, occupational support, and integrated TB-

HIV management in improving treatment outcomes. Addressing these multifaceted factors through targeted interventions could enhance survival rates and overall care for MDR-TB patients.

## REFERENCES

- Ayuningsih, Z., & Wahyono, T. Y. M. (2019). Faktor-Faktor yang Berhubungan dengan Kematian Pasien TB MDR Selama Masa Pengobatan di Indonesia Tahun 2015-2017. *Pro Health Jurnal Ilmiah Kesehatan*, 1(2).
- Baluku, J. B., Mukasa, D., Bongomin, F., Stadelmann, A., Nuwagira, E., Haller, S., Ntabadde, K., & Turyahabwe, S. (2021). Gender differences among patients with drug resistant tuberculosis and HIV co-infection in Uganda: a countrywide retrospective cohort study. *BMC Infectious Diseases*, 21(1), 1093. <https://doi.org/10.1186/s12879-021-06801-5>
- Dlatu, N., Longo-Mbenza, B., & Apalata, T. (2023). Models of integration of TB and HIV services and factors associated with perceived quality of TB-HIV integrated service delivery in O. R Tambo District, South Africa. *BMC Health Services Research*, 23(1), 804. <https://doi.org/10.1186/s12913-023-09748-2>
- Dlatu, N., Longo-Mbenza, B., Oladimeji, K. E., & Apalata, T. (2023). Developing a Model for Integrating of Tuberculosis, Human Immunodeficiency Virus and Primary Healthcare Services in Oliver Reginald (O.R) Tambo District, Eastern Cape, South Africa. *International Journal of Environmental Research and Public Health*, 20(11). <https://doi.org/10.3390/ijerph20115977>
- Harahap, D. W. S., Andrajati, R., Sari, S. P., & Handayani, D. (2024). Medication Adherence among Drug-Resistant Tuberculosis (DR-TB) Patients at Universitas Indonesia Hospital. *Jurnal Respirologi Indonesia*, 44(3), 196–200. <https://doi.org/10.36497/jri.v44i3.775>
- Hase, I., Toren, K. G., Hirano, H., Sakurai, K., Horne, D. J., Saito, T., & Narita, M. (2021). Pulmonary Tuberculosis in Older Adults: Increased Mortality Related to Tuberculosis Within Two Months of Treatment Initiation. *Drugs & Aging*, 38(9), 807–815. <https://doi.org/10.1007/s40266-021-00880-4>
- Kosgei, R. J., Callens, S., Gichangi, P., Temmerman, M., Kihara, A.-B., David, G., Omesa, E. N., Masini, E., & Carter, E. J. (2020). Gender difference in mortality among pulmonary tuberculosis HIV co-infected adults aged 15–49 years in Kenya. *PLoS One*, 15(12), e0243977.
- Machmud, P. B., Gayatri, D., & Ronoatmodjo, S. (2021). A survival analysis of successful and poor treatment outcome among patients with drug-resistant tuberculosis and the associated factors: a retrospective cohort study. *Acta Medica Indonesiana*, 53(2), 184.
- McQuaid, C. F., Horton, K. C., Dean, A. S., Knight, G. M., & White, R. G. (2020). The risk of multidrug- or rifampicin-resistance in males versus females with tuberculosis. *European Respiratory Journal*, 56(3), 2000626. <https://doi.org/10.1183/13993003.00626-2020>
- Przybylski, G., Dabrowska, A., Pilaczyńska-Cemel, M., & Krawiecka, D. (2014). Unemployment in TB patients - ten-year observation at regional center of pulmonology in Bydgoszcz, Poland. *Medical Science Monitor* :

- International Medical Journal of Experimental and Clinical Research*, 20, 2125–2131.  
<https://doi.org/10.12659/MSM.890709>
- Singh, B., Cocker, D., Ryan, H., & Sloan, D. J. (2019). Linezolid for drug-resistant pulmonary tuberculosis. *The Cochrane Database of Systematic Reviews*, 3(3), CD012836.  
<https://doi.org/10.1002/14651858.CD012836.pub2>
- Sotgiu, G., Centis, R., D'Ambrosio, L., Alffenaar, J.-W. C., Anger, H. A., Caminero, J. A., Castiglia, P., De Lorenzo, S., Ferrara, G., Koh, W.-J., Schecter, G. F., Shim, T. S., Singla, R., Skrahina, A., Spanevello, A., Udwardia, Z. F., Villar, M., Zampogna, E., Zellweger, J.-P., ... Migliori, G. B. (2012). Efficacy, safety and tolerability of linezolid containing regimens in treating MDR-TB and XDR-TB: systematic review and meta-analysis. *European Respiratory Journal*, 40(6), 1430–1442.  
<https://doi.org/10.1183/09031936.00022912>
- Tola, H. H., Tol, A., Shojaeizadeh, D., & Garmaroudi, G. (2015). Tuberculosis Treatment Non-Adherence and Lost to Follow Up among TB Patients with or without HIV in Developing Countries: A Systematic Review. *Iranian Journal of Public Health*, 44(1), 1–11.
- Wang, J., Zhou, M., Chen, Z., Chen, C., Wu, G., Zuo, Y., Ren, X., Chen, Z., Wang, W., & Pang, Y. (2020). Survival of patients with multidrug-resistant tuberculosis in Central China: a retrospective cohort study. *Epidemiology and Infection*, 148, e50.  
<https://doi.org/10.1017/S0950268820000485>
- Widyasrini, E. R., & Probandari, A. N. (2017). Factors Affecting the Success of Multi Drug Resistance (MDR-TB) Tuberculosis Treatment in Residential Surakarta. *Journal of Epidemiology and Public Health*, 2(1), 45–57.
- Wotale, T. W., Lelisho, M. E., Negasa, B. W., Tareke, S. A., Gobena, W. E., & Amesa, E. G. (2024). Identifying risk factors for recurrent multidrug resistant tuberculosis based on patient's record data from 2016 to 2021: retrospective study. *Scientific Reports*, 14(1), 23912.  
<https://doi.org/10.1038/s41598-024-73209-x>