


Application of Predictive Models for Tuberculous Meningitis Outcome: A Comparative Analysis of Decision Tree and Logistic Regression Approaches

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ABSTRACT

Background: Tuberculous meningitis remains one of the most severe complications of tuberculosis infection. This study evaluated critical factors influencing mortality among tuberculous meningitis (TBM) patients and compared the predictive efficacies of logistic regression and decision tree models. **Methods**: A retrospective cohort analysis using medical records from 65 TBM patients at R.D. Kandou Hospital from January 2018 to July 2021. Patient outcomes were assessed with the Glasgow outcome scale (GOS), and the mortality risk was calculated. Key predictors of mortality identified by both multivariate logistic regression and the decision tree were compared using the receiving operating characteristic (ROC) curve. **Result**: Multivariate logistic regression analysis identified SGOT levels at admission (aOR: 1.06; CI95% 1.02-1.09; p=0.001), length of stay (aOR: 0.81; CI95% 0.71-0.92; p=0.002), and positive nuchal rigidity (aOR: 41.78; CI95% 3.41-512.27; p=0.004) as significant predictors of mortality. Decision tree analysis highlighted the British Medical Research Council (BMRC) stage, temperature, and potassium levels below 4.3 as critical predictors. Both models showed comparable predictive performance on the ROC curve, with no significant difference (0.85 vs. 0.95; p = 0.074). **Conclusion**: These results suggest that decision tree analysis is a viable alternative to logistic regression for predicting mortality in TBM patients, providing complementary insights into outcome-related factors. Further research is needed to refine these predictive models.

Keywords: Decision tree, logistic regression, outcome determinants, tuberculous meningitis.

ABSTRAK

Latar belakang: Meningitis tuberkulosis (TBM) tetap merupakan salah satu komplikasi paling parah dari infeksi tuberkulosis. Penelitian ini bertujuan mengevaluasi faktor yang memengaruhi mortalitas pasien meningitis tuberkulosis (TBM) dan membandingkan kemampuan prediktif analisis regresi logistik dengan analisis pohon keputusan. **Metode**: Studi kohort retrospektif ini menggunakan rekam medis 65 pasien TBM di Rumah Sakit R.D. Kandou dari Januari 2018 hingga Juli 2021. Luaran pasien dinilai menggunakan *Glasgow outcome scale* (GOS), dan dilakukan penghitungan risiko mortalitas. Prediktor utama mortalitas yang diidentifikasi oleh regresi logistik multivariat dan pohon keputusan dibandingkan menggunakan kurva *receiving operating characteristic* (ROC). **Hasil**: Analisis regresi logistik multivariat mengidentifikasi tingkat SGOT saat admisi (aOR: 1,06; CI95% 1,02-1,09; p=0,001), lama hospitalisasi (aOR: 0,81; CI95% 0,71-0,92; p=0,002), dan adanya kaku kuduk (aOR: 41,78; CI95% 3,41-512,27; p=0,004) sebagai faktor prediktif mortalitas yang signifikan. Analisis pohon keputusan menunjukkan stadium British Medical Research Council (BMRC), suhu, dan tingkat kalium di bawah 4,3 sebagai faktor signifikan. Kedua model menunjukkan kinerja prediktif yang sebanding pada kurva ROC, tanpa perbedaan yang signifikan (0,85 vs. 0,95; p = 0,074). **Kesimpulan**: Hasil ini menunjukkan bahwa analisis pohon keputusan dapat menjadi alternatif yang efektif dari regresi logistik dalam memprediksi mortalitas pasien TBM, memberikan informasi tambahan mengenai faktor-faktor yang terkait dengan luaran pasien TBM. Diperlukan penelitian lebih lanjut untuk menyempurnakan model prediktif ini. **Ferrdy Pratama Wijaya, Arthur H.P. Mawuntu, Sarah Muharomah, Melke J. Tumboimbela, F.L. Fredrik G. Langi. Aplikasi Model Prediksi untuk Luaran Meningitis Tuberkulosis: Analisis Komparatif antara Pendekatan Analisis Pohon dan Regresi Logistik.**

Kata Kunci: Pohon keputusan, regresi logistik, determinan luaran, meningitis tuberkulosis.

INTRODUCTION

Tuberculous meningitis (TBM) remains one of the most severe complications of tuberculosis infection. Worldwide, TBM accounts for a mortality rate exceeding 20% despite constituting only 1% of the total cases.[1] There is an increasing interest in accurately predicting the outcome of TBM, as this allows risk stratification and ensures more targeted medical care for specific patients. Such predictions enable clinicians to make informed decisions on the most appropriate

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strategies for individual patients, assisting in patient counseling and communication. This capability also aids resource allocation and public health planning.

However, the inherent complexity of TBM, characterized by various determinants, presents significant challenges to diagnosis and treatment, influencing patient outcomes. Several tools have been developed to aid clinicians in predicting the disease's prognostic outcomes. Logistic regression models are commonly used, but they have limitations such as variable co-linearity, intricate variable interactions, and difficulties in identifying high-risk groups.[2] In several studies, the decision tree has emerged as an alternative strategy to counteract the limitations of other traditional parametric tests.[3] Existing data has showcased the effectiveness of the decision tree in facilitating the early detection of disease and in identifying prognostic data for treatment.[2,4] Moreover, it can stratify risk for patients using data from various covariates and offers easily interpretable decision rules applicable in clinical practice.[2] Additionally, it excels at identifying the very high- or very low-risk clinical subgroups.[5]

Previous research regarding the decision tree model for predicting tuberculosis outcomes has been primarily focused on using the regression tree to predict outcomes for general tuberculosis infections or to inform treatment choices.[6,7] Some studies also explored the incidence risk of multi-drug-resistant TB, comparing the sensitivity and specificity of logistic regression to that of the decision tree.[3] However, few studies have exclusively examined the predictive accuracy of TBM. In this study, we aim to evaluate and compare the effectiveness of decision tree models with logistic regression models in predicting the mortality outcomes of TBM patients.

METHODS

Study Design and Data Collection

Data were obtained from a non-matching retrospective cohort study conducted from January 2018 to July 2021 at RD. Kandou Hospital, a tertiary teaching hospital located in the central north of Celebes, Indonesia. Data on all newly diagnosed tuberculous meningitis (TBM) patients were obtained. Diagnosis of TBM was based on clinical criteria and the Lancet (Marais) consensus diagnostic criteria (possible and probable).[8] All patients under the age of 18 years were excluded due to regional law restrictions or if they had incomplete medical records.

A total of 65 patients were included in the study. Information on 45 independent variables was included in the dataset **(Table 1)**. This included basic demographics and health-related information. Specifically, the following data were collected: age (the age when the patient was admitted into the hospital); gender; education level (less than or equal to 9 years or more than 9 years of schooling); marital status (never married or ever-married); and insurance (government insurance or other). Health-related information included past medical history, clinical presentations, and examination variables such as fever with duration, headache and its duration, lapse of consciousness (LOC) and its duration, seizure, visual disturbances (including blindness or blurry vision), hemiparesis, history of cough, history of previous brain infection, history of diabetes, and HIV status. The BMRC staging system for severity measurement was also used. Severity of TBM upon admission according to the BMRC clinical criteria: BMRC I: I am fully conscious and have no focal deficit (GCS 15); BMRC II: GCS 11-14 or GCS 15 with focal neurological deficit; BMRC III: seizures (GCS <10) and severe neurological deficit

Table 1. Glasgow outcome scale (GOS).

Score	Functional Status	Description
1	Death	Severe injury or death without recovery of consciousness
2	Vegetative State	Severe injury with extended unconsciousness and persistent decline in higher mental functions
3	Severe Disability	Severe injury requiring permanent assistance in daily life
4	Moderate Disability	Independent in daily life; employment possible but may require special equipment
5	Mild Disability	Mild injury with minor neurological and psychological deficits

Additionally, data regarding weight, height, BMI, vital signs, Glasgow coma scale score upon admission, abnormal pupil findings, meningeal signs, and abnormal motor examination results were obtained. Measurements of Marais criteria were also obtained during this time. Laboratory data, obtained from the first available results in the medical records, included hemoglobin, thrombocytes, leukocytes, sodium, potassium, blood glucose, SGPT, SGOT, and HIV rapid test results. Cerebrospinal fluid analysis, available in 19 patients, included total white blood cell count, red blood cell count, protein, glucose ratio, mononuclear cells, and polymorphonuclear cell counts. Radiological results for chest x-rays and head CT scans were categorized as normal or abnormal. Medication data were classified based on the administration of antituberculosis therapy (OAT only) and whether corticosteroids or antibiotics were added.

Measurement of the Outcome

Outcomes were assessed to determine the status of patients as either deceased or alive at the conclusion of management. Additionally, the Glasgow outcome scale (GOS) was utilized to categorize patient outcomes into three levels: good (scores 4-5), poor (scores 2-3), and very poor (score 1), providing a comprehensive scoring system as outlined in **Table 2**. GOS scores were assigned by examiners who were blinded to any secondary insult data. Furthermore, the duration of each patient's hospitalization was documented.

Statistical Analysis

A description of our baseline data was provided. Categorical variables were presented as frequencies and percentages. All data were tested for normal distribution using the Shapiro-Wilk normality test. Normally distributed variables were presented as means and standard deviations (SD); those not normally distributed were presented as medians and interquartile ranges (IQR). All statistical analyses were performed using R statistical software version 14.5. A two-tailed P-value of less than 0.05 was considered statistically significant.

Logistic Regression

Bivariate and multivariate regressions were conducted. The final model was selected based on forward selection and the AIC


Table 2. Patient demographic and clinical profile.

Characteristic	n (%)	Mean ± SD	Median (Q1-Q3)
Demographic Characteristics			
Age (years)	-	-	36.0 (25.0 - 50.0)
Gender			
Female	16(25)	-	-
Male	49(75)	-	-
Education			
≤9 years	11(17)	-	-
>9 years	54(83)	-	-
Ethnicity			
Minahasa	48(74)	-	-
Other	17(26)	-	-
Insurance		-	-
Government	62(95)	-	-
Other	3(5)	-	-
Medical History			
Fever	53(82)	-	-
Duration of Fever (days)	-	-	6.0 (1.5 - 12.0)
Headache	52(80)	-	-
Duration of Headache	-	-	12.0 (5.0 - 21.0)
Altered Consciousness	59(91)	-	-
Duration of Altered Consciousness	-	-	4.0 (2.0 - 7.0)
Seizures	12(18)	-	-
Vision Disturbances	4(6)	-	-
History of Cough	27(42)	-	-
History of Diabetes Mellitus	3(5)	-	-
HIV Positive	27 (42)	-	-
Clinical Examination			
BMI (kg/m^2)	-	-	21.0 (19.5 - 22.5)
Systolic Blood Pressure (mmHg)	-	-	120.0 (110 -130.0)
Diastolic Blood Pressure (mmHg)	-	-	70.0 (70.0 - 80.0)
Heart Rate	-	89.2 ± 16.0	-
Temperature (°C)	-	-	36.8 (36.7 - 37.6)
Hemiparesis	13(20)	-	-
Thwaites Score (n=19)			
≤4 points	17(26)	-	-
>4 points	2(3)	-	-
Glasgow Coma Scale	-	-	11.0 (9.0 – 13.0)
Pupil Abnormalities	6(9)	-	-
Meningeal Sign	43(66)	-	-
Cranial Nerve Paresis	28(43)	-	-
Marais			
Possible	41(63)	-	-

score. The model was expressed as $f(yi) = \beta 0 + \beta 1Xi$ where f() is a link function for logistic regression, y is the outcome variable, $\beta 1$ is the regression coefficient vector, X is the covariate matrix, and i is the subject index in the analysis. The goodness of fit was tested using the Hosmer-Lemeshow test. The results of the regression model were reported as estimates, with 95% confidence intervals and P-values.

Regression Trees

Binary recursive partitioning methods were employed to construct regression trees. The R-tree implementation permits only splits on individual variables, not on linear combinations of predictor variables. At each node, the split that maximized the reduction in deviance was selected. All 34 candidate predictors described in **Table 1** were used. After the initial regression tree was grown, it was pruned using ten-fold cross-validation on the derivation dataset to determine the optimal number of leaves. Predictions for the validation dataset were obtained using the pruned tree. The regression tree models were fitted using the tree function in the R TREEÒ package. Pruning of the trees was performed using the prune.tree function. Node heterogeneity was assessed by deviance, and the optimal tree size was then selected to minimize deviance. If two tree sizes resulted in the same minimum deviance, the smaller tree size was chosen. To reliably estimate error, 10–100 iterations of 2–10-fold stratified cross-validation were used to assess the performance as indicated by changes in the area under the receiver operating characteristic curve (AUC). The final regression tree, fitted to the derivation sample, was then used to make predictions for subjects in the validation sample.

Comparative Analysis

The predictive performance of TBM outcomes between the final logistic regression model and the regression tree was compared using ROC curve analysis. The ROC curve was constructed, and the Z-value was calculated from the area under the curve and standard deviation. The corresponding P-value was used to discern differences between the statistical models. The significance threshold was set at $\alpha = 0.05$.

Probable	24(37)	-	-
BMRC			
I	6(9)	-	-
II	31(48)	-	-
III	28(43)	-	-
Supporting Laboratory			
Hemoglobin (g/dL)	-	11,3± 2,2	-
Platelet Count (×10^3 /µL)	-	287,0±130,3	-
White Blood Cell Count (10^3 /µL)	-	-	9.8 (6.9 – 13.9)
Sodium Levels (mg/dL)	-	130,1± 7,9	-
Potassium Levels (mg/dL)	-	3.7±0.6	-
Blood Sugar Levels (mg/dL)	-	-	100(89.0-113.0)
SGPT (mg/dL)	-	-	23.0(16.0-33.0)
SGOT (mg/dL)	-	-	23.0 (17.0-38.0)
CSF Analysis Result			
Total WBC Count in CSF (/mL)	-	-	300.0 (22.5-355.0)
CSF Protein Levels (mg/dL)	-	-	70.0(10.0-220.0)
CSF Glucose Ratio	-	-	0.4(0.3-0.6)
Mononuclear Cells in CSF (/mL)	-	-	20.0(2.5-87.5)
Polymorphonuclear Cells in CSF (/mL)	-	-	10(2.0-70.0)
Radiology Result			
Abnormal Chest X-Ray	44(68)	-	-
Abnormal CT Scan (n=35)	29(83)	-	-
Treatment			
OAT			
INH	1(2)	-	-
INH, ETH	5(8)	-	-
INH, ETH, PZA	56(90)	-	-
Corticosteroid	49(79)	-	-
Antibiotic	42(68)	-	-
Outcome			
Glasgow Outcome Scale	-	-	3.0(1.0-4.0)
Good (4-5)	27 (42)	-	-
Poor (2-3)	14 (21)	-	-
Very Poor (1)	24 (37)	-	-
Length of Hospital Stay (Days)	-	-	14.0(7.0-21.0)
Survival Status			
Alive	41(63)	-	-
Deceased	24(37)	-	-

Abbreviations: HIV: Human immunodeficiency virus; BMI: Body mass index; BMRC: British Medical Research Council; SGPT: Serum glutamic pyruvic transaminase; SGOT: Serum glutamic oxaloacetic transaminase; CSF: Cerebrospinal fluid; WBC: White blood cell; OAT: Obat anti-tuberkulosis; INH: Isoniazid; ETH: *Ethambutol*; PZA: *Pyrazinamide*.

RESULTS

Descriptive Statistics of the Samples

This study encompassed 65 patients, with their characteristics detailed in **Table 3**. The majority were male (75%), had over 9 years of education, belonged to the Minahasa ethnic group, and were covered by government insurance. Most patients presented with fever and headache, and all exhibited varying degrees of altered consciousness. Seizures were observed in 18% of cases, and 42% were HIV positive. Regarding the Marais criteria, the majority were classified as 'possible,' with 48% falling under BMRC grade II. Over 90% of patients received standard OAT treatment, and 79% were treated with corticosteroids. Additionally, the majority were administered antibiotics alongside OAT. During the treatment period, 24 patients (37%) were deceased. This TBM mortality rate translates to a cumulative incidence of approximately 26 per 1000 person-days. Among the 41 survivors, 27 showed improved conditions (GOS score 4-5), while the remainder were in a poor state (GOS score 2-3), necessitating close post-hospitalization monitoring.

Logistic Regression Analysis

The results of the regression model are presented in **Table 4**. Nuchal rigidity was identified as a significant determinant of mortality in our study ($p<0.05$). Notably, there was a significant increase in the odds ratio after adjusting for other covariates (cOR: 3.91, 95% CI: 1.14-13.50; aOR: 41.78, 95% CI: 3.41-512.27). This substantial difference between the crude and adjusted odds ratios suggests a strong confounding effect. Additionally, the wide confidence interval in the adjusted model may indicate a small sample size or high variability in one of the groups analyzed. Additionally, increased levels of SGOT (aOR: 1.06, 95% CI: 1.02-1.09) and length of stay (aOR: 0.81, 95% CI: 0.71-0.92) demonstrated a significant association with mortality in TBM. However, after adjustment for other covariates, neither BMRC stage III not the use of antibiotics was significantly associated with mortality in TBM patients.

Decision Tree Analysis

Figure 1 illustrates a decision tree model for mortality prediction in TBM patients, highlighting three critical predictors across six nodes, including four terminal ones. BMRC < 3 emerges as the most decisive factor, splitting


the patient population into two branches. Those with BMRC < 3 show a 35% survival rate, with further differentiation at a potassium threshold of 4.3. For patients with BMRC ≥ 3, temperature < 37°C does not significantly alter survival outcomes, with 20% difference in survival rates (43% vs. 23%).

Figure 2 presents the receiver operating characteristics (ROC) curves created to compare the predicted results of the logistic regression and decision tree models. The area under the curve (AUC) was found to be 95% in the logistic regression model and 85% in the decision tree model (DeLong's AUC Difference test, p = 0.074). According to the analysis, the logistic regression model performed slightly better but the difference between the two was not statistically significant.

DISCUSSION

Our cohort predominantly consisted of male patients (75%) with a median age of 36 years old, aligning with the demographic trends observed in TBM studies worldwide.[9–12] The highest prevalence of symptoms such as loss of consciousness (91%), fever (82%), and headache (80%) in our sample mirrors findings from Wang, *et al*, (2019).[13] Sixty-six percent of our patients exhibited meningeal signs, including neck stiffness, similar to findings in other studies.[9,14] The median Marais score was 8, and the majority of patients were in BMRC stage II (48%), which is consistent with previous research conducted in Indonesia.[9] In total, 24 patients (37%) died during hospitalization, resulting in a 26 per 1000

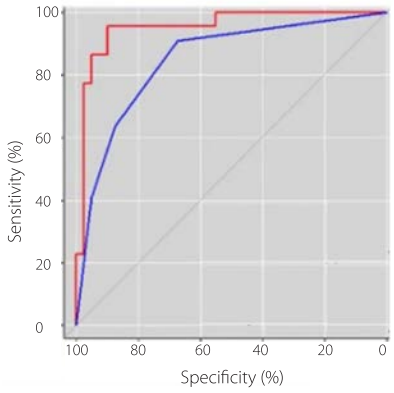

Figure 2. ROC curve comparison of logistic regression and decision tree models.

person-day cumulative incidence, which is higher than that reported in studies conducted in Vietnam,[1,15] but similar to that of a study conducted in Malaysia and several resource-constrained settings around the world.[11,13,16–19] This may be related to our cohort presenting with more severe symptoms compared to other studies, as the more serious the disease, the worse the treatment outcome.

In bivariate logistic regression, we found that BMRC stage III, SGOT levels at admission, length of stay, antibiotic use, and positive meningeal signs statistically significantly increase the patient's odds of mortality due to TBM. However, after adjustment with other factors, BMRC stage III and the need for antibiotics were not statistically significant, with OR changes of more than 10%, indicating a confounding factor.

Patients with BMRC stage III were 4 times more likely to die compared to those with stage I and II in this study, although this was not statistically significant (aOR: 4.06; p = 0.065). This finding is in line with several previous studies where clinical symptoms such as positive nuchal rigidity accompanied by a high BMRC stage (stage II and III) increase the risk of mortality, as it indicates that the TBM process has spread to the intraparenchymal brain and caused more damage.[11,13] Despite a high BMRC stage being consistently associated with a poor prognosis of TBM, other factors such as impaired consciousness, motor deficit, and cisternal effacement play a role in the mortality of patients, in line with our results, indicating a confounding factor.[20]

The SGOT value (aOR: 1.06; CI95% 1.02-1.09; p=0.001) was statistically significant but

Table 3. Logistic regression analysis of mortality outcomes in tuberculosis meningitis patients.

Variable	Crude Odds Ratio			Adjusted Odds Ratio		
	OR	95% CI	p-value	OR	95% CI	p-value
Positive Nuchal Rigidity	3.91	1.14 – 13.50	0.031*	41.78	3.41 – 512.27	0.004*
BMRC Stage III	6.62	2.16 – 20.28	0.001*	4.06	0.76 – 21.65	0.101
SGOT Value	1.02	1.00 – 1.05	0.080	1.06	1.02 – 1.09	0.001*
Length of Stay	0.87	0.80 – 0.95	0.001*	0.81	0.71 – 0.92	0.002*
Antibiotic Use	3.00	0.86 – 10.52	0.086	6.70	0.89 – 50.44	0.065

Abbreviations: OR: odds ratio; BMRC: British Medical Research Council; GOS: Glasgow outcome scale; SGOT: Serum glutamic oxaloacetic transaminase. *p-values are significant if <0.05

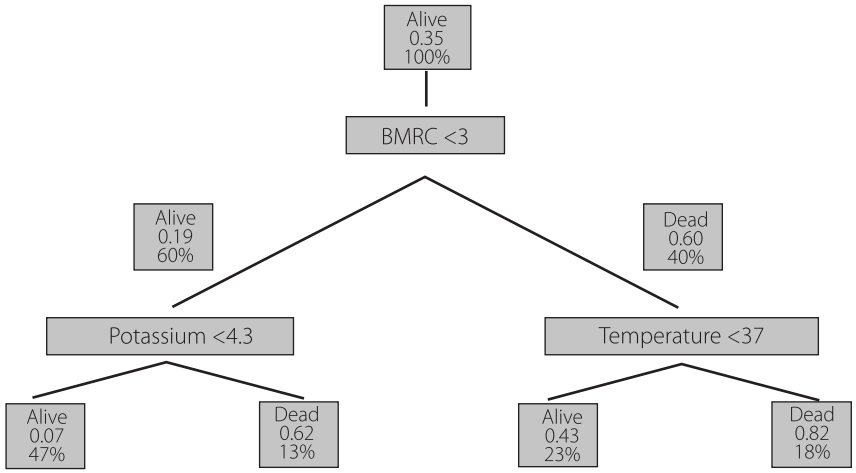

Figure 1. Decision tree model for predicting mortality outcome in TBM patients.

* the percentage next to the outcomes (dead vs. alive) at each terminal node of the tree represent the probability of that outcome within that particular subgroup, while the percentages next to the subgroup sizes represent the proportion of the total population that has reached that node following the specified path through the tree.

clinically may not be useful in clinical care as the increase in odds ratio per mg/mL of SGOT values is very small. Anti-tuberculous treatment is known to be the cause of liver injury, causing drug-induced hepatitis with increased levels of transaminases.[21] Generally, an increase in transaminase with signs of hepatotoxic effect is not unexpected, as all TB medication is liable to cause liver injury, with even higher dosages used for TBM. Furthermore, some patients may have other drugs, such as anti-seizure drugs, that can cause a transient rise in liver enzyme level.[22] However, there is no increase in mortality data related to an increase in SGOT level. Signs of liver dysfunction are particularly likely to be found in severe disseminated forms of tuberculosis, including tuberculous meningitis, with patients of stage III TBM developing significantly higher enzyme levels than those at stage II.[22] This may be related to actual tuberculous involvement in the liver or to the liberation of mycobacterial products related to the factor of development of liver dysfunction.[23,24] However, several studies showed no association between laboratory or imaging findings and poor outcome, especially in adult TBM with BMRC stage III; the common clinical factors aren't effective enough to predict the outcome.[25]

After controlling for other variables in the model, each one-day increase in LOS decreased the odds of death by 19% (95% CI 0.71–0.92; p = 0.002). Unlike the data from other studies, most previous data showed that after a cutoff time of hospitalization on the longer side, there will be an increased risk of a poor neurological outcome, especially in older patients.[26] However, data from Kerala showed that a shorter duration of stay was associated with mortality in TBM patients.[14] This may be due to the fact that patients presenting in this study tended to exhibit more severe symptoms, making the duration of hospitalization an indicator of treatment efficacy rather than the severity of the condition. Most patients presenting with severe conditions are likely to succumb quickly, resulting in a shorter overall hospital stay. Another possibility is that disease progression varies greatly among TBM patients; thus, despite the presenting stage being higher, the patient was not necessarily present at the hospital early, as found in another study.[27]

Nuchal rigidity was a significant determinant of mortality in our study (p<0.05). The association remained significant after adjusting for other covariates (aOR: 41.78; CI95% 3.41-512.27; p=0.004). However, the significant increase in the OR suggests the presence of a significant confounder, as indicated by a wide confidence interval. This outcome significantly exceeds initial estimates from the univariate model before adjusting for other variables. A study conducted by Thomas, *et al*, found that nuchal rigidity only showed diagnostic value in patients with severe meningeal inflammation, aligning with its role as a predictor of mortality in TBM patients. This is because more severe inflammation is associated with an increased risk of death.[28]

However, antibiotic use (aOR: 6.70; CI95% 0.89-50.44; p=0.065) was not a significant determinant after adjustment, possibly because most TBM patients must receive antibiotics; without them, death is likely. The delay in initiating antibiotic treatment is associated with mortality in TBM, with a delay of more than 3 days associated with a 70% increase in mortality.[17,29–31]

In the decision tree analysis, we found that the BMRC stage, in particular, which relates to severity and level of consciousness, emerged as a significant predictor of mortality in brain infection-related diseases.[32] This stage is consistently associated with a higher risk of mortality in patients with TBM, with advanced stages correlated with an unfavorable outcome.[33–35] Contrarily, a study by Erdem, *et al*, found that BMRC staging did not correlate with an unfavorable outcome and was unable to predict poor outcomes.[32]

Lower potassium, less than 4.3, was an important factor in our analysis. Neuroendocrine metabolic abnormalities are common in TBM, including gonadotropin deficiency, hyperprolactinemia, thyrotropin deficiency, corticotropin deficiency, and somatotropic hormone deficiency.[36] Additionally, electrolyte imbalances, related to symptoms such as vomiting and altered food intake, were observed.[37] Kidney dysfunction was also identified as a contributor to electrolyte disturbances in patients with TBM.[38] Hyperkalemia is also associated with adrenal insufficiency, with data consistently showing a lower likelihood of achieving high Glasgow outcome scale (GOS) values, thus indicating a more severe prognosis.[36] However, a study conducted in India indicated that endocrine dysfunction, in general, was not an independent predictor of increased mortality.[39]

Lastly, concerning body temperature, fever or a history of fever is included in almost every diagnostic category for TBM, despite not all patients with TBM presenting with fever. The presence of fever indicates a better immune response in patients with TBM, a disease that is strongly related to lower immunity and malnutrition. Patients co-infected with HIV likely exhibit a decreased inflammatory response, leading to significantly fewer cases of elevated peripheral WBC counts or neurological deficits. However, these patients tend to have worse outcomes.[11] Similarly, a study conducted in Indonesia found a strong association between fever and one-year mortality, consistent with the findings of our study.[40]

Our study showed that decision tree regression can be used as an alternative to logistic regression to predict mortality, as logistic regression's performance was not statistically significantly better than that of decision tree analysis. ROC comparison revealed no significant differences in the area under the curves for the logistic regression and decision tree models (0.85 vs. 0.95; p = 0.074). Different terminal nodes of the tree represent probabilities and effectively convey a data mining method for selecting determinants of mortality risk in TBM, a multifactorial disease. Logistic regression remains the most utilized method in TBM research and was superior in our study; however, tree models are the second most frequently used for model construction.[41] Darnila, *et al*, found that decision tree and random forest analysis are superior for analyzing the classification of TB based on treatment history in one of the provinces in Indonesia.[42] The use of the decision tree method renders the analysis unaffected by collinearity and reveals the interaction between the selected variables. Combined with logistic regression, these methods can complement each other.[43]

Strength and Limitations

This study faced several limitations. Firstly, it relied on secondary data from hospital


medical records, which may lead to incompleteness and variability in data quality. The retrospective nature of these records limits the ability to establish causality between factors and outcomes. Secondly, the study did not account for several potential determinants of patient outcomes during hospitalization, including comorbidities such as HIV status, detailed investigations on cerebrospinal fluid (CSF) and sputum in patients with pulmonary TB, treatment effectiveness, CD4+ levels in HIV-positive patients, and a history of BCG immunization. The small sample size, particularly for HIV status (only 42%), necessitates caution in interpreting the significance of these findings. Additionally, the lack of CD4 value observation in HIV-positive patients and the limited CSF data obtained (less than 30% of our sample) could further obscure the results.

Another limitation involves the potential for misclassification in the decision tree analysis, where cases might be assigned to one class despite belonging to another. These errors are indicated in the decision tree's leaf nodes as a result of pruning.[44] Despite these limitations, the study provides valuable insights into the factors influencing mortality in TBM patients. Future research should aim to address these limitations by incorporating a broader range of variables and employing prospective data collection methods to enhance our understanding of TBM patient outcomes.

CONCLUSION

The primary predictors of mortality identified from the logistic regression analysis, after adjustment, were nuchal rigidity and SGOT levels. Length of stay (LOS) also emerged as a significant factor. From the decision tree analysis, we found that BMRC stage and potassium levels were significant predictors of mortality outcome. Specifically, BMRC stage III at hospital admission was highlighted as a critical predictor influencing the risk of mortality, as determined by the decision tree model. Both analytical approaches proved to be comparable in predicting the outcomes of TBM. This underscores the necessity for further studies with more comprehensive variables and larger samples.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding this study.

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