

# BCG Vaccination as a Predictor of In-Hospital Mortality in Non-HIV Tuberculous Meningitis

Adri Naufan<sup>1</sup>, Edwin Ardiansyah<sup>2</sup>, Marda Arif Furqani<sup>3</sup>, Ahmad Rizal Ganiem<sup>3</sup>, Sofiati Dian<sup>3</sup>

<sup>1</sup>Resident, Department of Neurology, Faculty of Medicine Padjajaran University/Hasan Sadikin Hospital, Bandung

<sup>2</sup>Research Center for Care and Control of Infectious Disease (RC3ID), Padjajaran University

<sup>3</sup>Staff, Department of Neurology, Faculty of Medicine Padjajaran University/Hasan Sadikin Hospital, Bandung



## INTRODUCTION

- Tuberculous meningitis (TBM) is the most severe form of tuberculosis, with a mortality and disability among survivor up to 50% in HIV-negative patients.
- The Bacille Calmette–Guérin (BCG) vaccine is widely used and provides significant protection against severe tuberculosis, including meningitis in infants and young children
- The protective effect ov BCG vaccine tends to decline over time of vaccination, with reported efficacy decreasing from approximately 82% at 20 years post-vaccination to around 52% at 50–60 years against all forms of TB infection.
- In Indonesia, the BCG vaccine has been part of the national immunization program since 1977, with administration recommended during the neonatal period (≤1 month of age).
- Data and information regarding efficacys of BCG against TBM among adult patients are limited.



## METHODS

- This retrospective cohort study aimed to evaluate the association between BCG vaccination and in-hospital outcomes among adult patients with TBM without HIV.
- The diagnosis of TBM was established according to Marais criteria. Clinical presentation, laboratory findings, radiological results, vaccination history, and in-hospital outcomes (mortality) data were collected systematically.
- BCG vaccination history was determined based on history of immunization and the presence of a BCG scar on the upper arm.
- Statistical analysis was analyzed using Chi-square test for categorical variables, Mann–Whitney test for numeric variables, and multivariate analysis using logistic regression. A p-value <0.05 was considered statistically significant.



## CONCLUSION

Among adult TBM patients without HIV who receive BCG vaccination tend to present with less severe disease and had lower in-hospital mortality rates. Although TBM outcomes are influenced by multiple factors, these findings suggest that prior BCG vaccination may confer a protective effect against disease severity and mortality.

## REFERENCE

1. Nijman G, Imran D, Dian S, Ganiem AR, Estiasari R, Maharani K, et al. Tuberculous meningitis patient pathways and delays to diagnosis in Indonesia: a retrospective cohort study. *BMJ Public Health*. 2023 Nov 24;1(1)

2. Seid G, Alemu A, Dagne B, Gamtesa DF. Microbiological diagnosis and mortality of tuberculosis meningitis: Systematic review and meta-analysis. *PLoS One*. 2023 Feb 16;18(2):

3. Navarro-Flores A, Fernandez-Chinguel JE, Pacheco-Barrios N, Soriano-Moreno DR, Pacheco-Barrios K. Global morbidity and mortality of central nervous system tuberculosis: a systematic review and meta-analysis. *J Neurol*. 2022 Jul 15;269(7):3482–94.

4. Katelaris AL, Jackson C, Southern J, Gupta RK, Drobniowski F, Lalvani A, et al. Effectiveness of BCG Vaccination Against Mycobacterium Tuberculosis Infection in Adults: A Cross-sectional Analysis of a UK-Based Cohort. *J Infect Dis*. 2020 Jan 1;221(1):146–55.

5. Hart PE, McKenna TR, Kleinman JP, et al. Long-term efficacy of BCG vaccine in American Indians and Alaska Natives: A 60-year follow-up study. *JAMA*. 2004;291(17):2086–2091.



## RESULTS

Variabel	BCG Vaccination History		p-value
	Yes	No	
	N (%)	N (%)	
Sex Male	163 (57.6)	38 (45.8)	0.076
Fever	217 (77.8)	60 (75.9)	0.849
Headache	232 (84.4)	65 (84.4)	1
Altered consciousness	208 (73.5)	74 (89.2)	0.005*
Cranial Nerve Palsy	27 (11.5)	19 (26.4)	0.004*
Hemiparesis	166 (58.9)	53 (64.6)	0.417
TB Symptom	232 (82.0)	72 (86.7)	0.394
CSF Opening pressure	12.00 [10.00, 15.00]	12.00 [10.00, 13.00]	0.542
CSF Leukocytes	39.00 [4.50, 137.50]	51.00 [3.00, 140.50]	0.976
CSF Protein	131.00 [57.00, 264.00]	150.10 [62.00, 265.00]	0.654
Predominant Monocyte	215 (76.0)	58 (69.9)	0.328
CSF Blood Glucose Ratio	0.34 [0.20, 0.51]	0.33 [0.21, 0.49]	0.999
Hydrocephalus	94 (33.2)	26 (31.3)	0.85
Meningeal Enhancement	139 (49.1)	46 (55.4)	0.376
Tuberculoma	31 (11.0)	9 (10.8)	1
Infarct	47 (16.6)	15 (18.1)	0.884
Lungs TB	82 ( 29.0)	22 (26.5)	0.764
Lungs Extra TB	13 (4.6)	3 ( 3.6)	0.938
TBM Grade			
Grade 1	12 ( 4.3)	2 ( 2.5)	0.14
Grade 2	225 (80.9)	59 (73.8)	
Grade 3	41 (14.7)	19 (23.8)	
Marais score	12.00 [11.00, 14.00]	12.00 [11.00, 14.00]	0.653
In-Hospital Mortality	67 (24.0)	34 (41.0)	0.004*
Total	283	83	

**Table 1.** Comparison of Clinical, Laboratory, Radiological Features, and Outcomes in Tuberculous Meningitis Patients by BCG Vaccination Status

Variabel	In-Hospital Mortality		p-value
	Yes (101)	No (265)	
	N (%)	N (%)	
Sex Male	55 (54.5)	146 (55.1)	1
Fever	81 (81.8)	196 (75.7)	0.271
Headache	76 (82.6)	221 (85.0)	0.707
Altered Consciousness	97 (96.0)	185 (69.8)	<0.001*
Cranial Nerve Palsy	18 (22.0)	28 (12.4)	0.06
Hemiparesis	65 (65.0)	154 (58.3)	0.298
TB Symptom	87 (86.1)	217 (81.9)	0.416
CSF Opening pressure	12.00 [10.00, 14.75]	12.00 [10.50, 15.00]	0.518
CSF Leukocytes	34.00 [7.00, 121.00]	51.00 [4.00, 142.00]	0.469
CSF Protein	132.00 [52.00, 273.00]	132.00 [62.00, 261.50]	0.619
Predominant Monocyte	70 (69.3)	203 (76.6)	0.194
CSF Blood Glucose Ratio	0.32 [0.19, 0.49]	0.35 [0.20, 0.51]	0.36
Hydrocephalus	49 (48.5)	71 (26.8)	<0.001*
Meningeal Enhancement	46 (45.5)	139 (52.5)	0.287
Tuberculoma	9 (8.9)	31 (11.7)	0.564
Infarct	25 (24.8)	37 (14.0)	0.021
Lungs TB	49 ( 49.0)	137 (52.5)	0.634
Lungs Extra TB	3 (3.0)	10 (3.8)	0.956
TBM Grade			
Grade 1	2 (2.0)	12 (4.6)	<0.001*
Grade 2	64 (64.6)	220 (84.9)	
Grade 3	33 (33.3)	27 (10.4)	
Marais score	12.00 [11.00, 14.00]	12.00 [11.00, 14.00]	0.966
BCG Vaccination	67 (66.3)	216 (81.5)	0.003*
Total	101	265	

**Table 2.** Comparison of Clinical, Laboratory, Radiological Features, and Vaccination Status According to In-Hospital Mortality in Patients with Tuberculous Meningitis

- 366 adult TBM patients without HIV were included, comprising 283 patients with a BCG scar and 83 without a BCG scar.
- Patients without a BCG scar showed higher rated of decreased consciousness (89% vs. 74%; p = 0.005), cranial nerve palsy (26% vs. 12%; p = 0.004), and in-hospital mortality (41% vs. 24%; p = 0.004) compared to those with a BCG scar.
- In-hospital mortality was associated with decreased consciousness (96% vs. 70%), hydrocephalus (49% vs. 27%), severe TBM (33% vs. 11%), and absence of a BCG scar (34% vs. 19%) (p < 0.004).
- Multivariate analysis demonstrated that decreased level of consciousness and absence of BCG vaccination as independent predictors of in-hospital mortality.