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The correlation between ischemic lesions and tuberculoma incidence on head CT-Scan and clinical prognosis in tuberculous meningitis patients: A study at Hasan Sadikin Central General Hospital Bandung 2018

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ABSTRACT

Background: Central nervous system (CNS) TB disease occurs only in 2-5% of all tuberculosis patients but has high mortality rate up to 30% and often causes residual symptoms of neurological deficits, only 18% of the patient can return to normal neurological function. Computed Tomography Scan (CT scan) is the initial modality for detecting unique neuroradiological abnormalities in patients with tuberculous meningitis such as ischemic lesions and tuberculoma. Ischemic lesions and tuberculoma are associated with increased neurological complications in patients with tuberculosis and affect the clinical prognosis of tuberculous meningitis patients that can be assessed using Modified Rankin Score (MRS).

Objective: To review the correlation between ischemic lesion and tuberculoma on head CT-scan and clinical prognosis of tuberculous meningitis patient.

Methods: This study was an observational analytic study with a cross-sectional design. Sampling was done by consecutive admissions

in January 2015 to September 2016. The data were analyzed statistically using Chi-Square test.

Results: There were 22 subjects. The highest incidence is severe clinical prognosis, being highest found in 59.1% (13 patients). The result of the statistical test using Chi-Square test at 95% confidence degree shows that there is a statistically significant correlation between ischemic lesion and tuberculoma incidence on CT head examination and clinical prognosis of tuberculous meningitis patient Hasan Sadikin Central General Hospital Bandung (value $p \leq 0.05$).

Conclusion: There is a significant correlation between ischemic lesion and tuberculoma incidence on CT head scan and clinical prognosis of tuberculous meningitis patient at Hasan Sadikin Central General Hospital Bandung with p-value = 0.032 (value $p \leq 0.05$).

Keywords: tuberculous, meningitis, ischemic lesion, tuberculoma, CT scan, prognosis, Modified Rankin Score

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BACKGROUND

Tuberculosis (TB), still considered a public health problem in the world, is one of the infectious diseases caused by *Mycobacterium tuberculosis* bacteria.¹ The 2014 data of World Health Organization (WHO) estimate that there were 9.6 million new tuberculosis cases, in which 1.5 million deaths were caused by tuberculosis. Most tuberculosis cases (58%) are in the Asia-Pacific and western Pacific countries, while 38% cases prevail in Africa.² Indonesia has more than 100 cases per 100,000 population. It is one of the countries bearing tuberculosis burden in the world and is categorized as the high burden country in 2015 WHO TB Surveillance list.³ Central nervous system tuberculosis (CNST) disease occurs only in 2-5% of all tuberculosis patients. However, the fact that the mortality rate is high—30% of the patients not getting treatment—and it often leaves

the surviving patients residual symptoms of neurological deficits, makes this disease dangerous. Of all the CNST patients who were otherwise cured, only 18% of them were able to return to normal neurological state.⁴⁻⁵

Tuberculous meningitis disease, the most common form of TB disease in the CNST, is marked with inflammation of the brain membrane (meninges) caused by the infection of the *Mycobacterium tuberculosis* originating from hematogenous spread of TB infection elsewhere, mainly from pulmonary tuberculosis.⁶ TB meningitis is triggered by the proliferation of tuberculosis bacteria in the lungs (primary tuberculosis) through blood circulation vessels. The bacteria reach an oxygen-rich central nervous system that forms a focus known as the Rich Focus. This concentration can be formed in meninges, cortex, subarachnoid, sub-pial, and

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subependymal. When this concentration becomes active and manifests, it can cause disease according to its spread locations in the central nervous system. The manifestation of tuberculosis spread in the central nervous system is tuberculous meningitis and tuberculoma.⁷

Faster, more cost-effective, and more significantly available than MRI or Magnetic Resonance Imaging, Computed Tomography Scan (CT scan) is an optional radiological modality expected to play a role in making precise and early diagnosis.⁸⁻¹⁰ Tuberculous meningitis in CT scan and MRI may provide tuberculoma parenchymal lesions and triad of neuroradiological symptoms such as meningeal enhancement in basal areas, in particular, hydrocephalus and ischemic lesions, particularly in basal ganglia. These neurologic symptoms are predictors in determining prognosis in patients with tuberculous meningitis.^{11,12} Ischemic lesions in CT Scan were found in 38% of the cases, and tuberculoma occurs in 5-30% of tuberculous meningitis cases.¹³⁻¹⁶

This study is aimed at investigating the correlation between the incidence of ischemic lesion and tuberculoma on CT head scans and clinical prognosis. The clinical prognosis are assessed using Modified Rankin Score (MRS) based on disability level divided by three: normal (MRS = 0), mild to moderate disability (MRS = 1-3), severe disability (MRS = 4-5).¹⁷⁻²⁰

RESEARCH DESIGN AND METHODOLOGY

This study is an observational analytic study with cross sectional design to measure independent and dependent variables at the same time. It utilized retrospective data in its statistical analysis to find out the correlation between the ischemic lesion and tuberculoma on head CT scans and the degree of prognosis in adult tuberculous meningitis patients at dr. Hasan Sadikin Central General Hospital Bandung. This study has been granted ethical approval (No. LB.04.01/A05/EC/030/II/2018).

Sampling was performed by collecting the data, which had been read by radiologists in the field of neuroradiology, of the patients having had undergone head examination with CT scan in 2015-2016. The simple random sampling method was employed to obtain 22 sample sizes by selecting the data that met the inclusion criteria. Using Modified Rankin Score (MRS), the clinical prognosis was assessed when the patients were discharged from the hospital.

The collected data were processed in the computer to transform data into information. Univariable analysis was meant to describe the characteristics of study subjects including age, sex, incidences of ischemic lesions and tuberculoma on CT head scans, and the clinical prognosis of tuberculous meningitis at Dr. Hasan Sadikin General Hospital Bandung. The data were presented in quantities and percentages.

By utilizing two variable Chi-Square test with categorical data type, the bivariable analysis was run to examine the correlation between the incidence of ischemic lesion and tuberculoma and clinical prognosis of the tuberculous meningitis patients gained through CT head scans at dr. Hasan Sadikin Central General Hospital Bandung. Data analysis was performed using Statistical Product and Service Solution (SPSS) program for Windows version 18.0 at 95% confidence level and with $P \leq 0.05$.

RESULTS

This study had a sample size of 22 people. Their average age was 30 years, with standard deviation of 13 years, median 26 years old, the youngest age being 17 years old, and the oldest being 60 years. The most significant distribution of sample population was in the age group 21- 35 years, namely 11 people (50.0%). 77.3% of the sample study subjects or 17 people were male, while 22.7% of them or 5 people were female. The results are available in [Table 1](#).

The results of the CT head scans of the sample population showed that ischemic lesions occurred in as many as nine people (40.9%) and tuberculoma in as many as seven people (31.8%). The clinical prognosis was divided into three categories, normal (MRS = 0), mild-moderate (MRS = 1-3) and severe (MRS = 4-5). The severe clinical prognosis was found in 13 samples (59.1%), followed by nine samples (40.9%) showing a mild-moderate prognosis and no sample study subject exhibited good prognosis (0%). The results are available in [Table 2](#) and [3](#).

The samples were then divided into four categories based on CT scan images, namely ischemic lesions without tuberculoma, ischemic lesions with tuberculoma, tuberculoma without ischemic lesions and neither ischemic lesions nor tuberculoma. Ischemic lesions without tuberculoma were found to have the severe prognosis of 87.5% ($p = 0.032$, CI = 95%). These results are available in [Table 4](#).

Table 1 Characteristics of research subjects based on age and sex of patients with tuberculous meningitis at dr.Hasan Sadikin Central General Hospital Bandung

Variable	N	%
Age (years)		
Average (SD) : 30.14 (13.09)		
Median: 26		
Minimum: 17		
Maximum: 60		
≤20 years	6	27.3
21-35 years	11	50.0
26-50 years	3	13.6
>50 years	2	9.1
Sex		
Male	17	77.3
Female	5	22.7
Total	22	100.0

Table 2 The correlation between the incidence of ischemic lesion and tuberculoma on head CT scan and clinical prognosis of tuberculous meningitis patients in dr. Hasan Sadikin Central General Hospital Bandung

Variables	Clinical Prognosis based on MRS								P value
	Normal		Mild-Moderate		Severe		Total		
	n	%	n	%	n	%	n	%	
Ischemic lesion and tuberculoma									0.032
Ischemic lesion with tuberculoma	0	0	0	0.0	1	100.0	1	100.0	
Ischemic lesion without tuberculoma	0	0	1	12.5	7	87.5	8	100.0	
Tuberculoma without ischemic lesion	0	0	5	83.3	1	16.7	6	100.0	
Without tuberculoma and without ischemic lesion	0	0	4	57.1	3	42.9	7	100.0	

DISCUSSION

The result of this study showed that the average age of patients with tuberculous meningitis was 30.14 (standard deviation of 13.09). It confirms the study result by Anuradha et al. in 2010 revealing 31 (standard deviation of 12) as the mean age of TB meningitis, and the study result by Gu et al. revealing 32.9 (standard deviation of 18.6) as the mean age of

TB meningitis.^{19,20} The characteristics of the study subjects by age and gender can be seen in Table 1.

The average age group in this study was the productive age, proving the claim stated in the National Guidelines for Tuberculosis Control in Indonesia that the productive age group is the one most affected by tuberculosis and its complications. In line with studies by Rock et al. in 2008, Subur et al. in 2014 and Gu et al. in 2014, this study also proved that the gender distribution of patients with TB meningitis was mostly men.^{1,20,21} That men are more prone to tuberculous meningitis is possibly related to data which according to 2015 Global Tuberculosis Report, in general, there were more adult males suffering from tuberculosis.³ Also, Davila et al. in 2008 said that one of the four variations of TLR8 gene of the X chromosome, namely rs3764880 allele A in men, causes a man to be more prone to the infection by *Mycobacterium tuberculosis* bacteria.²²

The result of the head CT scans of the sample population showed that ischemic lesions were found in as many as nine people (40.9%) while tuberculoma was discovered in as many as seven people (31.8%). The characteristics of the findings of the CT head scans are assessed in Figure 1.

That less tuberculoma found in the sample was possibly related to Monterio et al.'s statement in 2013 that the highest distribution of intracranial tuberculoma happens to children and immunocompromised patients, whereas the mean age in this study sample fell into the productive category.²³ The most dominant prognosis found in the sample population was 59.1% severe prognosis. The probable cause is the fact that the study was conducted at a referral center hospital where the sample patients obtained were those whose initial clinical conditions already showed enough severe conditions. The characteristics of prognosis in the sample population are available in Figure 2.

With $p = 0.032$ ($p < 0.05$), this study indicates that there is a correlation between the incidence of the ischemic lesion and tuberculoma on the CT head scans and the clinical prognosis of tuberculous meningitis at dr. Hasan Sadikin Central General Hospital Bandung. The results are available in Table 2.

These findings were in line with researches done by Baba et al. in 2016 ($P = 0.019$) and Wasay et al. in 2014 ($p = 0.001$ [$p < 0.001$]) which found that imaging features such as ischemic lesions and tuberculoma were associated with severe prognosis. Table 2 also shows that ischemic lesions with tuberculoma as well as ischemic lesions without tuberculoma were related to a more severe clinical prognosis. These findings are also consistent with the research

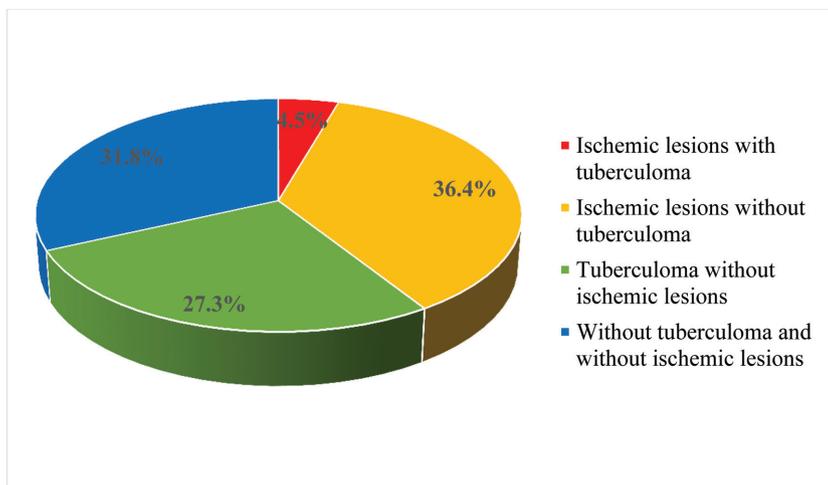


Figure 1 Characteristics of research subjects based on the incidence of ischemic lesions and tuberculoma on the CT head scans of the tuberculous meningitis patients

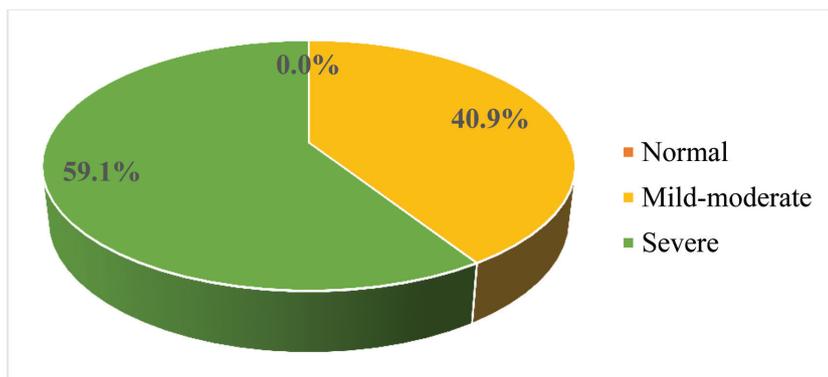


Figure 2 Characteristics of study subjects based on the clinical prognosis of the tuberculous meningitis patients

done first by Baba et al. 2014 and Wasay et al. in 2014.¹⁷⁻¹⁸ One explanation for this is the fact that ischemic lesions, as one form of cerebrovascular abnormalities, is triggered by *Mycobacterium tuberculosis*. It leads to manifestation, such as stroke, which is directly related to decreased MRS scores.

CONCLUSION

With $p = 0.032$ ($p \leq 0.05$), there is a significant correlation between the incidence of ischemic lesions and tuberculoma on the CT head scans and the clinical prognosis of tuberculous meningitis patients

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