



Research Article

## The body mass index profiles in chronic pulmonary aspergillosis: trend and variability in post tuberculosis patients

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### ABSTRACT

Tuberculosis (TB) is the leading risk factor for chronic pulmonary aspergillosis, especially in patients with residual cavitory lesions after completion of TB therapy. The body mass index (BMI) is one of the established markers in predicting the mortality of CPA. However, the data regarding BMI profiles of CPA patients in Indonesia is still limited. We evaluated the BMI profiles of CPA patients among post-TB patients. Patients were diagnosed as CPA based on clinical, radiology, and the *Aspergillus* IgG test. Fifty patients with a mean age of 35 years were included; 13 patients met the criteria of CPA. The overall median BMI in these patients was 21. The median BMI in the CPA group was 19.3. The lowest (19.8) median BMI value was observed in the positive *Aspergillus* IgG group (11.5 – 30 mg/L), with a minimum BMI of 14.7 and a maximum BMI of 29.2. The differences in median BMI across CPA and non-CPA groups and *Aspergillus* IgG levels were not statistically significant. However, there is a trend that lower BMI was distributed among patients with positive *Aspergillus* IgG. More than one-third of CPA patients in this study were classified as underweight. Future study is necessary to depict better the BMI profiles on a larger scale of populations of CPA in Indonesia to achieve better diagnosis and management of CPA.



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### INTRODUCTION

Chronic pulmonary aspergillosis (CPA) is a chronic respiratory disease characterized by progressive lung parenchyma destruction and persistent respiratory symptoms. Pulmonary tuberculosis (TB) is the major risk factor for CPA (Denning, Pleuvry, & Cole, 2011; Page et al., 2019; Rozaliyani et al., 2020). According to previous study, 8% of TB patients at the end of TB therapy posed a risk of developing CPA (Setianingrum et al., 2022). The TB incidence rate in Indonesia is 354 per 100.000 population, this rate placed Indonesia as the second-ranked country with the largest burden of TB (Ministry of Health Republic of Indonesia, 2023).

The prevalence of TB in certain areas is affected by several factors, one of them is nutritional status (Bhargava, 2016; Cegielski, Arab, & Cornoni-Huntley, 2012; Liu, Tang, Xiang, & He, 2022; Lönnroth, Williams, Cegielski, & Dye, 2010). A single unit decrease in BMI reduces TB incidence by 13.8% (Lönnroth et al., 2010). Previous study from Indonesia revealed that malnutrition exists in 87% of TB patients (Pakasi, Karyadi, Dolmans, Van Der Meer, & Van Der Velden, 2009).

The link between body mass index (BMI) and the prognosis of CPA is well established (Kimura et al., 2021; Lowes et al., 2017; Zhong et al., 2022). The decrease in mortality of CPA by 11% is attributed to the single increase of BMI (Lowes et al., 2017). The simple formula of BMI bring advantages for use in all levels of healthcare facilities to help clinicians assess the progression of CPA. Our main objective was to investigate the BMI profiles of CPA patients among post-TB patients and to observe if there are correlations between BMI profiles and the *Aspergillus* IgG level.

### METHODS

This study was performed using serum samples archived in the Parasitology Laboratory, Faculty of Medicine, Universitas Indonesia. Sera were collected from 50 post-TB patients after completion of TB therapy. Proven CPA was diagnosed based on the three parameters: 1) at least one of these symptoms, including cough, chest pain, dyspnea, and/or fatigue  $\geq 3$  months, AND 2) positive *Aspergillus* IgG with automated ELISA test (Immulite 2000 testing system, Siemens, Germany) according to the manufacturer instructions AND 3) radiological features indicative of CPA (at least one of cavitation and/or fungal ball). The information regarding BMI and the sera collection for the *Aspergillus* IgG were gathered during patients' visits to the hospital after completing PTB therapy. The study was conducted at the Parasitology Laboratory, Faculty of Medicine, Universitas Indonesia. Ethical approval was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia (no. 95/UN2.F1/ETIK/2019).

The SPSS version 20.0 software (IBM, Armonk, NY, USA) was used to perform the statistical analyses. Categorical data were presented as numbers of cases and percentages. Fisher's exact tests or  $X^2$  tests were used for categorical variables for CPA and non-CPA groups. The Mann-Whitney U test was used to detect the difference between non-parametric continuous variables. Comparison of median results across different *Aspergillus* Ig-G groups was assessed using Kruskal-Wallis tests. A p-value of  $p < 0.05$  was considered statistically significant.



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**RESULTS**

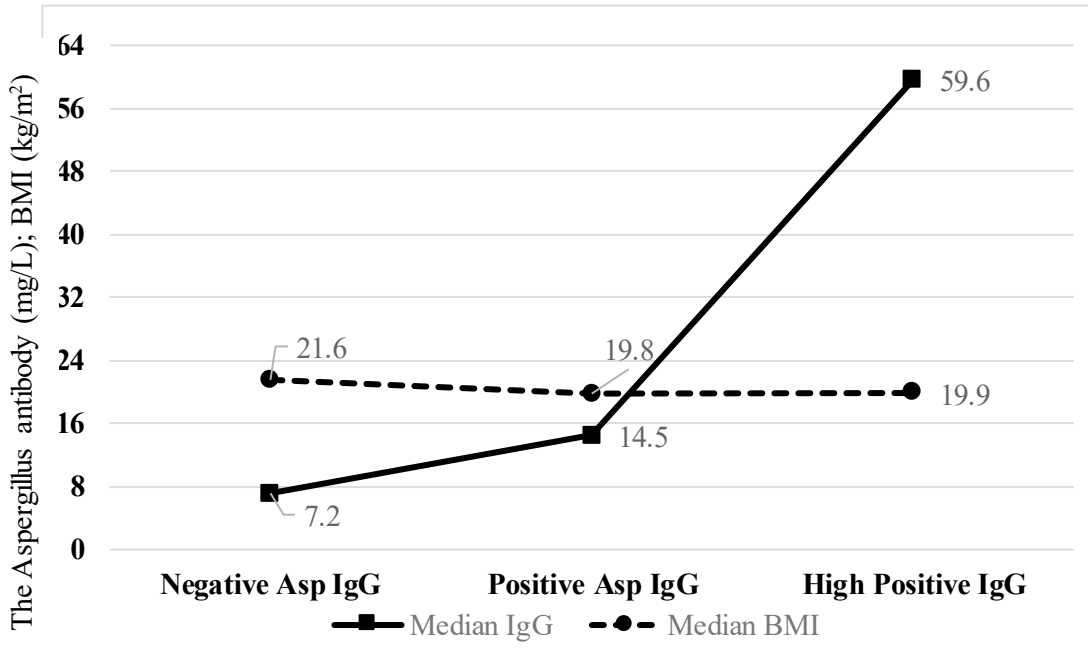
A total of 50 patients with post-TB therapy were included in this study. Table 1 shows the patient demographic characteristics of patients. The mean age was 35 years (range: 17-72 years; 20 patients (40%) were male. In the disease category, 13 patients (26%) were classified as the CPA group and 37 patients were classified as the non-CPA group. The most common symptom in the CPA group was fatigue 85% (n=11). There was a significant difference in the proportion of cough (31% in the CPA group vs 0% in the non-CPA group), dyspnea (46% in the CPA group vs 8% in the non-CPA group), and fatigue (85% in the CPA group vs 11%

in the non-CPA group). The overall median of BMI in these patients was 21, whereas the median BMI in the CPA group was 19.3.

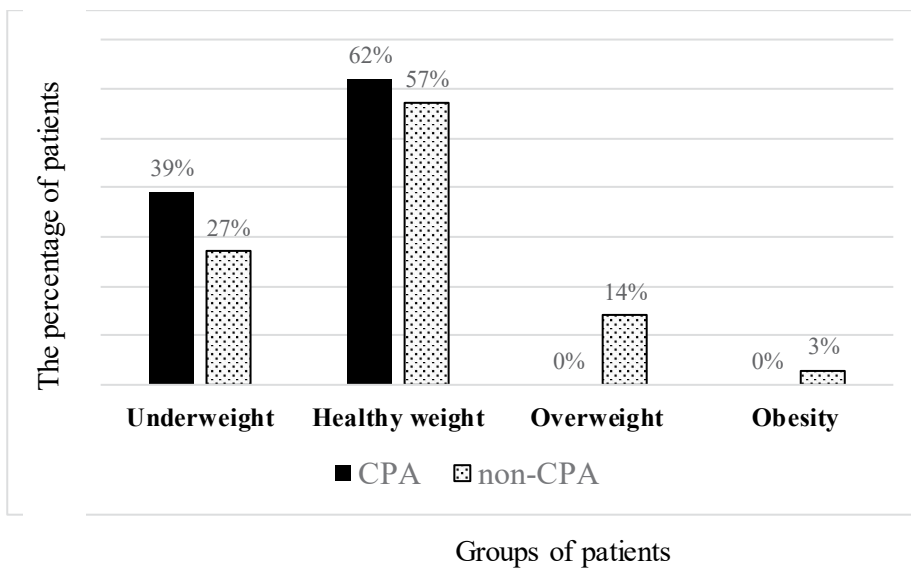
The median value of BMI test was varied across various *Aspergillus* IgG groups (Figure 1). The variability of BMI across three different groups of *Aspergillus* IgG level showed a p-value of 0.401. The lowest (19.8) median BMI value was observed in the positive *Aspergillus* IgG group (11,5 – 30 mg/L) with a level range of 14.7 – 29.2. The patients with the lowest (14.7) BMI in the positive *Aspergillus* IgG group met the criteria of CPA with *Aspergillus* IgG level 12.6 mg/L with respiratory chronic symptoms (dyspnea, chest pain, and fatigue).

**Table 1.** Demographic characteristics of patients

Symptoms	ALL (n=50)	CPA (n=13)	Non-CPA (n=37)	p-value
Gender				
Male	20 (40%)	6 (46%)	14 (38%)	
Female	30 (60%)	7 (54%)	23 (62%)	0.744
Age group				
> 60 years	6 (11%)	2 (15%)	4 (11%)	
≤ 60 years	44 (88%)	11 (85%)	33 (89%)	1
<b>Sign &amp; symptoms (≥3 months)</b>				
Cough	4 (8%)	4 (31%)	0 (0%)	0.003
Dyspnea	9 (18%)	6 (46%)	3 (8%)	0.006
Chest pain	2 (4%)	1 (8%)	1 (3%)	0.456
Fatigue	15 (30%)	11 (85%)	4 (11%)	<0.001
<b><i>Aspergillus</i> antibody IgG</b>				
Positive	20 (40%)	13 (100%)	7 (19%)	
Negative	30 (60%)	-	30 (81%)	<0.001
<b>Body mass index</b>				
Median	21 (14.4 – 36.4)	19.30 (14.7 – 24.1)	21.5 (14.4 – 36.4)	0.224



**Figure 1.** The variety level of body mass index (BMI) according to the *Aspergillus* IgG classifications.



**Figure 2.** The body mass index profiles of CPA and non-CPA patients.



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The distributions of the BMI is depicted in Figure 2. There were 39% (n=5) patients from the CPA group who were classified as underweight and 27% (n=10) patients in the non-CPA group (p=0.493). Overweight patients were only present in the non-CPA group (14%, n=5), resulting in p=0.309 compared to the CPA group. No significant differences were detected for the BMI groups between CPA and non-CPA groups. The comparison of BMI between healthy weight (62% in CPA vs 57% in the non-CPA group) and obesity (0% in CPA vs 3% in the non-CPA group) showed a p-value = 1.

## DISCUSSION

The purpose of this study was to investigate the BMI, demographic, and clinical characteristics of post-TB patients. This is the first study revealing the BMI profiles of CPA patients in Indonesia. This study is important because the variability of BMI is affected by ethnic groups worldwide (Kenangalem et al., 2013; Painter & Tabler, 2022). Asian ethnicities tend to have a lower BMI compared to the Black and Latino populations (Painter & Tabler, 2022). The overall median BMI of post-TB patients in our study (21) is the same as recent research from Singapore that investigated the BMI profiles of bronchiectasis patients with TB with a median BMI of 21.2 (Fong, Low, & Yui, 2022)

The median rate of BMI in CPA patients in our study was 19.3. This rate is slightly higher than other previous studies of CPA conducted in other countries with a BMI range from 17.1 to 18.98 (Nguyen et al., 2021; Ohara et al., 2016; Ohba et al., 2012). Malnutrition indicated with an underweight BMI is commonly found in CPA patients and becomes an independent predictor for mortality (Kimura et al., 2021; Lowes et al., 2017; Ohba et al., 2012).

The lowest BMI observed from this study is 14,40 from a non-CPA group patient with

an *Aspergillus* IgG level of 7,04 mg/L and persistent respiratory or systemic symptoms. The lowest BMI from the CPA group was 14,70 with severe bilateral cavitory lesions of TB in the early stages of TB therapy. There is the possibility that the BMI was lower than 14,70 at the time of TB diagnosis. A Van Lettow et al. study showed that the severity of radiological findings correlates with weight loss.

Previous studies revealed underweight is the major risk factor for TB (Choi et al., 2021). The poor clinical status reflected by BMI accompanied by severe lung cavitation is the perfect combination for the development of CPA in post-TB patients. TB and CPA as dual infections were reported in our previous study (Setianingrum et al., 2022). The effect of co-existence between CPA and TB on the BMI profiles of TB patients is required to be explored.

The proportion of underweight patients is higher in the CPA group than the non-CPA group, although this was not statistically significant (p=0,493). Also, the median BMI across different *Aspergillus* IgG groups was not statistically significant (p=0,401). There is a decrease trend of BMI in the positive *Aspergillus* IgG group (median BMI 21.6) compare to the negative *Aspergillus* IgG group. One of the limitations of this study is the small number of CPA cases. The high positive *Aspergillus* IgG group is defined by the *Aspergillus* IgG range >30 mg/L. There was only five patients classified into this group. In contrast, the number of patients in other *Aspergillus* IgG groups are 32 and 13. Therefore, future studies with a sufficient number of CPA cases might confirm our findings and elucidate the role of the BMI index in the progression of CPA in post-TB patients in Indonesia.





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### CONCLUSIONS

The BMI profile is a potential and simple tool to assess the prognosis of CPA. There is a need for future studies to understand better the interactions between the decrease in BMI and the increase in *Aspergillus* IgG levels in CPA patients. Furthermore, the co-existence between CPA with other conditions such as TB, bronchiectasis, and other pulmonary diseases might affect the fluctuation of BMI of patients.

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