

Findra Setianingrum^{1,2,3}, Anna Rozaliyani^{1,3,4}, Robiatul Adawiyah^{1,3}, Ridhawati Syam^{1,3}, Mulyati Tugiran^{1,3}, Cut Yulia I. Sari^{3,5}, Finny Nandipinto³, Johannes Ramnath⁵, Diah Handayani^{3,7}, Erlina Burhan^{3,7}, Martin C. Rumende⁷, Retno Wahyuningsih^{1,3,9}, Riina Rautemaa-Richardson^{2,10}, David W. Denning^{2,10}

¹Dept. of Parasitology, Faculty of Medicine Univ.Indonesia. ²Faculty Biology, Medicine and Health, Univ. of Manchester, and Manchester Academic Health Science Centre, UK. ³Pulmonary Mycosis Centre, Indonesia. ⁴Grha Permata Ibu Hospital, Indonesia. ⁵Jakarta Islamic Hospital, Indonesia. ⁶Dept. of Internal Medicine, Faculty of Medicine, Univ. Kristen Indonesia. ⁷Dept. of Pulmonology & Respiratory Medicine, Faculty of Medicine Univ. Indonesia ⁸Dept. of Internal Medicine, Faculty of Medicine, Univ. Indonesia. ⁹Dept. of Parasitology, Faculty of Medicine, Univ. Kristen Indonesia. ¹⁰National Aspergillosis Centre, Wythenshawe Hospital, UK.

Background

- Tuberculosis (TB) is the most common underlying disease of Chronic Pulmonary Aspergillosis (CPA).
- It can be estimated that there are some 17,561 new cases CPA after TB every year in Indonesia. The total estimate of CPA of ~83,000 patients.¹ There is no single study about CPA in PTB patients in Indonesia.

Aims

This study aims to estimate the optimal diagnostic cut-off for CPA among pulmonary TB in Indonesia.

Methods

- 203 patients at the end of their TB therapy, 90 healthy controls, and 100 lung disease control (no history or current TB) in Indonesia were recruited to the study.
- *Aspergillus* (Asp)-IgG level was measured using automated Immulite (Siemens) and the Dynamiker (anti-galactomannan IgG) manual ELISA.
- Receiver operating curve (ROC) analysis was used to determine the optimum cutoff of the Asp-IgG level.

Results

Table 1. Asp-specific IgG comparison (Immulite)

Group	Median (mg/L)	Range (mg/L)
CPA cases (n=26)	20.3	7.8 - 630
End of treatment TB (n=177)	8.5	3.2 - 133
Healthy controls (n=90)	7.1	2.6 - 18.4
Disease controls (n=100)	7.7	3.2 - 200

Table 2. Asp-specific IgG comparison (Dynamiker)

Group	Median (AU/ml)	Range (AU/ml)
CPA cases (n=23)	140.9	42-500
End of treatment TB (n=168)	127.7	31.3-500
Healthy controls (n=90)	80.6	31.3-500
Disease controls (n=100)	88.7	31.3-500

- 26 of the 203 recruited patients (13%) had clinical and radiological features of CPA (Table 1 & 2).
- There were significant differences ($p < 0.001$) in the Immulite Asp-specific IgG levels between the the CPA group and the end of treatment TB group without CPA, the healthy controls and disease controls.
- There were significant differences ($p < 0.05$) in the Dynamiker Asp-specific IgG levels between the the CPA group compared to healthy controls and disease controls.

Table 3. AUC Immulite cutoffs in different groups

Groups	ROC AUC	95% CI	Optimal diagnostic cutoff	Sensitivity	Specificity	Youden J index
Healthy controls	0.926	0.873-0.979	11.5 mg/L	89%	88%	0.76
End of treatment TB	0.837	0.766-0.907	11.5 mg/L	89%	72%	0.61
Diseased controls	0.87	0.805-0.935	12.2 mg/L	85%	85%	0.69
Diseased controls	0.87	0.805-0.936	11.6 mg/L	89%	80%	0.69

Table 4. AUC Dynamiker cutoffs in different groups

Groups	ROC AUC	95% CI	Optimal diagnostic cutoff	Sensitivity	Specificity	Youden J index
Healthy controls	0.758	0.663-0.854	106.8 AU/ml	83%	69%	0.52
End of treatment TB	0.581	0.470-0.693	106.8 AU/ml	83%	40%	0.23
Disease control	0.704	0.598-0.810	91.6 AU/ml	87%	51%	0.38
Disease control	0.704	0.598-0.810	106.2 AU/ml	83%	55%	0.38

- Healthy controls and end of treatment TB therapy analyses produced a cutoff of 11.5 mg/L, while the disease control group showed a cutoff of 12.2 mg/L, compared with the previous study² cutoff for CPA of 10 mg/L (Table 3).
- Immulite cutoff of 11.5 mg/L resulted in the highest sensitivity and specificity for CPA cases vs healthy controls with AUC 0.926, sensitivity 89% and specificity 88% (Figure 1).
- Healthy controls and end of treatment TB therapy analyses produced a cutoff of 106.8 AU/ml, while the disease control showed a cutoff of 106.8 AU/ml and 91.6 AU/ml for Dynamiker, compared with the manufacturer's cutoff of 120 AU/ml (Table 4).

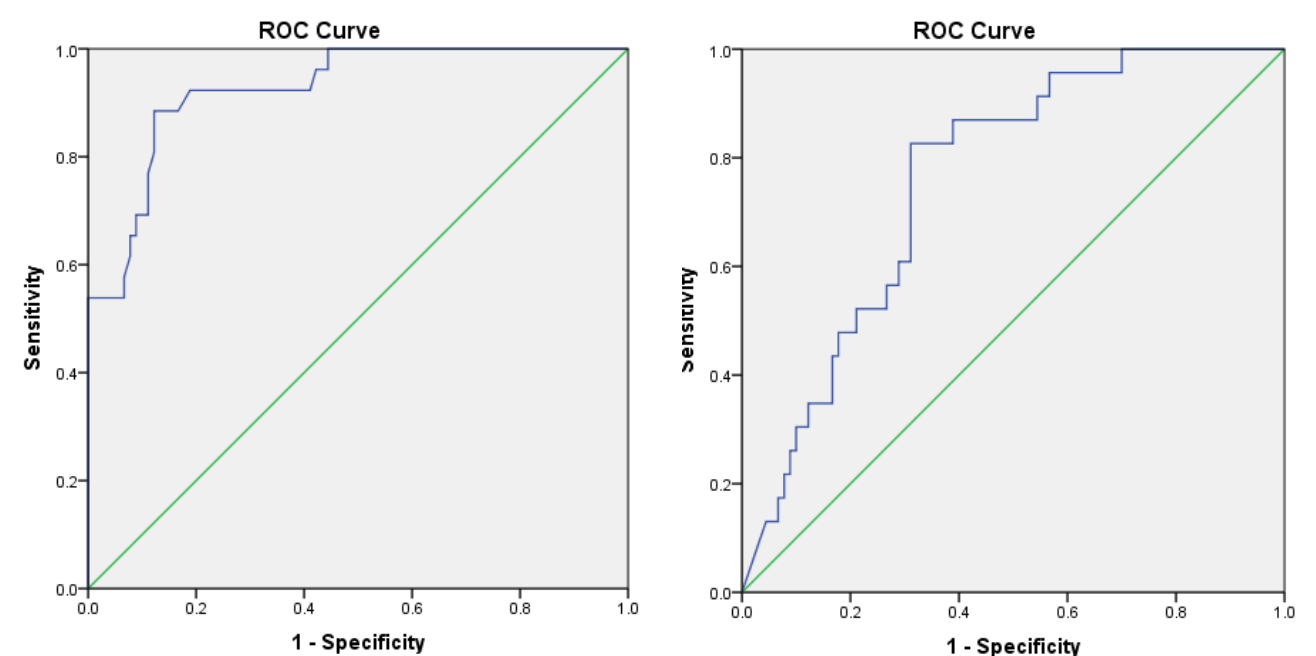


Figure 1. ROC curve Immulite (left) and Dynamiker (right) in healthy people

- There were 73 (38%) discordant results between the Immulite and Dynamiker tests using 11.5 mg/L for Immulite and 106.8 AU/mL as cutoffs.
- A moderate level of correlation was found between Immulite and Dynamiker with Spearman's rank analysis ($r_s = 0.5$, $p < 0.001$).
- The Asp-specific IgG level for CPA (at the end of TB treatment) compared with those without CPA is significantly different for Immulite but not Dynamiker assays. Culture extract antigens are used for Immulite while galactomannan is used in Dynamiker.

Conclusions

- Our study provides the first analysis of *Aspergillus*-specific IgG cutoffs for CPA in the Indonesian population.
- CPA appears to be common in TB patients in Indonesia.
- The currently used *Aspergillus*-IgG cutoff of Immulite and Dynamiker may require slight adjustment for CPA in the Indonesian population.

References:

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