



# The clinical usefulness of serum procalcitonin level in patients with scrub typhus

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## To the Editor,

Scrub typhus caused by *Orientia tsutsugamushi* is an endemic disease threatening a wide area of the Asia-Pacific rim, extending from Afghanistan to China, Korea, the Southwestern Pacific islands, and Northern Australia [1]. Scrub typhus is mainly diagnosed by serological testing [2]. However, diagnosing acute scrub typhus on the basis of serological testing alone is limited because antibody titres increase several days after illness onset. Therefore, for patients in the acute phase of scrub typhus, the condition must be diagnosed prior to laboratory confirmation on the basis of clinical presentation and patient history. The medical personnel could easily diagnose an acute scrub typhus if a patient had the typical eschar, and would treat him with appropriate antibiotics immediately. But, in the cases of the absence of eschar, diagnosing scrub typhus and administering appropriate antibiotics may be delayed, and delayed use of appropriate antibiotics is associated with increased risk of complications and death [3]. Procalcitonin (PCT) is a promising biomarker for identification of bacterial infections. In bacterial infections, serum PCT levels start to rise at 4 hours after the onset of systemic infection, and peak at between 8 and 24 hours [4]. PCT can be used as a rapid diagnostic biomarker to differentiate between bacterial sepsis

and systemic inflammatory response syndrome [4]. The level of PCT associated with *O. tsutsugamushi* infection is rarely investigated [5]. To the best of our knowledge, no study has focused on the usefulness of PCT for the diagnosis of acute scrub typhus.

In this study, we compared serum PCT levels of acute scrub typhus with that of *Escherichia coli* bacteraemia on the day of admission. In addition, we determined the optimal cutoff value of serum PCT levels for diagnosing acute scrub typhus. *E. coli* bacteraemia was defined as *E. coli* grown from blood culture taken on the day of admission. Acute scrub typhus was defined as an increased titre in the indirect immunofluorescence antibody test against *O. tsutsugamushi*  $\geq$  4-fold increased titre in the follow-up [2]. Serum PCT levels were assessed within the first 24 hours following admission. This retrospective study was conducted in Wonkwang University Hospital and Chonbuk National University Hospital in Korea between July and December 2011.

A total of 106 patients ( $\geq$  18 years old) with acute scrub typhus and 82 patients ( $\geq$  18 years old) with *E. coli* bacteraemia were included in the study. The mean ages of the patients with acute scrub typhus and with *E. coli* bacteraemia were 64.9 and 73.3 years, respectively. The mean serum PCT levels in patients with acute scrub typhus and with *E. coli* bac-

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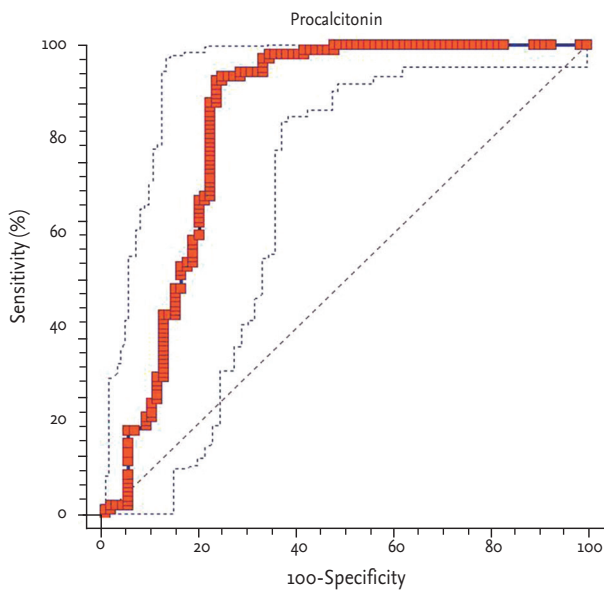
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**Table 1. Sensitivity, specificity, and odds ratio for acute scrub typhus according to cutoff value of PCT levels**

Cutoff value of PCT level, ng/mL	Sensitivity, %	Specificity, %	Odds ratio	95% Confidence interval
≤ 0.98	80.2	78.0	14.4	7.088–29.220
≤ 1.20	84.9	78.0	20.0	9.487–42.162
≤ 1.27	87.7	78.0	25.4	11.646–55.553

PCT, procalcitonin.



**Figure 1.** Receiver operating curve analysis of procalcitonin in acute scrub typhus patients. With a cutoff value of < 1.3 ng/mL, a sensitivity of 87.7%, a specificity of 78.0%, and an area under curve of 0.84.

teraemia were 0.90 and 43.7 ng/mL, respectively. Receiver operating characteristic curve analysis determined the optimal cutoff value of serum PCT to be 1.3 ng/mL with a sensitivity of 87.7% and a specificity of 78.0% (Fig. 1). Patients with PCT levels lower than 1.3 ng/mL had a 25.4 times higher risk for having acute scrub typhus than for having *E. coli* bacteraemia (Table 1).

A previous study reported the correlation between elevated PCT level and increased mortality [5]. In our study, we focused on usefulness of PCT for early diagnosis of acute scrub typhus and for differentiating other bacterial infections from acute scrub typhus in the scrub typhus endemic area. PCT levels in scrub typhus were markedly lower than in *E. coli* bacteraemia, which is a most representative bacterial infection, and optimal cutoff value for PCT was set at 1.3 ng/mL (87.7% sensitivity; 78.0% speci-

ficity). In addition, a PCT level lower than 1.3 ng/mL carried 21.9 times higher risk for having acute scrub typhus than that of *E. coli* bacteraemia using multiple linear regression analysis after adjustment for age and gender.

Our study suggests that PCT could be used for differentiating acute scrub typhus from other bacterial infections and for early diagnosis of acute scrub typhus. As you know, patients with other acute febrile illnesses, such as viral infection, also showed a low PCT level (≤ 1.3 ng/mL). Thus, serum PCT level should be considered along with the clinical findings to establish a diagnosis of scrub typhus. However, scrub typhus must be considered as a possible cause when acute febrile patients are presented with low PCT level (≤ 1.3 ng/mL) especially during the autumn season. The present study has some limitations. First, this study was retrospective in nature. Second, only *E. coli* bacteraemia cases were used for comparison, and *E. coli* bacteraemia cases are not entirely representative of all bacterial infections. In conclusion, serum PCT (≤ 1.3 ng/mL) may be useful as a supplementary test for diagnosis of acute scrub typhus.

**Keywords:** Procalcitonin; Scrub typhus; Escherichia coli

**Conflict of interest**

No potential conflict of interest relevant to this article was reported.

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**REFERENCES**

1. Kelly DJ, Fuerst PA, Ching WM, Richards AL. Scrub typhus: the geographic distribution of phenotypic and genotypic variants of *Orientia tsutsugamushi*. Clin Infect

- Dis 2009;48 Suppl 3:S203-S230.
2. Blacksell SD, Bryant NJ, Paris DH, Doust JA, Sakoda Y, Day NP. Scrub typhus serologic testing with the indirect immunofluorescence method as a diagnostic gold standard: a lack of consensus leads to a lot of confusion. *Clin Infect Dis* 2007;44:391-401.
  3. Yasunaga H, Horiguchi H, Kuwabara K, Hashimoto H, Matsuda S. Delay in tetracycline treatment increases the risk of complications in Tsutsugamushi disease: data from the Japanese Diagnosis Procedure Combination database. *Intern Med* 2011;50:37-42.
  4. Kibe S, Adams K, Barlow G. Diagnostic and prognostic biomarkers of sepsis in critical care. *J Antimicrob Chemother* 2011;66 Suppl 2:ii33-ii40.
  5. Peter JV, Karthik G, Ramakrishna K, et al. Elevated procalcitonin is associated with increased mortality in patients with scrub typhus infection needing intensive care admission. *Indian J Crit Care Med* 2013;17:174-177.