The Role of Procalcitonin Levels in Assessing the Severity of *Clostridium Difficile* Infection

Sir,

Clostridium difficile-associated disease (CDAD) is the most recognized cause of healthcare-associated infectious diarrhea and a major cause of morbidity and mortality in hospitalized patients.[1,2] Clinical manifestations range from mild or moderate watery diarrhea to fulminant, pseudomembranous colitis.[3] Because of the heterogeneous presentation of CDAD, early identification of severe illness may be crucial in the institution of prompt and proper management.[4,5] There is a paucity of research on biomarkers for the diagnosis for CDAD.[6] Procalcitonin (PCT) is a Food and Drug Administration (FDA)-approved biomarker that is produced by numerous cells in the body, specifically in response to bacterial infections (i. e., pneumonia and sepsis).[7,8] Its role in the identification of severe CDAD has not been validated.[9,10] This analysis was conducted in order to evaluate the role of PCT levels as a diagnostic adjunct in the identification of severe CDAD.

A retrospective chart review was conducted in two inner city hospitals in New Jersey. All patients > 18 years of age admitted between January 1, 2011 and August 2012 who were diagnosed with CDAD were eligible. CDAD was defined as having diarrhea (i. e., more than watery stools/24 h) plus a positive *Clostridium difficile* stool assay (positive enzyme immunoassay for toxin A/B test or polymerase chain reaction (PCR) test). Only patients who had a PCT level drawn within 24 h of confirmation of CDAD were included. The following data were collected: A. Markers of CDAD severity — white blood cell (WBC) count, serum creatinine, serum albumin, temperature, and blood pressure. b. Risk factors and other variables — age, gender, residence in a nursing home, concomitant suspected or confirmed acute bacterial infection, and Charlson comorbidity score. Severe CDAD was defined as presence of CDAD plus any one of the following: WBC > 15,000 cells/ml, fever (temperature > 38.2°C), and 50% increase in serum creatinine from baseline or hypotension (systolic blood pressure (SBP) < 90 mmHg or mean arterial pressure (MAP) < 60).

Logistic regression analysis was done to determine the association between severe CDAD and PCT, as well as the risk factors. Receiver operating characteristic (ROC) curve analysis was done to determine the best cutoff point for PCT. [Figure 1] Fifty-three patients were included in the

study, and their characteristics included the following: [Table 1] Mean age in years, 69.2 ± 19 (43.4%); male gender 41.5%; and patients with severe CDAD, 62.3%. Age, gender, concurrent bacterial infection, and residence in the nursing home did not affect PCT's association with severe CDAD.

PCT > 0.5 is a marker to identify severe CDAD; specificity 86.1%, sensitivity 88.2%, positive predictive value (PPV) 93.9%, and negative predictive value (NPV) 75.0%. [Figure 1] [Table 2].

PCT levels at > 0.5 μg/mL appear to be a good indicator of severe CDAD, with a very high PPV. [Table 3] Prospective, larger studies are needed to validate this finding. Further research is needed as to whether following PCT levels may be helpful in determining resolution of the disease, risk of relapse, or predict mortality.

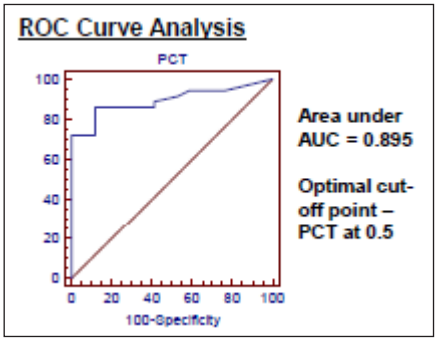

Figure 1: Logistic regression analysis was done to determine the association between severe CDAD and PCT and receiver operating characteristic (ROC) curve analysis was done to determine the best cut-off point for PCT

Table 1: Patient characteristics

Characteristic	*n* (%) patients
Mean Age in years	69.2±19
Male Gender	43.4
Nursing home resident	41.5
Patients with severe CDAD	62.3

Table 2: Odds ratio for how different variables are associated with severe CDAD

Variable	Odds ratio	95 CI %	*P* value
Procalcitonin	19.26	1.19 to 311.08	0.03
Age	0.99	0.91 to 1.08	0.79
Male Gender	0.63	0.04 to 10.29	0.74
Albumin	1.26	0.10 to 16.32	0.86
Charlson Score	1.18	0.65 to 2.12	0.59
Concomitant bacterial infection	1.14	0.04 to 33.66	0.94
Nursing home resident	3.11	0.08 to 126.83	0.55

Age, gender, concurrent bacterial infection and residence in nursing home did not affect procalcitonin's association with severe CDAD

Table 3: PCT > 0.5 as a marker to identify severe CDAD

Specificity	Sensitivity (%)	PPV (%)	NPV (%)
86.1%	88.2	93.9	75.0

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