Background

Antibiotic-associated colitis caused by Clostridium difficile (CD) is the most common cause of hospital-acquired diarrhea. The pathogenesis of CD colitis is mediated by bacterial toxins (toxins A & B), and the clinical manifestations range from asymptomatic carriage to life-threatening disease. It is postulated that CD infection (CDI) severity is determined at least partially by patient’s premorbid conditions, however, fecal bacterial toxin level may also be relevant. Nevertheless, this has not been widely studied.

Aim

To determine whether CD fecal toxin (CDT) level correlate with disease severity

Materials and Methods

A cross-sectional study was performed on seventy-three patients that were admitted to a large tertiary center during 2011-2015 and were tested positive for CDT. Patient data was collected as part of a previous study on the epidemiology of CDI. Charlson comorbidity index was calculated to assess for premorbid disease conditions. CDI severity was defined using the following accepted objective measures: leucocyte count of 15 x 10^3 /μL and/or creatinine which deteriorated by more than 1.5X baseline and/or albumin levels of 2.5g/dl. Mortality was documented within 30 days of CDI diagnosis. Fecal toxin A and B levels (ng/ml) were determined by modified qualitative ELISA (C. DIFFICILE TOX A/B II™, Techlab) on samples that were stored at -80°C.

Results

The study cohort included 73 patients (60% females), at a mean age of 68.7±17.7 years. Severe CDI, defined by leucocyte count, was associated with greater levels of CD fecal toxin (p=0.001) compared to mild/moderate disease. Additionally, CDT level correlated with leucocyte count (r= 0.515, p=0.001), but not with deterioration in creatinine or serum albumin levels. There was no difference in premorbid conditions between severe and mild/moderate patients. Adjustment for multiple confounding variables revealed that only leucocyte count (p=0.04), exposure to chemotherapy (p=0.016) and Charlson comorbidity index (p=0.019) remained significant predictors of CDT level.

Thirteen patients (15%) died within 30 days of CDI diagnosis. These patients had significantly (p=0.008) increased CDT levels (2676.3 ng/ml, range 200.6-5202.0) compared to those who survived (182.3 ng/ml, range 69.7-672.2) (Fig. 1), however, there was no significant difference in Charlson comorbidity index between the groups (p=0.6).

Conclusions

CDT level is associated with disease severity and with mortality rate. Therefore, measuring CDT level may be an objective and accurate way to define severity in CDI. This may be of specific importance with regard to early initiation of more aggressive therapy in cases where leucocyte count is not reliable such as in patients who suffer from other infectious diseases or in inflammatory bowel disease patients.