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LETTER

Absence of candidemia in critically ill patients with COVID-19 receiving selective digestive decontamination

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Dear Editor,

Candidemia in critically ill patients with coronavirus disease 2019 (COVID-19) is frequently observed [1], with incidence rates averaging 5.7% (range 0.8–14%) [2]. Main risk factors for invasive candidiasis include gastrointestinal *Candida* colonization, loss of intestinal epithelium integrity and immunosuppression. In critically ill COVID-19 patients SARS-CoV-2 infection of enterocytes may compromise the intestinal wall integrity and corticosteroids have been shown to be associated with COVID-19 associated candidemia (CAC) [2, 3]. Furthermore, several other risk factors may be present in these patients including prolonged admission in an intensive care unit (ICU), frequent use of broad-spectrum antibiotics, and possibly reduced quality of infection control prevention due to limited staff [2]. The mortality of CAC has been reported to be between 40 and 70%, but the attributable mortality of candidemia in these patients remains unknown [2].

We investigated the frequency of CAC in critically ill patients in our tertiary care university medical center since the beginning of the pandemic. In our ICU, patients with an anticipated admission duration of > 3 days or mechanical ventilation for > 2 days receive selective decontamination of the gastrointestinal tract (SDD) that involves the application of oral paste containing 2% polymyxin B, tobramycin and amphotericin B and the administration of 10 ml solution with 500 mg amphotericin B, 100 mg polymyxin B and 80 mg tobramycin into the gastric tube, in combination with four days of intravenous cefuroxime. This strategy aims to prevent Gram-negative bacteremia and ventilator-associated pneumonia and has been proven effective in the Dutch low-resistance setting [4]. Amphotericin B is aimed to prevent intestinal yeast overgrowth. Bacterial and yeast colonization is monitored twice weekly through oropharyngeal, sputum and rectal cultures.

Over a 30-month period (March 2020–November 2021), 378 patients were admitted to our ICU with COVID-19 confirmed by polymerase chain reaction. Review of medical and laboratory records showed no cases of CAC, which corresponds with an incidence of 0% (95% confidence interval 0–0.97%). The cohort involves patients with recognized risk factors for invasive candidiasis including long term ICU stay, presence of central vascular catheter and glucocorticoid therapy. During ICU stay, 53% of patients were colonized by *Candida* and median time to decolonization was 7 days (Table 1/supplementary Fig. 1) [1]. The frequency of CAC was compared with that in a cohort of 569 COVID-19 ICU patients not receiving SDD at University Hospitals Leuven, Belgium, since March 2020. Eight CAC cases were observed (1.4%), which represents a low prevalence compared with the literature, but is significantly higher than observed in our SDD cohort (95% CI 0.19–2.7%; $p = 0.0207$).

SDD has previously been shown to be associated with a low incidence of candidemia in critically ill patients. Between 1994 and 2013, only 51 candidemia cases were observed among 12,491 ICU patients receiving SDD [5]. Of these, only 10 cases were observed after yeast

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Table 1 Characteristics of the COVID-19 cohort

Number of patients	378
Age, mean (range)	61 (16–93)
Apache II score, mean (range)	17.0 (1–38)
Mean duration of ICU stay per patient (days)	18.8 (1–89)
Number of patients with ICU stay of < 5 days	62 (16%)
Number of patients receiving SDD	352 (93%)
Number of patients with diabetes	79 (21%)
Number of patients with central vascular catheter	310 (82%)
Number of patients on mechanical ventilation	309 (82%)
Number of patients with renal replacement therapy	45 (12%)
Number of patients receiving IL6- inhibitors	188 (50%)
Number of patients receiving dexamethasone	274 (72%)
Number of blood culture sets (aerobic/anaerobic), mean per patient during ICU stay	6.5 (0–31)
Number of patients with *Candida* colonization	199 (53%)
Median time to *Candida* decolonization (days)	7 (1–53)

decolonization was achieved and were considered SDD failures, which corresponds with an incidence of 0.08% [5]. A meta-analysis of 54 observational studies of ICU patients found a mean candidemia incidence of 1.5% (95% 1.2–1.9), which is similar to the 1.4% rate in COVID-19 ICU patients not receiving SDD at University Hospitals Leuven [6]. The observed proportion among our cohort (0%; 95% CI 0.0- 0.97%) of SDD recipients is substantially lower than the mean proportion among 43 cohorts of SDD recipients in ICU (2.4%; 1.6–3.1%)" [6]. A limitation of our study was that we did not assess the impact of SDD on multi-drug-resistant bacterial infection, COVID-19 associated pulmonary aspergillosis and mortality. A clinical trial evaluating empiric micafungin in ICU-patients prevented invasive candidiasis but failed to show an impact on survival [7]. Our observation suggests that SDD is effective to decolonize yeast from COVID-19 patients in the ICU, and may help to prevent candidemia in this patient group.

Supplementary Information
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Declarations

Conflicts of interest
JBB reported grants from Gilead Sciences and F2G. JAS has received unrestricted educational and resarch grants from MSD and has been an advisor to Pfizer. JW reported grants from Gilead Sciences, MSD and Pfizer, and non-financial support from Gilead Sciences, Pfizer and MSD. PEV reported grants from Gilead Sciences, MSD, Pfizer and F2G, and non-financial support from OLM and IMMY. All reported grants were outside the submitted work.

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