Clinical Microbiology and Infection 30 (2024) 1486–1487

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Letter to the Editor

Lower (1,3)-β-D-glucan sensitivity and *in vitro* levels in *Candida auris* and *Candida parapsilosis* strains: author's response

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ARTICLE INFO

Article history:
Received 28 May 2024
Accepted 30 May 2024
Available online 6 June 2024

Editor: L. Leibovici

Keywords:
Candida albicans
Candida auris
Candida parapsilosis
CVC
Glucan

To the Editor;

We thank Adelman et al. [1] for their comment on our paper on lower *in vitro* and *in vivo* levels of (1,3)-β-D-glucan (BDG) in cases of infections caused by *Candida auris* and *Candida parapsilosis* as compared with *Candida albicans* [1,2]. Adelman et al. [1] suggested that contamination of a central venous catheter (CVC), defined as the growth of *Candida* in the blood cultures drawn from a CVC and the absence of growth in blood cultures from a peripheral vein, which is potentially more frequent in intensive care unit (ICU) patients, might have been the cause of lower serum BDG levels, as in such cases there was no systemic infection [1]. We appreciate raising the issue of the value of peripheral vein blood cultures in the ICU, as many studies on the performance of BDG did not specify if blood cultures were performed from CVC only or not [3–5].

We analysed the hypothesis advanced by Adelman et al. [1] and for the following reasons, found it an unlikely explanation for the differences in BDG content among these three species in our centre.

First, the possibility of CVC colonization might be a plausible explanation for lower serum BDG levels, but it should have no effect on the *in vitro* BDG levels, which could not be influenced by the presence or absence of systemic infection. Indeed, all the isolated strains were handled in the same manner after the initial growth. They were stored at −80°C, then thawed and cultured, and the same quantity of colonies was suspended for the *in vitro* BDG testing. Despite the same fungal burden, there were significantly lower levels of *in vitro* BDG in cases of *C auris* and *C parapsilosis* as compared with *C albicans.*

Second, while most cases of *C auris* candidemia occurred in ICU-admitted patients, most cases of *C parapsilosis* candidemia, which was also associated with lower BDG levels, occurred in patients outside the ICU.

Finally, to carefully evaluate if CVC colonization might have an effect, we reviewed our clinical data on the positivity of blood cultures from a CVC and from a peripheral vein. Although all patients reported clinical signs of symptoms at the time of blood collection and no surveillance cultures were performed, in ten patients (eight of them admitted to an ICU), the blood culture from a peripheral vein drawn within 24 hours from the diagnosis of candidemia was either not performed or negative (six cases of *C auris*, three cases of *C parapsilosis,* and one case of *C albicans* infection). We excluded them from the analysis and focused on the remaining 36 patients who had a peripheral vein blood culture(s) positive for *Candida*. *In vitro* BDG was available for all of them, and serum BDG for 32 of them. There was a still highly significant difference in the BDG levels, both *in vivo* ($p = 0.006$) and *in vitro* ($p < 0.001$), among the three species. In particular, for serum BDG, the median BDG levels were 63 pg/mL (interquartile range [IQR] 13–165) for *C auris*, 57 pg/mL (IQR 19–393) for *C parapsilosis,* and 438 pg/mL (IQR 182–520) for *C albicans*, compared with, respectively, 50 pg/mL (IQR 15–161), 57 pg/mL (IQR 18–332), and 372 pg/mL (IQR 102–520) reported for the whole cohort [2]. With the

DOIs of original article: https://doi.org/10.1016/j.cmi.2024.02.012, https://doi.org/10.1016/j.cmi.2024.05.010.
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https://doi.org/10.1016/j.cmi.2024.05.024

important limitation of a very low number of cases, the sensitivity of serum BDG levels in these 32 patients was 50% (95% CI, 22–78) for *C auris*, 43% (95% CI, 12–80) for *C parapsilosis,* and 85% (95% CI, 54–87) for *C albicans*. The *in vitro* BDG levels in these 36 patients were 428 pg/mL (IQR 361–573) for *C auris*, 826 pg/mL (IQR 712–960) for *C parapsilosis,* and 1089 pg/mL (IQR 824–1289) for *C albicans*, compared with, respectively, 463 pg/mL (IQR 379–648), 755 pg/mL (IQR 511–930), and 1080 pg/mL (IQR 830–1276) in the whole cohort [2].

Therefore, even after excluding patients who might have had CVC colonization rather than true infection, the species of *C auris* and *C parapsilosis* isolated in our centre contained and released lower levels of BDG compared with *C albicans* strains. Analyses from other *C auris* clades or *C parapsilosis* strains might be useful to further confirm the generalizability of our findings.

Author contributions

Data analysis and writing—M.M.; data curation—N.U. and L.M.; conceptualization and review—all authors.

Transparency declaration

Author M.M. reports study grant from Gilead paid to the institution; speaker/adviser fees from Allovir, BioMérieux, Gilead, Janssen, Moderna, Mundipharma, and Pfizer, all outside the submitted work. M.B. reports grants from: Angelini, Shionogi, Cidara, Gilead, Pfizer, and MSD. and personal fees for adviser/consultant and/or speaker/chairman from Angelini, BioMerieux, Cidara, Gilead, Menarini, M.S.D., Pfizer, Roche, and Shionogi, outside the submitted work. No external funding was received.

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