P1939

High Prevalence of Invasive Candidiasis in Neonates in Southeast Asia and the Pacific

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BACKGROUND

Neonates, particularly those born prematurely or requiring prolonged hospitalisation, are vulnerable to invasive fungal infections. These infections are associated with high neonatal morbidity and mortality. Antifungal resistance is rising globally and contributes to this morbidity and mortality burden, particularly where a lack of efficacious therapies are available. The 2022 WHO Fungal Priority Pathogen list (FPPL) identified major data gaps in the epidemiology of fungal infections and their associated resistance patterns in low- and middle-income countries (LMICs). Access to affordable antifungal therapy in LMICs is limited and may be exacerbated by the growing burden of antifungal resistance.

METHODS

We conducted a multicentre international observational study across 5 clinical sites in Southeast Asia and the Pacific to evaluate the prevalence of neonatal candidiasis, as part of the NeoSEAP study. Clinical and microbiological data for neonates with clinical sepsis were retrospectively reviewed and positive blood cultures yielding *Candida* spp. across a 24-month period (January 2019 – December 2020) were collated. Duplicate cultures were removed, and antifungal susceptibility patterns evaluated, where resources were available to ascertain these data.

	Sri Lanka	Indonesia			Tonga	
Site	**Colombo**	**Jakarta**	**Bandung**	**Surabaya**	**Nuku'alofa**	**Total**
Significant pathogen isolated in blood culture	117	612	347	137	30	1243
***Candida* spp. isolated in blood culture**	6 (5%)	21 (3%)	22 (6%)	11 (8%)	0 (0%)	60 (5%)
Susceptibility testing for *Candida* spp. performed	2	12	21	7	0	42 (70%)

Anti-fungal resistance by species, where available (n=42)

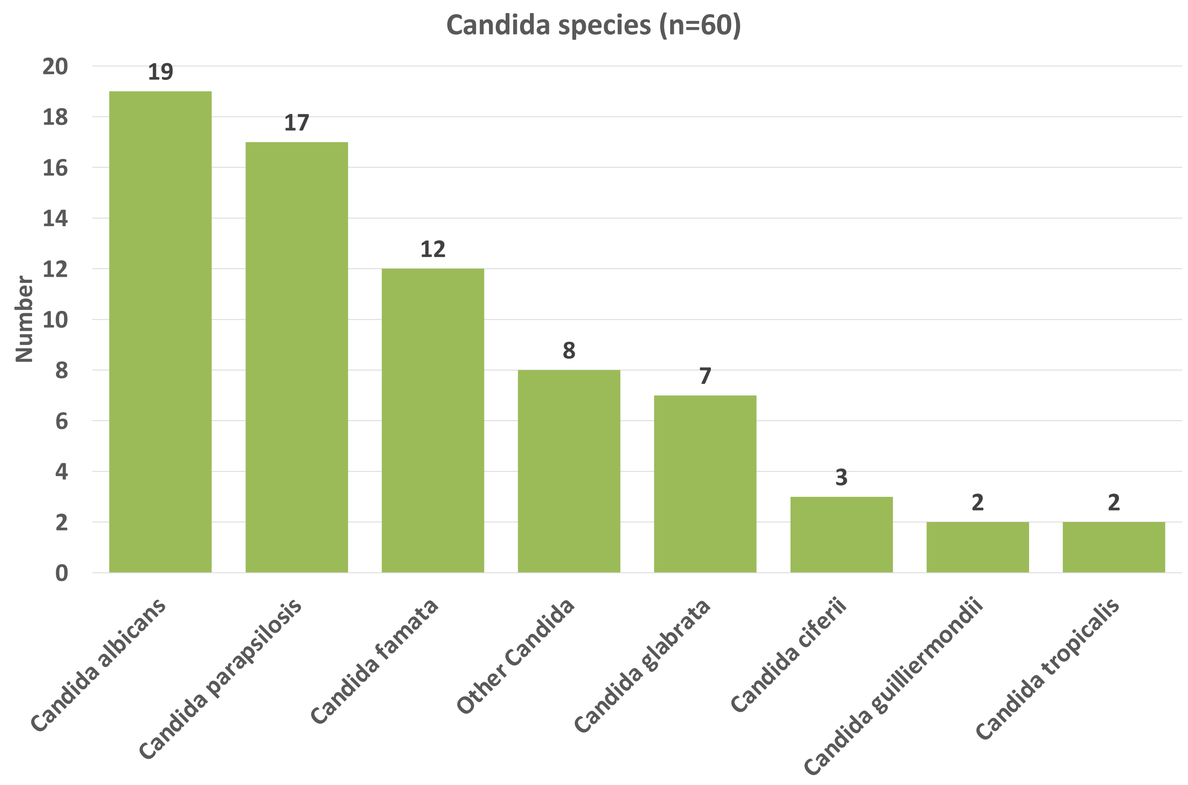
	Fluconazole			Voriconazole			Amphotericin			Caspofungin			Micafungin			Flucytosine		
Pathogen	**T**	**R**	**%**	**T**	**R**	**%**	**T**	**R**	**%**	**T**	**R**	**%**	**T**	**R**	**%**	**T**	**R**	**%**
C. albicans	14	0	0	13	0	0	13	0	0	13	0	0	13	0	0	3	0	0
C. parapsilosis	15	3	20	15	0	0	15	1	7	15	0	0	15	0	0	7	0	0
C. glabrata	0	0	0	5	0	0	5	0	0	5	4	80	5	3	60	2	0	0
C. guilliermondii				2	0	0	2	0	0	2	0	0	2	1	50	2	0	0
C. tropicalis	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0
C. ciferii				3	0	0	3	1	33									
Other *Candida* spp.	2	0	0															

T= Number tested; R= Number resistant; % = proportion

RESULTS

Data were collated from 5 clinical sites in Indonesia, Sri Lanka and Tonga. Of 5,740 blood cultures collected in neonates with clinical sepsis, 1,243 (22%) yielded true pathogens of which 60 (5%) revealed invasive candidiasis as the cause of infection. Antifungal susceptibility data were available for 42 of these isolates. *Candida albicans* was the most common species isolated (19/60) followed by *Candida parapsilosis* (17/60); the latter revealed fluconazole-resistance in 17% of isolates tested (3/15).

Several *Candida spp.* demonstrated considerable resistance to common antifungal agents which may complicate treatment outcomes (Table 2)..



CONCLUSIONS

These data provide important insights into the prevalence of invasive fungal infections in neonates, in a region of the world where the burden of morbidity and mortality due to neonatal sepsis remains high. Most importantly, these data have identified the prevalence of 'critical' and 'high' priority fungal pathogens – as defined by the WHO FPPL, *Candida albicans* and *Candida parapsilosis* – as responsible for the majority of invasive fungal infections in neonates.

Importantly, *Candida parapsilosis* may be responsible for outbreaks in neonatal intensive care units (given its propensity for biofilm formation), so ongoing surveillance, and stringent infection, prevention and control strategies when this pathogen is isolated are necessary.

The challenges in ascertaining complete antifungal resistance data within our cohort highlights the importance of enhanced mycology diagnostic capacity and improved surveillance in LMIC settings. In the future, comprehensive prospective surveillance studies are needed to fill the knowledge gaps regarding the burden of fungal disease in neonates.

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