Assessment of a QCMD proficiency programme for molecular diagnosis of systemic Candida infection.

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INTRODUCTION

Systemic Candida infections are associated with high mobility and mortality rates in vulnerable patient groups particularly in Intensive Care Units or similar clinical settings. Treatment delays are common because of slow turnaround time of traditional diagnostic methods such as culture. The introduction of molecular diagnostics has had a considerable impact on reducing the time to treatment from 67.5 hours based on blood culture results to 31 hours[1]. Hence if a patient presenting with septic shock, caused by Candida, is treated within 24 hours this will significantly increase survival and lowers treatment costs[2]. This highlights a need for progressive microbiology diagnostics and for reliable molecular diagnostic techniques. In 2012 QCMD whose primary aim is to establish and develop international proficiency testing programmes introduced a pilot External Quality Assessment (EQA) scheme. The aim of this scheme was to assess the ability of diagnostic laboratories to detect and differentiate Candida species at clinically relevant levels.

FIGURE 1 – Distribution of assays type

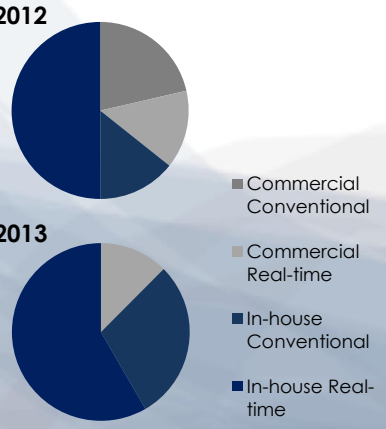

FIGURE 2 – Laboratory performance over two distributions

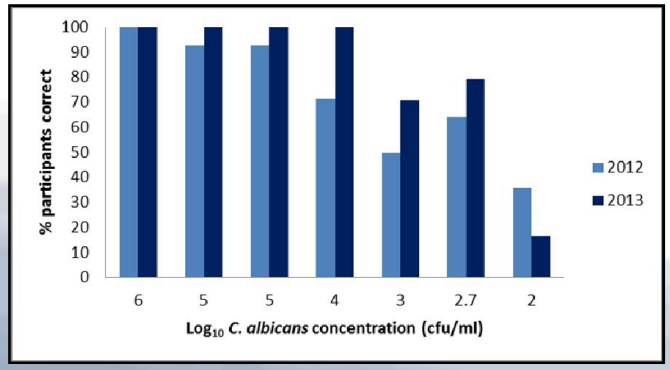

TABLE 1 – Sample identification results from the 2013 distribution

Sample content	Sample conc. CFU/ml	Sample Matrix	Total datasets n=24		Sample ID reported		Sample identification							
							C. albicans		*C. glabrata*		*C. albicans/ C. glabrata*		Other	
			n	%	n	%	n	%	n	%	n	%	n	%
Candida albicans	1.0 x 10E6	Plasma	24	100	11	45.8	10	90.9					1	9.1
Candida albicans	1.0 x 10E5	Plasma	24	100	11	45.8	10	90.9					1	9.1
Candida albicans	1.0 x 10E5	Plasma	24	100	11	45.8	10	90.9					1	9.1
Candida albicans	1.0 x 10E4	Plasma	24	100	11	45.8	10	90.9					1	9.1
Candida albicans	1.0 x 10E3	Plasma	17	70.8	9	52.9	7	77.8					2	22.2
Candida albicans	5.0 x 10E2	Plasma	19	79.2	8	42.1	7	87.5					1	12.5
Candida albicans	1.0 x 10E2	Plasma	4	16.7	2	50	2	100						
Candida glabrata	1.0 x 10E5	Plasma	17	70.8	11	64.7			9	81.8			2	18.2
C. albicans/ C. glabrata	1.0 x 10E5/ 1.0 x 10E5	Plasma / Plasma	24	100	11	45.8	2	18.2			8	72.7	1	9.1
Candida Negative		Plasma	24	100										
Candida Negative		TE Buffer	24	100										

RESULTS

In 2012, 18 participants registered for the programme from 13 different countries, 11 participants provided 14 datasets for analysis. In 2013 the participation increased to 32 participants from 17 countries, 22 participants provided 24 datasets for analysis.

Analysis showed that in-house developed assays both conventional and real-time were predominant in this programme (2012, 64% and 2013, 87.5%) (figure 1) in contrast to many EQA programmes, this is perhaps due to an emerging interest in the diagnoses of invasive fungal infections and limited availability of commercial assays in this area.

Early indications are that the assays used in this EQA programme are performing well

- Being able to detect *C. albicans* down to concentrations of around 100 CFU/ml (figure 2).
- 91% were able to correctly identify *C. albicans* in samples with a concentration of 10000 CFU/ml (table 1).
- 70% of laboratories identified a mixed sample containing both *C. albicans* and *C. glabrata*.

Encouragingly of the labs that submitted identification information no labs misidentified any samples and were either unable to identify or narrowed the identity to 1 or 2 species.

METHODS

QCMD panels were produced containing eleven samples containing various concentrations of Candida spp. (*Candida albicans* and *Candida glabrata*). Panels were distributed to registered participants worldwide in both 2012 and 2013. The programme was coordinated and analysed by the QCMD Neutral Office.

CONCLUSIONS

In this EQA programme the majority (greater than 70%) of laboratories correctly identified at least 6 panel members in both years. In the future the challenge will be enhanced by introducing different species and lower clinically relevant concentration of Candida as well as potential antifungal resistant strains as they become increasingly important clinically. It may also be beneficial to assess the turnaround time of laboratory results to determine if these assays could be utilised to achieve the patient diagnosis within the 24 window to substantially improve mortality and morbidity rates.

REFERENCES

1- Bloos *et al.* J Crit Care. 2013
2 - Kollef *et al.* Clin Infect Dis. 2012