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Paper Poster Session
Update in fungal resistance and susceptibility

Notable trend of increase in azole non-susceptible Candida tropicalis causing invasive candidiasis in China, August 2009 to July 2014

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Background: *C. tropicalis* is an important pathogen causing invasive candidiasis (IC). Worldwide, *C. tropicalis* has become the first to fourth leading cause of IC. Furthermore, resistance to azoles, particularly to fluconazole, is increasingly being reported in *C. tropicalis* isolates. Here we report a notable and continuous increase in azole non-susceptibility among *C. tropicalis* causing IC in China in the past half-decade.

Material/methods: Between August 2009 and July 2014, 585 *C. tropicalis* isolates were collected from ten hospitals from the China Hospital Invasive Fungal Surveillance Net (CHIF-NET) study. The *in vitro* susceptibility of isolates to nine antifungal drugs - fluconazole, voriconazole, itraconazole, posaconazole, caspofungin, micafungin, anidulafungin, amphotericin B and 5-flucytosine - was determined using Sensititre YeastOne™ YO10 methodology, following the manufacturer's instructions. Current available species-specific clinical breakpoint (CBPs) or epidemiological cut-off values (ECVs) were used for interpretation of results.

Results: Overall, 22.1% and 19.5% of isolates were non-susceptible to fluconazole and voriconazole, respectively, with 10.4% of the isolates showing cross-resistance to both. Over five years, there was a significant decrease in azole susceptibilities, particularly during the last two years. As shown in the Figure, the non-susceptible rate of *C. tropicalis* isolates to fluconazole and voriconazole continuously increased from 10.4% to 42.6% for fluconazole, and from 10.4% to 39.1% for voriconazole, with the rate accelerating in the fourth (2013) and fifth (2014) years. The prevalence of fluconazole-voriconazole cross-resistant isolates also increased from 6.6% to 21.7%. In addition, the fluconazole and voriconazole MIC_{50} and GM MIC values in the fifth year were 1- to 3-fold higher than those in the first year, while the MIC_{90} values also notably increased by over five fold. Moreover, although all isolates remained of wild-type phenotype to itraconazole and posaconazole, the GM MIC and MIC_{50} values for these two drugs also rose by over two fold, and the MIC_{90} values had a 4-fold increase in the study period. In comparison, all *C. tropicalis* isolates included in the present study were of wild-type to amphotericin B, and only 0.7% of isolates were of non-wild type phenotype to 5-flucytosine. Over 99% of the isolates remained susceptible to all three echinocandin agents tested. In addition,

during the five years of surveillance, there were no significant changes (within ±1 dilution) in MIC_{50}, MIC_{90}, and GM MIC values for these drugs.

Conclusions: Our findings show an unusual high-level of fluconazole and voriconazole resistance, and a significant trend of decreasing azole susceptibility among *C. tropicalis* isolates from IC in China for the period August 2009 to July 2014, which is particularly notable during the last two years. Further study is needed to identify the contributing factors, so that effective control measures can be devised and implemented to control the situation.

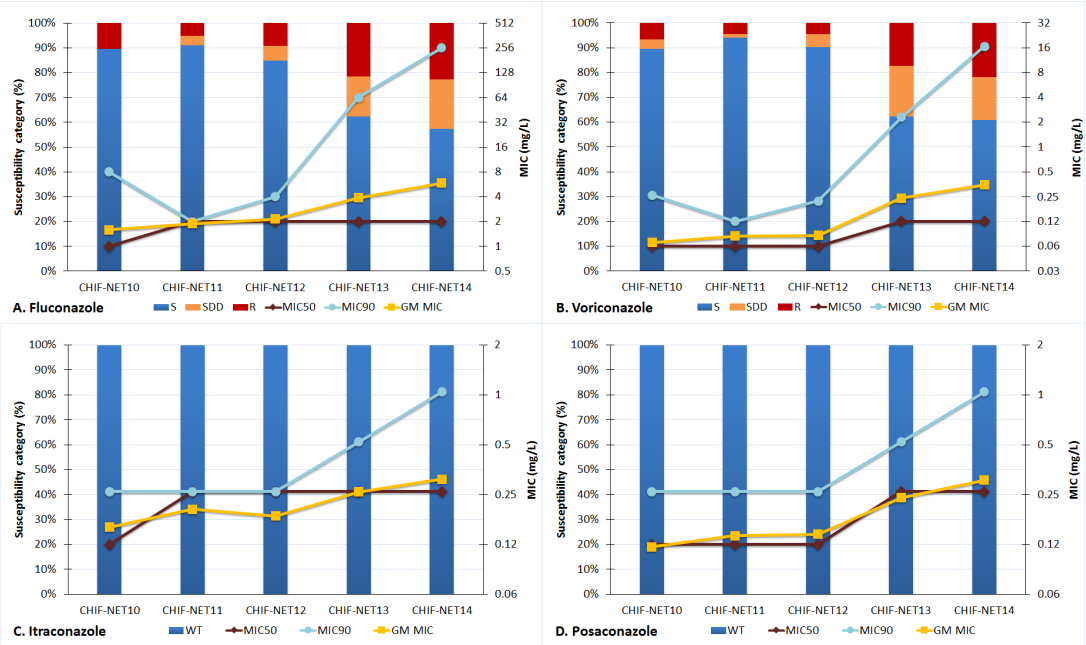

Figure.