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Emergence of *Candida auris* in Israel, 2021

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INTRODUCTION

- Candida auris* has spread through healthcare systems worldwide, and is associated with resistance to multiple antifungal drugs, invasive infections and high case fatality rates.
- Infections with Clade 4 were first identified in Israel in 2014. A significant increase in cases was observed in 2021.
- We report on laboratory-based surveillance of *C. auris* infections in Israel.

METHODS

- Study population:** All patients with *C. auris* isolates from all Israeli hospitals and long-term care facilities between January 2014 and November 2021
- Isolates suspected as *C. auris* were sent to the national reference mycology laboratory at the Tel Aviv Medical Center.
- Species-level identification was done using internal transcribed spacer (ITS) PCR and sequencing.
- Antifungal drug susceptibility testing was performed using broth microdilution according to CLSI methodology.
- Multilocus sequence typing (MLST) was performed using 4 housekeeping genes (ITS, LSU, RPB1 and RPB2). Sequences were concatenated and aligned using MUSCLE, and a phylogenetic tree was constructed with the neighbor joining method and 2000 bootstrap replications.
- Clinical data was recovered retrospectively from the patients' medical records.

Fig. 1 Epidemic curve of *C. auris* in Israel 2014-2021

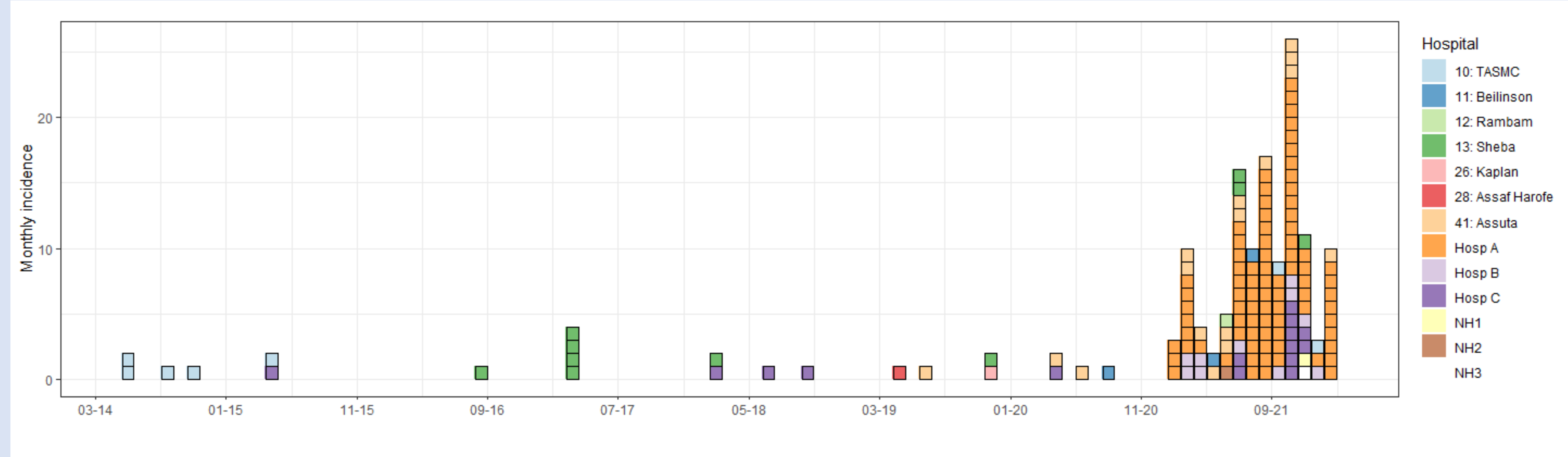
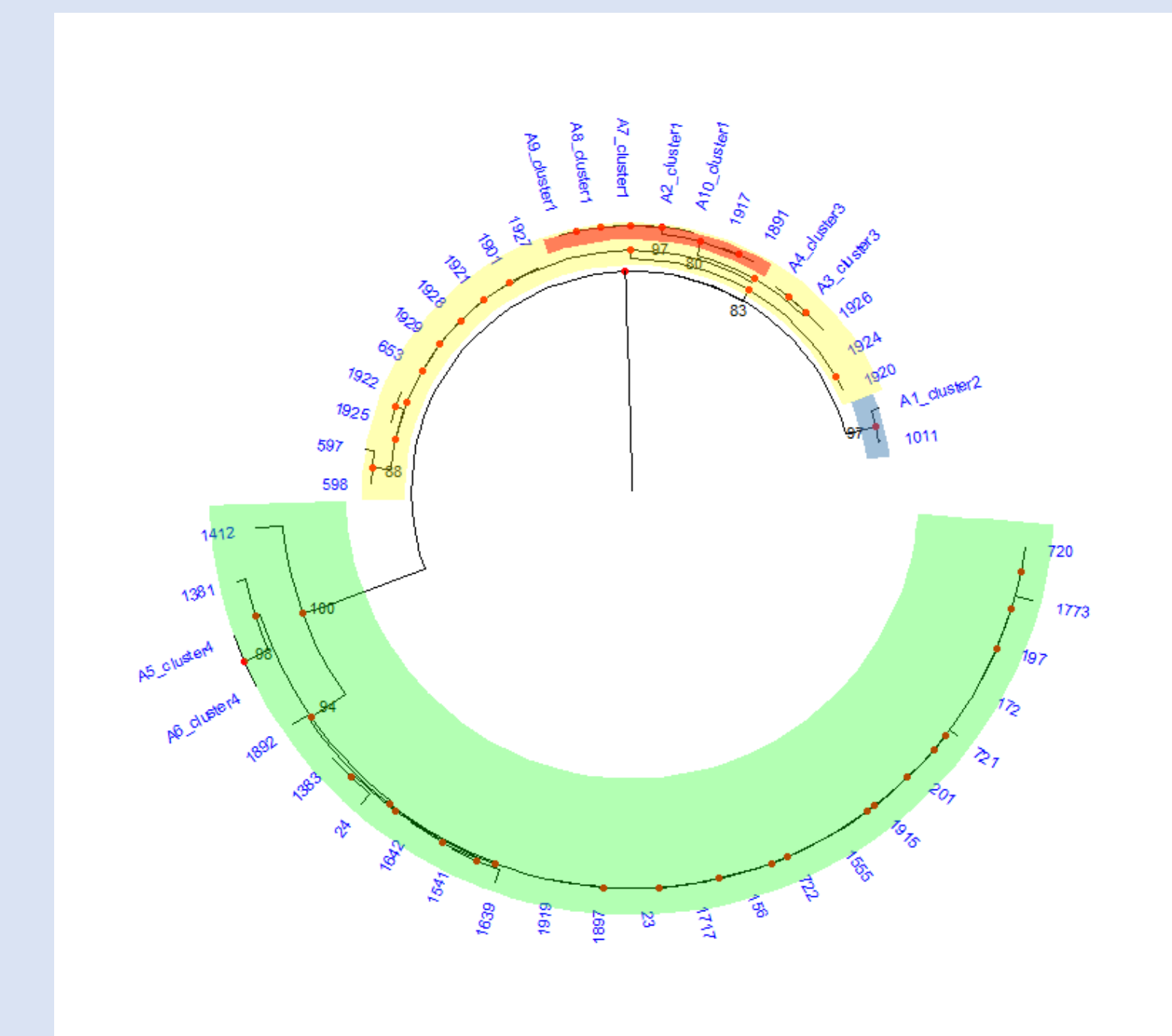


Fig. 2 Genetic relatedness of *C. auris* isolates



Genetic relatedness of 31 clinical isolates assessed using MLST. Clade 1 (Red), Clade 2 (Grey), Clade 3 (Yellow) and Clade 4 (Green)

Fig. 3 Drug Resistant Organisms carriage

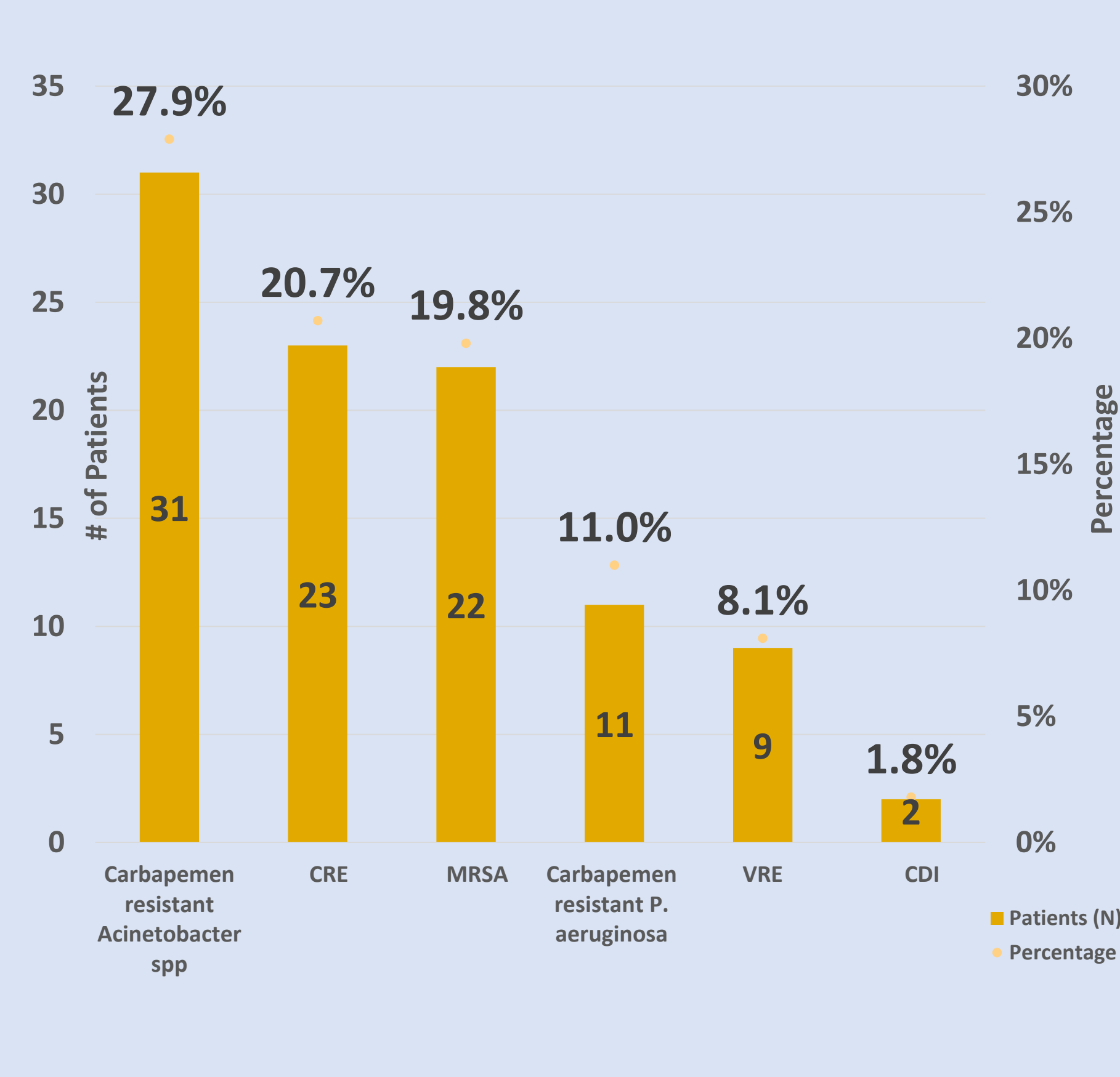
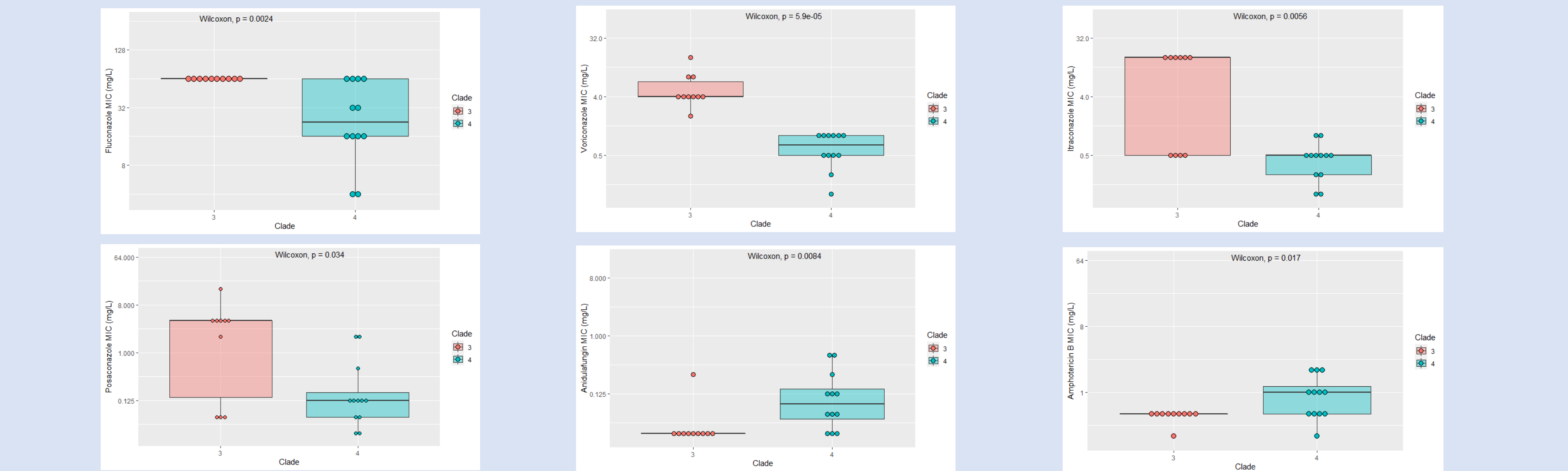


Figure 4. MIC differences- Clade 3 vs Clade 4



MIC distribution for six antifungal drugs, compared between Clade 3 and Clade 4 clinical isolates..

Table 1 Clinical characteristics

Variable	N (%)
Background	
Sex	
Male	76 (68.5)
Female	35 (31.5)
Age, years	66 ± 18.6
Charlson Comorbidity Index	2.3 ± 2.0
Admission source	
Home	79 (71.2)
LTCF	27 (24.3)
Other hospital	5 (4.5)
Functional level	
Independent	58 (52.3)
Functional dependence	53 (47.7)
Drug Resistant Organisms carriage	59 (53)
In hospital exposure	
ICU stay prior to <i>C. auris</i>	58 (52.2)
Mechanical ventilation	85 (76.5)
Antifungal exposure	13 (11.8)
Antibiotic exposure	96 (86.5)
COVID19 documented infection	37 (33.6)
Microbiology	
Isolates	
clinical	56 (50.5)
screening	55 (49.5)
Bloodstream isolates	19 (17.1)
Outcomes	
Crude hospital death (all patients)	37 (33)
In-hospital death <i>C. auris</i> fungemia	7/19 (37)
Length of hospital stay, days	42 ± 35

RESULTS

- A total of 111 patient-specific *C. auris* isolates were identified in Israel between January 2014 and November 2021.
- Of these, 94 (84.6%) patient-isolates were identified in 2021, a 38.7-fold increase over the previous annual incidence (**Fig.1**).
- Clinical data were collected on 111 patients (**Table 1**).
- 56 (50.5%) were clinical isolates and 55 (49.5%) screening isolates.
- 19 bloodstream isolates were identified, 10 of them in 2021.
- 37 (33.6%) patients were hospitalized with COVID19. Median time from COVID19 diagnosis to recovery of *C. auris* was 26 days.
- Drug resistant bacterial organisms were recovered from 59 (53%) patients (**Fig.3**).
- Only 12% of patients with *C. auris* were previously exposed to antifungal drugs.
- Of isolates collected in 2021, 77/94 (82%) originated in 3 hospitals (A, B and C). In all 3 hospitals, cases were first associated with COVID19 units, and subsequently were identified in other units.
- MLST was performed on 31 isolates. Clade 4 predominated from 2014 through 2020 (15/16 isolates). In contrast, in 2021, 9 of 15 isolates (60%), all from hospital A, were identified as clade 3, 2 isolates (13.3%), both from hospital B, were clade 1, and 4 isolates (26.6%) were clade 4 (**Fig.2**).
- Isolates from clade 3 had higher mean MIC of fluconazole, itraconazole, voriconazole, and posaconazole, and lower mean MIC of anidulafungin and amphotericin B compared to isolates from clade 4 (**Fig. 4**).
- The crude hospital mortality rate was 33.3% (37/111).

CONCLUSIONS

- There is an ongoing multihospital outbreak of *C. auris* infections in Israel.
- Identification of distinct *C. auris* clades in different hospitals suggests multiple importation events into the country, and accelerated spread driven by infection control deficiencies at COVID19 units.
- Urgent implementation of infection control measures across healthcare facilities is required.