

# The investigation of *in vitro* activity of ceftaroline, vancomycin and teicoplanin for methicillin-resistant *Staphylococcus aureus* isolates



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## Objectives

Methicillin-resistant *Staphylococcus aureus* (MRSA) strains have previously been considered as resistant to all beta-lactam agents, however the introduction of cephalosporins with anti-MRSA activity, i.e. ceftaroline and ceftobiprole, necessitated an update in this consideration. Until recently, vancomycin has been used as the first choice treatment option for serious infections due to MRSA, however the demonstration of treatment failure and increased mortality in infections due to MRSA strains with vancomycin minimal inhibitory concentration (MIC) of  $\geq 1$  mg/L resulted in search for alternative agents. Ceftaroline fosamil is indicated for the treatment of community acquired bacterial pneumonia and acute bacterial skin and skin structure infections. In our study we aimed to determine the MIC values for vancomycin (VA), teicoplanin (TEC) and ceftaroline fosamil (CFT) in a collection of clinical MRSA isolates.

## Methods

MRSA strains (n = 105) isolated from clinical specimens between 2012 and 2015 were included in the study. The isolates were identified with MALDI-TOF MS instrument (Bruker Daltonics, Germany). Initial antimicrobial susceptibility testing was performed using VITEK 2 instrument (bioMérieux, France).

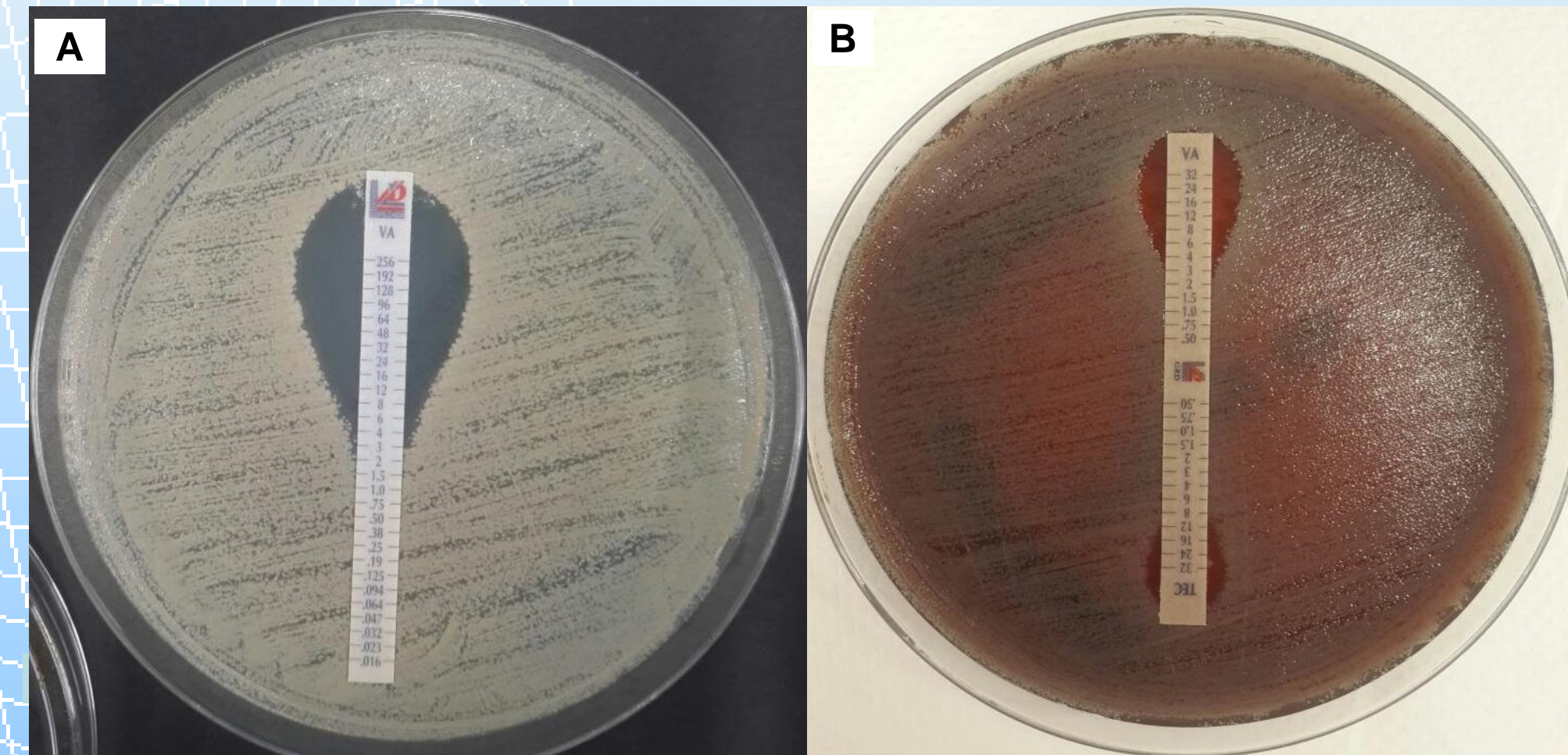
Isolates stored at  $-80^{\circ}\text{C}$  in cryo vials were retrieved and broth microdilution (BMD) was performed for CFT (Astra Zeneca), VA and TEC (Sigma) following the EUCAST methodology. For a single MRSA isolate with VA MIC value of 4 mg/L, VA and VA/TEC glycopeptide resistance detection (GRD) MIC test strip (Liofilchem, Italy) was used. *Staphylococcus aureus* ATCC 29213 was used as the control strain.

## Results

MIC<sub>50</sub> and MIC<sub>90</sub> values of the strains were determined as 0.5 mg/L and 1 mg/L for VA, 0.5 mg/L and 2 mg/L for TEC and CFT, respectively (Table 1). When evaluated with the current EUCAST clinical breakpoints, nonsusceptibility was observed in 0.9% (n = 1), 1.9% (n = 2) and 23.8% (n = 25) of the study isolates for VA, TEC and CFT, respectively. The MRSA isolate with VA MIC of 4 mg/L in BMD method also demonstrated an MIC of 4 mg/L with VA gradient strip test, and with VA/TEC gradient strip the values 4/16 mg/L were obtained (Figure 1).

**Table 1.** The *in vitro* activity of vancomycin, teicoplanin and ceftaroline for clinical MRSA isolates (n = 105)

	MIC (mg/L)			Susceptibility (%)
	MIC range	MIC <sub>50</sub>	MIC <sub>90</sub>	
<b>Vancomycin</b>	0.125 – 4	0.5	1	99.1
<b>Teicoplanin</b>	0.125 – 4	0.5	2	98.1
<b>Ceftaroline</b>	0.125 – 2	0.5	2	76.2



**Figure 1.** Phenotypic test results of the MRSA strain with VA MIC of 4 mg/L.

A) VA MIC test strip: VA MIC = 4 mg/L

B) GRD MIC test strip: VA MIC = 4 mg/L, TEC MIC = 16 mg/L

## Conclusion

- Even though ceftaroline fosamil has not entered into clinical practice in our country yet, ceftaroline susceptibility among clinical MRSA isolates was determined as 76.2%.
- Among the study MRSA isolates we detected an isolate with VA MIC of 4 mg/L which is nonsusceptible to vancomycin according to EUCAST breakpoints and confirmed as glycopeptide intermediate *S. aureus* by using GRD MIC test strip.
- We also observed two teicoplanin resistant isolates with TEC MIC of 4 mg/L.