LETTER TO EDITOR / CARTA AL EDITOR

Study of susceptibility to vancomycin from clinical isolates of *Staphylococcus aureus*

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Vancomycin has been considered for over 40 years as the primary treatment option for Methicillin-Resistant *Staphylococcus aureus* (MRSA) strains. However, excessive, indiscriminate, or inappropriate use has led to the appearance of MRSA strains with intermediate resistance (VISA) and total resistance to vancomycin (VRSA)[1]. In Central America, particularly in Honduras, no VRSA strains have been reported. However, it is vitally important to implement an epidemiological surveillance program where this isolation can be traced since its appearance has been considered a severe public health problem in the last two decades[2]. By 2002, the first two VRSA strains were isolated, specifically in Michigan and Pennsylvania. Since then, a total of 52 VRSA isolates have been reported worldwide. The only country in Latin America that has reported VRSA strains is Brazil[3]. In this sense, we have carried out an assay to determine the MIC of the 96 clinical isolates of *S.aureus* obtained from patients who attended two of the essential hospital centers in Tegucigalpa, Honduras: the Hospital Escuela (HE) and the Honduran Institute of Social Security (IHSS). The samples were the same with which we studied resistance to methicillin, and it is a follow-up to the study that was previously published in this journal[4]. The MIC of *S. aureus* to vancomycin was determined using the E-test® strips (Solna, Sweden) under the same conditions reported in the previous study[4] and based on what is recommended by the CLSI5 (figure 1). The cohort points to determine the susceptibility and resistance of *S.aures* to vancomycin can be seen in Table 1.

Of the 96 clinical isolates of *S. aureus*, none showed a MIC greater than 2 µg/mL, so we considered them all

VSSA *	VISA	VRSA
CMI ≤ 2µg/mL	CMI de 4 a 8 µg/mL	≥ 16 µg/mL

Table 1. Cohort points for the interpretation of susceptibility/ resistance to vancomycin.

* *S. aureus* Susceptible to Vancomycin.

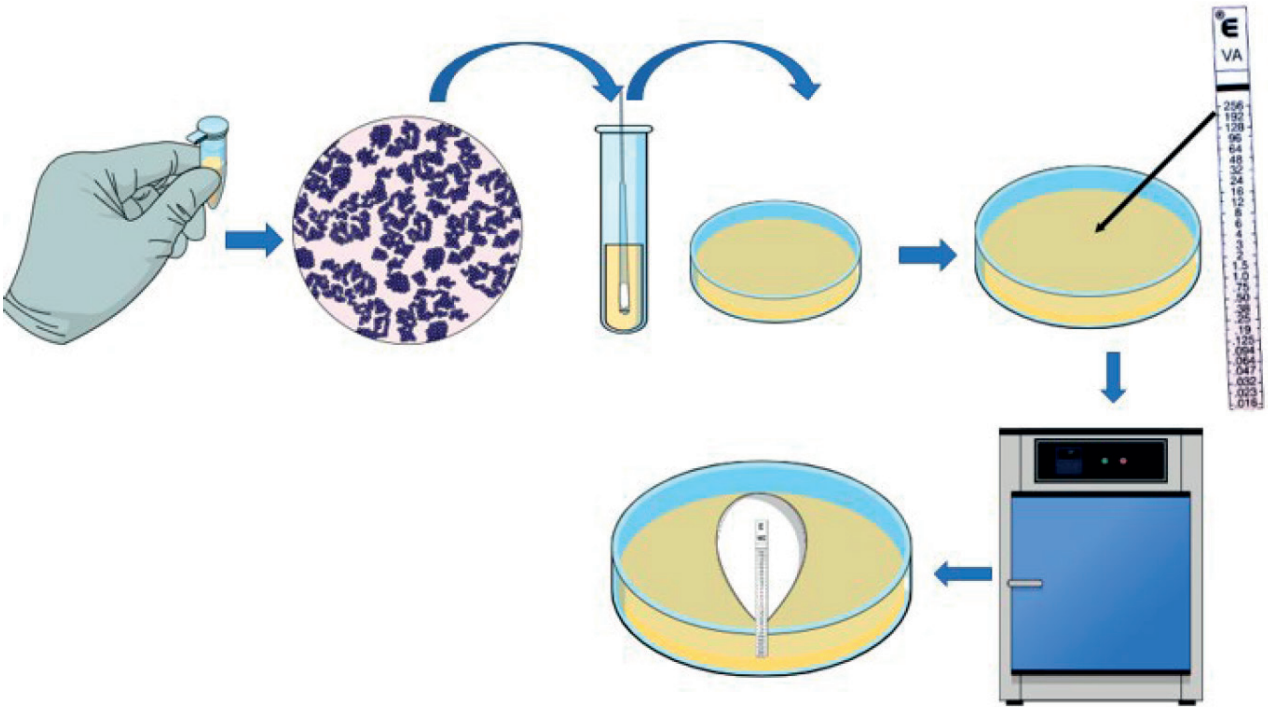

Figure 1. Schematic procedure for the detection of the MIC of *S. aureus* by vancomycin.

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susceptible to vancomycin (SVSA). However, 3 isolates showed a MIC of 2 µg/mL right at the cohort point or the upper limit allowed by the CLSI. To make sure of these values, we repeated the test using the Vitek-2 technique. The distribution of the isolates can be seen in Figure 2A. 50% showed a MIC ≤ 0.75 µg/mL (MIC50) and 90% a MIC ≤ 1.5 µg/mL (MIC90). Figure 2B shows the S.aureus plaque with the vancomycin E-test® strip marking a halo at 2 µg/mL.

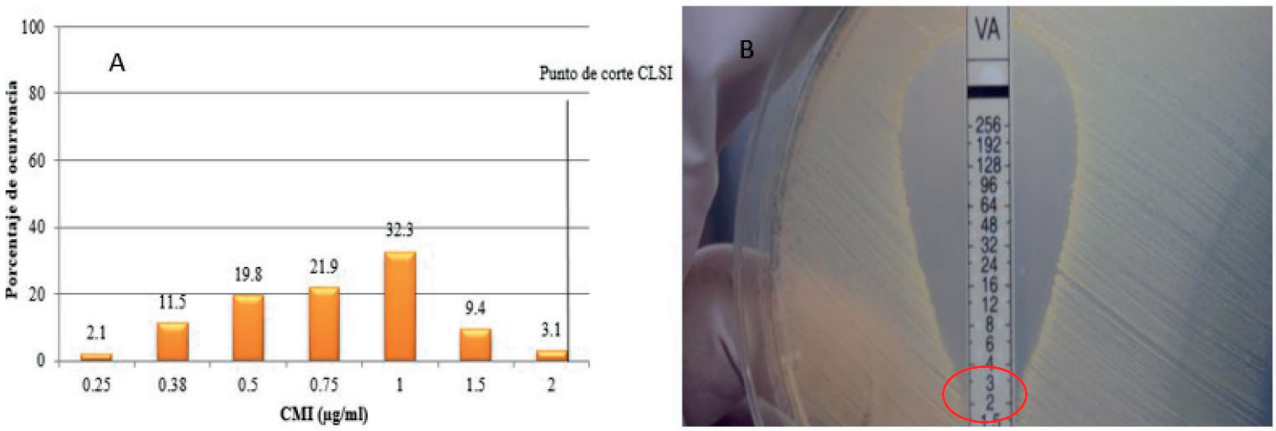

Figure 2. A. Percentage of occurrence and MIC of clinical isolates of *S. aureus* to vancomycin. B. MIC of 2 µg/mL to vancomycin of one of the three clinical isolates of *S. aureus*.

Although neither VISA nor SARV strains were found, the 3 isolates with MICs of 2 µg/mL are of concern since VISA strains could arise from heterogeneous intermediate resistance or VISAh strains. According to the literature, VISAh strains present MICs below 2 µg/mL, as found in our trials, which could lead to this phenomenon[6]. These findings coincide with several studies where it has been found that 30% to 50% of the *S. aureus* isolates had a vancomycin MIC of 2 µg/mL and that present heterogeneous intermediate resistance[6,7]. However, confirming the results with other official techniques was impossible since they were costly and difficult to implement. The reference test analyzes the population profile of the area under the curve (PAP-AUC), using increasing concentrations of antibiotics[8,9]. However, an alternative method for detecting these strains is E-test GRD, which consists of a double strip of increasing concentrations of vancomycin and teicoplanin, which is cheaper[8].

Similarly, several authors who have studied the relationship between the vancomycin MIC of *S. aureus* strains and the efficacy of treatment with this drug have reported that when the MIC increases from 0.5 to 2 µg/mL, the chances of therapeutic failure. However, the strains continue to be classified as susceptible. Therefore, a vancomycin MIC of 2 µg/mL is a poor predictor of response to vancomycin therapy[10].

In this context, we could be in the presence of VISAh strains, so more specific studies are required to confirm it. For this reason, we recommend reducing the indiscriminate use of vancomycin in these hospitals, as well as the active participation of medical, pharmaceutical, and clinical laboratory personnel in the implementation of the necessary methods for the identification and permanent monitoring of strains with reduced susceptibility to vancomycin. as well as the generation and application of a comprehensive epidemiological surveillance program.

Author Contributions

Conceptualization, LS, and NR; Methodology, LS, LE, and LCE. Data analysis, LS and NR; Validation of assays, LE and LCE; writing, proofreading, and editing, LS, NR, LE and LCE; Supervision, LE and NR. Project management, NR, and LE. All authors have read and approved the publication of this manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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