

DETECTION AND ANTIBIOTIC SUSCEPTIBILITY TEST OF ENTEROCOCCUS SPP. FROM DIFFERENT CLINICAL SAMPLES IN DUHOK CITY/ IRAQ

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ABSTRACT

Enterococci a variety of species and formerly believed to be of no medical importance; recently they emerged as life threatening multidrug-resistant (MDR) nosocomial pathogens. *Enterococcus faecalis* and *Enterococcus faecium* make up the majority of clinical isolates. Furthermore, these bacteria are naturally resistant to most commonly used antibiotics. The study assesses the prevalence of Enterococcus spp. in different clinical samples; pinpoints the prevalence of species causing infection in this area and finally analyzes the patterns of drug resistance of these isolates. A total of 560 samples were collected and plated on blood and chocolate agar. Species identification and antibiotic susceptibility testing were performed using automated VITEK 2 system. Four species of Enterococci were isolated: *E. faecalis* (74%), *E. faecium* (18%) and only (4%) of each *E. gallinarum* and *E. avium*. *E. faecalis* had a (100%) rate of resistance to Gentamycin. *E. faecium*, a rate of (100%) resistance to Benzylpenicillin. *E. gallinarum* showed complete resistance to a variety of antibiotics. *E. avium* showed complete resistance to Ampicillin and Tetracycline. Enterococci represent an infection control challenge in the region, a careful usage of antibiotics and implementation of infection control practices is believed to reduce the risk of infection.

KEYWORDS: Enterococcus genus, Nosocomial pathogens, Antibiotic resistance, Vitek 2 system.

INTRODUCTION

Enterococci are gram-positive cocci shaped bacteria. They are facultative anaerobes that are catalase negative and non-spore formers (Bin-Asif and Abid Ali, 2019). Enterococcus is a large genus of lactic acid bacteria belonging to the phylum Firmicutes of Enterococcaceae family. The Enterococci genus consists of large variety of species, 58 species have been identified so far, the ones currently most common and clinically significant are *E. faecalis* and *E. faecium*. They mostly colonize the upper and lower parts of the human gastrointestinal tract, the oral cavity and genital tract (García-Solache & Rice, 2019).

Studies have found that both *E. faecium* and *E. faecalis*, both clinically significant species, have developed capacity to bind collagen present on the surface of human cells (Rich, 1999). Furthermore, studies have shown that *E. faecalis* is inherently more virulent than *E. faecium* and has greater ability to acquire virulence factors (Moellering, 1992).

Enterococci are not toxin producers; their virulence mainly is attributed to properties like durability, structure, their ability for production of gelatinase (gelE), catalase (kcat), haemolysis (cylL/S), bacterial antagonism (enterocins) and biofilm formation via enterococcal surface protein (Esp) as well as virulence potential with innate or acquired resistance to antibiotics (Ali et al., 2013; Miller et al., 2016)

The ability of these bacteria to form biofilms promote adherence to catheters, dental prostheses, and heart valves. Biofilm production limits their sensitivity to antibiotic penetration leading to persistent infections (Ch'ng et al., 2019); this also protects enterococci from phagocytic attacks and allows the exchange of virulence genes in multispecies biofilms (Ch'ng et al., 2019; Khalil et al., 2022, Kristich et al., 2014)

Even though these bacteria are regarded as part of the normal flora of human intestinal tract, they can still cause many types of infections and some of them may be difficult to treat specially in the nosocomial setting (Van Schaik et al., 2010). Enterococci bacteria are now considered

a common cause of UTI, bacteremia, endocarditis and they can also on rare occasions cause intra-abdominal infections (IAI) and meningitis. Enterococcal infections are most often associated with surgery of burn wounds, pressure and leg ulcer and finally diagnostic or therapeutic UTI procedures. Infections reported in newborns and infants are most commonly catheter related and may lead to meningitis (Vu and Carvalho, 2011; Moellering, 1992; Teixeira et al., 2011)

Enterococci species have recently emerged as opportunistic pathogens mainly associated with hospital settings particularly patients hospitalized for long periods of time (Bruni and Sparo, 2016). It was formerly believed that enterococcal infections were endogenous, that is; the infection originated as opportunistic pathogens from the patient's own normal flora (Escolà-Vergé, 2019). However, studies have confirmed that resistant strains of enterococci spread from patient to patient in the hospital. Furthermore, these microorganisms colonize hospital staff and namely nurses, becoming part of their bowel flora, which in turn transfer the bacteria to patients. (Reyes et al., 2016)

The European Centre for Disease Prevention and Control (2011-2012) report that enterococci are estimated to cause about 8% of healthcare-associated infections in Europe. The ECDC has categorized them as pathogens posing a major threat to healthcare systems. (Fernández-Hidalgo and Escolà-Vergé, 2019).

Enterococcus genus is now one of the common causes of human infections. And during the pandemic, a high number of this type of infection was reported. However, it is unclear why the number of Enterococcus infections raised during COVID-19 (Bonazzetti et al., 2020; Toc et al., 2020).

Furthermore, there seems to be a causal relationship between Enterococcus spp. and bloodstream infections (BSIs) developed among COVID-19 patients. Two of the dominant species responsible were *E. faecalis* (1.8%) and *E. faecium* (8.4%) (Gaibani et al., 2021)

Species mostly associated with medical concerns include: firstly, *Enterococcus faecalis* making up the majority of clinical isolates (85%-90% in most laboratories), followed by *Enterococcus faecium* (5%-10% of strains encountered clinically). And recently there have been increased reports of infections due to *Enterococcus durans*, *Enterococcus avium*, *Enterococcus raffinosus*, *Enterococcus*

gallinarum, and *Enterococcus casseliflavus* as well (Moellering, 1992).

Recently *Enterococcus faecium* has become one of the most commonly isolated species of bacteria from critically ill patients in the United States. It has been reported to be isolated almost as often as *Enterococcus faecalis* from a variety of clinical samples (Hodel-Christian & Murray, 1991; Kristich et al., 2014)

The treatment of infections caused by Enterococci has become one of the most challenging issues facing clinicians. The increase of strains that are resistant to nearly all bactericidal antibiotics has become an extreme concern (Hodel-Christian & Murray, 1991; Kristich et al., 2014). The genus of Enterococcus is inherently resistant to cephalosporins, clindamycin, aminoglycosides and trimethoprim-sulfamethoxazole (García-Solache & Rice, 2019).

The objective of this study is to identify and determine the rate of the different Enterococci species in the different types of clinical samples and also to determine the sensitivity and resistance rate of these bacteria against different types of antibiotics which help to give an idea about the spreading of this bacteria in Duhok city and also what are the best treatments of it.

Materials and methods

Sample collection

A total of 560 clinical samples were collected from patients with bacterial infections visiting Vin hospital in Duhok city, Iraq from October 2021 to October 2022. The samples included: urine, HVS (high vaginal swabs), blood, sputum, cerebrospinal fluid (CSF), wound, semen, and throat swabs. All samples were collected in accordance with aseptic sample collection protocols and procedures in sterilized containers. All samples were directly processed in the Microbiology lab. in Vin hospital

Culture and Gram staining

Samples were cultured on both blood and chocolate agar under controlled sterilized condition. Media were prepared according to manufacturing instructions. Cultures were then incubated at 37°C for 20-24 hours. Standardized procedure of Gram staining was done for all samples. All of the media and reagents were obtained from (Difco/ United States). The species of Enterococcus were confirmed and differentiated using the VITEK 2 Compact System with a Gram-positive detection card (GP BioMérieux, France), which employs the fluorogenic methodology for identification.

Antibiotic Sensitivity testing

The VITEK 2 system with a Gram-positive susceptibility card (AST - P 640 BioMérieux, France) was used to perform the antibiotic susceptibility pattern of Enterococcus isolates.

RESULTS

The identification of Enterococcus isolates

For the purpose of this study a total of 560 clinical samples were collected from patients with suspected bacterial infections that visited Vin medical complex/ Duhok; from October 2021 to October 2022; of which 53 (9.4%)

samples were identified as bacterial infection caused by Enterococcus spp.

The clinical samples positive for Enterococci spp. included 18 (33.9%) urine samples, 15 (26.4%) HSV/ Vaginal swab samples, 9 (18.8%) blood samples, 3 (5.6 %) sputum samples, 2 (3.7%) CSF samples, 2 (3.7%) wound samples, 1 (1.8%) semen sample, 1 (1.8%) throat swab and 2 (3.7%) other types of samples (Table 1). Four main species of enterococci were isolated during our research. Of which, the number of *E. faecalis* isolates were 39; 74%, those of *E. faecium* were 10; 18%) and only 2 (4%) of each *E. gallinarum* and *E. avium* (Table 2).

Table (1): Number and frequency of Enterococci isolated from each type of sample

Type of sample	Number of <i>E. faecalis</i> isolates in each type of sample/ (%)	Number of <i>E. faecium</i> isolates in each type of sample/ (%)	Number of <i>E. gallinarum</i> isolates in each type of sample/ (%)	Number of <i>E. avium</i> isolates in each type of sample/ (%)
Urine	14	3	1	0
HVS/ Vaginal swab	11	3	1	0
Blood	6	2	0	1
Sputum	2	1	0	0
CSF	1	1	0	0
Wound	1	0	0	1
Semen	1	0	0	0
Throat swab	1	0	0	0
Other samples	2	0	0	0

Table (2): Frequency and percentage of each Enterococci sp. isolated from patients

Microorganism	Number of isolates	Percentage out of 53 (%)
<i>E. faecalis</i>	39	74 %
<i>E. faecium</i>	10	18 %
<i>E. gallinarum</i>	2	4 %
<i>E. avium</i>	2	4 %

Antibiotics sensitivity patterns

The antibiotic resistance frequency and rates for all four isolated species are exhibited in

(Tables 3,4,5 and 6). *E. faecalis* isolates showed the highest resistance towards gentamycin (100%) followed by tetracycline (92%); but only

(15%) resistance rate for Benzylpenicillin while for ampicillin it showed a very low rate of (10%). The highest sensitivity rate (100%) was reported for the antibiotics Linezolid, Daptomycin and Tigecycline. These were followed by the antibiotics: Teicoplanin and Trimethoprim/ Sulfamethoxazole with the rate

(90%, 97%) respectively. Finally, Levofloxacin which also relatively revealed good effectivity toward the isolates (82%) followed by Clindamycin and Ciprofloxacin with a rate of (79%) and Vancomycin and Erythromycin antibiotics with the rates (77% and 69%) respectively (Table 3)

Table (3): Susceptibility test of *E. faecalis* isolates (N=39)

	Antibiotics	Frequency of sensitive <i>E. faecalis</i> / Percentage	Frequency of Resistant <i>E. faecalis</i> / Percentage	Intermediate
1	Benzylpenicillin	33 (85%)	6 (15 %)	0
2	Ampicillin	35 (90 %)	4 (10 %)	0
3	Ciprofloxacin	31 (79 %)	8 (21%)	0
4	Levofloxacin	32 (%)	7 (18%)	0
5	Clindamycin	31 (79%)	8 (21%)	0
6	Erythromycin	27 (69%)	12 (31%)	0
7	Linezolid	39 (100%)	0	0
8	Daptomycin	39 (100%)	0	0
9	Teicoplanin	35 (90 %)	4 (10%)	0
10	Vancomycin	30 (77 %)	9 (33 %)	0
11	Tetracycline	3 (8 %)	36 (92 %)	0
12	Tigecycline	39 (100%)	0	0
13	Gentamycin	0	39 (100%)	0
14	Trimethoprim/ Sulfamethoxazole	38 (97%)	0	1 (3%)

E. faecium isolates (Table 4) showed an extremely high rate of resistance (100%) for both Benzylpenicillin and Gentamycin. Also, for both ampicillin and Tetracycline, the isolates showed a very high rate of resistance (80%). Similar to *E. faecalis* isolates, *E. faecium* isolates showed the highest rate of sensitivity (100%) towards Linezolid, Daptomycin and

Tigecycline; followed by Trimethoprim/Sulfamethoxazole and Teicoplanin with the rate (90%, 80%) respectively. Both Ciprofloxacin and Levofloxacin showed a sensitivity rate (80%); Clindamycin, Vancomycin and Erythromycin revealed sensitivity rate (50%, 40% and 70%) respectively.

Table (4):Susceptibility test of *E. faecium* isolates (N=10)

	Antibiotics	Frequency of sensitive <i>E. faecium</i> / Percentage	Frequency of Resistant <i>E. faecium</i> / Percentage	Intermediate
1	Benzympenicillin	0	10 (100%)	0
2	Ampicillin	2 (20%)	8 (80%)	0
3	Ciprofloxacin	8 (80%)	0	2 (20%)
4	Levofloxacin	8 (80%)	1 (10%)	1 (10 %)
5	Clindamycin	5 (50%)	5 (50%)	0
6	Erythromycin	7 (70%)	3 (30 %)	0
7	Linezolid	10 (100%)	0	0
8	Daptomycin	10 (100%)	0	0
9	Teicoplanin	8 (80%)	2 (20 %)	0
10	Vancomycin	4 (40%)	6 (60%)	0
11	Tetracycline	2 (20%)	8 (80%)	0
12	Tigecycline	10 (100%)	0	0
13	Gentamycin	0	10 (100%)	0
14	Trimethoprim/ Sulfamethoxazole	9 (90%)	1 (10%)	0

Tables 5 and 6 represent the resistance and sensitivity patterns for both *E. avium* and *E. gallinarum* isolates in our study. It was noteworthy to state that since only two isolates of each of these species were detected in this study, the results may not reflect the true and accurate sensitivity patterns. Even so, the isolates of *E. avium* and *E. gallinarum* revealed a high sensitivity of (100%) to the antibiotics Levofloxacin, Linezolid, Daptomycin, Tigecycline and Trimethoprim/

Sulfamethoxazole while only *E. avium* isolates showed complete sensitivity to Teicoplanin. Benzylpenicillin, Ciprofloxacin, Erythromycin, Clindamycin showed moderate activity (50%) against both isolates. *E. gallinarum* showed an extremely high rate of resistance (100%) for Ampicillin, Teicoplanin, Vancomycin, Tetracycline and Gentamycin. While the most resistance showed by *E. avium* isolates was against Ampicillin, Tetracycline and Gentamycin.

Table (5): Susceptibility test of *E. gallinarum* isolates

	Antibiotic	Frequency of sensitive <i>E. gallinarum</i> / Percentage	Frequency of Resistant <i>E. gallinarum</i> / Percentage	Intermediate.
1	Benzylpenicillin	1 (50%)	1 (50%)	0
2	Ampicillin	0	2 (100%)	0
3	Ciprofloxacin	1 (50%)	1 (50%)	0
4	Levofloxacin	2 (100%)	0	0
5	Clindamycin	1 (50%)	1 (50%)	0
6	Erythromycin	1 (50%)	1 (50%)	0
7	Linezolid	2 (100%)	0	0
8	Daptomycin	2 (100%)	0	0
9	Teicoplanin	0	2 (100%)	0
10	Vancomycin	0	2 (100%)	0
11	Tetracycline	0	2 (100%)	0
12	Tigecycline	2 (100%)	0	0
13	Gentamycin	0	2 (100%)	0
14	Trimethoprim/ Sulfamethoxazole	2 (100%)	0	0

Table (6): Susceptibility test of *E. avium* isolates

	Antibiotic	Frequency of sensitive <i>E. avium</i> / Percentage	Frequency of Resistant <i>E. avium</i> / Percentage	Frequency of Intermediate <i>E. avium</i> / Percentage.
1	Benzylpenicillin	1 (50%)	1 (50%)	0
2	Ampicillin	0	2 (100%)	0
3	Ciprofloxacin	1 (50%)	1 (50%)	0
4	Levofloxacin	2 (100%)	0	0
5	Clindamycin	1 (50%)	1 (50%)	0
6	Erythromycin	1 (50%)	1 (50%)	0

7	Linezolid	2 (100%)	0	0
8	Daptomycin	2 (100%)	0	0
9	Teicoplanin	2 (100%)	0	0
10	Vancomycin	1 (50%)	1 (50%)	0
11	Tetracycline	0	2 (100%)	0
12	Tigecycline	2 (100%)	0	0
13	Gentamycin	0	2 (100%)	0
14	Trimethoprim/ Sulfamethoxazole	2 (100%)	0	0

DISCUSSION

The genus of Enterococci is most commonly known as normal bowel flora in humans, but more recently many cases of opportunistic pathogenicity has been associated with Enterococci, leading to serious and life-threatening infections such as UTI, endocarditis, bacterial vaginosis and even sepsis.

For the purpose of this study a total of 560 clinical samples were collected from patients who visited Vin medical complex/ Duhok, of which 53 (9.4%) samples were identified as Enterococcus spp. in different clinical samples. This percentage is almost identical to that found in the European Centre for Disease Prevention and Control (ECDC, 2011-2012) in which it was found that Enterococcus spp. are the third most frequently isolated microorganisms in healthcare-associated infections with a rate of (9.6%), furthermore, it was found that the percentage of Enterococcal infections varied between 4.5% in the Czech Republic and Norway and more than 20% of all microbial infections in Denmark and Sweden in the same research. Our results were also consistent with data reported in Europe, 2017 stating that 9.6% of all reported nosocomial infections were of Enterococci (Bhardwaj, 2020).

This study showed higher rates of Enterococcal infection than those found in: a Canadian study where only 3% of the nosocomial infections were reported to be due to Enterococci bacteria (Simner et al., 2015), a study in Kolkata, India in which the rate was (7.3%) in different clinical samples

(Chakraborty et al., 2015), and another report in New Delhi, India reported (5.9%) Enterococci infections (Purohit et al., 2017). Finally, a study in Ethiopia where the overall prevalence of Enterococci was 5.5% (Toru et al., 2018) and more studies which reported ranges between 5.0 and 6.2% (Tseng et al., 2008; Marcus et al., 2011; Olawale et al. 2011; Kabew et al., 2011)

the results of this study also showed slightly higher results than those reported in a number of studies such as the one in Istanbul, Turkey reporting 3.2% (Ipek et al., 2011) 1.4% in São Paulo (Lo et al., 2013) and 2.7% in Port Sudan in all age groups (Shingeray et al., 2013); These variances in prevalence might be due to the use of different methodological design (retrospective and cohort), the study area and country and finally the study period. This study also reports lower prevalence of Enterococcal infection than 11% reported from Malaysia (Noor Shafina et al., 2015); 20.8% from Pakistan (Toru et al., 2018); and 15.3% from Tanzania (Aamodt et al., 2015). The differences in the regions and the plan of the study may be behind the differences of the results.

Most recent studies of clinically significant Enterococci show that the two species most commonly being clinically problematic are *E. faecalis* and *E. faecium*. The prevalence of *E. faecalis* being notably higher than that of *E. faecium*, followed by other species, mostly *E. gallinarum* and *E. avium* as shown in study by (Guzman et al., 2016, as cited in Krawczyk et al., (2021) where the most common species are *E. faecalis* with a very high rate of (80–90%) and subsequently *E. faecium* with a rate of (5–

15%). These results are evident in our work, where the prevalence of *E. faecalis* was (74%), that of *E. faecium* was (18%) and only (4%) for each *E. gallinarum* and *E. avium* (Table 1).

Our results are almost identical to those reported in Saudi Arabia that showed the prevalence of *E. faecalis* to be (72.7%), that of *E. faecium* to be (22.8%) and the prevalence of each *E. gallinarum* and *E. avium* to be only (2.2%) (Alotaibi & Bukhari, 2017).

The Enterococci species distribution obtained in this study is also comparable to the results reported in a study in Riyadh, Saudi Arabia in which the frequency of *E. faecalis* was found to be (69.2%) followed by *E. faecium* (11.3%), *E. avium* (2.1%) and *E. gallinarum* (1.3%) (Salem-Bekhit et al., 2012). as mentioned before that the variation and similarity in the results may depend on many factors like the deference in the geographic region and also how much the roles of infection controls are applied in each region, which may affect the spreading of nosocomial and opportunistic bacteria.

Similarly, in a study from Iran testing clinically important Enterococci species reported the major species associated with infection to be *E. faecalis* with a rate of (57%) followed by *E. faecium* (43.0%) forming of the isolates (Kafil & Asgharzadeh, 2014).

These results were also consistent with two studies found in India; one reported *E. faecalis* as the major isolate (76%), followed by *E. faecium* (24.0%) (Sreeja & Prathab, 2012); and another study which reported (90.85%) *Enterococcus faecalis* followed by (8.50%) *Enterococcus faecium* and (0.65%) *Enterococcus gallinarum* (Chakraborty et al., 2015).

Finally, our results are comparable to a study in Italy showing that the most isolated species is *E. faecalis* (82.2%) followed by *E. faecium* (17.8%) (Boccella et al., 2021) and another study done as part of the SENTRY Antimicrobial Resistance Surveillance Program showing the prevalence of *E. faecalis* to be the highest, representing 57.2% of Enterococci isolated in Canada, 60% in USA and 76.8% in Latin America; *E. faecium* to be the second most common 19.3% in Canada, 20% in USA and 4.6% in Latin America, followed by *E. avium* and *E. gallinarum* with much lower rates that varied with the geographic region ranging from 0.3% to 3.3% among other species (Low et al., 2001).

Only one resource, in Iran, reported higher incidence of *E. faecium* (64.8%) being isolated than the usually most common isolated species *E. faecalis* (32.84%) (Purohit et al., 2017)

The clinical samples positive for Enterococci spp. In our study showed most common isolation (33.9%) from urine samples followed by: (26.4%) HSV/Vaginal swab samples, (18.8%) blood samples, 3 (5.6 %) sputum samples, 2 (3.7%) CSF samples, 2 (3.7%) wound samples, 1 (1.8%) semen sample, 1 (1.8%) throat swab and (3.7%) other types of samples.

These results are almost consistent with the study by Boccella et al. (2021) that found the prevalence of Enterococcal infection among different clinical samples to be as follows: urine cultures (32.5%), vaginal swabs (19.4%), wound swabs (15.9%), blood cultures (8.2%), sputum (2.6%), sperm cultures (0.6%), and others (16.9%); and another study by Alotaibi & Bukhari (2017) done in Saudi Arabia, which reported Enterococcal detection in 95 (41.4%) Urine samples, 63 (27.2%) blood samples and 45 (19.4%) wound swabs; these were the most commonly involved specimens. Our results are slightly

Our results were comparably higher than those found in India where Enterococci was found accountable for 8.45% of urinary, 4.53% wound swab or pus, 4.23% blood and 4.43% high vaginal swab isolates; causing 7.3% of all nosocomial infections in the area. The study showed a significantly high number of nosocomial infections caused by Enterococci where nosocomial urinary tract infection by Enterococci was as high as (66%) and (19.6%) in wound infections (Chakraborty et al., 2015)

In another study, the highest number of isolates was recovered from urine (61.5%), followed by; pus (19.8%), blood (5.5%), wound (3.2%), vaginal (1%), semen (1%) at a Tertiary Care Center of Eastern Nepal. (Karna et al., 2019). And finally, our results are lower than those reported in New Delhi, India where isolates from urine were (51.2%) and those from blood and pus were (30 %) and (18.8%) respectively (Purohit et al., 2017). The differences in the results may depend on the number of each type of samples that were tested for isolating the Enterococcus spp. and differences in methodology.

Antibiotic patterns

This study showed high sensitivity rate of all Enterococcus spp. isolates against linezolid, Tigecycline, and Daptomycin antibiotic with rate

100%, and this may be due to the fact that these antibiotics are less commonly used in our area, while they revealed high resistance to Tetracycline, Benzylpenicillin and ampicillin except *E. faecalis* which has high sensitivity to both Benzylpenicillin and ampicillin antibiotics. These results have relative resemblance to a study done by (Boccella et al., 2021) in Italy which report that *Enterococcus faecalis* showed a high rate of resistance to tetracycline, gentamicin. while being highly sensitive to ampicillin (96.7%), ampicillin/sulbactam (99.4%), linezolid (99.4%), teicoplanin (98.5%) and tigecycline (98.9%) this may be due to the abuse of these medications in Italy.

Enterococcus faecium, in our research on the other hand, showed high resistance to ampicillin (80%), Benzylpenicillin (100%) this agrees with Boccella et al, 2021 which revealed that *Enterococcus faecium* shows high resistance to ampicillin (84.5%) and Benzylpenicillin.

Another study which reported a progressive increase in *E. faecium* infections, has found it to be more resistant to penicillin and aminoglycosides. This is attributed to production of the enzyme 6-acetyl transferase and more penicillin-binding proteins (Sood et al., 2008)

Enterococci showed a high rate of sensitivity for linezolid in this study, which is the first Oxazolidinones antibiotic approved for clinical use. It shows great activity against a wide spectrum of multidrug resistant Gram-Positive bacteria; such as sensitive and resistant strains of *Staphylococcus aureus*, vancomycin-sensitive and vancomycin-resistant strains of *Enterococcus* as well as against *Streptococcus pneumoniae*. (Zimmer et al., 2003)

Another antibiotic that showed high activity in this study was Daptomycin. Which is one of the few antibiotic options for infections caused by ampicillin and vancomycin resistant Enterococci, such as vancomycin-resistant *Enterococcus faecium* (Satlin et al., 2019)

As mentioned previously that both Linezolid and Daptomycin are of the less used antibiotics in our region, this may be the primary reason behind the fact that these antibiotics are still very active against Enterococci -among other bacteria- that has not yet become resistant to them.

Tigecycline also has high activity towards Enterococci, it was considered to have high activity against vancomycin-resistant *Enterococcus* isolates. This is a broad-

spectrum antibiotic usually used as a last resort against infections caused by multi drug resistant Gram negative and Gram-positive bacteria.

A high resistance to gentamycin and tetracycline were also detected in this study. This is also mentioned in a study done in the eastern region of Saudi Arabia, which revealed high resistance to erythromycin, gentamycin and tetracycline suggesting the diverse geographical distribution of MDR Enterococcus isolates in Saudi Arabia (Farman et al., 2019)

Gentamicin is one of the most commonly used aminoglycosides used against Enterococci. Unfortunately, Enterococci has gained high resistance against it due to the acquisition of aminoglycoside resistance genes (Daikos et al., 2003)

A high prevalence of high-level resistance to both erythromycin and tetracycline was documented by certain studies; the multidrug efflux pump systems in the Enterococci are believed to be responsible for tetracycline resistance (Ahmadpoor et al., 2021).

High-level resistance to vancomycin was also recorded in this study which is encoded by a different cluster of genes referred to as the vancomycin-resistance gene cluster (eg, vanA, vanB, and vanD gene clusters) (Chen & Xu 2015). Enterococcal isolates exhibited a high rate of sensitivity to Ciprofloxacin and levofloxacin which agrees with a study reporting that these antibiotics have a good activity against Enterococci bacteria (Drago et al., 2001).

Finally, it is worthy of mentioning that the Enterococci are a genus of highly resistant bacteria to a broad range of antibiotics, such as cephalosporins and sulfonamides (Kristich et al., 2014). They represent a major infection control challenge because of their intrinsic resistance to many antibiotics as well as their ability to acquire additional resistance by gaining certain resistance genes through the transfer of plasmids and transposons. Furthermore, they can disseminate easily in the hospital setting, thus, a careful and controlled usage of antibiotics and the implementation of infection control practices is believed to reduce the risk of these infections. All these reasons have unfortunately led Enterococci to become significant pathogens worldwide, especially with respect to nosocomial and iatrogenic infections (Moellering, 1992; Teixeira et al., 2011; Farman et al., 2019).

CONCLUSION

Enterococci represent an infection control challenge and is one of the most common nosocomial pathogens in our region. *Enterococcus faecalis* and *Enterococcus faecium* make up the majority of clinical isolates of Enterococci. These bacteria are resistant to many used antibiotics like Gentamycin and Tetracycline, while they are highly sensitive to other antibiotics like linezolid and Daptomycin antibiotics. A careful usage of antibiotics and implementation of infection control practices is believed to reduce the risk of Enterococci infection.

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