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RISK FACTORS AND OUTCOMES OF ENTEROCOCCUS SPECIES ISOLATED FROM CLINICAL SPECIMENS

Microbiology

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ABSTRACT

Introduction: Enterococci are the most common aerobic and facultative anaerobic gram-positive cocci. They show intrinsic resistance to many antibiotics, acquire resistance genes and are capable of transferring resistance genes. Immunosuppression, abdominal surgery, structural abnormalities of urinary tract, long hospital/ICU stay, previous antibiotic use, mechanical ventilation, etc. are all risk factors for enterococcal infections. **Objectives:** A study was undertaken to find out the risk factors and outcomes of *Enterococcus* species isolated from clinical specimens. **Material and Methods:** Single enterococcal isolates recovered from clinical specimens received for bacterial culture in this hospital during a period of one and half years were included in the study. Clinical details of the patient and risk factors were noted down in a structured proforma. Enterococci were identified and speciated by standard biochemical tests. Patient was followed up to see the outcome. **Results:** Total 96 enterococci were isolated during this period from hospitalized patients, out of which 86 were *Enterococcus faecalis*, 8 *E. faecium* and 2 *E. solitarius.* Out of these, 4.2% isolates were vancomycin resistant enterococci. Out of 96, 52.1% had a hospital stay >7 days, 28.1% were on mechanical ventilation and 19.8% had central line insertion. In this study, 26% patients with enterococcal infection expired. Mortality among patients with *E. faecium* infection was more (62.5%) than among patients with *E. faecalis* infection (23.3%). Mortality in patients whose hospital stay was >7 days was 42%, whereas those on mechanical ventilation was 48.1% and those with central line insertion was 52.6%. **Conclusion:** This study revealed that in enterococcal infections, hospital stay of >7 days, mechanical ventilation and central line insertion are significantly associated with mortality.

KEYWORDS

Enterococcus species, VRE, Risk factors, Outcome.

INTRODUCTION

Enterococci are the most common aerobic and facultative anaerobic gram-positive cocci, which are well adapted for survival and persistence in a variety of adverse environments, including sites of infections and inanimate hospital surfaces. Enterococci, once regarded by many as harmless commensals, have emerged as one of the most important nosocomial pathogens worldwide and are associated with high mortality. They are formidable pathogens because of their resistance to antimicrobial agents, allowing them to survive and thrive in the hospital environment, where antibiotic usage is high [1].

Enterococci have emerged as one of the leading clinical challenges for physicians due to its intrinsic and acquired resistance to vancomycin, resistance to high concentration of aminoglycosides and its ability to produce β-lactamases, which are responsible for causing serious or life-threatening infections [2].

Risk factors for multi-drug resistant enterococci are patients with chronic renal failure, patients with hematologic malignancy, neutropenia, immunosuppression, critically ill patients in the intensive care unit (ICU), diarrhea, organ transplant recipient and severe underlying illnesses [3]. Other risk factors include prolonged hospitalization, the need for intra-hospital transfer to another ward, surgical exploration or other surgical procedures, use of enteral feeding tubes, proximity to a patient harboring multi-drug resistant enterococci, the use of sucralfate, prior antimicrobial therapy having no anti-enterococcal activity, anti-cancer chemotherapeutic agents, immunosuppressants and anti-inflammatory drugs, renal insufficiency, malignancies, comorbidities, and surgical procedures [3]-[5].

Due to increasing use of antineoplastic, biological and other immunosuppressive agents, enterococcal infections have become a major cause of nosocomial infections [6], [7]. Empirical use of antibiotics, absence of national guidelines for screening patients for multi-drug resistant bacteria and lack of sufficient information and programs to control rapid spread of enterococci has led to increased mortality caused by enterococcal infections [3]-[5]. Mortality due to VRE

are high (25-50%) since they are often seen in immunocompromised hosts [8], [9].

This study was undertaken to identify the different risk factors and to assess the outcome of patients with enterococcal infections.

MATERIAL AND METHODS

It was a prospective study conducted in a tertiary care hospital in Mumbai during a period of one and a half years, after prior consent from the Institutional Ethics Committee. Single enterococcal isolates recovered from clinical specimens including urine, pus, blood culture, respiratory samples, body fluids, etc. received for bacterial culture was included in the study.

Clinical details of the patient and risk factors were noted down in a structured proforma. Ninety-six enterococci were identified and speciated by standard biochemical tests [10]. Vancomycin susceptibility was performed on Mueller Hinton agar by using E-strip method (HiMedia) for detecting Minimum Inhibitory Concentration (MIC). All the patients were followed up to see the outcome.

RESULTS

Out of total 96 enterococcal strains isolated, 86 were *Enterococcus faecalis*, 8 were *E. faecium* and 2 were *E. solitarius.* Vancomycin resistance was seen in 4% isolates. Table 1 & Fig. 1 show the predisposing and risk factors compared with mortality in patients with enterococcal infections. 69.8% patients had history of previous use of antibiotics, 45.8% patients were catheterized and 41.7% patients had past history of surgery.

Fig. 2 shows the outcome of the patients with enterococcal infections. Out of 96, 26% (25/96) patients expired, 56.3% (54/96) were discharged after cure and 17.7% (17/96) went against medical advice. Of the patients who expired, 52% was from pus/wound infections, 28% was from sepsis, 12% from urinary tract infections, 4% from respiratory infections and 4% from central line insertion. Out of 96, 4.2% isolates were vancomycin resistant enterococci.

Table 1: Predisposing/risk factors compared with mortality in 96 patients with enterococcal

Predisposing/risk factors	Present No. (%)	Mortality No. (%)	p value	Significance**
Previous use of antibiotics	69.8 (67)	19 (28.4%)	0.4737	NS

Hospital stay >7 days	52.1 (50)	21 (42%)	0.0055	S
Catheterization	45.8 (44)	14 (31.8%)	0.3705	NS
Past history of surgery*	41.7 (40)	10 (25%)	1.00	NS
Mechanical ventilation	28.1 (27)	13 (48.1%)	0.0292	S
Central line insertion	19.8 (19)	10 (52.6%)	0.0349	S

*Maximum patients had undergone abdominal surgery (11), followed by head, neck & face surgery (6) and orthopedic surgery (5); **NS = not significant, S = significant.

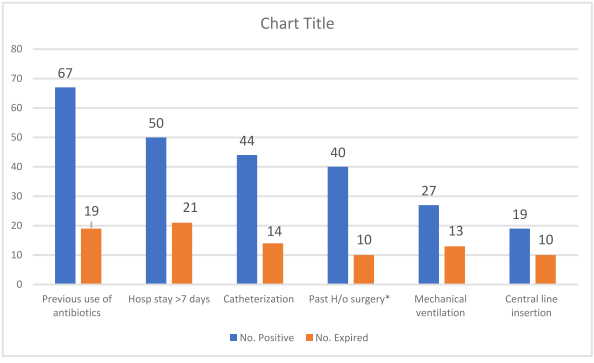

Fig 1: Predisposing/risk factors compared with mortality in 96 patients with enterococcal infections

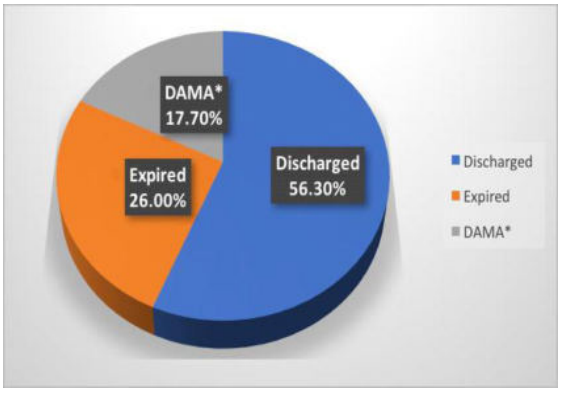

Fig. 2: Outcome of 96 patients with enterococcal infections

Fischer's exact test was done for each predisposing and risk factor separately by preparing a 2*2 table. Hospital stay >7 days, mechanical ventilation and central line insertion turned out to be significantly associated with mortality, whereas previous use of antibiotics, catheterization and past history of surgery were not associated with mortality.

Table 2 shows mortality in different species of enterococci. Five patients with *E. faecium* infection expired (blood culture 2, wound swab 2, urine 1). Twenty patients with *E. faecalis* infection expired (pus & wound swab 11, blood culture 5, urine 2, tracheal secretion 1, CL tip 1). Mortality among patients with *E. faecium* infection was more (62.5%), than among patients with *E. faecalis* infection (23.3%). By Fisher's exact test, mortality in *E. faecium* was statistically significant in comparison to *E. faecalis* (p value= 0.029). Two patients with *E. solitarius* infection did not expire. Mortality in VRE infection in this study was 50% (2/4) and both of them were *E. faecium*.

Table 2: Mortality in different species of enterococci (n=96)

Enterococcus species	No. positive	No. expired (%)
E. faecium	08	05 (62.5)
E. faecalis	86	20 (23.3)
E. solitarius	02	00 (00)

DISCUSSION

Overall 26% patients with enterococcal infection expired (Fig. 2). Mortality among patients with *E. faecium* infection was more (62.5%), than in patients with *E. faecalis* infection (23.3%). By Fisher's exact test, mortality in *E. faecium* was statistically significant as compared to *E. faecalis*. In the study by Noskin et al [9], E. *faecium* showed significant association (50%) with mortality. McBride et al [8] also reported that *E. faecium* has significant association with mortality.

50% patients with enterococcal infection were hospitalized for more than 7 days. By Fisher's exact test, duration of hospital stay of more than 7 days was highly associated with mortality (p value = 0.0055) (Table 1). Studies by Carmeli et al [18] and Edmond et al [12] have also shown duration of hospital stay of mean 8 days is associated with mortality.

Amongst various predisposing/risk factors seen in 96 patients, 27% patients were on mechanical ventilation and 19% had central line insertion. By Fisher's exact test, the predisposing/risk factors associated with mortality were mechanical ventilation (p value= 0.0292) and central line insertion (p value= 0.0349). Previous use of antibiotics, catheterization and past history of surgery were not significantly associated with mortality (Table 1).

Mortality in VRE infection in this study was 50% (2/4) and in both the patients, *E. faecium* were isolated. The duration of hospital stay was more than 7 days in both these patients. One was a case of intracranial hemorrhage and one was a case of chronic kidney disease with renal failure. Both of them were on mechanical ventilation and central line insertion. Taneja et al [15] have reported 25% (2/8) mortality in patients with VRE. Our study is almost similar to the study by Bhavnani et al [13], who reported 52% mortality in VRE patients. Mortality due to VRE infection ranged from 19% to 64% in different studies. However, in the studies by De et al [19] and Oberoi et al [20] none of the patients with VRE died.Table 3 shows the mortality percentage in VRE infected patients in different studies, which ranged from 19% to 64%.

Table 3. Mortality seen in VRE infected patients

Study	Year	Mortality in VRE infected patients
Linden et al [11]	1996	46%
Edmond et al [12]	1996	37%
Bhavnani et al [13]	2000	52%
Vergis et al [14]	2001	19%
Taneja et al [15]	2004	25%
DiazGranado et al [16]	2005	64%
Haas et al [17]	2010	23%
Present study	2017	50%

CONCLUSION

This study highlighted the independent risk factors for enterococcal infections. Significant risk factors for enterococcal infection were hospital stay >7 days, mechanical ventilation and central line insertion. These were significantly associated with mortality. Mortality in *E. faecium* was statistically significant in comparison to *E. faecalis*.

In cases complicated by bacteremia or intra-abdominal infections, enterococci are usually pathogenic with a high mortality rate, that must be handled carefully. Studies on risk factors for the onset of enterococcal infections provide useful information for clinicians, enabling improved prognosis, reduced hospitalization and the proper use of antimicrobial agents through early treatment intervention. Nevertheless, additional prospective studies are necessary to confirm the present findings.

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