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Original article

MDR enterococcal urinary isolates with associated co-morbidity and mortality in a tertiary care hospital- A novel dilemma

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Abstract

Introduction: Isolation of multi-drug resistant enterococci from urine samples of hospitalized patients may be considered as one of the underlying factors in determining final outcome in these patients at the time of discharge. **Materials and Methods:** A pilot study was conducted in a super-specialty hospital between March and July, 2014 to generate preliminary data on association between isolation of MDR *Enterococcus spp*. from urine samples with co-morbidity status and prediction of subsequent short term mortality rate (over the next three years) in hospitalized patients.Urine samples received from 1839 consecutive hospitalized patients were subjected to bacterial culture and sensitivity. Urine samples from forty patients repeatedly yielded *Enterococcus spp.* which were identified up to genus level. Antibiotic sensitivity of these isolates was carried out by modified Kirby Bauer disk diffusion method. Those strains with significant resistance to two or more different groups of antibiotics, often including, but not limited to, vancomycin were labeled as multi-drug resistant (MDR). The original version of the Charlson Index (CI) was used to assess co-morbidity and short term mortality rate among patients with and without urinary MDR *Entrerococcus spp*. isolates respectively. **Results:** The percentage susceptibility of *Enterococcus spp*. to antibiotics was as follows: Amoxyclav (42.5%), ciprofloxacin (27.5%), levofloxacin (30%), norfloxacin (42.5%), linezolid (92.5%), gentamicin-120 µg (10%), vancomycin (82.5%) and teicoplanin (82.5%) respectively. Out of 40 *Enterococcus spp.* isolates, thirty six (90%) were labeled as MDR. All the 36 patients with MDR urinary *Enterococcus spp*. isolates had high co-morbidity and short term mortality rate (>85%/year) respectively and seventeen of these patients expired. **Conclusions:** The isolation of MDR *Enterococcus spp*. from urine samples of hospitalized patients should not be ignored. Due consideration should be given to antibiogram before taking final therapeutic decision. Further

studies should be conducted to evaluate the existence of any significant association between isolation of MDR *Enterococcus spp.* from urine samples of hospitalized patients and co-morbidity and subsequent short term mortality rate.

Key-words: Multi drug resistant, *Enterococcus spp.*, Charlson's index

Introduction

Enterococcus spp. are one of the major causes of nosocomial and community-acquired infections which have posed enormous challenges for clinicians in the recent years due to the evolution of antimicrobial resistance The past two decades have witnessed rapid emergence of multi-drug resistant (MDR) *Enterococcus spp*. Outbreaks of nosocomial infection caused by *Enterococcus spp.* exhibiting high level aminoglycoside resistance, ß-lactamase enzyme associated penicillin resistance and vancomycin resistance have been reported in different parts of the world.[1]

Inherent and acquired resistance of *Enterococcus spp*. to several currently available antibiotics leaves limited therapeutic options and results in the selection and spread of MDR strains in hospitals.[2] Empirical use of antibiotics; prolonged hospitalization; invasive procedures like intra-abdominal surgery, endotracheal intubation, intravenous and urinary catheterization; chronic debilitating illnesses like renal insufficiency; exposure to specific contaminated surfaces within patient-care areas; absence of national guidelines for screening patients for MDR bacteria and lack of sufficient information and programs to control rapid spread of *Enterococcus spp.* are some of the important risk factors associated with the emergence of debilitating and life threatening infections caused by MDR *Enterococcus spp*.[1],[3],[4]

Materials and Methods

A pilot study was conducted in a super-specialty hospital between March and July, 2014 to generate preliminary data on association between isolation of MDR *Enterococcus spp*. from urine samples with co-morbidity status and prediction of subsequent short term mortality rate (over the next three years) in hospitalized patients. Urine samples received from 1839 consecutive hospitalized patients (admitted in wards and Intensive Care Units) were subjected to bacterial culture and sensitivity. Urine samples from forty patients repeatedly yielded *Enterococcus spp.* which were identified up to genus level using standard biochemical tests.[5] However, due to some unforeseen circumstances, further speciation of these isolates could not be performed. The microscopic findings of all 40 urine samples showed presence of abundant pus cells and bacteria. Antibiotic sensitivity of these isolates was carried out by modified Kirby Bauer disk diffusion method using *Enterococcus faecalis* (ATCC 29212) as control. Following antibiotics: Amoxyclav (Amoxicillin/Clavulanic acid- 20/10µg), ciprofloxacin (30µg), levofloxacin (5µg), norfloxacin (10µg), nitrofurantoin (300µg), linezolid (30µg), teicoplanin (30µg),

vancomycin (30µg) and gentamicin (120µg) were used. All the antibiotic discs were procured from Himedia except gentamicin (120µg), which was prepared in-house.[6] Those strains with significant resistance to two or more different groups of antibiotics, often including, but not limited to, vancomycin were labeled as multi-drug resistant (MDR).[1] Relevant clinico-epidemiological details of these patients were subsequently obtained from Medical records as per the proforma formulated. The original version of the Charlson Index (CI) was used to assess co-morbidity and short term mortality rate among patients with and without urinary MDR *Entrerococcus spp*. isolates respectively.[7]

The CI consists of nineteen items corresponding to the following co-morbid conditions: Myocardial infarction,congestive heart failure,peripheral vasculardisease,cerebrovascular disease, dementia,COPD,connective tissue disease,peptic ulcer disease,diabetes mellitus,hemiplegia,leukemia, moderate to severe chronic kidney disease, malignant lymphoma,solid tumor, liver disease, AIDS. Each of these conditions may increase mortality in patients based on their severity and is assigned a score. Age grouping of patients into five categories namely (<40, 41-50, 51-60, 61-70 and 71-80 years respectively) is done and each of these age groups is also assigned a score from 0 to 4 respectively. The sum of co-morbidity and age group scores (as applicable for different patients) is calculated. A score of 0–1 points signifies no co-morbidity, 2 points low and > 3 points high co-morbidity respectively. This score is also used to predict short term mortality rate of different patients as follows: 0 points: 12% mortality/year; 1–2 points: 26% mortality/year; 3–4 points: 52% mortality/year and > 5 points: 85% mortality/year respectively[7] .

Results and Discussion

All 40 (100%) patients were having an indwelling urinary catheter and thirty (75%) of these were febrile. The mean age (± S.D.) of these 40 patients was 57.2±15.5 years, twenty six (65%) of whom were females. All 40 (100%) patients had been administered antibiotics empirically. Thirty (75%) and ten (25%) of these 40 patients had been hospitalized in the preceding month and resided in an extended care facility respectively. The percentage susceptibility of *Enterococcus spp*. to all the aforementioned antibiotics was as follows: Amoxyclav (42.5%), ciprofloxacin (27.5%), levofloxacin (30%), norfloxacin (42.5%), linezolid (92.5%), gentamicin-120 µg (10%), vancomycin (82.5%) and teicoplanin (82.5%) respectively. Out of 40 *Enterococcus spp.* isolates, thirty six (90%) were labeled as MDR. The co-morbidity status and predicted short term mortality rate of patients with and without urinary MDR *Enterococcus spp*. Isolates has been depicted in Table 1. Seventeen of the 36 patients with MDR *Enterococcus spp*. urinary isolates expired.

Table-1: Co-morbidity status and predicted short term mortality rate of patients with and without urinary MDR *Enterococcus spp*. isolates

Co-morbidity status of 36 patients with urinary MDR *Enteococcus spp*. isolates			**Co-morbidity status of 4 patients without urinary MDR *Enterococcus spp*. isolates**		
No co-morbidity (%) Score: 0-1	**Low co-morbidity (%) Score: 2**	**High co-morbidity (%) Score: >3**	**No co-morbidity (%) Score: 0-1**	**Low co-morbidity (%) Score: 2**	**High co-morbidity (%) Score: >3**
Nil (0)	Nil (0)	36 (100)	Nil (0)	Nil (0)	4 (100)

Predicted short term mortality rate of 36 patients with urinary MDR *Enteococcus spp.* isolates (%)				**Predicted short term mortality rate of 4 patients without urinary MDR *Enteococcus spp*. isolates (%)**			
12%/year	**26%/year**	**52%/year**	**85%/year**	**12%/year**	**26%/year**	**52%/year**	**85%/year**
Nil (0)	Nil (0)	Nil (0)	36 (100)	Nil (0)	Nil (0)	4 (100)	Nil (0)

This is one of the first studies in which Charlson's co-morbidity index has been used to categorize co-morbidity status and predict subsequent short term mortality rate in hospitalized patients from whom urinary MDR *Enterococcus spp*. isolates were obtained. The results obtained in the present study point towards a probability of strong association between isolation of MDR *Enterococcus spp*. from urine samples of hospitalized patients and high level of co-morbidity (co-morbidity score>3) and subsequently high short term mortality rate (>85%/year). Out of 36 patients with urinary MDR *Enterococcus spp.* isolates, 17 (47.2%) expired. While blood cultures of 14 of these patients were sterile, contaminants in the form of Gram positive aerobic spore bearing bacilli were isolated from blood samples of remaining three patients. MDR *Enterococcus spp.* were also isolated from wound discharge samples of two of these patients. Medical records revealed prolonged administration of imipenem, amikacin, colistin in all 17 patients irrespective of the organism(s) isolated and antibigrams provided by the laboratory. All 4 (100%) patients without urinary MDR *Enterococcus spp.* isolates were alive at the time of discharge.

Mortality due to *Enterococcus spp*. infection is difficult to ascertain because severe co-morbid illnesses are common. Enterococcal sepsis has been implicated in 7% to 50% of fatal cases.[1] In the present study, it is difficult to attribute the cause of deaths to infections with MDR *Enterococcus spp* because of limitations like small sample size, inability to speciate enterococcal isolates and non-isolation of *Enterococcus spp*. from blood samples of all 17 patients who expired.

Conclusion

The isolation of MDR *Enterococcus spp*. from urine samples of hospitalized patients should not be ignored. The pathogenic status of these isolates may be ascertained keeping in mind the clinical picture, microscopic findings, presence of indwelling urinary catheter and history of inadvertent antibiotic administration. Due consideration should be given to antibiogram before taking final therapeutic decision. Also, new criteria laid down by Magiorakos AP et al may be used to classify *Enterococcus spp*. into multi-drug resistant (MDR), extremely-drug resistant (XDR) and pan-drug resistant (PDR) more accurately.[3] Further studies should be conducted to evaluate the existence of any significant association between isolation of MDR *Enterococcus spp.* from urine samples of hospitalized patients and co-morbidity and subsequent short term mortality rate.

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