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ANTIMICROBIAL SENSITIVITY PATTERNS OF URINARY ENTEROCOCCI AND IMPLEMENTATION OF ANTIMICROBIAL STEWARDSHIP IN GRASS ROOT LEVELS:A RETROSPECTIVE OBSERVATIONAL STUDY.

Clinical Microbiology

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ABSTRACT

Enterococci are matter of concern because of their ability to acquire resistance to broad spectrum antibiotics.Variations in the antibiotic sensitivity patterns can pose a threat to treatment of drug resistant enterococci. Antibiotic resistance patterns reported from a medical unit having a microbiology laboratory can provide valuable guidance to treatment and rational use of antibiotics. Out of the 318 samples of bacteriuria patients 37.10% yielded enterococcus sp.The mean age of patients with enterocccus positive urine cultures was 27 years.Females (53.38%) were slightly affected more than males (46.61%).Enterococcus sp. Showed (99.15%)sensitivity to linezolid,followed by nitrofurantoin (89.83%),doxycycline (54.23%),Amoxycillin-clavulinic acid (27.96%),ciprofloxacin (22.03%) and gentamicin (20.33%).Urinary enterococci of ICU patients were more resistant to amoxycillin clavulinic acid(90% resistance) as compared to OPD patients(48.14%)[p-value 0.0144].Resistance to ciprofloxacin was >70% in both ICU and OPD[p-value 0.003]. Treatment of urinary enterococci should be based on local/hospital antibiograms.Intensive care units should be more cautious while using broad spectrum antibiotics which show high resistance trends in local antibiograms.

KEYWORDS

Enterococci, Multidrug Resistance, Antimicrobial Resistance, Antimicrobial Stewardship.

INTRODUCTION

Enterococci are components of normal flora of humans and other animals. Studies have shown pathogenic potential of these organisms proving them to be a source of hospital acquired infections[1].Urinary tract infections by enterococci are one of the most common infections in humans.Most of these infections are hospital acquired and are sometimes associated with urinary tract abnormalities.Enterococcal infections were initially thought to be endogenous speading from the individual's own bowel flora but now it is clearly documented that resistant strains of enterococci can spread from patient to patient inside hospitals. These organisms are intrinsically resistant to a number of antimicrobial agents.In addition to intrinsic resistance,acquired resistance is found in all naturally occurring strains of enterococci.

Antimicrobial resistance (AMR) is a serious threat in global healthcare. Multidrug resistant organisms can lead to antibiotic-treatment response failure when periodic local antibiotic susceptibility reports are not available.Behavioral patterns of an organism in terms of antibiotic sensitiivity in the intensive care setting and outpatient setting sometimes differ.

So, the aim of this study is to look into the sensitivity of urinary enterococci to commonly used antibiotics and its variations in antibiotic susceptibility patterns.This study can guide in rational use of antibiotics and can help in implementing antimicrobial sterwardship when the concerned organism is in question.

MATERIALS AND METHODS

This retrospective data analyis was conducted in the Department of Microbiology of Midnapore Medical College and Hospital,West Bengal.The period for which this analysis was done was from November 2019 to December 2021.

The laboratory protocol for studying and analysis of samples were as follows: early morning clean catch midstream urine sample was collected in wide mouthed sterile screw capped container from clinically suspected patients.

With a calibrated microloop,0.001 ml of urine was cultured into cysteine lactose electrolyte deficient agar, Mac conkey agar, Blood agar and Mueller Hinton agar plates. After overnight incubation at 37 degree centigrade for 24 hours colony counts yielding growths > 10^5 /ml was considered as significant in urine sample.

Enterococcus species were confirmed by gram stain characteristics, catalase negativity, blackening of bile esculin agar, PYRase test, heat tolerance test (growth in broth at 60 degree centigrade for 30 minutes), salt tolerance test (growth in presence of 6.5% Nacl)[3]. Further confirmation was done by sugar fermentation testing which included lactose,mannitol,glucose,arabinose and growth in potassium tellurite agar.

Antimicrobial susceptibility testing performance was done on Mueller Hinton Agar with six commonly used antibiotics.Amoxycillin clavulinic acid (30 microgram), Nitrofurantoin (300 microgram), gentamicin (10 microgram), Doxycycline (30 microgram), Ciprofloxacin (10 microgram) and linezolid (30 microgram) were tested. The antibiotic sensitivity pattern was noted on 5% Mueller Hinton agar by modified Kirby-Bauer disk diffusion method[4]. The antibioltic susceptibility patterns were were interpreted as per Clinical and Laboratory Standards Institute(CLSI) guideline M100,34th edition[5]. Ethical standards as per Helsinki declaration 1975 as revised in 2000 was followed while conducting the study. Microsoft excel and Microsoft word(version 8.1) were used to generate the tables and figures. Results are based on descriptive statistics.

RESULTS

Out of the total urine cultures samples received for processing from November to 2019 to December 2021, 318 were found to be positive for some organism. Among the 318 bacteriuric patients, 118(37.10%) yielded enterococcus species. The other bacteria isolated from urine samples received during this study period were Escherichia coli, Candida albicans, Candida nonalbicans, Staphylococcus epidermidis, Klebsiella sp.Morganella sp.

Out of the 118 enterococcus positive urine cultures, Intensive Care Unit(ICU) patients contributed11(9.32%). The mean age of patients with enterococcus positive urine cultures was 27 years. Females 63(53.38%) were slightly affected more than males 55(46.61%).

117(99.15%) urinary enterococci in these samples were sensitive to linezolid followed by 106(89.83%) sensitive to nitrofurantoin, 64(54.23%)sensitive to doxycycline, 33(27.96%) sensitive to amoxyclav, 26(22.03%) sensitive to ciprofloxacin and 24(20.33%) sensitive to gentamicin.

84(71.18%) urinary enterococcoci were found to be multidrug resistant (gentamicin, ciprofloxacin, doxycycline)..

Urinary enterococci of Intensive Care Unit(ICU) patients showed (>90%) resistance to Amoxycillin-clavulinic acid as compared to the OPD patients(48.14%)(p-value 0.014456). Resistance to ciprofloxacin was >70% in both ICU and OPD(p value>0.003422).

The resistance patterns of urinary enterococci is described below in table 1 and chart 1.

Table 1. Resistance Patterns Of Urinary Enterococcus Sp.to Six Antibiotics In This Study

Antibiotics	% Susceptible	% Resistant
Amoxycillin-Clavulinic Acid (AMC)	33(27.96%)	85(72.03%)
Ciprofloxacin (CIP)	26(22.03%)	92(77.96%)
Doxycycline (DOX)	64 (54.23%)	54(45.76%)
Nitrofurantoin (NIT)	106(89.83%)	12(10.16%)
Gentamicin (GEN)	24(20.33%)	94(79.66%)
Linezolid (LZ)	117(99.15%)	1(0.84%)

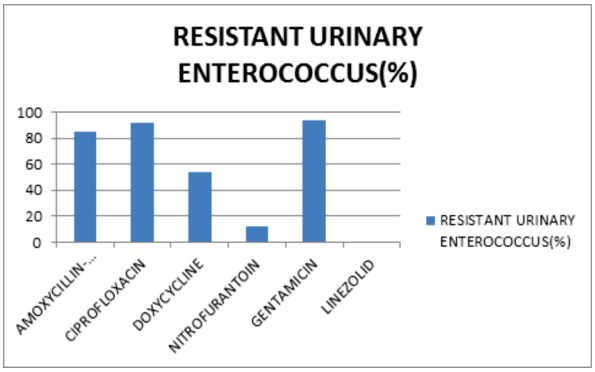

Chart 1.

DISCUSSION

The rapid emergence of resistant enterococci especially in hospital setting can be attributed to the fact that these organisms are nosocomial and multidrug resistant pathogens as they are exposed to multiple antibiotics in hospitals throughout the world. Multidrug resistance is defined as acquired non susceptibility to at least one agent in three or more antimicrobial categories.

Enterococci have evolved a number of efficient mechanisms for transfer of resistance genes which are responsible for the multidrug resistance of this bacteria.. They exchange plasmids via conjugation and also exchange resistance genes on transposons in the absence of plasmids[1].Single step mutations can lead to high level resistance to streptomycin and increased intrinsic resistance to penicillins[1]. Bacteriophages also transfer resistance genes among enterococci[1]. Because of the unique ecological niche of enterococci in gastrointestinal tract they come into close contact with gram positive and gram negative organisms and can exchange genes via conjugation with staphylococci, streptococci, listeria and other gram positive organisms and also have been shown to exchange resistance genes with Escherichia coli[1]. Thus it is quite obvious that these organisms can develop resistance in hospital settings.

Stringent antimicrobial stewardship in all levels of healthcare (Inpatient and Outpatient) is therefore need of the hour.

The prevalence of enterococcus from urinary isolates in this study was 37.10%.Most of the enterococcal isolates were from urine [1]. Most of the studies done on enterococcus support this finding.

The gender distribution showed females slightly more effected than males.. A study done by Bharti,et al. showed similar findings where the females were affected more than males by enterococcal UTI.

In our study, 22.88% urinary enterococcus was isolated from Outpatient department attending patients and the remaining77.12% were isolated from hospitalized patients. The Intensive Care Unit (ICU) patients comprised of 9.32% of urinary enterococcal isolates. This finding corroborated with the study by Barman,et al.[2] wher 76.34% enterococcus were from hospitalized patients and 23.66% were from OPD patients.

99.15% was sensitive to linezolid(Resistance 0.85%) and 89.83% was sensitive to Nitrofurantoin.In a similar studies,100% sensitivity to linezolid 82% sensitivity to nitrofurantoin was noted.[6,7]26% of the isolates were sensitive to ciprofloxacin which corroborated with findings of Barman et al.[2]

71.18% was multidrug resistant (gentamicin, ciprofloxacin, doxycycline). This finding was somewhat similar to a study in Pune, India, where the prevalence of multidrug resistance among 63% of enterococcal isolates were noted.

Doxycycline sensitivity was found to be 54% in our study. [8]Tetracycline resistance can be attributed to presence of tet (M), tet (O), tet (S), tet (K), and tet (L) genes.[9]

Tigecycline is the first bacteriostatic glycylcycline approved for clinical use with a 20-fold higher ribosomal affinity than tetracycline. This antibiotic retains activity against ~99.5% of VRE with a MIC_{90} of 0.25 µg/mL. Resistance is associated with mutations in efflux pumps (similar to the multidrug and toxin extrusion pumps in S. aureus) and mutations in rpsJ, a gene encoding ribosomal protein S10, which often occur in response to tigecycline exposure. [10]

ICU patients showed >90% resistance to Amoxycillin-clavulinic acid and OPD patients showed 48.14% resistance to the same antibiotic.(p-Value 0.014456).Resistance to ciprofloxacin was >70% in ICU as well as OPD patients(p-value 0.003422).Comparison study between antibiotic resistance of Amoxycillin-clavulinic acid was found to be limited.

The high prevalence of multidrug resistant enterococci in tertiary care centers especially ICU maybe due to the use of broad spectrum antibiotics while initiating treatment.

Behavioral patterns of bacteria change from time to time due gene mutations and changes in environmental factors.Antibiograms should be published from time to time by the tertiary health care facilities and local private diagnostic centers having microbiology laboratory. Narrow spectrum antibiotics with good sensitivity to the organism in question should be chosen.Antibiotic policy should be reviewed and modified as per the most recent available antibiogram of the region.District hospitals can refer to the antibiograms published by the nearest tertiary health care facility.A committee on rational use of antibiotics can be formed with the available resources in all health care facility.The local health department has to take an active interest in this direction.Advice on usage of narrow spectrum antibiotics with references from peer reviewed literature and guidelines published by infectious disease societies/state and national health departments can be included in microbiology reports.This will prevent unnecessary prescription of the inappropriate antibiotics.

The World Health Organisation(WHO) has identified a list of priority pathogens that pose a critical threat to human health due to their resistance to antimicrobials latest in 2024.Medical practitioners need be aware of this update.The NMC NAP-AMR module for prescribers can be an useful guidance resource for practitioners.This document also states that communication between clinicians and laboratory is vital and clinicians should be aware of rapid diagnostic tests and use them appropriately.The decision of starting antibiotics empirically should be governed by local epidemiology and hospital antibiogram.Cascade reporting by microbiology labs can prevent misuse of antibiotics.The MIC therapeutic Index(BMQ Ratio) is a better indicator of therapeutic efficacy.Selective reporting is reporting of results for specific antimicrobial agents based on defined criteria unrelated to antibiotic susceptibility results.This approach can be adopted for promotion of Antibiotic stewardship.[11]

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