Original Article

Multi Drug Resistant Nosocomial Pathogens in Intensive Care Units of a Tertiary Care Hospital in Karachi

Ishrat Irfan Ali,[1] Irfan Ali Khan,[2] Muhammad Kashif Munir[3]

Abstract

Objective: To evaluate occurrence of nosocomial infections and antibiotic susceptibility patterns of bacterial pathogens isolated from Intensive Care Units (ICUs) in a tertiary care hospital of Karachi-Pakistan.

Methods and Results: One thousand and fifty clinical isolates were identified following standard protocols. Their antibiograms were evaluated and a clinical correlation was made to measure their pathogenic status and method of acquisition of infection. Fifty-six percent isolates were identified as Acineto-bacter baumannii, 13.2% as Pseudomonas aeruginosa, 11.2% as Staphylococcus aureus (MRSA), 8.8% as Klebsiella pneumoniae, 4.1% as Vancomycin resistant Enterococci (VRE), 2.7% as Escherichia coli (ESBL), 1.2% as Klebsiella spp, 1.1% as coagulase negative staphylococcus, 0.7% as Salmonella typhi and 0.2% as salmonella spp. All the isolates exhibited different resistance patterns against conventional antibiotics. Majority of them were Multi Drug Resistant (MDR).

Conclusions: In this study, Acinetobacter baumannii isolates revealed a pathogenic potential of around 56% were identified by antimicrobial susceptibility patterns. In our study, majority of Pseudomonas aeruginosa, Staphylococcus aureus, Klebsiella pneumoniae, Vancomycin resistant Enterococci, E.coli, and Klebsiella spp were found to be multi drug resistant. High antimicrobial resistance in the ICU is an alarming situation, and calls for imperative measures leading to careful selection/use of antimicrobials while treating different infections. This study is expected to help infection control agencies to take robust steps to control nosocomial infections in developing countries.

Key words: Prevalence; resistance patterns; clinical correlation; nosocomial status.

[1] Research Scholar
Department of Microbiology, The University of Karachi
[2] Research Scholar, The RNA Institute, University at Albany, USA
[3] Research Officer, Pakistan Medical Research Council TB Research Centre, King Edward Medical University Lahore

Date of Submission: 20-10-2016
Date of Acceptance for Publication: 18-01-2017
Conflict of Interest: None
Funding Source: None

Contribution

All Authors have contributed in Study Design, Data Collection, Data Analysis, Data Interpretation, Manuscript Writing and Approval.

Introduction

Nosocomial infections are defined as the infections that are not present at the time of the admission to hospital and appear within 48 to 72 hours after admission or within 10 days after discharge.[1] The World Health Organization (WHO) has reported that, globally, the highest frequency of nosocomial infections occurs in Intensive Care Units (ICUs) of hospitals. Infection rates are higher among patients with risk-factors, such as, very young/old age, underlying disease, compromised immune system and prolong use of different medical devices.[2] Prolong hospitalization associated with nosocomial infections leads to increased morbidity and mortality.[3,4] Patient in the intensive care unit (ICU) has a 5 to 7 fold higher chance of acquiring nosocomial infection.[5]

Nosocomial infections constitute a serious problem in the developing countries including Pakistan, where precise guidelines for hospital infection control and prevention are yet to be defined.[6] Hospitals of both large and small cities of Pakistan are facing multi facet

Corresponding Author: Muhammad Kashif Munir, Research Officer PMRC TB Research Centre, King Edward Medical University, Lahore
Email: munir_gemini81@yahoo.com

problems which included prolonged hospital stays, long term disability, huge additional costs of health care, high costs of hospital expenses for patients and their families and unnecessary deaths due to extensive prevalence of nosocomial infections and the emergence of multi-drug-resistant bacterial strains.[7,8] In Pakistan, authentic literature on hospital acquired infections and ICU-associated infections are scanty.[9,10] This study, therefore, reports the prevalence of nosocomial infections at a tertiary care hospital over a period of 20 months (Dec 2010-July 2012). Additionally, the study also evaluates the antibiograms of bacterial isolates and compares it with clinical correlates of the individuals participating in this study.

Patients and Methods

One thousand and fifty cases were selected from different ICUs, such as medical ICUs, medical high dependency unit (HDU) and surgical ICUs (male and female), of a tertiary care hospital in Karachi-Pakistan. The cases reported as nosocomial infection were selected for the study. A consent form was designed for this purpose.

Samples (blood, urine, tracheal secretion, pus swab, bronchial washing, catheters, intravenous devices and tips) were collected from the patients who were admitted to the ICUs and confirmed as nosocomially infected. Data on the date and the site of infection, patient's demographic information and the devices used were collected for microbiological processing.[11] The bacterial strains were preserved in Luria broth (Sigma-Aldrich St. Louis, MO) containing 20% glycerol at stored at -80°C until further analysis for, phenotypic and genotypic characteristic.

Base line microbiological characterization was conducted using standard methods.[12,13] Following standard microbiological methods, the pathogens were cultured using following growth media: Blood agar, Mac Conkeys's agar, CLED (Cysteine lactose electrolyte deficient) agar, S.S (Salmonella Shigella) agar, Chocolate agar, SIM (sulpher, indole and motility) medium, TSI (triple sugar iron) agar, Simmon citrate agar and Urease medium.[11-13]

Antibiotic susceptibility tests were performed and results were interpreted according to National Committee for Clinical Laboratory Standards (CLSI/NCCLS).[11] Antibiotic susceptibility/resistance was determined using the Kirby–Bauer disk diffusion test on Mueller–Hinton agar.[12,13] Susceptibility/resistance was tested against a panel of antimicrobial agents, which included Amp (Ampicillin 10µg), AMC (Amoxycillin 10µg/Calvulanic acid), TZP (Tazobactam 110µg), CXM (Cefuroxime 30µg), CTX (Cefotaxime 5µg), CRO (Ceftriaxone 30µg), CAZ (Ceftazidime 30µg), FEP (Cefipime 30µg), ATM (Aztreonam 30µg), MEM (Meropenem 10µg), IPM (Imipenem 10µg), G (Gentamicin 10µg), AK (Amikacin 10µg), C (Chloramphenicol 30µg), SXT (Co-trimoxazole), TOB (Tobramycin 10µg), SCF (Salbactam 30µg/ Cefoperazone 75µg), NA (Nalidixic acid 30µg), VA (Vancomycin 30µg), E (Erythromycin 15µg), DA (Fusidic acid 10µg), FD (Clindamycin 2µg), AK (Amikacin 30µg) and CIP (ciprofloxacin 5µg). Additionally, CAZ (Ceftazidime 30µg), Ceftazidime-Calvulanic acid (30µg /10µg), CTX (Cefotaxime 30µg), Cefotaxime-Calvulanic acid (30µg /10µg) were used for ESBL *E.coli* confirmation.

Results

Although a variety of clinical samples were collected from individuals, a higher frequency of bacterial isolates was recovered from catheters and other devices used in the ICUs. A total of 60% of the isolates were obtained from catheters, while 30% and 10% isolates were obtained, respectively, from different mechanical devices and central intravenous lines (Figure 1).

A Total of 1050 bacterial isolates were confirmed as nosocomial pathogens from clinical specimens like urine, blood, catheter tubes, bronchial washing, tracheal secretions, pus swabs and intra venous devices.

Total 1000 urine samples and catheter tips were collected for culture and sensitivity from the patients suspected of nosocomial UTI. Among them 630 (60%)

samples were distinguished as Nosocomial UTI.

The most frequently isolated pathogen was E.coli which was isolated 420/630 .*Klebsiella pneumoniae* was 73/630, *Pseudomonas aeruginosa* was revealed as 62/630, Klebsiella spp isolated as 43/630 and Coagulase negative staph aureus was 32/630.all samples were first confirmed as nosocomial infections.

These infections mainly VAP (Ventilator associated Pneumonia) which is a great concern in patient of ICUs.VAP rate was8.9 infections per 1000 ventilator days. Other most frequent infections were from Tracheal tubes. Total 315 samples were confirmed as nosocomial infected which were 30% of the total samples. The most commonly isolated pathogen was *Acinetobacter baumannii* 97/315, *Pseudomonas aeruginosa* was 77/315, Mechicillin resistant staph aureus (MRSA) were 43/315.we have found 49/315 Vancomycin resistant Enterococci(VRE) and 49/315 *Klebsiella pneumoniae*.

Bloodstream infections also a big threat and source of mortality. During our study we have collected 567 samples to proceed and only 10% (N= 105) were identified as nosocomial infections and multi drug resistant. Most frequently isolated pathogen was *Acinetobacter baumannii* 57/105 followed by *Pseudomonas aeruginosa* 21/105, *Klebsiella pneumoniae* 12/105, MRSA 08/105, VRE 06/105 and E coli 03/105.

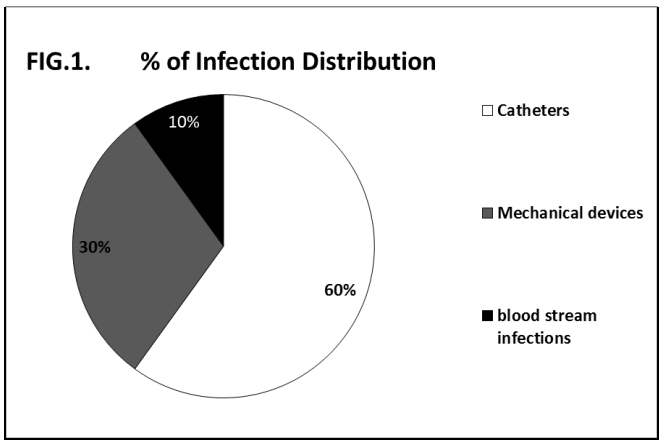

Fig. 1: *Distribution of infections.*

Based on cultural characteristics and biochemical assays, isolates were identified. Fifty six percent multidrug drug organisms were *Acinetobacter baumannii*, 13.2% *Pseudomonas aeruginosa,* 11.2% *Staphylococcus aureus* (MRSA), 8.8% *were Klebsiella pneumoniae*, and 4.1 % as Vancomycin resistant *enterococci* (VRE). In addition, 2.7% isolates were identified as *E.coli* (ESBL), 1.2% isolates as *Klebsiella spp*, 1.1% as coagulase negative *Staphylococcus*, 0.7% as *Salmonella typhi* and 0.2% as other *Salmonella* spp. (Figure 2 A, B and C).

Isolated pathogens shown multidrug resistance against tested antibiotics. Most of the isolates were resistant to Amoxicillin + Calvulanic Acid, Piperacillin/Tazobactam, Ciprofloxacin, Imipenem, ceftriaxone, Amikacin and Co-trimoxazole. The most frequent and resistant Pathogen was found as *Acinetobacter baumannii* for which we have found Polymixin B as a drug of choice. Among 56% Acinetobacter we have found 94% resistant to all antibiotics except polymyxin B and only 6% were showing sensitivity to polymixin B, Tobramycin, Caftazidime, Pipracillin/ Tazabactum and Gentamycin.

As far as *Pseudomonas aeruginosa* concern, among 13.2% we have found ciprofloxacin, Gnetamycin imipenem, ceftazidime, Meropenum, oflaxacillin/ciprofloxacin and amikacin as resistant drugs.in case of *staphylococcus aureus*, Cloxacillin, Clindamycin, Gentamycin, Tetracycline, Amikacin, Cotrimoxazole, - Ofloxacin/Ciprofloxacin,penicillin and erythromycin were resistant.

The resistant profile of *Klebsiella pneumoniae* Ampicillin, Amikacin, Cefixime, Cefotaxime, Ceftriaxone, Cotrimoxazole, Gentamicin, Ofloxacin/ Ciprofloxacin, Aztreonam, Tazobactam and Meropenem were resistant.among 4.1% Vancomycin resistant Enterococci we have found Ampicillin,Tetracycillin, Amikacin, Vancomycin, Cotrimoxazole, Ofloxacin/ Ciprofloxacin and gentamycin as resistant antibiotics.

During our study, we have found 2.7% E.coli as clinical isolates. The antibiotics which were found resistant are as; Amikacin, Ampicillin, Cefixime, Cefotaxime, Ceftriaxone, Cotrimoxazole, Ofloxacin/ Ciprofloxacin,Tazobactum and Gentamycin (Fig. 2 A, B, C).

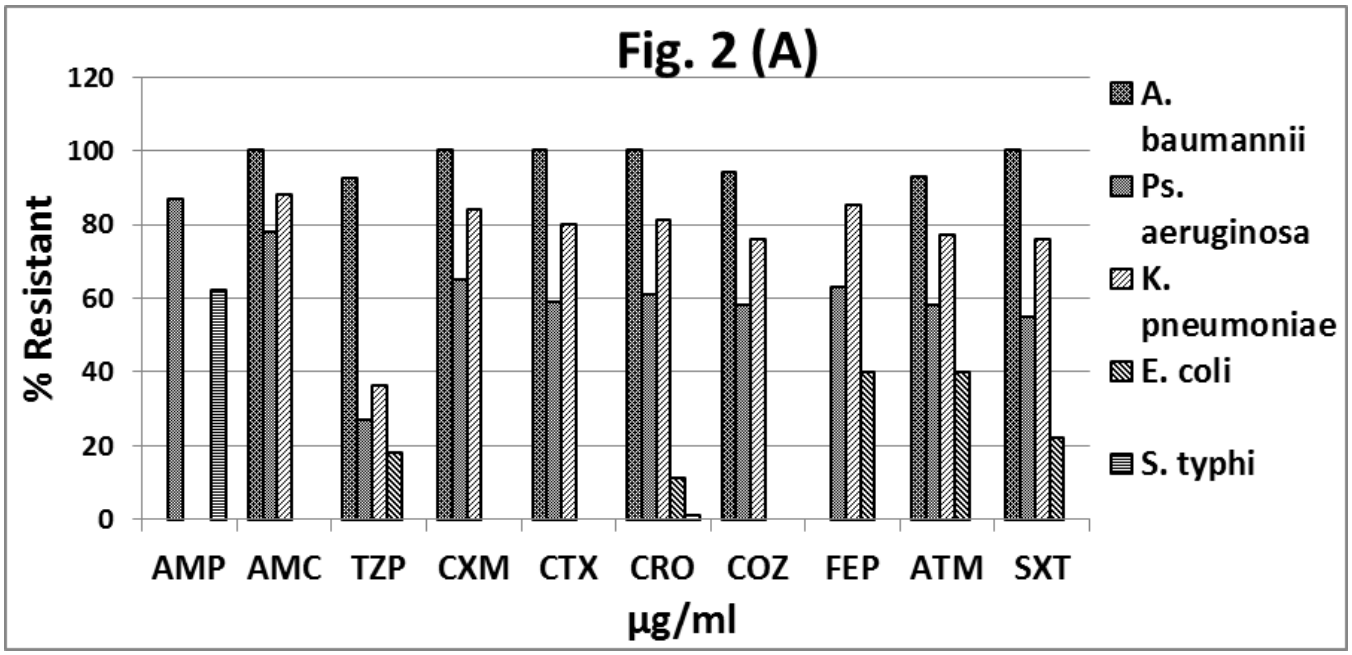

Fig. 2 (A): *Antimicrobial drug resistance pattern of Gram negative organisms; Acinetobacter baumannii, Pseudomonas aeruginosa, Klebsiella Pneumoniae, Escherichia coli and Salmonella typhi, against Amp (Ampicillin 10µg), AMC (Amox10µg/Calvulanic acid), TZP (Tazobactam 110µg), CXM (Cefuroxime 30µg), CTX (Cefotaxime 5µg), CRO (Ceftriaxone 30µg), CAZ (Ceftazidime 30µg), FEP (Cefipime 30µg) and ATM (Aztreonam 30µg).*

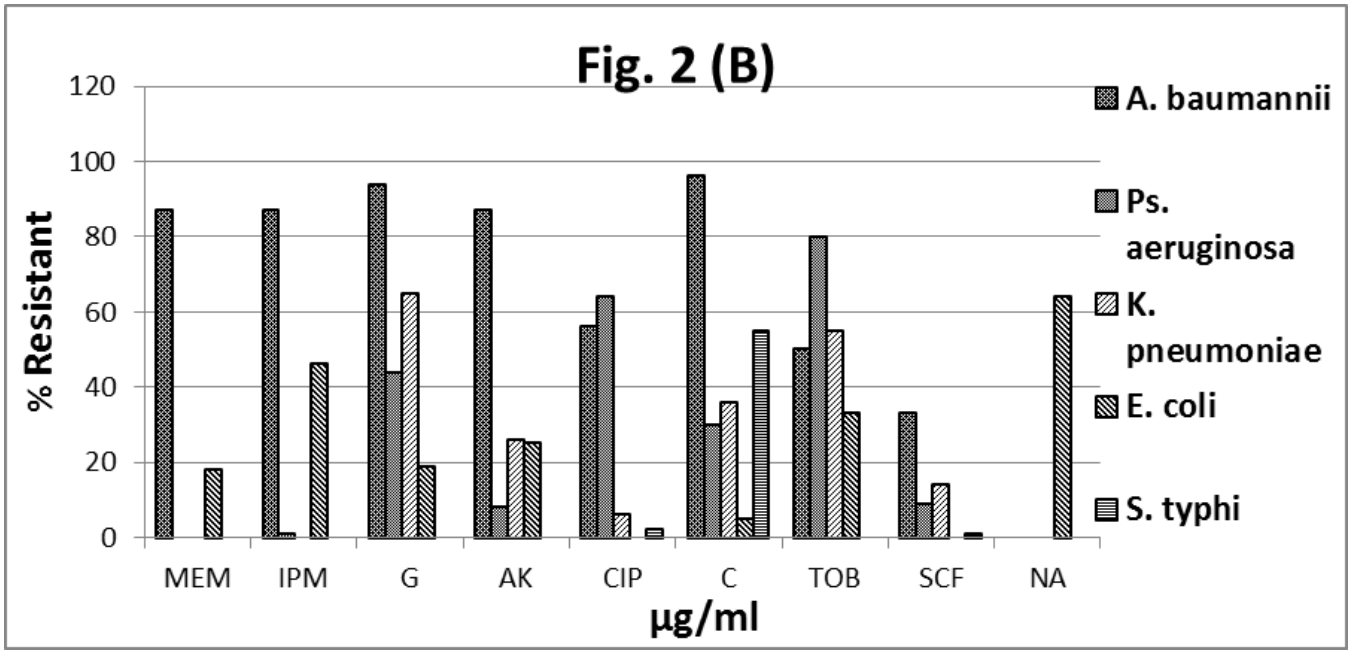

Fig. 2 (B): Antimicrobial drug resistance pattern of Gram negative organisms; *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella Pneumoniae*, *Escherichia coli* and *Salmonella typhi*, against MEM (Meropenem10µg), IPM (Imipenem 10µg), G (Gentamicin 10µg), AK (Amikacin 10µg), CIP (ciprofloxacin 5µg), C (Chloramphenicol 30µg) SXT (Co-trimoxazole) TOB (Tobramycin 10µg), SCF (Salbactam 30µg/Cefoperazone 75µg), NA (Nalidixic acid 30µg).

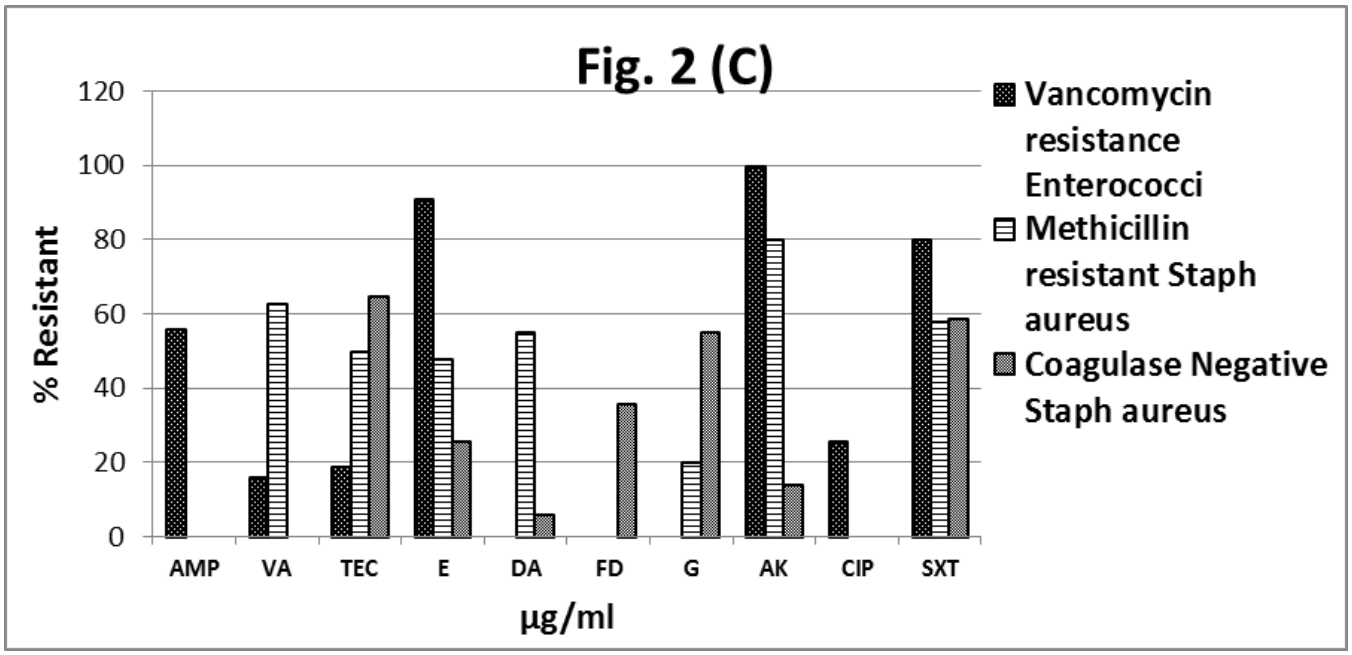

Fig. 2 (C): Antimicrobial drug resistance pattern of Gram positive organisms; Vancomycin resistant *enterococci* (VRE), Methicillin resistant *Staphylococcus aureus* (MRSA) and coagulase negative *Staphylococcus aureus* against; Amp (Ampicillin 10µg), VA (Vancomycin 30µg), TEC (Teicoplanin 30µg), E (Erythromycin 15µg), DA (fusidic acid 10µg), FD (Clindamycin 2µg), G (Gentamicin 10µg), AK (Amikacin 30µg), CIP (ciprofloxacin 5µg), SXT (Co-trimoxazole).

Discussion

The rational for this study was to study the prevalence of nosocomial pathogens isolated from patients admitted in ICUs of tertiary care hospital and to investigate the antimicrobial resistance profile of the isolates against frequently prescribed antibiotics. According to antibiograms, the rate of prevalence of multi drug resistant (MDR) pathogens was higher compared to the other areas of the hospital (environment). Multi drug resistant *Acinetobacter baumannii* was the most common pathogen, followed by *Pseudomonas aeruginosa* and *Staphylococcus aureus* (MRSA) which demonstrated higher levels of resistance. This observation is different from other studies conducted in developed countries, e.g. the SENTRY antimicrobial surveillance program (Europe 1997 – 1998 and North America, 2001),[22-26] in which *S. aureus* was reported as the most common nosocomial pathogen followed by *P. aeruginosa* and *E. coli* in 25 ICUs.[18,19,27]

This study revealed, around 60% catheters associated nosocomial infections, 30% different mechanical devices associated and 10% were found as blood stream infections as shown in Fig. 1. Nosocomial urinary tract infections were the most frequently occurring infections in patients admitted in ICUs with indwelling urinary catheters. We have found 25.5% *Acinetobacter baumannii*, 15.5% *Pseudomonas aeruginosa*, 10.8% *Staphylococcus aureus*, 7.5% *Klebsiella pneumoniae* and 7.4% *Escherichia coli*. These strains were having high rates of resistance to most antibiotics.

We have found 30% of nosocomial infections from different invasive mechanical devices in ICUs, in which Ventilator associated pneumonia and surgical sites infections were most predominant. The Ventilator associated pneumonia in patients was 22.3% and 7.7% were the frequency of wounds and surgical site infections. During our study we have also found 10% nosocomial infections related to central line associated blood stream infection which were causing bacteremia and septicemia.

This is very clear that following infection control guidelines is very important factor to control nosocomial MDRs pathogens. As far as antimicrobial resistance concern, in our study majority of isolated organisms were multi drug resistant as shown in Fig. 2 (A, B, C). Our observations revealed, 94% *A. baumannii* isolates from ICUs were resistant to all tested antibiotics but were sensitive to Polymixin B.[28,29] The 2nd Most frequently isolated MDR was *P. aeruginosa* and as previous studies reported, we did not find increasing

rate of amikacin resistance. We have found significant higher rate of resistance against ciprofloxacin, Chloramphenicol, Co-trimoxazole, Tobramycin, Ampicillin, AMC (Amox/Calvulanic acid), (Cefuroxime Cefotaxime, Ceftriaxone, Cefipime and ATM (Aztreonam. As far as MRSA concern, among total isolating ratio was 11.2% from which 33% were MRSA and showed resistance against Vancomycin, Amikacin, Co-trimoxazole.[25,27]

The data out of the present research work in Pakistan, suggest that application of conventional agents for the empirical treatment become complicated by the nosocomial pathogens with accelerated resistance to antibiotics. Efforts to control multi drug resistant bacterial strains in Pakistani hospitals, significant scientific societies and government agencies have only partially been successful.[7,30,31] Rigorous mutual efforts are compulsory to preserve the efficiency of existing antimicrobial agents, by following the principles of antimicrobial stewardship.[2,32]

The main solution of the problem is to follow infection prevention and control guidelines such as proper hand hygiene and correct application of basic precautions while applying invasive procedures. These are simple techniques to prevent hospital acquired infections and for implementation of the patient safety guidelines there will be strict need of monitoring of staff and their way of delivering care to patients.

Acknowledgements

We would like to deeply express our thanks to Dr. Junaid Mahmood Alam and Ms. Nuzhat Ansari for their generous support and encouragement.

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