Original Article

Trend of Increased Resistance to Antibiotics in Intensive Care Unit Isolates of a Tertiary Care Hospital Over Two Years 2009 & 2010

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Objective: To asses the antibiotic resistance pattern of Intensive Care Unit bacterial isolates over two year period; 2009 & 2010.

Material & Methods: This observational study was carried out on Intensive Care Unit isolates of Services Hospital Lahore in the Microbiology section of Department of Pathology, Services Institute of Medical Sciences Lahore. All samples processed for microbial cultures were tested for anti-biotic sensitivity / resistance pattern studied and compared.

Results: In 2009,790 samples & in 2010 886 samples were submitted from ICUs to Microbiology Section for culture. Of these, 42% and 46% were culture positive respectively. Gram negative isolates were 294 in 2009 & 308 in 2010. Resistance to all drugs tested was exhibited by 26 (8.78%) and 39 (12.60%) isolates in 2009, 2010. The total number of Acinetobacter isolated increased to 102 in the year 2010 from 74 in the year 2009 with 28 more Acinetobacters than in 2009 and the number exhibiting extensive drug resistance doubling to 28 from 14. Resistance to Imipenem, Tazobactem and Amikin drugs increased in Acinetobacters, Klebsiella and resistance of E coli to Imipenem also increased but decreased in Pseudomonas and E coli. ORSA and coagulase negative staphylococci with Oxacillin resistance were also on the rise, doubling in number from 12 to 25 and 14 to 31 in 2009 & 2010.

Conclusion: Acinetobacter species are on the rise in the intensive care units as is their extensive and multi drug resistance pattern. Increasing Carbepenem resistance is alarming limiting our therapeutic options. Judicious use of antibiotics and curtailing nosocomial infections would deter this upward trend.

Keywords: Acinetobacter, Pseudomonas aeruginosa, EDR, Imipenem, Amikin, Tazobactam, ORSA

Introduction

Nosocomial infections now concern 5-15% of hospitalized patients and can lead to 25-30% infections in patients admitted to intensive care units (ICU).[1] The total estimate of nosocomial infections over a 12 month period in 1975-1976 was >2 million patients with an expected rise of 4 million per year in 1984.[2,3] Hospital-based programs of surveillance, prevention, and control of nosocomial infections were developed during the 1950s and refined in the United States during the 1960s and 1970s.[4] Evaluation of the nosocomial prevention and control program in United States from 1970-1976 by SENIC (Study of the Efficacy of Nosocomial Infection Control) however revealed that due to implementation in a few hospitals, the decline in nosocomial infection rate was 6% of the 2 million patients instead of the expected 32%.[5,2]

ICU acquired infection itself is an independent risk factor for hospital mortality.[6] Risk factors include increased length of stay (>48 hours), mechanical ventilation, trauma, central venous, pulmonary artery and urinary catheters.[7] ICUs in countries with limited resources have rates of device associated, health-care associated infection (HAIs) including central line related blood stream infection (CLAB), ventilator associated infection (VAP), and catheter associated urinary tract infection (CAUTI) three to five times higher than North America, Western Europe and Australian ICUs.[8] The pathophysiology of nosocomial infections include colonization of host by potentially dangerous pathogens from exogenous and endogenous sources e.g methicillin resistant *Staphylococcus aureus* (MRSA), Vancomycin resistant *enterococcus* (VRE), azlo resistant candida spp. and extended spectrum beta lactamases (ESBLs).[9]

Acinetobacter and *Pseudomonas* have emerged as important nosocomial pathogens in critically ill patients. Moreover they show a multiple drug resistance pattern, which is defined as drug resistance

to three groups of antimicrobial drugs on primary isolation of the microorganism.[10]

HAI result in increased length of stay, mortality and cost. CDC released cost range of dollar 28-45 billion.[11] With effective control programs compared to 2001, in 2009 there was a reduction of 58% CLABS and 27000 lives with dollar 1.8 billion health costs saved.[12]

Material and Methods

This cross-sectional, observational study was carried out at the Microbiology Section, Department of Pathology, Services Institute of Medical Sciences Lahore from the period 2009 and 2010 on intensive care units of Services Hospital Lahore. Clinical specimens were obtained from Medical and Surgical ICUs. These included tracheal aspirates, sputum, urine, urine catheter tips, central venous tips, blood, body fluids and pus. These samples were transported to the laboratory within 2 hours of collection.

Samples were cultured onto appropriate culture media as Blood agar, Mac Conkey's agar, Chocolate agar, CLED, Sabouraud's medium. Culture plates were incubated aerobically for 24-48 hours at 37^0C. Isolates were identified by colony morphology, Gram's staining, catalase, coagulase, oxidase and biochemical tests.

Antimicrobial sensitivity testing was performed on Mueller Hinton agar using Kirby-Bauer Disc Diffusion Method in accordance to Clinical and Laboratory Standard Institute Guidelines.[13]

Antibiotic discs used for Gram negative bacteria were Ampicillin, Augmentin, Ceftrioxone, Cefoperazone, Doxycycline, Azectam, Ofloxacin, Imipenem, Amikin & Tazobactam. Antibiotic discs used for Gram positive isolates were Ampicillin, Augmentin, Vancomycin, Oxacillin, Ciproxin, Erythrocin,

Table-1: Culture results of ICU specimens received in microbiology in 2009, 2010.

Year	ICU Samples	Negative Cultures	Positive Cultures	Gram postive cocci	Candida	Contamination
2009	790	409 (51.7%)	331 (41.89%)	39 (4.93%)	43 (5.4%)	7 (0.88%)
2010	886	388 (43.79%)	408 (46%)	92 (10.38%)	86 (9.7%)	4 (0.45%)

Table-2: Gram negative isolates with their antibiotic resistance pattern in 2009.

Microorganism isolated	Total (n=296) N %	Sensitive	EDR (n=26) % =8.78	IPM R (n=58) %=19.59	AK R (n=131) %=44.25	TZP R (n=135) %= 45.60
Acinetobacter	74 (25%)	60	14 (18.91%)	30 (40.54%)	49 (66.22%)	48 (64.86%)
Pseudomonas	88 (429.73%)	83	5 (5.68%)	19 (21.59%)	37 (42.04%)	40 (45.45%)
Klebsiella	58 (19.59%)	56	2 ESBL3 (3.44%)	04 (6.39%)	18 (31.03%)	15 (25.86%)
E Coli	76 (25.67%)	71	5 ESBL11 (6.58%)	5 (6.58%)	27 (35.52%)	32 (43.24)

Table-3: Gram negative isolates and their antibiotic resistance pattern in 2010.

Microorganism isolated	Total (n=308) N %	Sensitive 237	EDR (n=39) % =12.66	IPM R(n=50) %=16.23	AK R (n=137) %= 44.48	TZP R (n=128) %= 41.55
Acinetobacter	102 (33.11%)	74	28 (27.45%)	32 (31.37%)	58 (56.86%)	60 (58.88%)
Pseudomonas	81 (26.29%)	77	4 (4.93%)	03 (3.7%)	31 (38.86%)	23 (28.39%)
Klebsiella	65 (21.10%)	61	4 ESBL 2 (6.15%)	06 (9.23%)	24 (36.9%)	18 (27.69%)
E coli	60 (19.48%)	57	3 ESBL 5 (5%)	09 15%)	24 (40%)	27 (45%)

Table-4: Break-up of gram positive cocci isolated from different samples from ICU.

Year; No	Total Staphylococci	Staphylococcus Aureus Oxacillin R	Staphylococcus Aureus Oxacllin S	Staphylococci Coagulase negative	Streptococci
2009; 40	34 (85%)	12 (30%)	01 (2.5%)	21 (42.5%)	06 (15%)
2010; 92	78 (84.78%)	25 (27.17%)	22 (23.91%)	31 (33.69%)	14 (15.21%)

Fucidic acid. All the antibiotic discs used in the present study were manufactured by Oxoid UK.

Multi Drug Resistant (MDR) organisms were resistant to at least three groups of antibiotics and Extensive Drug Resistant (EDR) organisms were resistant to all drugs tested. The results were analyzed statistically by application of appropriate tests to determine the frequency of antibiotic resistance.

Results

The number of samples processed in Microbiology from ICUs comprised 6% in 2009 and 9% in 2010 of the total samples submitted to the Department of Pathology. Out of the total 790 samples in 2009, 409 did not show any growth. Bacterial growth was yielded by 331 samples and Candida was isolated in 43 cultures. In 2010, of the 886 samples, 408 samples were culture positive for bacteria and 388 culture negative. Candida was isolated from 86 cultures. Some cultures were contaminated (4% &7% ; 2009 & 2010 respectively) hence excluded from positive cultures in both the years (**Table 1**).

The culture results of Gram negative isolates are shown in **Table 2** and **3**. The four most common pathogens isolated are grouped and compared. In 2010, of the sixteen Enterobacteriaceae (other than shown in tables) extensive resistance was exhibited by one Proteus and MDR by 2 of the 11 isolates; 2 Providencia were MDR out of 5. In 2009 of the 27 isolates none showed extensive resistance whereas 3 Enterobacter had MDR pattern .

Antibiotic resistant patterns to three important groups like Imipenem, Amikin, Tazobactam are tabulated in **Table 2** & **3**. The other groups of drugs like Penicillin and Cephalosporins, Quinolones showing mostly resistant patterns are not mentioned here.

Similarly Gram positive isolates are shown in **Table 4**. Oxacillin Resistant Staphylococcus aureus (ORSA) as well as Oxacillin Sensitive Staphylocoocus aureus (OSSA) were resistant to septran, gentacin and erythrocin. Streptococci were also resistant to these drugs.

Discussion

The number of patients admitted to hospitals is increasing annually and so is the number of patients to intensive care units. Half of all pneumonias and life threatening blood stream infections occur in ICUs.[14] They are most frequently isolated from respiratory tract[15,7] urinary tract[16] and wounds[17] in such a setting. However, in some studies blood is the most common[18] or second most common specimen[15] to yield *Acinetobacter*.

The Gram negative bacteria both fermenters and non-fermenters have emerged as prominent nosocomial pathogens. The nosocomial pathogens are showing an alarming increase in *Acinetobacter* species with a Multi Drug Resistant pattern or extensive resistant pattern (EDR) in these high dependency units.[10] In the present study, in 2010 non-fermenters comprised almost 60%(n= 183) of positive cultures (n=308). The most prevalent bacterium was *Acinetobacter* (n=102) with 67 (65.7%) samples from upper respiratory tract mainly from the trachea 63 (61.76%) samples. *Pseudomonas aeruginosa* were 81 with 43 (53.1%) samples from respiratory tract, tracheal samples being 37 (45.7%). In 2009 non -fermenters comprised 54.7% (n=162) bacteria of positive cultures (n=296). The predominant organism in 2009 was *Pseudomonas aeruginosa* (29.72%) followed by *E coli* (25.67%) and *Acinetobacter* (25%) of positive cultures. Eighty-six samples were from trachea only.

The total number of extensive drug resistance gram negative isolates belonging to the groups in **Tables 2** & **3** were 39 out of the n=308 positive cultures (12.66%) in 2010 compared to 26 of total n=296 positive cultures (8.78%) in 2009. The increase in EDR pathogens was by 23.88% in a year.

The year 2010 exhibited an 8% increase in the total *Acinetobacter* isolates with 8.54% increase in EDR. This increase is not much compared to 51% over an 8 year period from 2001-2008 in a military medical centre based USA study.[10] EDR *Acinetobacters* comprised (71%) of the total 39 EDRs isolated that year. A study from Rawalpindi, Pakistan reports 181 (66%) MDR *Acinetobacter* and 33 (18%) EDR *Acinetobacter* out of 276 isolates.[19] Falgas & Kopterides 2006 state that use of carbepenems and third generation cephalosporins is related to MDR *Acenatobacter baumanni* phenotype.[20] In the present study the rest of the Gram negative groups expressed a combined resistance of (3.6%) of the total 308 isolates. In 2009 *Acenatobacter* comprised 25% of 296 positive cultures with 19% of the group exhibiting EDR pattern. However the combined resistance (4.05%) of the other pathogenic groups was more (0.45%). This increase was contributed mainly by *E coli* which were 16 more in number than in 2010 and EDRs (2% more than 2010) with 11 ESBLs (14.5% of 76 *E coli* isolates); 5 of them also EDRs, adding to the resistant group. However there was a decrease in this trend in 2010 (6 EDRs less) with *Acinetobacter*

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