

Prospective Evaluation and Mortality Outcome of Nosocomial Infections in Medical Intensive Care Unit at Tertiary Care Teaching Centre in Mumbai

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Abstract

Background: Hospital acquired infections are a worldwide phenomenon and infection rates in ICU's have been documented to be ranging from 12% to 45%.

Methods and material: To study epidemiology of nosocomial infections and its clinical outcome.

Study design and setting: It is a prospective observational study; carried out in the Medical intensive care unit (MICU) of a tertiary care teaching hospital.

Results and conclusion: 205 patients developed nosocomial infection. The commonest nosocomial infections developing in MICU were Ventilator Associated Pneumonia (VAP); hospital acquired pneumonia followed by urinary tract infection. 94.1% isolates were Gram-negative and Gram-positive contributing to 2.5%, of which most common organisms isolated were Klebsiella, Acinetobacter and *E. coli*.

93.4% of blood stream infections were associated with intravenous lines, 68.1% of pneumonia with intubation, 91.7% of UTIs were associated with urinary catheter. As number of risk factors increase, like duration of mechanical ventilation, prolonged ICU stay (60.0%), increasing age, and number of organs failed, mortality increased significantly. Sensitivity of *E. coli* isolates to carbapenams, polymyxin was 100%. Klebsiella and Acinetobacter showed a maximum sensitivity to carbapenem, polymyxin followed by piperacillin-tazobactam. 75.1% of patients with nosocomial infections improved and mortality in current study was 30.3%.

Keywords: Critical illness; Nosocomial infection; Antibiotics

Introduction

A Nosocomial infection also called "Hospital acquired infection" can be defined as: "An infection occurring in a patient, in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge and also occupational infections among staff of the facility" [1].

The term "Healthcare associated infection" is now widely used instead of the traditional "Nosocomial infection" and is defined by the Centre for Disease Control and Prevention (CDC) "as a localized or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s). There must be no evidence that the infection was present or incubating at the time of admission to the acute care setting" [2].

The most frequent nosocomial infections are blood stream infections, urinary tract infections, lower respiratory tract infections and infections of surgical wounds. The WHO studies, and others, have shown that the highest prevalence of nosocomial infections occurs in intensive care units and in acute surgical and orthopaedic wards. Infection rates are higher among patients with increased susceptibility because of old age, underlying disease, or chemotherapy. In the USA the most frequent type of infection, hospital wide is urinary tract infection (36%), followed by surgical site infection (20%), bloodstream infection (BSI), and pneumonia (both 11%) [3]. In France, the most common infection sites are urinary tract infections (30.3%), pneumonia (14.7%), infections of surgery sites (14.2%), infections of the skin and mucous membrane (10.2%), other respiratory infections (6.8%) and bacterial infections/blood stream infections (6.4%) [4].

A prevalence survey conducted under the auspices of WHO in 55 hospitals of 14 countries representing 4 WHO Regions (Europe, Eastern

Mediterranean, South-East Asia and Western Pacific) showed an average of 8.7% of hospital pts had nosocomial infections. At any time, over 1.4 million people worldwide suffer from infectious complications acquired in hospital [5]. The highest frequencies of nosocomial infections were reported from hospitals in the Eastern Mediterranean and South-East Asia Regions (11.8 and 10.0% respectively), with a prevalence of 7.7 and 9.0% respectively in the European and Western Pacific Regions [6]. International comparisons of nosocomial infection rates in various countries are as follows United States (10%), France (21.6%), Italy (6.7%), United Kingdom (10%), Finland (8.5%), and India (19.7%) [3,7-11].

A 6-year surveillance study from 2002-2007 involving intensive care units (ICUs) in Latin America, Asia, Africa, and Europe, using CDC's NNIS definitions (National nosocomial infection surveillance), revealed higher rates of central-line associated Blood Stream Infections (BSI), Ventilator Associated Pneumonias (VAP), and catheter-associated urinary tract infections than those of comparable United States ICUs [12]. In 2005, the National Healthcare Safety Network (NHSN) was established by CDC with the purpose of integrating and succeeding previous surveillance systems at the Centres for Disease

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Control and Prevention [13]. Percentage of most frequently isolated nosocomial organisms as per CDC, National Nosocomial Infection Surveillance (NNIS) system (January1990-March1996) and the top 3 pathogens in various nosocomial infections are shown in Tables 1 and 2 [13-17].

Material and Methods

It is a prospective observational study done in the Medical Intensive Care Unit (MICU) of a tertiary care teaching public hospital and, we aimed, to study rates of nosocomial infections (as per CDC definitions of nosocomial infections in adults) [18-21], sites of infections and risk factors involved, empirical antibiotics used in treatment and its effectiveness by studying culture sensitivity of various body fluids/secretions, time of initiation of antibiotics, effects of anti biogram on clinical outcome. We included all adult patients (pts), who have been admitted in critical care unit for more than 48 hours. Patients, who already have an infection and were on antibiotics within less than 48 hours, were followed for superadded infections. We excluded surgical, immunocompromised pts, and those below 12 years of age. Institute's Ethics committee approval was taken. After valid written informed consent, all patients were assessed, investigated, and treated as per the existing practices without disturbing their routine care appropriate for the disease condition till either the patient was discharged from MICU or expired. All hospital infection control practices were strictly adhered to. All the routine investigations done in MICU patients were taken into consideration. We noted all the haemodynamic parameters Type and class of antimicrobial drugs used, route of administration, dosage and its frequency, duration of antimicrobial drug used, reason for

selection of drug, reason for change of drug were noted. Resistance and sensitivity of various organisms isolated in present study to the drugs used to treat patients in current study were those that were supplied under government schedule.

Study Design and Setting

It is a prospective observational study; and was carried out in the MICU of a tertiary care, teaching, public hospital in India over a period of 2 years.

Statistical Analysis

Outcome of each nosocomial infection was classified as either survived (improved) or expired. Data thus obtained was statistically analysed, using Pearson Chi-square test and logistic regression analysis using SPSS software.

Results

Out of 2935 patients admitted to MICU during the study period, 205 patients developed nosocomial infections, with an incidence rate of 14.31% during study period. Results are noted in Tables 3-5.

Discussion

Nosocomial infection rates in ICU's have been documented to be highest of all hospital acquired infections, ranges from 12% to 45%. The data from various studies shows variable results of nosocomial infection in MICU statistics, Ak et al. reported 25.6% mortality, Ustan et al. reported 45.4%, Madani N et al. reported 14.5%, Sax et al. reported 29.7%, Habibi et al. reported 34.1%, Rizvi et al. reported 39.7%, and Present study had 14.31% mortality rate [22-27].

In present study, majority of patients (85 pts) developing nosocomial infections were between age group of 21-40 years (41.5%) and 29.8% (61 pts) patients were between age group of 41-60 years which may be explained by the higher incidence of patients in age group of 21-40 years getting admitted with complications. The mean age of patients was 44.29 years in present study. Dahmash et al. included patients with age ranging from 14 to 100 years with median age being 54 years [28]. In another study done by Gagneja et al. it was found that 21.61% of patients were in age group of less than 17 years, 42.15% in 18-64 years and 36.38% were of more than 65 years of age [29]. The present study showed higher mortality rate in age group of >80 years (50%) followed by second peak in the age group between 41-60 years (36.1%) which was not statistically significant.

In current study, 63.4% (130 pts) of MICU patients developing nosocomial infections were males while females (75 pts) contributed to 36.6% of total cases. In study done by Dahmash et al. 51.4% were males while 48.6% were females [28]. Most frequently identified nosocomial infections in current study were pneumonia (65.9%) (VAP responsible for 44.9% of cases), Urinary Tract Infections (UTI) (17.6%) followed by wound infections (9.3%). Habibi et al. showed that 77% had pneumonia, 24% had urinary tract infection, and 9% had blood stream infection which is comparable to our study [26]. Ak et al. and Moreno et al. showed that blood stream infection was most common infection followed by VAP and UTI [22,30]. While, Lyytikainen et al. showed Surgical Site Infection (SSI) (29%) being most common followed by UTI (19%) [10].

In current study, most frequently isolated organisms were *Klebsiella pneumoniae* (35.1%), *Acinetobacter baumannii* (24.9%) and *E. coli* (16.5%). Kallel et al. showed multidrug-resistant *P. aeruginosa* (44.7%) and *A. baumannii* (21.3%) being most frequently isolated

Pathogens	Percentage
<i>Staphylococcus aureus</i>	13
<i>E. coli</i>	12
Coagulase negative staphylococcus	11
Enterococcus	10
<i>Pseudomonas aeruginosa</i>	9
Enterobacter	6
<i>Candida albicans</i>	5
<i>Klebsiella pneumoniae</i>	5
<i>Proteus mirabilis</i>	3
Other Candida	2
Other fungi	2
<i>Serratia marcescens</i>	1
Acinetobacter species	1

Table 1: Percentage of most frequently isolated nosocomial organisms as per CDC.

Infection	Organisms
Bloodstream infections	Coagulase-negative staphylococci (38%)
	Enterococcus (11%)
	<i>S. aureus</i> (9%)
	<i>Candida albicans</i> (5.5%)
Pneumonia	<i>P. aeruginosa</i> (22%),
	<i>S. aureus</i> (17%)
	<i>Haemophilus influenzae</i> (10%)
Urinary tract infections	<i>Escherichia coli</i> (19%)
	<i>C. albicans</i> (14%)
	<i>P. aeruginosa</i> (13%)
Surgical site infections	<i>S. aureus</i> (20%)
	<i>P. aeruginosa</i> (15%)
	Coagulase-negative staphylococci (14%).

Table 2: The top 3 pathogens in various nosocomial infections.

Sr. no.	Parameter (n=205)	Mortality (%)	Mortality in nos.	p-value
1.	Age group			
	≤20 yrs	6.8%	2 out of 12 pts	
	21-40 yrs	41.5%	34 out of 51 pts	
	41-60 yrs	29.8%	22 out of 39 pts	
	61-80 yrs	21.0%	16 out of 27 pts	0.463
2.	>80 yrs	1%	1 out of 1 pt	
	Distribution among the cases of sex			
	Male	64.6%	83 out of 130 pts	-
	Female	35.4%	26 out of 75 pts	
3.	Length of ICU stay (days)			
	<7	47.2%	17 out of 36 pts	
	8-15 days	36.6%	37 out of 110 pts	
	16-30 days	23.8%	12 out of 44 pts	0.061
	>30 days	60%	9 out of 15 pts	
4.	No. of organs involved and final outcome			
	0	9.9%	7 out of 71 pts	
	1	41.9%	31 out of 74 pts	0.599*1/10 ⁸
	2	58 %	29 out of 50 pts	
	3	77.8%	7 out of 9 pts	
	4	100%	1 out of 1 pt	
5.	Antibiotic used and final outcome			
	Started empirically	56.4%	22 out of 39 pts	
	Started empirically and modified according to	31.9%	52 out of 163 pts	
	Culture sensitivity			0.017
	According to culture sensitivity	33.3%	1 out of 3 pts	
6.	Mechanical ventilation in days and outcome			
	≤7			
	>7	52%	26 out of 50 pts	0.254*1/10 ¹¹
	No mechanical ventilation	59.1%	39 out of 66 pts	
		11.2%	10 out of 89 pts	
7.	Nosocomial infection and final outcome			
	Ventilator associated pneumonia	56.5%	52 out of 92 pts	
	Urinary tract infection	27.8%	10 out of 36 pts	0.523*1/10 ⁹
	Wound infection	42.1%	8 out of 19 pts	
	Blood stream infection	26.7%	4 out of 15 pts	
	Hospital acquired pneumonia	2.3%	1 out of 43 pts	

*Multiplication, pts-patients

Table 3: Association amongst the cases and final outcome.

organisms [31]. Ak et al. reported that 68.8% of the isolates were Gram-negative, 27.6% were Gram-positive [22]. While present study showed 94.6% isolates being Gram-negative with Gram-positive organisms contributing to only 1.5% isolates. Ak et al. reported that 3.6% of the isolates were fungi, which is comparable with our study which showed 3.9% of the isolates being fungi. [22].

In current study, 66.7% isolates of *Acinetobacter baumannii*, 73.6% isolates of *Klebsiella pneumoniae* and 64.7% isolates of *E. coli* were ESBL (Extended spectrum beta lactamases). Most common infection caused by ESBL organisms was pneumonia (71.6%) with VAP contributing to 52.3% of cases followed by UTI (15.6%). Isolate from pts with VAP caused by ESBL organisms was *Acinetobacter baumannii* (49.1%) followed by *Klebsiella pneumoniae* (40.4%). While most common isolate patients with UTI caused by ESBL organisms

was *Klebsiella pneumoniae* (70.6%). In present study, no significant difference in mortality was found among the patients with nosocomial infections caused by non-ESBL organisms (42.1%) and those caused by ESBL organisms (43.1%). The mortality was higher in cases with non-ESBL strains of *Acinetobacter baumannii* (70.6%) as compared to ESBL strains (55.9%). While in case of *Klebsiella pneumoniae* ESBL strains (39.6%) were associated with higher mortality as compared to non-ESBL strains (10.5%). In case of *E. coli*, mortality was almost equal in both ESBL (31.8%) and non-ESBL (33.3%) strains. Fagon et al. showed that pneumonias occurring in ventilated patients were especially those due to *Pseudomonas* or *Acinetobacter* species and were associated with considerable mortality (71.3%) in excess of that resulting from the underlying disease alone, and significantly prolong the length of stay in the MICU [32].

In present study, organism's isolated from patients with UTI were *E. coli* (55.5%), *Klebsiella pneumoniae* (25.0%) and *Pseudomonas aeruginosa* (16.7%). Bagshaw et al. reported their findings as *E. coli*, *Pseudomonas*, *Enterococcus* and *Candida* [33]. In similar study done

Risk factor	Number of patients	Percentage
Outcome of nosocomial infection		
Expired	75	36.6%
Survived	130	63.4%
Organs involved		
Respiratory system	72	35.12%
Renal	50	24.3%
Neurological	48	23%
Hepatic	23	11.2%
Cardiovascular	10	4.9%
Hematological	2	1%
Invasive procedures		
Central Lines	198	96.6%
Foley's catheterization	190	92.6%
Nasogastric tube	169	82.6%
Intubation	106	51.7%
Tracheostomy	23	11.2%
Dialysis	21	10.2%
Diabetes mellitus		
Present	37	18%
Absent	168	82%
Hypertension		
Present	31	14.6%
Absent	175	85.4%
Chronic obstructive airway disease		
Present	26	12.7%
Absent	179	87.3%

Table 4: General characteristics of the study population based on parameters.

Infection	Organisms
Bloodstream infections	<i>Klebsiella pneumoniae</i> (40%)
	<i>Acinetobacter Boumannii</i> (33.3%)
	Coagulase negative staphylococcus (20%)
Pneumonia	<i>Klebsiella Pneumoniae</i> (73.6%)
	<i>Acinetobacter Boumannii</i> (66.7%)
	<i>E. coli</i> (64.7%)
Urinary tract infections	<i>E. coli</i> (55.4%)
	<i>Klebsiella pneumoniae</i> (25%)
Wound infections	<i>Pseudomonas aeruginosa</i> (16.7%)
	<i>Klebsiella pneumoniae</i> (31.6%)
	<i>Pseudomonas aeruginosa</i> (21%)

Table 5: The top 3 pathogens in various nosocomial infections in current study.

by Laupland et al. the most common UTI aetiologies were found to be Enterococcus species (24%), *Candida albicans* (21%), and *Escherichia coli* (15%) [34]. There were no *Candida* species isolated from patients with nosocomial UTI in our study which is in contrast to other studies mentioned above [33,34].

In the current study, organism's isolated from patients with nosocomial pneumonia were *Klebsiella pneumoniae* (37.8%), *Acinetobacter baumannii* (32.6%) and *Pseudomonas aeruginosa* (12.6%). A 5 years (2004-2009) study done by Gagneja et al. reported *Pseudomonas aeruginosa* (30-50%) as most common organism followed by *Klebsiella* species, they also reported that the rate of isolation of *Acinetobacter* species increased from 11.78% (2004-2005) to 25% (2008-2009) becoming the second most common isolate [29]. Trivedi et al. showed enteric Gram-negative organisms were commonest isolates (61.9%), followed by *Staph aureus* (29.8%) [35]. While in present study, 94.8% of isolates causing nosocomial pneumonia were Gram-negative organisms.

In present study, 42.4% of isolates causing VAP were *Acinetobacter baumannii* followed by *Klebsiella pneumoniae* (29.3%), *Pseudomonas aeruginosa* (10.9%). Chatre and Fagon showed that *Staphylococcus aureus*, *Pseudomonas* and Enterobacteriaceae were most common among isolates causing VAP [36]. Richard et al. reported their findings as *Pseudomonas* and *Acinetobacter* being most common organisms causing VAP [37]. In another study done by Japoni et al. most commonly isolated organisms were *Acinetobacter*, MRSA (methacillin resistant staphylococcus aureus), *Pseudomonas* and MSSA (methacillin sensitive staphylococcus aureus) [38]. While Esperatti et al. showed that non-fermenter, enteric Gram-negative bacilli and MSSA were most commonly isolated from patients with VAP [39].

In current study, most common bloodstream infection isolates were *Klebsiella pneumoniae* (40.0%), *Acinetobacter baumannii* (33.3%) and Coagulase Negative Staphylococci (CONS) (20.0%). Edmond MB et al. found that Gram-positive organisms accounted for 64% of cases, Gram-negative organisms accounted for 27%, and 8% were caused by fungi with most common organisms being CONS (32%), *Staphylococcus aureus* (16%), and Enterococci (11%) [40]. Laupland et al. showed *Staphylococcus aureus* (18%), CONS (11%), and *Enterococcus faecalis* (8%) being most common bloodstream infection isolates [41]. Thus Edmond et al. differs from our study where Gram-negative organisms were most common bloodstream infection isolates (80.0%) demonstrating the changing trends of the isolates [40].

In present study, most common isolates from wound infection were *Klebsiella pneumoniae* (31.6%) followed by *Pseudomonas aeruginosa* (21.0%). Peromet et al. showed that most common organisms isolated from pressure ulcers were *Proteus mirabilis*, group D streptococci, *Escherichia coli*, *Staphylococcus* species, *Pseudomonas* species, and *Corynebacterium* organisms [42].

In present study, 93.4% of blood stream infections were associated with central lines, 68.1% of pneumonia with intubation, 91.7% of UTI's were associated with urinary catheter. Rosenthal et al. reported that VAP posed the greatest risk (41% of all device-associated infections or 24.1 cases [range, 10.0 to 52.7 cases] per 1000 ventilator days), followed by Central Venous Catheter (CVC)-related bloodstream infections (30% of all device-associated infections (DAI) or 12.5 cases [range, 7.8 to 18.5 cases] per 1000 catheter days) and catheter-associated urinary tract infections (29% of all device-associated infections or 8.9 cases [range, 1.7 to 12.8 cases] per 1000 catheter days) [43].

In current study, patients with 1-2 risk factors (100%) had better

survival than those with 3 or more risk factors (60.1%). Majority of patients in present study (85.5%) stayed for more than 7 days in MICU, mortality rate was high in patients with prolonged ICU stay (60.0%) followed by second peak in patients with ICU stay of less than 7 days (47.2%), most of these patients were referred from other hospitals in moribund condition. Wong et al. showed that the mortality for long-stay patients approached 50% which is comparable with our finding [44]. Similar finding was observed in the study done by Laupland et al. [45] While Williams et al. showed that an increase in length of stay was not independently associated with an increased risk of hospital mortality with most of hospital deaths occurring within the first 10 days in ICU [46].

The patients on mechanical ventilation (56.0%) had higher mortality as compared to non-ventilated patients (11.2%), and as duration of mechanical ventilation increases, mortality also increased significantly. The risk factors such as Diabetes mellitus, hypertension, COAD and duration of mechanical ventilation were found to be associated with development of VAP, but association was not statistically significant. (Table 6) This is in contrast to the study done by Craven and Steger which showed that host factors, oropharyngeal and gastric colonization, cross-infection, and complications from the use of antibiotics and nasogastric and endotracheal tubes increased the risk of bacterial VAP [47].

In current study, increasing age was associated with higher risk, whereas Diabetes Mellitus, female sex, foley's catheter were not statistically associated with risk of developing ICU-acquired UTI in logistic regression analysis (Table 7). In a study done by Bagshaw and Laupland it was found that indwelling urinary catheters, increased duration of urinary catheterization, female sex, length of stay in a ICU, and preceding systemic antimicrobial therapy were associated with risk of developing ICU-acquired UTI [33]. No differences in vital signs on admission, routine blood tests, APACHE II and TISS scores (therapeutic intervention scoring system), or overall hospital mortality rate were observed among patients who developed an ICU-acquired UTI as compared with those who did not.

In present study, it was found that 88.21% isolates of Enterobacteriaceae, 93.75% isolates of *Acinetobacter baumannii*, 89.4% isolates of *Klebsiella pneumoniae*, and 81.5% cases of *E. coli* were resistant to ceftriaxone. But this finding is in contrast to studies done by Moreno et al. and Rosenthal et al. and Cuellar et al. in western world which

Variables	B	S.E.	Wald	df	Sig.	Exp(B)
Risk factor-Diabetes mellitus (No)	-0.261	0.673	0.150	1	0.698	0.770
Risk factor-Hypertension (No)	0.609	0.693	0.772	1	0.380	1.838
Risk factor-COAD (No)	-0.473	0.818	0.334	1	0.563	0.623
Risk factor-Mechanical Ventilation (<7days)	-	-	0.552	2	0.759	-
Risk factor-Mechanical Ventilation (>7 days)	-0.358	0.482	0.552	1	0.457	0.699
Risk factor-Mechanical Ventilation (No)	-22.776	4246.692	0.000	1	0.996	0.000
Constant	1.671	1.065	2.464	1	0.117	5.318

B: Coefficient for the constant in the null model (also called the "intercept")

S.E.: Standard error around the coefficient for the constant

Wald: Wald chi-square test

Df: Degree of freedom

Sig: Significance

Exp (B): Exponentiation of the B coefficient

VAP: Ventilator Associated Pneumonia

Dependent variable encoding: For VAP yes, it's 1

Table 6: Binary Logistic Regression between 'VAP' as Dependent variable and a set of Independent (Predictor) variables.

Variables	B	S.E.	Wald	df	Sig.	Exp(B)
Risk factor-Diabetes mellitus (No)	0.428	0.516	0.689	1	0.407	1.534
Age (years)	0.027	0.011	5.728	1	0.017	1.027
Sex (Female)	0.198	0.386	0.264	1	0.608	1.219
Risk factor-Foley's catheter (Yes)	-0.361	0.703	0.264	1	0.608	0.697
Constant	-2.887	1.008	8.195	1	0.004	0.056

B: Coefficient for the constant in the null model (also called the "intercept")

S.E.: Standard error around the coefficient for the constant

Wald: Wald chi-square test

Df: Degree of freedom

Sig: Significance

Exp (B): Exponentiation of the B coefficient

UTI: Urinary Tract Infection

Dependent variable encoding: For UTI yes, it's 1

Table 7: Binary Logistic Regression between 'UTI' as Dependent variable and a set of Independent (Predictor) variables.

showed resistance of Enterobacteriaceae to ceftriaxone was between 40-50% [31,43,48]. In current study, 48.9% isolates of *Acinetobacter baumannii*, 25.4% isolates of *Klebsiella pneumoniae*, and 4.3% cases of *E. coli* were resistant to piperacillin-tazobactam and it was found that about 37.5% isolates of *Pseudomonas aeruginosa* were resistant to ciprofloxacin, whereas studies done by Rosenthal et al. and Cuellar et al. found resistance between 40%-70% [43,48] Further, 84.2% isolates were sensitive to meropenem, while 93.8% isolates were sensitive to imipenem. Resistance of *Pseudomonas aeruginosa* to imipenem was found to be low (6.2%) which is in contrast to other studies done by Moreno et al. and Cuellar et al. which reported resistance in the range of 13-38% [30,48]. In present study, sensitivity of *Staphylococcus aureus* and CONS to methicillin was not tested. In studies done by Rosenthal et al. and Cuellar et al. it was found that methicillin resistant *Staphylococcus aureus* were in range of 75-95% [43,48]. Emerging drug resistance may be explained by the indiscriminate use of antibiotics in developing countries like India.

In present study, sensitivity of *E. coli* isolates to Carbapenems and Polymyxin was 100%. While *Klebsiella pneumoniae* and *Acinetobacter baumannii* showed a maximum sensitivity to carbapenem, polymyxin followed by piperacillin-tazobactam. *Pseudomonas aeruginosa* showed a maximum sensitivity to piperacillin-tazobactam followed by Imipenem. In current study 100% isolates of ESBL organisms were resistant to amoxicillin-clavunate and ceftriaxone. 60.0% isolates of ESBL *Acinetobacter baumannii*, 74.5% isolates of ESBL *Klebsiella pneumoniae* and 94.1% isolates of ESBL *E. coli* were sensitive to piperacillin-tazobactam. While 75.0% isolates of ESBL *Acinetobacter baumannii*, 88.6% isolates of ESBL *Klebsiella pneumoniae* and 100.0% isolates of ESBL *E. coli* were sensitive to meropenem. 100% isolates of ESBL organisms were sensitive to Carbapenems. While 79.2% isolates of ESBL *Acinetobacter baumannii*, 95.6% isolates of ESBL *Klebsiella pneumoniae* and 100.0% isolates of ESBL *E. coli* were sensitive to Imipenem. Günseren et al. showed that amikacin, ciprofloxacin and imipenem were effective against, respectively, 41.3%, 48.2% and 92.0% of the ESBL producers, however, only 12.5% of these were susceptible to piperacillin-tazobactam and Cefepime was found to be active against 35.5% of these problem pathogens [49]. Thus our observations found that there is changing trend of organisms causing nosocomial infection and also change in the sensitivity patterns of these organisms to various antibiotics.

Resistance of Gram-negative organisms isolated from patients with lower respiratory tract infections to various antibiotics in current study is ceftriaxone 86.0%, ceftazidime 85.7%, piperacillin-tazobactam 18.4%, gentamicin 73.3%, amikacin 57.8%, netilmycin 53.6%, ciprofloxacin 71.4%, meropenam 31.9% and imipenam 34.8%.

Gagneja et al. showed increasing trend of resistance of Gram-negative organisms to third generation cephalosporins, amoxicillin/clavulanic acid and piperacillin-tazobactam and declining trend of resistance to aminoglycosides, they also showed increasing trend of resistance to carbapenems [29]. Thus, judicious use of older/newer antimicrobial agents is essential to prevent the emergence of multidrug-resistant bacteria in the ICU.

In our study, 3 out of 10 patients with swine flu were females while 7 were males and most common nosocomial infection was lower respiratory tract infection (70%) with HAP contributing to 50% of cases. The most common organism isolated was *Klebsiella pneumoniae* (80%) with ESBL strains contributing to 50% cases followed by *Acinetobacter baumannii* (20%). Out of 10 patients, 4 required mechanical ventilation. 3 patients had 1-2 risk factors while remaining 6 had 3 or >3 risk factors. Piperacillin-tazobactam was used in 70% cases; mostly in combination with levofloxacin (50%). The mortality in patients on mechanical ventilation was 50% and those without ventilation, was 16.7%. 70% patients of swine flu with nosocomial infection survived while 30% died.

In current study, antibiotics were started empirically in 19% cases, while in 79.5% patients antibiotics were started empirically and modified according to culture sensitivity report. Antibiotics started after culture sensitivity report in only 1.5% cases. In present study, ceftriaxone, Piperacillin-tazobactam, Meropenem was started empirically in 51.3%, 35.9%, 5.1% cases and after culture sensitivity reports in 38%, 67.5%, 17.8% cases respectively. The mortality was significantly higher (56.4%) in patients in whom antibiotics started empirically as culture sensitivity report were not made available before the patient had died, as compared to those in whom antibiotics were started empirically and modified according to culture sensitivity report or antibiotics started after culture sensitivity report (32.6%). No significant difference in mortality was found between, in those with antibiotics started empirically and modified according to culture sensitivity report and antibiotics started only after culture sensitivity report.

In our study, we found the statistically significant association between types of nosocomial infections and final outcome. In study done by Esperatti et al. it was found that the type of isolates and outcomes are similar regardless of whether pneumonia is acquired or not during ventilation, indicating they may depend on patients' underlying severity rather than previous intubation [39]. It was seen that patients with Glasgow coma score ≤ 10 at the time of admission had significantly high mortality as compared to patients with >10 . Knaus et al. showed that the mortality was 40.0% in patients with single organ failure as against 98% in three or more organ failure which was consistent with our findings [50]. The commonest procedure performed was insertion of central venous lines in almost 96.58% of patients. It was done especially in cases of circulatory shock, acute renal failure and pulmonary edema for fluid management purpose. Intubations were performed 106 patients (51.7%) mostly for ventilatory support but also for prophylactic purposes to secure the airway. Tracheostomies were performed in 11.2% of the total patients who required prolonged ventilatory support. Amongst the 21 patients who received dialysis, 12 survived, while 9 died. Described by Knaus et al. the mean APACHE II score at time of admission in our study was 16.85; we found that as APACHE II score increases, mortality also increased significantly [50].

In present study, need of mechanical ventilation and elevated APACHE II score at the time of admission were associated with higher mortality while length of MICU stay between 16-30 days were

Variables	B	S.E.	Wald	df	Sig.	Exp(B)
Number of risk factor (Yes)	1.075	0.730	2.168	1	0.141	2.930
Age (years)	-0.013	0.010	1.630	1	0.202	0.987
APACHE II Score at time of admission	0.136	0.024	32.914	1	9.63*1/10¹⁰	1.145
Sex (Female)	-0.436	0.363	1.443	1	0.230	0.646
<i>Klebsiella pneumoniae</i> ESBL (No)	-0.503	0.412	1.492	1	0.222	0.605
<i>Acinetobacter baumannii</i> ESBL (No)	-1.425	0.461	9.565	1	0.002	0.241
Constant	-1.717	0.999	2.956	1	0.086	0.180

B: Coefficient for the constant in the null model (also called the "intercept")

S.E.: Standard error around the coefficient for the constant

Wald: Wald chi-square test

Df: Degree of freedom

Sig: Significance

Exp (B): Exponentiation of the B coefficient

*****: Multiplication

Dependent variable encoding: For Expired yes, it's 1

Table 8: Binary Logistic Regression between 'Final outcome' as Dependent variable and a set of Independent (Predictor) variables.

associated with less mortality in a logistic regression analysis. No statistical significance between factors such as number of risk factors, age, gender and final outcome was found in our study by logistic regression analysis (Table 8). Yologlu et al. showed that extrinsic risk factors such as urinary catheter, mechanical ventilation, total parenteral nutrition, intubations, antimicrobial treatment prior to nosocomial infections, nasogastric catheter and central catheter were associated with nosocomial infections [51].

Conclusion

Thus our observations found that there is changing trend of organisms causing nosocomial infection as compared to the western world, compared to our study where it is multidrug resistant Gram-negative organisms and also change in the sensitivity patterns of these organisms to various antibiotics possibly due to their indiscriminate use.

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