Journal of Advanced Research in Medicine
Volume 9, Issue 1 - 2022, Pg. No. 1-10
Peer Reviewed & Open Access Journal

Research Article

Current Pattern and Clinico-Bacteriological Profile of Healthcare Associated Infections in an ICU Setting: A Study from a Tertiary Care Centre in Delhi

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DOI: https://doi.org/10.24321/2349.7181.202201

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How to cite this article:
Wasi S, Daga MK, Mawari G, Kumar N, Sharma U, Hussain M, Baveja CP. Current Pattern and Clinico-Bacteriological Profile of Healthcare Associated Infections in an ICU Setting: A Study from a Tertiary Care Centre in Delhi. J Adv Res Med. 2022;9(1):1-10.

Date of Submission: 2022-01-31
Date of Acceptance: 2022-02-11
Date of Publication: 2022-02-14

A B S T R A C T

Background: Global prevalence of healthcare associated infections (HAIs) ranges anywhere between 7% and 12% as per WHO estimates. This study was undertaken to understand the pattern and types of HAI at a selected healthcare facility and to determine the common causative agents and their antibiotic susceptibility profile.

Methods: One hundred consecutive patients diagnosed with HAI were enrolled and monitored; the causative organisms isolated on culture were recorded and their sensitivity profiles were generated.

Results: There were a total of 110 HAIs with 10 patients having two infections each. 69 patients had ventilator associated pneumonia (VAP), 21 patients had catheter associated urinary tract infection (CAUTI) patients, 20 patients had central line associated bloodstream infection (CLABSI), and 10 patients had both VAP and CAUTI. All of the HAIs were device associated. 76 pathogens were isolated on culture. No organism was isolated in 40 HAI. Majority (94.7%) of the organisms were gram-negative and all were multidrug resistant. Seventy-seven of the enrolled patients expired while 23 patients were discharged from the hospital.

Conclusions: This study demonstrated that HAIs occur in patients of all age groups; younger patients were not spared. Majority of the HAIs were caused by multidrug resistant gram-negative bacteria and were associated with high mortality. Acinetobacter species was the most common organism associated with HAI.

Keywords: Healthcare Associated Infections (HAIs), Ventilator Associated Pneumonia (VAP), Catheter Associated Urinary Tract Infection (CAUTI), Central Line Associated Bloodstream Infection (CLABSI)

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Introduction

Healthcare associated infections (HAIs), also known as hospital acquired infections or nosocomial infections are one of the leading causes of morbidity and mortality among hospitalized patients. At any given time, approximately 1.4 million patients are affected with HAI worldwide, with global prevalence ranging anywhere between 7% and 12%, as per WHO estimates.[1] Published literature from Indian subcontinent has indicated heterogeneity in reported prevalence with numbers ranging anywhere between 11-83%.[2] HAIs are also a matter of concern in developed countries; however, in developing countries, the magnitude of the problem remains underestimated or even unknown because the diagnosis of HAI is complex and surveillance activities needed to guide interventions require expertise and resources. Prolonged stay in the hospital, presence of medical comorbidities, indwelling catheters along with patient related and environmental factors contribute significantly to the development of HAIs.[3,4] Most frequently diagnosed HAIs are catheter associated urinary tract infection (CAUTI), surgical site infection (SSI), ventilation associated pneumonia (VAP), and catheter related blood stream infection (CRBSI).[2,3,5] There is increased reporting of multidrug resistant organisms as the cause of these infections. The present study was conducted to investigate the pattern and types of HAIs, the causative pathogens and their antimicrobial susceptibility profile in current scenario of increasing antimicrobial resistance and changing microorganisms.

Methodology

This study was a prospective observational study conducted in the Department of Medicine, Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi, India, over a period of one year. Adults more than 18 years of age who had no evidence of infection at the time of admission were included in the study if they developed an infection after a minimum of 48 hours after admission. Any patient below the age of 18 years, patients with pre-existing central line or indwelling urinary catheters or who were known immunocompromised (HIV, malignancy, on immunosuppressants) were excluded from the study. Informed consent was obtained from all the patients. Admitted patients were monitored daily for development of infection during hospital stay. Identification of infection was done based on clinical suspicion and subsequent diagnostic tests. Diagnosis of HAI was based on the Centre for Disease Control diagnostic criteria. The first 100 consecutive patients diagnosed with HAI were enrolled in the study. Clinical history, relevant physical examination, primary diagnosis, and demographic details of all the enrolled patients were obtained. Devices present at any time during hospital stay were noted. Their date of insertion, date of change, date of removal, and total duration was noted. Baseline CBC, Biochemical tests, markers, cultures, chest X ray and other relevant radiological investigations for all the patients were done on admission. These tests were repeated on suspicion of infection or when required. Specific site cultures were also sent on suspicion of infection. Various pathogenic organisms isolated on culture were recorded. Bacterial isolates were subjected to gram staining, hanging drop for motility, catalase and oxidase tests. Their identity was established by a battery of biochemical tests like fermentation of sugars, indole test, citrate utilization test, urease production test and production of H_2S on TSI as per standard protocol. Antibiotic susceptibility testing was performed by Kirby-Bauer's disk diffusion method on Muller-Hinton agar (Hi Media, Mumbai, India) in accordance with the standards of the Clinical Laboratory Standards Institute (CLSI—formerly National Committee for Clinical Laboratory Standards [NCCLS]) guidelines. The panel of antimicrobial agents employed has been given in Supplementary Table 1.

Table 1.Primary reasons for admission in study subjects in different HAI

	HAI (n=100)	VAP (n=69)	CLABSI (n=20)	CAUTI (n=21)
Infectious	31	22	8	6
Neurological	22	15	2	8
Respiratory (None-Infectious)	15	11	3	1
Cardiac	12	7	4	1
Renal	8	5	1	2
CLD	3	2	1	0
Other	9	7	1	3

Study Definitions

Infection that developed after a minimum of 48 hours of admission was considered as HAI.

A pneumonia, where the patient was on mechanical ventilation for more than two calendar days on the date of event with day of ventilator placement being day one and the ventilator was in place on the date of event or the day before, was considered as VAP. If the ventilator was in place prior to inpatient admission, the ventilator day count begins with the admission date to the first inpatient location. Primary bloodstream infection (BSI) is a laboratory confirmed bloodstream infection (LCBI) that is not secondary to an infection at another body site. Secondary BSI is thought to have seeded from a site-specific infection at another body site. A LCBI where an eligible BSI organism is identified and an eligible central line is present on the day of event or the day before is considered as a CLABSI. UTIs are defined using symptomatic urinary tract infection (SUTI) criteria and

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202201

asymptomatic bacteraemia urinary tract infections (ABUTI) criteria. A UTI where an indwelling urinary catheter was in place for more than two calendar days on the date of event with day of device placement being day one and an indwelling urinary catheter was in place on the date of event or the day before, is considered as a CAUTI. If an indwelling urinary catheter was in place for more than two consecutive days in an inpatient location and then removed, the date of event for the UTI must be the day of device discontinuation or the next day for the UTI to be catheter-associated.

Statistical Analysis

The collected data were entered into MS Excel and analyzed on the SPSS 22 software. The quantitative data were analyzed using mean and SD, while the qualitative data were analyzed using proportions. The antibiogram was constructed based on different types of HAI and the antibiotic susceptibility profile was analyzed.

Results

A total of 100 patients diagnosed with HAI were enrolled in our study, out of which 10 patients had 2 infections each, resulting in a total of 110 hospital acquired infections. The age of the patients with HAI ranged from 18 to 75 years with mean(±SD) being 42 (±17) years and median being 42 years. The age of patients with VAP ranged from 18 to 75 years with a mean (±SD) of 42.2 (± 16.8) years and a median age of 42 years. The age of patients with CLABSI ranged from 18 to 75 years with mean (±SD) of 37.3 (± 17.8) years and a median age of 32.5 years. The age of patients with CAUTI ranged from 18 to 72 years with a mean (±SD) age of 43.7 (±19.3) years and a median age of 50. The number of males (61) was more than females (39) in our study. Gender distribution of patients with VAP, CLABSI, CAUTI, and HAI overall HAI is shown in Figure 1. The details of primary reasons for admission in study subjects in different HAI have been shown in Table 1. Since there were 10 patients with both VAP and CAUTI, the diseases were overlapping. All HAIs were device associated. Out of 100 patients with HAI, VAP was present in 69 patients, CLABSI was present in 20 patients, and 21 patients had CAUTI. There were 10 patients with both VAP and CAUTI and 6 patients with VAP had secondary bloodstream infection. The total duration of hospital stays for all enrolled patients ranged from a minimum of 5 days to a maximum of 50 days with a mean (±SD) of 21.16 (±11.85) days and a median of 20 days. The duration of hospital stays of 100 patients for 110 HAIs ranged from 3 to 30 days with mean (±SD) and median being 10.85± (6.69) days and 10 days respectively. The mean (±SD) duration of mechanical ventilation in VAP patients was 10.26 (±6.28) days, the median was 9 days, and the range was between 3 to 30 days. The number of patients who were tracheostomized before developing VAP was 19 (27.5%) while 50 patients (72.5%) were not tracheostomized. Patients with single intubation who developed VAP were 59 (85.5%) while 10(14.5%) were reintubated. Duration of catheterization before development of infection ranged from 3 to 30 days with a mean (±SD) of 10.86 (±6.89) days and a median of 10 days. The mean duration of catheterization for people with CLABSI was 13.35 days, the median was 11 days, and the range was of 4 to 30 days. The mean(±SD) and median durations of catheterization before CAUTI were 10.43(±5.90) days and 10 days respectively, and the range was of 3 to 22 days. Out of the 100 patients, 29 patients had history of hospitalization for a minimum of 2 days within past 3 months, while the remaining 71 patients did not have any prior hospitalization during the same time. All of the patients were given antibiotics in the hospital before development of infection. Out of the 100 patients enrolled in the study, 77 (77%) expired and 23 patients (23%) were discharged from the hospital. There were 8 patients with both VAP and CAUTI who expired. The outcomes of all enrolled patients and the outcomes among different organisms causing HAI are shown in Figure 2. A total of 76 pathogens were isolated on culture which accounted for the nosocomial infections in these patients. No organism could be isolated from 40 cases of HAI. The detailed distribution of 76 organisms isolated in patients of HAI are shown in the Figure 3 and Figure 4 shows the sensitivity pattern of each organism to different antimicrobial agents. Details of antibiotic susceptibility profile of different organisms to various antimicrobial agents are included in Supplementary Tables 1 to 7.

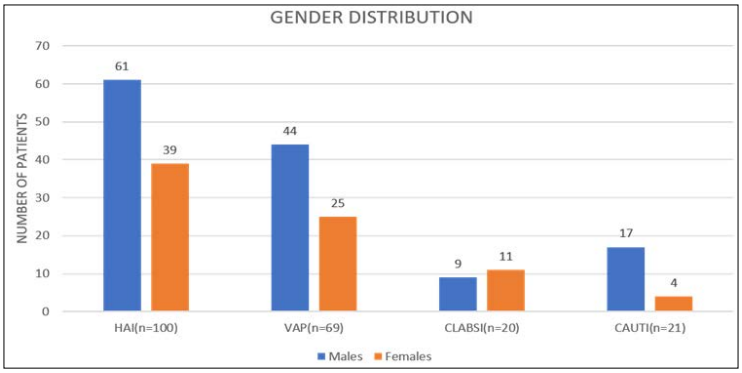

Figure 1.Gender distribution of patients with VAP, CLABSI, and CAUTI, and HAI overall

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202201

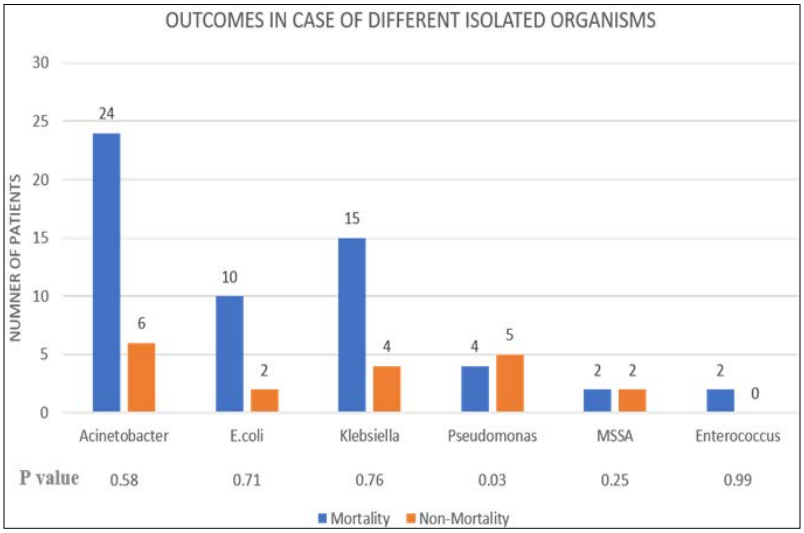

Figure 2.The outcome among patients with HAI caused by different organisms (along with P values)

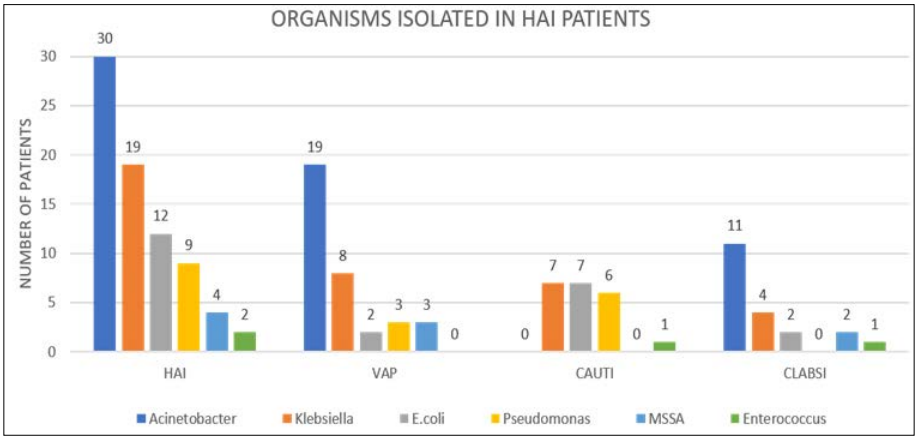

Figure 3.Distribution of organisms isolated in patients of HAI

Discussion

In our study, all the HAIs were associated with the use of invasive devices and majority (92%) of the patients were admitted in ICUs. VAP comprised majority (69%) of the infection followed by CAUTI (21%) and CLABSI (20%). The WHO quotes that the risk of acquiring HAIs is significantly higher in intensive care units (ICUs), with approximately 30% of patients affected by at least one episode of HAIs.[4] The present study was carried out exclusively in ICU setup. The pattern of distribution of diseases in our study was similar to multiple prior published studies. U.S National Nosocomial Infection Surveillance system reports that three major infection sites comprised 68% of all reported infections; nosocomial pneumonias were most frequent, followed by UTIs and primary bloodstream infections (BSIs), and the vast majority of infections were associated with the use of invasive devices (87% of primary BSIs, 83% of nosocomial pneumonias, and 97% of UTIs were associated with central intravenous lines, mechanical ventilation, and urinary catheter respectively).[5] In a prospective observational study by Habibi et al, pneumonia (77%) was the most common infection followed by UTI (24%) and bloodstream infection (24%).[6] Pooled rates of VAP, CLABSI, and CAUTI were 9.4/1,000 mechanical ventilator–days, 5.1/1,000 central line–days, and 2.1/1,000 urinary catheter–days respectively, as reported by International Nosocomial Infection Control Consortium from India.[7]

Demographics

Majority of the patients in our study were young and belonged to 18-30-year age group category (36% overall; 34.8% in VAP, 50% in CLABSI, and 33% in CAUTI). This was contrary to the common finding; that age > 60 year predisposes patients to develop HAI and can be attributed to the varying population characteristic.[4,8,9] When examining gender distribution, males (61) were more common than females (39) in our study. Gender of the patient per se did not have a strong correlation with increased risk of HAI overall as seen in EPIC II study and many other Indian studies.[3,10,11] However, when breaking down the infection into VAP and CAUTI, male gender has been demonstrated to be a risk factor of VAP and female gender likewise for the development of CAUTI. Cook et al in their seminal paper

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202201

published on risk factors of VAP showed higher proportion of male gender afflicted with VAP.[12] Similarly, Rello et al in their large epidemiological study published on VAP showed that male gender strongly correlated with development of VAP.[13] Whether this is causal or correlational is still unknown; however, higher proportion of males smoke in India and are thus predisposed to the development of COPD in comparison to females. This could possibly offer an explanation for higher incidence of VAP in males in our study. Nineteen percent of patients in our study who developed CAUTI were females. Female gender is a non-modifiable risk factor for development of CAUTI.[14] Female patients are susceptible to developing CAUTI, owing to the differences in urethral anatomy, with female urethra being relatively short and wide with straight path into the bladder, making it easy for bacterial entry.

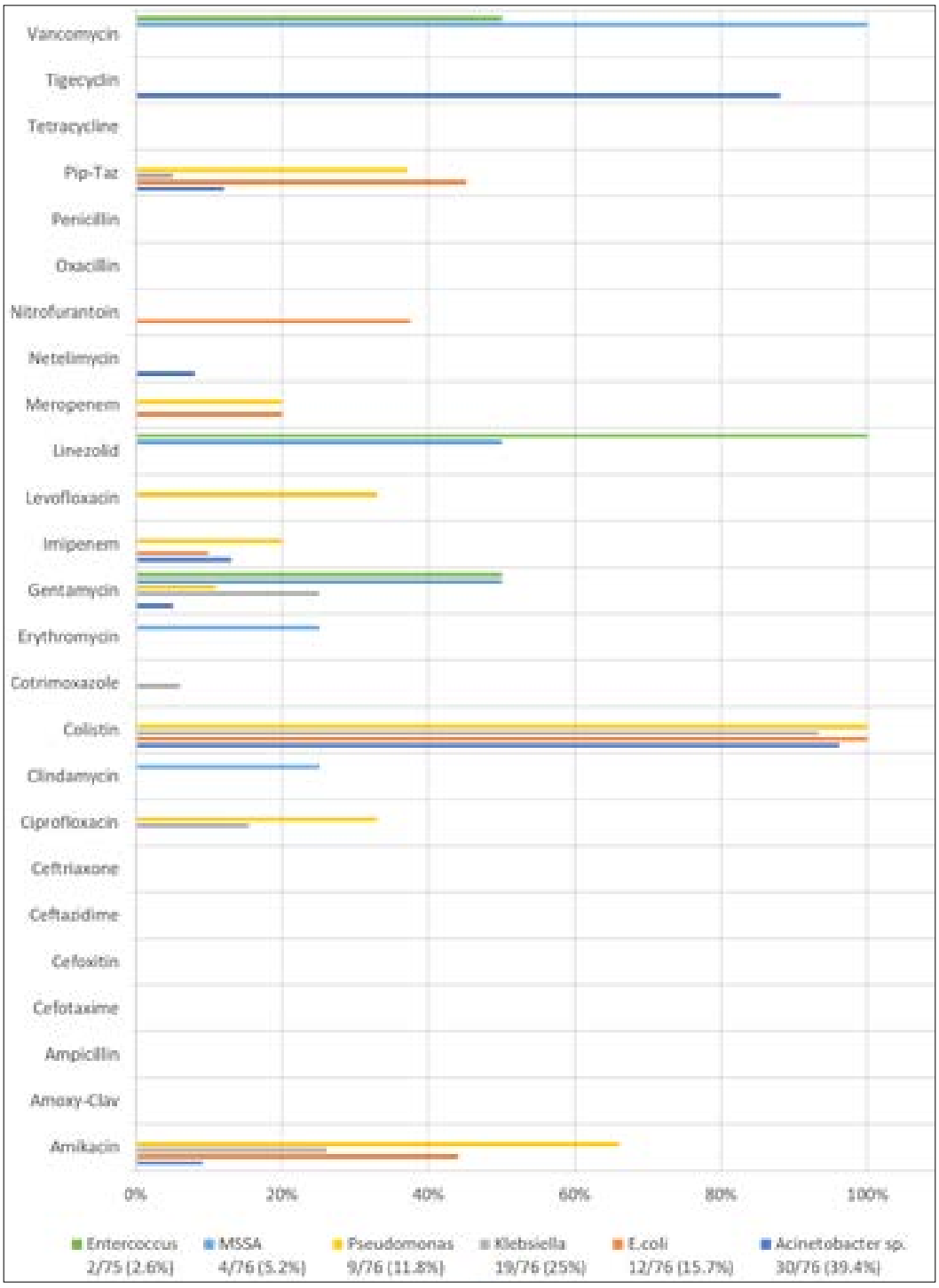

Figure 4.Sensitivity patterns of organisms to different antimicrobial agents

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202201

Organisms Isolated and Antibiotic Sensitivity Profile

A total of 76 pathogens were isolated on culture and accounted for the nosocomial infections in these patients. Majority (92%) were gram-negative organisms and only 8% were gram-positive. All of the isolated organisms were multidrug resistant. The global scenario shows that gram-positive infections are more prevalent in the Western world ICUs. However, gram-negative bugs dominate in India and Asia-Pacific region.[3,7,15] In Asian ICUs, gram-negative isolates constituted 74% as compared to 58% in Western Europe, while gram-positive isolates constituted 34% in Asian ICUs and 49% in Western Europe.[3] Our findings are in corroboration with the other worldwide studies. The National Nosocomial Infections Surveillance System reported a significant increase in the proportion of Acinetobacter among all gram-negative aerobes during the 17 years of the study period.[16] Acinetobacter was also the predominant (39.5%) causative organism in our study. Resistance shown by organisms from developing countries are higher than in developed countries, which is clearly proven in our study. Study from China, analyzing the resistance rate of *Acinetobacter baumannii* and *Pseudomonas aeruginosa,* showed that the resistant rate of *Acinetobacter baumannii* to Meropenem has increased from 32% to 83% in the last 10 years, for piperacillin/tazobactam it has increased from 44.8% to 78.4%. The resistance rate of *P. aeruginosa* to imipenem has been increasing as well, which was 30.3% in 2006 and 45.6% in 2015.[17] High resistance rates have been reported by adult and pediatric ICUs from 40 hospitals in 20 cities of India to International Nosocomial Infection Control Consortium.[7] Numerous studies from developing counties including India show the same of high levels of sensitivity to colistin and high levels of resistance to broad spectrum antibiotics.[6,11,18] Our study shows similar findings. In Ghanshani et al study, all Enterobacteriaceae and pseudomonas were ≥ 95% sensitive to colistin, Klebsiella and Pseudomonas were > 50% resistant to 3rd generation cephalosporin and carbapenems, while E. coli was still > 50% sensitive to carbapenems and Acinetobacter > 50% sensitive to 3rd generation cephalosporin.[11] Gram-positive organisms showed zero sensitivity to penicillin, oxacillin, and tetracycline. MSSA were 100% sensitive to vancomycin, and 50% sensitive to linezolid and gentamycin. Enterococcus was 100% sensitive to linezolid, 50% sensitive to vancomycin. In Dutta et al. study *Staphylococcus aureus* and Enterococcus were 100% sensitive to linezolid and vancomycin and more than 50% resistant to gentamicin, erythromycin, and ciprofloxacin.[18] Similar findings were seen in Ghanshani et al study.[11] Our study and numerous studies worldwide are in concordance. Indiscriminate use of antibiotics for prolonged and inappropriate duration is the possible explanation of such high levels of multidrug resistance in the organisms.

Conclusion

HAI is a major adverse event of healthcare causing significant morbidity, mortality, and economic burden for all patients and healthcare facilities. HAIs can affect patients from all age groups and even the younger population is not spared. Prolonged and indiscriminate use of invasive devices, which is not uncommon among ICUs, is a major preventable risk factor of HAI. Most frequent HAI was VAP followed by CAUTI and CLABSI.

In our study causative organisms were predominantly gram-negative bacteria unlike western countries where majority of HAIs were due to gram-positive bacteria. Acinetobacter was the most common organism isolated from the patients with HAI. All of the isolated organisms were multidrug resistant and associated with high mortality.

Limitations of the Study

- The sample size of the study was small, therefore statistical power of the study is low.
- Our study cannot give information on anaerobic and fungal causative pathogens of HAI as no special culture techniques were employed to isolate them.
- High mortality seen in our study could be due to the severity of the disease they were admitted with and also due to lack of state-of-the-art ICU care.

Declarations

Ethics Approval

This study was conducted only after approval from the Institutional ethics committee, Maulana Azad Medical College, New Delhi.

Funding

No organized funding source was used for the study.

Acknowledgements: None

Conflict of Interests: None

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ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202201

Supplementary Tables

Table 1.Panel of antimicrobial agents employed against various microbes

Enterobacteriaceae	Pseudomonas	Gram-positive bacteria
Ceftriaxone	Ceftazidime	Linezolid
Cefotaxime	Meropenem	Vancomycin
Meropenem	Ciprofloxacin	Clindamycin
Imipenem	Levofloxacin	Penicillin
Piperacillin-tazobactam	Piperacillin-tazobactam	Erythromycin
Gentamicin	Gentamicin	Gentamicin
Netilmicin	Amikacin	Cefoxitin
Amikacin	Imipenem	Oxacillin
Ciprofloxacin	Colistin	Tetracycline
Co-trimoxazole		
Colistin		
Tigecycline		
Ampicillin		
Nitrofurantoin		
Ceftazidime		

Table 2.Susceptibility profile of Acinetobacter species (n=30)

*Antibiotic (isolates tested)	Resistant (%)	Sensitive (%)	Intermediate (%)
Ceftriaxone (19)	19 (100.0)	0	0
Ceftazidime (14)	14 (100.0)	0	0
Cefotaxime (5)	-	-	-
Meropenem (20)	19 (95.0)	0	1 (5.0)
Imipenem (23)	18 (78.3)	3 (13.1)	2 (8.7)
Piperacillin-Tazobactam (24)	18 (69.2)	3 (11.5)	3 (11.5)
Gentamicin (19)	18 (94.7)	1 (5.3)	0
Netilmicin (13)	12 (92.3)	1 (7.7)	0
Amikacin (22)	19 (86.4)	2 (9.1)	1 (4.5)
Ciprofloxacin (19)	19 (100.0)	0	0
Levofloxacin (13)	13 (100.0)	0	0
Colistin (26)	1 (3.9)	25 (96.1)	0
Tigecycline (8)	0	7 (87.5)	1 (12.5)
Ampicillin-sulbactam (2)	-	-	-
Cotrimoxazole (14)	14 (100.0)	0	0

*Not all organisms were tested for all antibiotics.

ISSN: 2349-7181
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Table 3.Susceptibility profile of E. coli organism (n=12)

*Antibiotic (isolates tested)	Resistant (%)	Sensitive (%)	Intermediate (%)
Ceftriaxone (9)	9 (100.00)	0	0
Ceftazidime (2)	-	-	-
Cefotaxime (6)	6 (100.0)	0	0
Meropenem (5)	4 (80.0)	1 (20.0)	0
Imipenem (10)	9 (90.0)	1 (10.0)	0
Piperacillin-Tazobactam (11)	6 (54.5)	5 (45.5)	0
Gentamicin (4)	-	-	-
Netilmicin (1)	-	-	-
Amikacin (9)	4 (44.4)	4 (44.4)	1 (11.1)
Cotrimoxazole (7)	7 (100.0)	0	0
Amoxiclav (3)	-	-	-
Colistin (7)	0	7 (100.0)	0
Ampicillin (8)	8 (100.0)	0	0
Ciprofloxacin (5)	5 (100.0)	0	0
Levofloxacin (8)	8 (100.0)	0	0
Nitrofurantoin (8)	5(63.5%)	3(37.5%)	0

*Not all organisms were tested for all antibiotics.

Table 4.Susceptibility profile of Klebsiella sp.(n=19)

*Antibiotic (isolates tested)	Resistant (%)	Sensitive (%)	Intermediate (%)
Ceftriaxone (17)	17 (100.0)	0	0
Ceftazidime (1)	-	-	-
Cefotaxime (5)	-	-	-
Meropenem (12)	10 (83.3)	0	2 (16.7)
Imipenem (15)	12 (80.0)	1 (6.7)	2 (13.3)
Piperacillin-Tazobactam (18)	17 (94.4)	1 (5.6)	0
Gentamicin (12)	9 (75.0)	3 (25.0)	0
Netilmicin (8)	8 (100.0)	0	0
Amikacin (19)	13 (68.4)	5 (26.3)	1 (5.3)
Cotrimoxazole (15)	14 (93.3)	1 (6.7)	0
Amoxiclav (8)	8 (100.0)	0	0
Colistin (15)	1 (6.7)	14 (93.3)	0
Ampicillin (12)	12 (100.0)	0	0
Ciprofloxacin (13)	10 (76.9)	2 (15.4)	1 (7.7)
Levofloxacin (3)	-	-	-

*Not all organisms were tested for all antibiotics.

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202201

Table 5.Susceptibility profile of MSSA organism. (n=4)

*Antibiotic (isolates tested)	Resistant (%)	Sensitive (%)	Intermediate (%)
Erythromycin (4)	3 (75.0)	1 (25.0)	0
Penicillin (4)	4 (100.0)	0	0
Clindamycin (4)	3 (75.0)	1 (25.0)	0
Linezolid (2)	1 (50.0)	1 (50.0)	0
Vancomycin (4)	0	4 (100.0)	0
Tetracycline (3)	3(100)	0	0
Gentamycin (4)	2 (50)	2 (50.0)	0
Oxacillin (4)	4 (100)	0	0
Ciprofloxacin (3)	3 (100)	0	0
Cefoxitin (3)	3(100)	0	0

*Not all organisms were tested for all antibiotics.

Table 6.Susceptibility profile of Pseudomonas sp. (n=9)

*Antibiotic (isolates tested)	Resistant (%)	Sensitive (%)	Intermediate (%)
Ceftazidime (8)	8 (100.0)	0	0
Gentamycin (9)	7 (77.8)	1 (11.1)	1 (11.1)
Piperacillin-Tazobactam (8)	5 (62.5)	3 (37.5)	0
Meropenem (5)	4 (80.0)	1 (20.0)	0
Imipenem (5)	4 (80.0)	1 (20.0)	0
Amikacin (6)	2 (33.3)	4 (66.7)	0
Ciprofloxacin (6)	4 (66.7)	2 (33.3)	0
Levofloxacin (3)	-	-	-
Colistin (6)	0	6(100)	0

*Not all organisms were tested for all antibiotics.

Table 7.Susceptibility profile of Enterococcus sp. (n=2)

*Antibiotic (isolates tested)	Resistant (%)	Sensitive (%)	Intermediate (%)
Erythromycin (2)	2 (100.0)	0	0
Penicillin (2)	2 (100.0)	0	0
Clindamycin (2)	2 (100.0)	0	0
Linezolid (2)	0	2 (100.0)	0
Vancomycin (2)	0	1 (50.0)	1 (50.0)
Gentamycin (2)	1 (50.0)	1 (50.0)	0

*Not all organisms were tested for all antibiotics.

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.202201