

INFECTIONS AND ANTIMICROBIAL RESISTANCE TRENDS IN ADULT INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL IN EASTERN INDIA

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ABSTRACT

Background: Nosocomial or health care associated infections/ Hospital acquired infection are currently the leading issue in modern clinical practice especially in critical care areas like Intensive care units.

Aim: A prospective observational study was carried out to gather a baseline data of the locally prevalent Pathogens and their antibiotic sensitivity pattern in our Intensive care unit (ICU) over a period of one year in order to plan specific infection control practices.

Methods: All 207 patients included in the study were followed up at frequent intervals (3rd day) for development of symptoms of nosocomial infections (VAP/CAUTI/ CVC-BSI/SSI) till discharge /death. Diagnosis of central vascular catheter-associated bloodstream infection (CVC-BSI), catheter-associated urinary tract infection (CAUTI) and ventilator-associated pneumonia (VAP) were done. For multi-drug resistant Gram negative Organisms double disk synergy test & EDTA disk synergy test were done for ESBL & MBL detection respectively. We did not look for AmpC/ KPC production.

Results: Overall Hospital acquired infection (HAI) rate was 30.3% and 27.71% HAIs per 1000 ICU days. Lower respiratory tract infections were the commonest followed by catheter associated Urinary tract infections. Gram negative organisms were leading over gram positive organisms. *Klebsiella pneumoniae* and *Acinetobacter baumannii* were the more common isolates. Incidence of extended spectrum beta-lactamases and Metallobetalactamases among Gram negative bacteria's was high. Pan drug resistance including tigecycline was noted in 9.6% cases.

Conclusion: HAI rates due to Multi-drug resistant Gram negative bacterial pathogen are too high, with an increased incidence of non- fermenters. A robust hospital infection control program would probably be the best solution to the current HAI issues.

Keywords: Central vascular catheter-associated bloodstream infection (CVC-BSI), catheter-associated urinary tract infection (CAUTI), Extended spectrum beta-lactamases, Hospital acquired infection (HAI), Metallobetalactamases, ventilator-associated pneumonia (VAP)

INTRODUCTION

Nosocomial Infection/ Hospital acquired Infection / Health care associated infections (NI/HAI/HCAI) are not only the leading cause of increased mortality, but adversely affect the quality of life. Grave

economic burden is an added curse.^{1,2} HAIs can occur in pre-morbid patients as well as apparently immunocompetent patients who undergo invasive procedures. There is a five to ten fold rise in the incidence of such infections in the Intensive care units (ICU).³ As the name suggests the care in ICU is always more intensive with more invasive life lines and procedures including surgeries, mechanical ventilation, longer length of stay, more IV and parenteral, tube feeding and parenteral nutrition. As per INNIC studies rate of ventilator-associated pneumonia is 16 per 1000 ventilator days, that is, 3 times higher than in US; the rate of central line-associated bloodstream infection is 7 per 1000 central lines-days, that is, 3 times higher than in US; and the rate of catheter-associated urinary tract infection is 6 per 1000 urinary catheter- days, that is, also 3 times higher than in US.(INNIC).The incidence of HAI in India is ranges somewhere between 4-28% . The reasons for this discrepancy are varied. There is a paucity of data on prevalence of NI from eastern part of India using the standardized definitions HAI rates per 1000 device days. One of the milestone study done on HCAI was by International Infection control Consortium (INICC) at Kalinga Hospital, Bhubaneswar. Health care associated infections are caused by a wide array of microorganisms carried by the patients themselves or acquired from the hospital ecosystem/ health care workers thus differing across different patient populations and the ICU settings. Because of the large disease burden and the consequences attributable, there is a great interest and need to accurately diagnose, and find out the incidence of HAI. The knowledge of the local microbial flora in each setting is crucial for a more effective and rationalized therapy.

With the above background we envisaged the present study to provide a baseline data of the locally prevalent nosocomial pathogens, their antibiotic sensitivity pattern in our ICU and the overall incidence of HAIs in order to guide the development of specific infection control policies and protocols. We aim at development of a reliable methodology for further periodic surveillance of HAI at regular intervals to monitor the impact of infection control practices.

MATERIAL AND METHODS

This was a prospective observational study conducted in Microbiology dept. in collaboration with the Medical intensive care unit (MICU) of our hospital, over a period of one year from Feb 2016 to Jan 2017. The study was approved by the institute research and ethical committees. Informed consent was taken from the patients' next of kin.

Inclusion criteria: All adult patients directly admitted to or transferred from wards to the ICU with more than 48hrs stay within and one or more invasive devices in situ were included in this study.

Exclusion criteria: Patients inhabited for less than 48 hours or died within 48hours were excluded.

Relevant clinical data such as patients vitals, length of stay, details of medication and instrumentation, associated co morbid conditions and the average severity of illness score(ASIS) were collected as per the designed proforma.

Study was performed on 207 patients reporting to microbiology lab of the institute. Patients included in the study were followed up at frequent intervals (3rd day) for development of symptoms of nosocomial infections (VAP/CAUTI/ CVC-BSI/SSI) till discharge /death.

Sampling and Culture Techniques

Diagnosis of central vascular catheter-associated bloodstream infection (CVC-BSI), catheter-

associated urinary tract infection (CAUTI) and ventilator-associated pneumonia (VAP) were done as per CDC-NNIS definitions, as they are adapted internationally. For VAP, in most cases, a deep tracheal aspirate from the endotracheal tube was cultured aerobically and gram-stained, for CVC-BSI, CVC were removed aseptically and the distal 5 cm of CVC was amputated and cultured using a standardized semi quantitative method [15]. Concomitant blood cultures were drawn percutaneously in nearly all cases. A urine sample was aseptically aspirated from the sampling port of UC and cultured quantitatively for diagnosing CAUTI. Pus/tissue or wound swab was collected for detection of SSI from suspected cases. In all cases, standard laboratory methods were used to identify microorganisms, and a standardized susceptibility test was performed using Kirby- Bauer's Method as per CLSI guidelines.

For multi-drug resistant Gram negative Organisms double disk synergy test & EDTA disk synergy test were done for ESBL & MBL detection respectively. We did not look for AmpC/ KPC production. MRSA strains identified using cefoxitin (30µg) disks and D zone test was used for inducible clindamycin resistance. Vancomycin Resistant *Enterococcus* (VRE) was detected using Hi-comb Strip (Hi-media).

RESULT

HAI Rate: Total aggregate ICU days: 7469.5 days, Mean length of stay - 9.5 days. Overall HAI rate was 30.3% (207/681) and 27.71% (207/7469.5x 1000) HAIs per 1000 ICU days.

Site specific Infection: The infection rate was highest in lower respiratory tract (51%) followed by urinary tract infections (21%), wound infections (13%) and blood stream infections (12%).

Risk factors: The major risk factors associated with development of nosocomial infections were diabetes mellitus, cerebro vascular accidents with hypertension, complicated malaria, advanced age, chronic kidney disease, Trauma, surgery, length of stay beyond 96hrs, recent broad antibiotic history and invasive procedures such as endotracheal intubation, urinary catheter or central lines for longer duration. Association of development of infection in ICU with length of stay, duration of invasive device use and prior antibiotic use was statistically significant ($p \leq 0.05$).

Organisms: Major infections found in ICU were due to gram negative bacterias. *Klebsiella pneumoniae* was the most common (34%) followed by *Acinetobacter baumannii* (21%), *Pseudomonas aeruginosa* (18%) *Escherichia coli* (15%), *Staphylococcus aureus* (9%) and *Enterococcus faecalis* (6%). A major junk of NIs were due to *Candida* spp. (17%).

Resistance pattern: Lowest resistance was seen for carbapenems, Piperacillin-tazobactam & cefoperazone-sulbactam combinations. Incidence of ESBLs and MBLs among GNB was high and 69% of the *K. pneumoniae* & 80% of the *E. coli* were phenotypically confirmed ESBL producers. Twelve percent of *Klebsiella pneumoniae* and 13% of *E coli* were carbapenem resistant and 19% of the *Pseudomonas* spp and 37% of the *Acinetobacter* species harbored MBLs. Pan drug resistance including tigecycline was noted in 9.6% cases. Among gram positive organisms, occurrence of MRSA was 65% in this study, none was resistant to Vancomycin. 4% of the infections were caused by *Enterococcus* and 22.2% showed resistance to Vancomycin.

Antibiotic prescribing pattern in our ICU: The most common antibiotics prescribed in our ICU were

piperacillin-tazobactam and meropenem for gram negative coverage and linezolid for gram positive bacteria's, most of the time (55%) it was empirically prescribed. In 42% cases suspicion of infection was microbiologically confirmed.

DISCUSSION

NI is the derivative of two Greek words nosos [disease] and komein [to care for]. CDC/NHSN surveillance definition states: a healthcare-associated infection is a localized or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s) that was not present on admission to the acute care facility and all the elements of a CDC/NHSN site-specific infection criterion were first present together on or after the 3rd calendar day of admission to the facility (day of hospital admission is day 1).

Nosocomial Infections in ICUs, especially those caused by antibiotic-resistant pathogens, is a critical issue, imparting an adverse healthcare outcome for the patient hospitalized in an ICU.

Pathophysiology and risk factors of HAI: In a review, J L Vincent mentions, nosocomial infection develops due to variable interactions of two basic pathophysiologic factors: decreased host defences and colonization with pathogenic or potentially pathogenic bacteria. Depressed defences are quite obvious in critical care setups, as a result of concurrent co-morbidities leading to immune paralysis and increased risk of infection. There are a number of causes for both exogenous and endogenous colonization with microbes. Endogenous bacterial colonization is related to the underlying health problems, more use of external devices/invasive procedures as well as prolonged use of various antibiotics. Among them use of antibiotics in particular is of concern; antibiotics can exert selective pressure on patient's normal flora and replace it by more pathogenic flora. A good number of studies have identified prior use of high end antibiotics as a major risk factor of NI with MDR pathogens as well as *Candida* infections in ICUs.

Epidemiology: The incidence of HAI varies with the type of clinical set-up, the patient population and the defining criteria. As per the INICC study, the single study using standardized criteria, the HAI rate was of 4.4%. The quoted range in India is somewhere between 4% - 28%. In this study the HCAI rate was 27.7 per 1000 ICU days, higher than that of INICC findings, but consistent with findings of other studies. A six-month study conducted in the intensive-care units in the All India Institute of Medical Sciences (AIIMS), New Delhi, found that 140 of 1,253 patients (11%) had 152 hospital-acquired infections. Study of 493 patients in a tertiary teaching hospital in Goa found that 103 people (21%) developed 169 infections⁴⁸.

Site specific infections: The respiratory system (35.92%) was the most common site of infection in the ICU, followed by septicemia (19.41%) and wound infections (6.79%). In a study by Singh S et al VAP was the lead infection, the overall infection rate for CA-UTI, IV-CRBSI, and VAP were found to be 0.6, 0.48, and 21.92 per 1000 device days, respectively.**In a study from 21 adult ICUs from 10 different states of India the baseline VAP rate was 17.43/1000 mechanical ventilator days and in comparison to USA the rate was tenfold higher, 1.8 VAP rate/1000 MV days determined by the CDC NSHN.

Organisms and Antimicrobial resistance: Gram negative organisms were the most common isolates and among them *Klebsiella pneumoniae* was the commonest pathogen in our study, while in other studies NFGNB, esp. *P. aeruginosa* predominated. Findings of INICC from different ICUs of India reported 87.5% *S.aureus* as methicillin resistant. Over all prevalence of MRSA from different parts of India is somewhere between 30-85%. Approximately, INICC findings: 2.6% *Enterococcal* infection, 33.3% VRE.

Antibiotic prescribing pattern: Costs associated with HAI are much more than non HAI cases and half

of the expenditure is due to antibiotics. Apart from cost, the issue of concern is resistance to antimicrobials. N K Ganguly et al mentions that 'Drug selection pressure' is the single most important factor in the evolution of drug resistance in bacteria. In a Meta analysis it is evident that primary care antibiotics by and large is important in development of antibiotic resistance. The effect may last 1-12months and probably is an important driver for the high endemic levels of antibiotic resistance in the community. Antibiotics were started empirically in 64% of the cases; the infections were confirmed in 45.91% cases only.

CONCLUSION

HAI rates due to MDR Gram Negative bacterial pathogen are too high, with an increased incidence of non-fermenters. In fact emergence of pan drug resistance (PDR) is on the rise. Due to lacunae in many aspects of infection control in a health care setup with special mention of hand hygiene practices the ideal goal of total elimination is practically impractical. However a structured & fully functional hospital infection control committees of paramount importance. Regular Surveillance, Implementation of an updated and revised antibiotic policy based on the local resistance pattern of the prevalent organisms in the particular hospital set up with optimized antimicrobial usage, strict Adherence to hand hygiene practices and cordial Liaison between the Microbiologist and the Physicians/ Surgeons would never the less be an appropriate attempt to address the ongoing scenario.

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Table 1: Distribution of Isolates from different clinical samples

Gram negative organism	N (%)	ET secretion	Urine	Pus	Blood	Central line tip
<i>Klebsiella pneumoniaea.</i>	57 (34)	40	3	7	6	1
<i>Acinetobacter baumannii</i>	35 (21)	29	-	4	1	1
<i>Pseudomonas aeruginosa</i>	31(18)	22	2	5	2	-
<i>Escherichia coli</i>	15(8)	2	9	4	-	-
<i>Enterobacter spp</i>	3(1.4%)	2	-	1	-	-
<i>Citrobacter freundii</i>	2(.9%)	-	2	-	-	-
<i>Proteus mirabilis</i>	2(.9%)	-	1		1	-
Gram positive organism						
<i>Staphylococcus aureus</i>	17(9)	4	-	4	7	2
<i>Enterococcus species</i>	9 (6)	-	4	2	3	-
<i>Candida species</i>	36 (17)	7	22	1	5	1
Total	207	106 (51%)	43 (21%)	28(13%)	25 (12%)	5 (2%)

Table 2: Frequency of Pan drug Resistant Organisms

Organisms	Resistance to all Antibiotics (n=20) (9.6%)
<i>Acinetobacter species</i>	10 (50%)
<i>Pseudomonas species</i>	05(25%)
<i>Klebsiella pneumonia</i>	03(15%)
<i>Escherichia coli</i>	02 (10%)