DOI: 10.7860/JCDR/2017/23076.9150

Original Article

Internal Medicine Section

Healthcare Associated Infections in a Resource Limited Setting

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ABSTRACT

Introduction: Health Care associated Infections (HAI) are the most common complications affecting the hospitalized patients. HAI are more common in developing and under developed countries. However, there are no systematic surveillance programs in these countries.

Aim: To find out the burden, predisposing factors and multidrug resistant organisms causing HAI in a resource limited setting.

Materials and Methods: This prospective observational study was done at Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER). Patients aged 13 years or more with stay of more than 48 hours in a 16 bedded Medical Intensive Care Unit (MICU) between November 2011 and April 2013 were included in the study. Patients were prospectively followed up till discharge or death for the development of HAI. Device associated HAI like Ventilator Associated Pneumonia (VAP), Catheter Related-Blood Stream Infection (CR-BSI) and Catheter Associated-Urinary Tract Infections (CA-UTI) were studied. Standard laboratory methods were used for identification of microorganisms causing HAI and to test their antibiotic sensitivity.

Results: A total of 346 patients were included in the study with median age of 38 years. Common indications for admission to Medical Intensive Care Unit (MICU) were poisoning (31.5%); neurological illness (23.4%) like Guillian-Barre syndrome, tetanus, meningitis, encephalitis; respiratory illness (14.5%) like pneumonia, acute respiratory distress syndrome and tropical infections (7.2%) like malaria, scrub typhus, leptospirosis. Fifty percent (174/346) patients developed one or more HAI with VAP being the most common. The rates of HAI per 1000 device days for VAP, CR-BSI, CA-UTI were 72.56, 3.98 and 12.4, respectively. *Acinetobacter baumannii* was the most common organism associated with HAI. Multidrug resistance was seen in 74% of the isolates.

Conclusion: The burden of HAI, especially with MDR organisms, in resource constrained setting like ours is alarming. There is urgent need for infection control and monitoring system to reduce HAI.

Keywords: Cross infections, Hospital infections, Nosocomial infections

INTRODUCTION

HAI are the most common complications affecting the hospitalized patients. Studies have revealed that prevalence of HAIs in developing countries are twice as compared to European countries and incidence of HAIs acquired in ICU of developing countries is triple as compared to USA [1]. However, accurate estimates of burden of HAI from developing countries cannot be made because of lack of countrywide surveillance programs and data.

Recently concluded study of Device Associated Healthcare Associated Infections (DA-HAI) from 50 countries [2] showed that although the device use is similar, HAI and bacterial resistance are higher in developing countries. Few studies are available from India addressing the burden of HAI and the rates of HAI reported are varying widely from 0.38% to 34.1% [3-10]. Profile of HAI varies between the institutes and also various ICU of a hospital. It is felt that if the reporting of HAI from hospitals in India and other developing countries is made mandatory, it will help in acknowledging and tackling the alarming rates of these infections [11]. The present study was done with the objective of finding out the burden of major HAI, factors predisposing to HAI and drug resistant microorganisms in MICU of this tertiary care teaching hospital.

MATERIALS AND METHODS

Setting: This prospective study was conducted in MICU of our hospital between November 2011 and April 2013. It's a 16 bedded MICU with overall Doctor: Patient ratio of 1:4 and Nurse: Patient ratio of 3:4. The study was approved by the Ethics Committee of JIPMER. A written informed consent was taken from legally accepted representative of all subjects prior to induction into the study.

Inclusion criteria: All patients admitted to MICU aged 13 years or more and those who have stayed in MICU for more than 48 hours were included in the study.

Exclusion criteria: Patients were excluded if the initial cultures taken within 48 hours of admission to MICU yielded microorganisms or if the succeeding cultures yielded the same microorganisms as the initial organisms (community acquired) or if patient discharged or died within 48 hours of hospital stay.

Minimum sample size required for the study was calculated as 323 based on the expected prevalence of healthcare associated infections as 30% with 5% absolute precession and 95% confidence interval. Information on demographics, clinical, laboratory investigations and interventions done were recorded using a structured proforma. At baseline, cultures of urine and tracheal aspirate (if patient's trachea was intubated) were sent to microbiology laboratory for isolation of pathogens and antimicrobial sensitivity testing. Repeat urine samples were sent for all patients after 48-72 hours. Further, tracheal aspirate and blood samples were sent if VAP and CR-BSI respectively were suspected. For suspected cases of VAP, deep tracheal aspirate from endotracheal tube was subjected to gram-staining and quantitative culture for identification of the organism. For suspected cases of CR-BSI, paired sample from the catheter and peripheral vein were subjected for semiquantitative culture; if the

catheter was removed catheter tip was also cultured. For suspected cases of CA-UTI, urine sample was aseptically aspirated from the sampling port of the catheter and subjected for quantitative culture. The resistance patterns and definitions of MDR, XDR and PDR were used as formulated by Magiorakos et al., [12]. In all cases, standard laboratory methods were used to identify microorganisms and a standardized susceptibility test was performed [13].

Definitions: VAP, CR-BSI and CA-UTI were defined as per the CDC/NHSN surveillance definition of health care associated infection and criteria for specific types of infections in the acute care setting [14].

STATISTICAL ANALYSIS

Descriptive statistics were used to report incidence rate and cumulative incidence of HAI, proportion of pathogens at various sites, and antibiogram of commonly isolated organisms. The associations between clinical factors and interventions with development of HAI were tested using Chi-square test. Association between duration of ICU stay, duration of intubation and mortality attributable to HAI were tested using independent student's t-tests or Mann-Whitney U test. To explore the independent factors associated with the infection, univariate analysis was carried out and factors found significant in univariate analysis were considered for multivariate logistic regression analysis. Rates of VAP, CR-BSI and CA-UTI per 1000 device days were calculated by dividing the total number of HAIs by the total number of specific device days and multiplying the result by 1000. All statistical analysis was carried out for two tailed significance at 5% level of significance and p-value < 0.05 was considered as significant. SPSS Version 20.0 (CDC, Atlanta, GA, USA) was used for data analysis.

RESULTS

A total of 346 patients were included in the study. The median age of patients admitted to MICU was 38 years (IQR = 26-55 years) and maximum number (n=78; 22.5%) of patients were in 20–29 years age group, and males 212 (61%) were more than females 134 (39%). Common indications for admission to MICU in present study were poisonings 109 (31.5%), neurological diseases 81 (23.4%) like Gullian-Barre syndrome, tetanus, meningitis/encephalitis followed by respiratory illnesses 50 (14.5%) like ARDS, pneumonia, followed by other infections 25 (7.2%) such as Malaria, Scrub typhus and Leptospirosis. Of the 346 patients included in the present study, 335 (96.8%) required mechanical ventilation for more than 48 hours, all patients required Foley catheter for continuous bladder drainage and 114 (32.9%) required Central Venous Catheter (CVC) insertion.

During the study period of 18 months, 174/346 (50.2%) patients experienced at least one episode of HAI. There were total of 292 episodes of HAI with VAP being the most common 237 (81%), followed by CA-UTI 50 (17.2%) and CR-BSI 5 (1.7%). A total of 169/346 (48.8%) patients developed at least 1 episode of VAP of which 86 patients had early onset VAP and 83 patients had late onset VAP. *Acinetobacter baumannii* (45%), *Pseudomonas aeruginosa* (26%) and *Klebsiella pneumonia (13%)* were the most common organisms causing VAP. Microbiology of early and late VAP did not differ significantly except for all 9 episodes of VAP due to *Escherichia coli* were late VAP. The risk of HAI was more in patients with duration of hospital stay of more than five days and in patients with more severe illness as expressed by median SAPS II score. However, other clinical characteristics were similar in patients with or without HAI [Table/Fig-1].

Duration of mechanical ventilation, reintubation and tracheostomy were associated with significantly higher risk for development of VAP. Patients who underwent reintubation and tracheostomy were at 3.42 and 7.97 times, respectively, more at risk of developing VAP when compared to patients who had not underwent the respective procedures [Table/Fig-2]. Risk of VAP, CA-UTI and CR-BSI were directly proportional to the duration of endotracheal tube, Foley catheter and CVC placement in-situ, respectively [Table/Fig-3].

Acinetobacter baumannii was the most common organism causing hospital acquired infections (135 isolates), followed by *Pseudomonas aeruginosa* (84 isolates), *Klebsiella pneumoniae* (49 isolates) and *Escherichia coli* (34 isolates). Majority of the *Acinetobacter baumannii* isolates were resistant to the commonly used antibiotics like amikacin (75%), piperacillin-tazobactum (73%) and meropenem (83%). Similarly, *Pseudomonas aeruginosa* was resistant to amikacin (43%), piperacillin-tazobactum (60%) and meropenem (54%). Seventy three percent isolates of *Acinetobacter baumannii,* 65% isolates of *Pseudomonas aeruginosa* and 90% isolates of *Klebsiella pneumonia* were sensitive to cefaperazone-sulbactum. Among *Escherichia coli,* 91% were sensitive to amikacin and 100% were sensitive to piperacillin-tazobactum and imipenem. The other organisms causing HAI, their antibiotic sensitivity patterns and percentages of MDR isolates are listed in [Table/Fig-4,5].

During the study period, 42 patients with HAI died as compared to 28 patients without HAI. Though, the mortality was higher in patients with HAI (24.1%) as compared to those without HAI (16.2%), the difference was not statistically significant (p = 0.069).

Characteristics	No HAI (n = 172) Number (%)	HAI (n = 174) Number (%)	p-value
Duration of stay < 5 days	84 (48.83%)	10 (5.75)	< 0.001
> 5 days	88 (51.16%)	164 (94.25)	
SAPS II score (Median)	26	30	0.59
Age 0-60 years	151 (87.79%)	140 (80.46%)	0.062
> 60 years	21 (12.21%)	34 (19.54%)	
Sex Male	109 (63.37%)	103 (59.20%)	0.425
Female	63 (36.63%)	71 (40.80%)	

[Table/Fig-1]: Association of HAI with different clinical parameters (n = 346).

Exposure		No VAP	VAP	p-value	Odds ratio(CI)
Reintubation	No	155	136	0.000	3.42 (1.664 – 7.03)
	Yes	11	33		
Tracheostomy	No	157	116	0.000	7.97 (3.778 – 16.813)
	Yes	9	53		

[Table/Fig-2]: Odds ratio of developing VAP with reintubation and tracheostomy (n = 335*).
*335 out of the total sample size of 346 patients, needed tracheal intubation and mechanical ventilation

DISCUSSION

During 18 months of study period, 50.2% of our patients had developed one or more of the HAIs and the incidence of HAI in our study were 74.9 per 1000 device days. The rates of HAI per 1000 device days for VAP, CA-UTI and CR-BSI were 72.56, 12.4 and 3.98 respectively. These rates are significantly higher as compared to most of the recent studies published from different parts of India [Table/Fig-6]. VAP rates were uniformly higher in all the studies except in the study done by Datta P et al., [6]. It is possible that

HAI type	Number (n)	Median duration (days)	Mini-mum duration	Maximum duration	p-value
VAP	169	11	2	68	< 0.05
No VAP	166	4	0	27	
CA-UTI	44	16	4	65	< 0.05
No CA-UTI	302	8	0	68	
CR-BSI	5	20	2	60	< 0.05
No CR-BSI	109	7	11	43	

[Table/Fig-3]: Risk of HAI with duration of device placement in situ (n= 346).

Organism	Ceftriaxone		Amikacin		Ciprofloxacin		Tetracycline		Piperacillin-tazobactum		Cefaperazone-sulbactum		Meropenem		Cloxacillin		Vancomycin	
	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R
A. baumannii	8.5	91.5	25.2	74.1	17.1	79.7	40.6	56.3	27.3	72.7	72.9	22.4	17	83	-	-	-	-
P. aeruginosa	19.1	78.9	53	43.3	24.1	60.2	-	-	40	60	65.3	27	46.1	53.9	-	-	-	-
K. pneumonia	31.9	67	75.5	24.5	51	44.7	75	25	100	0	91	9	65.5	34.5	-	-	-	-
E. coli	29	71	91	9	18.7	75	100	0	100	0	100	0	69.6	30.4	-	-	-	-
S. areus	66.6	33.4	-	-	-	-	100	0	-	-	-	-	-	-	75	25	100	0

[Table/Fig-4]: Antibiotic susceptibility of the common microorganisms.
S – Sensitive, R – Resistant (S + R may not be 100%, remaining strains are intermediate sensitive). All values are in percentages (%)

Organism	Episodes of HAI	MDR isolates (%)
Acinetobacter baumannii	135	102 (75.5%)
Pseudomonas aeruginosa	84	53 (63%)
Klebsiella pneumonia	49	21 (42.8%)
Escherichia coli	34	10 (29.4%)
Providnecia	11	8 (72.7%)
Staphylococcus aureus	8	1 (12.5%)

[Table/Fig-5]: Multi drug resistant microorganisms causing HAI.

continuous subglottic suctioning done in their ICU has led to lower rates of VAP.

Duration of ICU stay was found to be significantly higher in patients with HAI in our study as seen in previous studies, but we didn't find increased risk of HAI with age dichotomized at 60 years. Also, we didn't find gender to be a risk factor for HAI similar to the study by Datta P et al., [6]. Increased risk of HAI with longer duration of ICU stay could be explained by serious comorbidities, greater exposure to pathogens, and frequent invasive procedures.

High HAI in our study was mainly due to VAP with 48.8% patients developing VAP during the study period which is higher as compared to other studies from India [3,5,15,16]. The most common organisms isolated from patients with VAP in our study are gram negative organisms like *Acinetobacter baumannii, Pseudomonas aeruginosa* and *Klebsiella pneumonia.* Similar organisms were isolated in previous studies [3,5,17]. *Pseudomonas aeruginosa* was the most common organism causing VAP in study done by Gupta A et al., [16], but in our study, *Acinetobacter baumannii* was the most common organism which was similar to the study done by Shabina habibi et al., [3].

The rates of MDR organisms were very high in our study with rates as high as 75% for *Acinetobacter baumannii*, 63% for *pseudomonas aeruginosa* and 43% for *Klebsiella pneumonia*, the three most common organisms causing VAP. Even for organisms like *Providencia* which caused only 11 episodes of HAI, the rates of MDR isolates were as high as 72%. This is very alarming and similar to the high rates observed in previous study by Joseph et al., from this institute [5]. Surprisingly, prior antibiotic use, prior corticosteroid use which were shown as risk factors for VAP in previous study [5] especially in relation to MDR organisms were not observed to be significant in our study.

Possible explanations for high incidence of VAP in our setup include: firstly, lack of a proper hospital infection control and monitoring system which will have a great impact on regular surveillance and prevention of these infections; secondly, around 25% of our patients underwent tracheal intubation in emergency department and wards where due to crash intubations proper aseptic measures may not have been taken; thirdly, median 24 hour nurse to patient ratio in our ICU was 0.75, and a study [18] has shown that if the nurse-to-patient ratio was maintained >2.2 there will be a significant reduction in the incidence of HAIs in the ICU; fourthly, lack of proper education and awareness of hand washing, proper suctioning techniques, proper care of respiratory devices among doctors and nursing staff of ICU; fifthly, lack of dedicated and trained personnel to take care of ventilators and other instruments in ICU; and lack of optimal ventilation strategies like use of High Efficiency Particulate Air (HEPA) filters and higher air exchanges per hour. Because of the above mentioned factors, we consider our setting as resource limited.

The difference in mortality was not significant in patients with and without HAI in our study. This is in contrast to other studies where HAI is associated with increased mortality [19,20]. Reason for not observing a difference in mortality could be due to high risk of death due to the admitting indication rather than due to HAI.

LIMITATION

The study was limited to device associated infections as they are the most common causes of HAI and are largely preventable. Only Multidrug Resistant (MDR) organisms could be identified but not XDR or PDR because antibiotic susceptibility testing did not include all classes of antibiotics. Environmental surveillance was not done among ICU environment and among health care workers. Compliance of hand washing among ICU residents and staff was not studied.

CONCLUSION

There is a high burden of HAI and MDR organisms in resource limited setting. All efforts must be made to reduce the duration of device use as HAI risk is directly proportional to duration of device placement in situ. Proper hospital infection control and monitoring system, adequate provision of well trained manpower with continued education of the staff on importance of hand hygiene may reduce the rates of hospital acquired infections.

Author (Reference no)	Period of study	Place of study	HAI incidence (%)	VAP*	CA-UTI*	CR-BSI*
Habibi s et al., [3]	2004-2005	New Delhi	34.1	31.4	11.2	3.4
Joseph NM et al., [5]	2006-2007	Puducherry	NA	30.6	NA	NA
Datta P et al., [6]	2010-2011	Chandigarh	29.1	6.0	9.08	13.8
Singh S et al., [7]	2009-2010	Pune	17.6	32	9	16
Mathai AS et al., [10]	2010-2011	Vellore	NA	40.1	NA	NA
Current study	2011-2013	Puducherry	50.2	72.5	12.4	3.9

[Table/Fig-6]: Burden of various healthcare associated infections in different parts of India [3,5-7,10].
*per 1000 device days; NA – information not available

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Aug 12, 2016**
Date of Peer Review: **Sep 09, 2016**
Date of Acceptance: **Nov 10, 2016**
Date of Publishing: **Jan 01, 2017**