ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 01 | January - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

FIVE YEARS TREND OF DEVICE ASSOCIATED HOSPITAL-ACQUIRED INFECTIONS IN A TERTIARY CARE HOSPITAL IN SOUTH INDIA-A PROSPECTIVE SURVEILLANCE STUDY.

Clinical Microbiology

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ABSTRACT

Surveillance of device-associated hospital-acquired infections (DA-HAI) in ICUs plays a vital role in hospital infection control & quality assurance and in understanding the changing trend and implementation of the antibiotic stewardship program. There is limited data on DA-HAI reported from Indian ICUs. The single-center study aimed to assess the burden, microbiologic profile, and the trend of DA-HAIs over five years based on active monthly surveillance data as a part of Infection control practices in a tertiary care hospital in South India. DA-HAI rates of ventilator-associated pneumonia (VAP), central line-associated bloodstream infection (CLABSI), and catheter-associated urinary tract infection (CAUTI) per 1,000 device-days were calculated by dividing the total number of DA-HAIs by the total number of specific device-days and multiplying the result by 1,000. Overall DA-HAI rate of 1.46 per 1000 device days of which CLABSI and VAP and CAUTI constituted 2.19, 2.09, and 0.42 per 1000 device days, respectively. Diabetes was the most common comorbidity associated with DA-HAI. In contrast to data from West gram negative organisms constituted the majority of etiological agents in DA-HAIs regardless of the duration in our study (82.45%), while gram positive organisms and fungi constituted only 17.54% & 0.87%, respectively. Notably, 96.15% of *Acinetobacter baumannii* isolates in VAP were carbapenem resistant (CR), while 54.54% *Klebsiella pneumoniae* were CR. In CLABSI 75% of *Enterococcus* isolates were vancomycin resistant (VRE). In CAUTI 20% of gram negative organisms were CR and all *Enterococcus faecium* isolates in were VRE. There was increasing trend of CR gram negative organisms causing DA-HAI.

KEYWORDS

Hospital-acquired infections (HAI), VAP, CAUTI, CLABSI, Surveillance.

INTRODUCTION:

Hospital-acquired infections (HAI) have been a significant cause of mortality in intensive care units (ICUs) worldwide **(1, 2).** Centers for Disease Control and Prevention (CDC) estimated that on any given day, 1 in 31 hospitalized patients has an HAI. Central line-associated bloodstream infection (CLABSI), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infection (CAUTI) are the typical device-associated hospital-acquired infections (DA-HAI) in ICUs **(3).** DA-HAI surveillance in the ICUs plays a vital role in hospital infection control and quality assurance **(4).**

Background:

Unlike the developed countries, DA-HAI surveillance in the ICUs in the developing world has been a challenge for many reasons. There is a wide variation of rates of DA-HAIs reported from various parts of India, ranging from 0.38% to 34.1% **(5-12)**; moreover, most previous Indian studies have included not more than two years of surveillance. We attempted to study the burden and microbiologic profile of DA-HAIs over five years in a single tertiary care center.

MATERIALS AND METHOD:

Study design & data collection: This study was conducted in a 550-bed tertiary care referral hospital over five years between January 2013 and December 2017. Active monthly surveillance was done for DA-HAIs under the guidance of an infection control practitioner (ICP), and we analysed our surveillance data from January 2013 to December 2017. The definitions of VAP, CLABSI, and CAUTI were as per CDC/NHSN guidelines **(13)**.

Statistical analysis: Data was analysed using Microsoft Excel 2010. DA-HAI rates of VAP, CLABSI, and CAUTI per 1,000 device-days were calculated by dividing the total number of DA-HAIs by the total number of specific device-days and multiplying the result by 1,000.

RESULTS:

In our study, males and females had a similar distribution (57.01 % males vs. 42.98 % females), with the majority belonging to the age groups >60 years (37.71%) and 40-59 years (34.21%). The comorbidities were diabetes mellitus (47%), CAD (14%), cerebrovascular accident (14%), and chronic obstructive pulmonary disease (9%); 8% of patients did not have any comorbid conditions.

Incidence of DA-HAIs

Over five years, total DA-HAIs were 114, with total device days of 79,695, making an overall DA-HAI rate of 1.46 per 1000 device days. CLABSI and VAP constituted the majority of DA-HAIs (2.19 and 2.09 per 1000 device days, respectively), while CAUTI incidence was the least (0.42 per 1000 device days).

The trend of DA-HAIs over five years

The overall incidence of DA-HAIs over five years was 2.12, 1.19, 0.83, 1.15, and 1.76 per 1000 device days in 2013,2014,2015,2016, and 2017 respectively. DA-HAIs showed a declining trend from initial rates in 2013 to the lowest in 2015 but again increased in 2017.

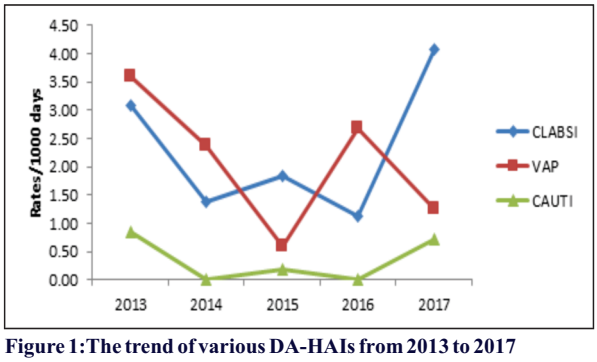

Figure 1:The trend of various DA-HAIs from 2013 to 2017

The number of device utilization days was initially high in 2013

(19,296 device days), decreased in 2014 (11,727 device days), only to rise steadily up to 2016 (17,327 device days), and again decreased in 2017 (15,834 device days).

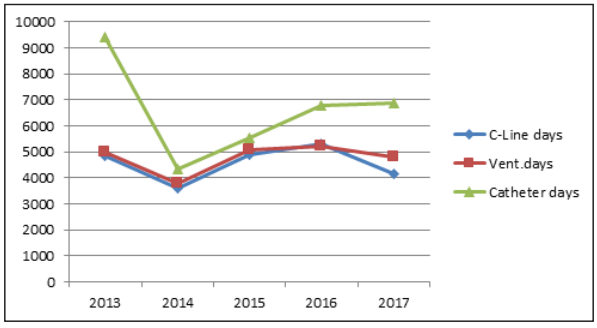

Figure2: The trend of Device utilization days from 2013 to 2017

Etiological agents in DA-HAIs

Gram negative organisms constituted the majority of etiological agents in DA-HAIs in our study (82.45%), while gram positive organisms constitute a minority (17.54%) and fungi were rare (0.87%). *Acinetobacter baumannii* was the most common organism (33.33%), followed by *Klebsiella pneumoniae* (22.8%), other gram negative bacteria (17.54%), *Enterococci* (7.89%), and *Pseudomonas aeruginosa* (7.89%).

Table1: Distribution of etiological organisms in VAP

Microorganism	n=50	%
Acinetobacter baumannii	**26**	52
Klebsiella pneumoniae	**11**	22
Pseudomonas aeruginosa	**5**	10
S.aureus	**5**	10
B.cepacia	**2**	4
Enterobacter spp.	**1**	2
Total	**50**	**100%**

32 out of 45 gram negative isolates (71.11%) causing VAP were carbapenem resistant (CR). Notably, 25/26 (96.15%) *A.baumannii* isolates wereCR while 6/11 (54.54%) *K.pneumoniae* isolates were CR. One out of five (20%) *P.aeruginosa* isolates was CR. The majority of *S.aureus* isolates (4/5; 80%) were methicillin-sensitive.

Comorbidities and mortality associated with VAP:

The predominant comorbidities in VAP were diabetes (41%), CAD (21%) and CVA (15%), COPD (6%), and CLD (4%), while 13% of patients had no comorbidities. Eighty-six percent of patients who suffered from VAP developed VAP after five days of mechanical ventilation (Late VAP), while 14% of patients developed VAP within five days of mechanical ventilation (Early VAP). The in-hospital crude mortality rate in patients who have suffered from VAP was 40% (20/50 patients).

Table 2: Distribution of etiological organisms in CLABSI

Microorganism	n=52	%
Klebsiella pneumoniae	**13**	25
Acinetobacter baumannii	**13**	25
Pseudomonas aeruginosa	**4**	7.69
E.coli	**1**	1.92
Enterobacter spp.	**2**	3.84
Serratia spp	**1**	1.92
Citrobacter spp.	**1**	1.92
B.cepacia	**5**	9.61
S.maltophila	**1**	1.92
S.aureus	**1**	1.92
Coagulase negative *Staphylococcus sp.*(CONS)	**5**	9.61
Enterococcus faecalis	**1**	1.92
Enterococcus faecium	**3**	5.76
Candida spp.	**1**	1.92
Total	**52**	**100%**

24 out of 41 gram negative isolates (58.53%) causing CLABSI were CR. Notably, *A.baumannii* isolates, which constituted the majority, were all CR (13/13; 100%), while a majority of *K.pneumoniae* isolates (9/13; 64.28%) were also CR. One out of four (25%) *P.aeruginosa* isolates was CR. All coagulase negative *Staphylococcus sp* (CONS) isolates were methicillin-resistant (5/5; 100%), while the single *S.aureus* isolate was methicillin-sensitive. The majority of *Enterococcus* isolates were vancomycin resistant (VRE) (3/4; 75%). The only fungus isolated was *C.tropicalis* which was fluconazole sensitive.

Comorbidities and mortality associated with CLABSI:

The predominant comorbidities in CLABSI were diabetes (46%), COPD (14%), and CVA (11%), while 13% of patients had no comorbidities. The in-hospital crude mortality rate in patients who have suffered from CLABSI was 0% (0/14 patients).

Site of central line placement:

The most common site of central line placement in patients with CLABSI was the internal jugular vein (53.84%), followed by femoral (42.30%) and subclavian sites (3.84%).

Table3: Distribution of etiological organisms in CAUTI

Microorganism	n=14	%
E.coli	7	50
K.pneumoniae	3	21.42
E.faecium	2	14.28
E.faecalis	2	14.28

Two out of ten gram negative isolates (20%) causing CAUTI were CR.Both *E.faecalis* isolates were penicillin/ampicillin sensitive, while both *E.faecium* isolates were VRE.

Comorbidities and mortality associated with CAUTI:

The predominant comorbidities in CAUTI were diabetes (62%) and CVA (23%), while 15% of patients had no comorbidities.

The in-hospital crude mortality rate in patients who have suffered from CLABSI was 0% (0/14 patients).

DISCUSSION:

Our study reports an overall DA-HAI rate of 1.43 per 1000 device days. The VAP rates, CLABSI, and CAUTI in our study were 2.09, 2.19, and 0.42 per 1000 device days, respectively. These rates are well below the rates reported in the latest INICC data summary, which included 703 ICUs in 50 countries from Latin America, Europe, Eastern Mediterranean, Southeast Asia, and Western Pacific World Health Organization regions where the rates of VAP, CLABSI, and CAUTI were 12.2, 4.19 and 4.82 per 1000 device days respectively **(14).** Our VAP and CLABSI rates are slightly higher, while our CAUTI rates are lower when compared with the recent CDC-NHSN DA-HAI data. **(15)**. DA-HAI studies in India vary in rates widely, as shown below.

Table 4: DA- HAI studies in India

DA-HAI Study	VAP**	CLABSI**	CAUTI**
Aravind et al . (16)	38.7	7.6	1.47
Sood et al . (17)	8.9	2.74	1.5
Gatti C et al. (18)	72.56	3.98	12.4
Datta P et al. (8)	6.04	13.86	9.08
Singh S et al. (6)	21.9	0.48	0.60
Jana et al. (19)	19.47	3.99	4.25
Narendranath et al. (20)	0.19	0.45	1.66
Sanjeev Singh et al. (21)	6.74	2.4	1.63

**Rates as per 1000 device days.

Compared to most prior Indian studies, our study reports lower incidence rates of VAP, CLABSI, and CAUTI. The reason for the lower incidence rate of DA-HAIs in our hospital compared to INICC data and data from most other Indian centers could be due to the presence of a DA-HAI team consisting of an infection control practitioner and infection control nurses who do active surveillance in the ICUs coupled by strong support from the hospital management in handling infection control issues related to DA-HAIs.

Overall, in our study, diabetes mellitus (DM) was the predominant comorbidity associated with patients who developed DA-HAI (47%) followed by cerebrovascular accident (14%) and chronic obstructive

pulmonary disease (9%), while 8% of patients had no comorbidities. In the study by Jana et al., the predominant comorbidities in patients who have acquired DA-HAIs in the ICU were malignancy, diabetes, and chronic obstructive pulmonary disease **(19)**.

While DA-HAI studies performed in the western ICUs traditionally demonstrate a high prevalence of gram positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA), *vancomycin-resistant enterococci* (VRE), studies from India and the Asia-Pacific region have shown a predominance of gram negative bacteria **(22).** The SOAP study, a multicenter, observational study conducted in 195 intensive care units in 24 European countries, reported an equal frequency of gram-positive and gram-negative organisms. **(23).**In Asian ICUs, gram negative isolates constituted 75% compared to 58% in Western Europe, while gram positive isolates constituted 33% in Asian ICUs and 49.9% in Western Europe **(1).** Gram negative organisms constituted an overwhelming majority in our study also (92.00%), while gram positive organisms constituted a minority (17.54%) and fungi were rare (0.87%). *Acinetobacter baumannii* was the most common etiological organism (33.33%). Our findings are in allegiance with multiple prior Indian studies, which indicate that patients admitted in Indian ICUs suffer from infections caused by gram negative organisms predominantly in contrast to the western scenario**.** *In our study,* 38/39 *A.baumannii* isolates (97.43%) were carbapenem resistant, while 15/26 *K.pneumoniae* isolates (61.53%) were carbapenem resistant. Our overall CR rate was 60.14% among gram negative isolates, higher than previous Indian studies **(19).**

Studies from the west have shown Gram.positive cocci, predominantly *S. aureus*, mainly methicillin-sensitive *S.aureus* (MSSA) and *Streptococcus pneumonia* as the most commonly isolated organisms in early-onset VAP **(24)** and gram.negative bacilli, methicillin-resistant *S.aureus* (MRSA) as the most common etiological agents of late-onset VAP (**25**). In contrast to western data, our study reports a majority of gram negative organisms as the causative organism in early and late VAP.In contrast with other Indian studies, which reported *P.aeruginosa* as one of the predominant pathogens causing VAP, our study found that *P.aeruginosa* contributed only to a minority of VAP isolates (5/50; 10%).

Regarding CLABSI, our study could not conclude whether the site of line placement was a predisposing factor for CLABSI since we did not have the data on the total number of patients in whom a particular site was used for central line placement. In our study, *A.baumannii* and *K.pneumoniae* were the predominant gram negative organisms causing CLABSI, while among the gram positive organisms, CONS was the most common, followed by *Enterococci*. Importantly all CONS isolates were methicillin-resistant, and a majority of *Enterococcus* isolates were vancomycin resistant. Interestingly, while candidemia has been increasingly reported as a cause of nosocomial bloodstream infection and fungal isolates causing CLABSI were reported at the rate of 5–15% in various Indian studies **(26-28);** they contributed to only 2% of isolates in our study.

As far as CAUTI is concerned, *E.coli* was the predominant etiological agent (50%), followed by K.pneumoniae (21.42%). Gram positive agents *E.faecalis* and *E.faecium* were responsible for minority of cases. In our study, both *E.faecalis* isolates were penicillin/ampicillin sensitive. In contrast, both the *E.faecium* isolates were vancomycin-resistant (VRE), leading to an overall VRE prevalence of 50%, which is considerably higher when compared to a recent study by Kulkarni et al. where VRE prevalence in CAUTI isolates was 18.75% (**29).** The emergence of *Enterococci,* particularly VRE in CAUTI, is a disturbing situation that demands a need for further studies to estimate the prevalence of VRE exclusively associated with CAUTI in India.

CONCLUSION:

DA-HAI rates in our tertiary care center were lower when compared to the recent INICC data (2010-15) and data from multiple Indian centers, which could be attributed to the presence of a DA-HAI team comprising an infection control practitioner and infection control nurses and active DA-HAI surveillance supported by the hospital management. Regardless of the duration of VAP gram, negative organisms were most common. Carbapenem resistant gram negative organisms causing DA-HAI are increasing. VRE is a concern for CAUTI. We conclude that a representative multicenter surveillance mechanism is urgently needed in India to detect and reduce DA-HAI rates. Similarly, a nationwide antimicrobial stewardship program is the need of the hour to minimize antimicrobial resistance.

Acknowledgement:
We are thankful to the entire infection control team of our hospital including infection control nurses who are tirelessly working for ensuring Infection control practices .We acknowledge the support of hospital administration for implementation of DA- HAI surveillance practices in the hospital and technical and moral support for the study.

Funding:
There was no funding from any organisation for the study. The Authors have no conflict of interest to disclose related to this study.

Ethical approval:
The study was based on active monthly surveillance data as a part of Infection control practices in a tertiary care hospital. The data was extracted from hospital infection control surveillance data system and clinical case sheet after approval of properly constituted Institutional Ethics Committee, in agreement with local regulations.

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