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STUDY OF MULTIDRUG RESISTANT ORGANISMS ISOLATED FROM MEDICAL DEVICE ASSOCIATED INFECTION.

Microbiology

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ABSTRACT

Background: Healthcare associated infections in general and device associated infections (DAI) in particular are common complications in hospitalized patients that take its toll in the form of high morbidity and mortality, and increased healthcare cost. Emergence of multidrug resistance organisms (MDRO)often negatively affects the outcome of the patient. The present study was conducted at a tertiary care teaching hospital of Maharashtra with aim to determine prevalence of MDRO like Methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), and carbapenem resistant Enterobacterales (CRE) in DAIs. **Methods:** A site-specific surveillance of DAI was conducted in Medical Intensive Care Unit (MICU) for a period of 2 years. Based on the criteria of Centers for Disease Prevention and Control's National Health Safety Network (NHSN) samples received from three DAI i.e.Catheter associated urinary tract infection (CAUTI), ventilator associated pneumonia (VAP) and catheter related blood stream infection (CRBSI) wereincluded in the study.The samples were processed as per the standard microbiological protocol. VITEK system was used to identify the pathogen along with its antimicrobial susceptibility profile. **Results:** The rates of CAUTI, CR-BSI and VAP were 5.14/ 1000 catheter associated days, 4.74/1000 catheter associated days and 4.25/1000 ventilator associated days respectively. A total of 52 (37.4%) Enterobacterales isolates were resistant to carbapenem (CRE). Out of 18 isolates of *S. aureus*, 7 (38.9%) were resistant to methicillin (MRSA) whereas 1 isolate of Enterococcus (n=7) was resistant to vancomycin (VRE). **Conclusion:** Emergence of multidrug resistance as a cause of healthcare associated infections in general and device associated infection (DAI) in particular often complicates the treatment and hence the outcome of patients in critical care areas. As seen in the present study, multidrug resistant organisms (MDRO) are common cause of DAI. Therefore the present study highlights the importance of strict adherence to institutional and national antimicrobial policy along with implementation of infection prevention and control policies to prevent emergence of DAI due to MDRO.

KEYWORDS

Healthcare associated infections, device associated infection, Multidrug resistant organism, methicillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus, carbapenem resistant Enterobacterales.

INTRODUCTION

In recent years, healthcare associated infections (HAI) and infections due to multidrug resistant organisms (MDRO) have emerged as an important threat.Nearly 1/3rd of HAI are due to presence of indwelling medical devices (IMDs).[1] IMDs are considered as inseparable part of modern medicine as they are the mainstay of management of medical and surgical cases.

Device-associated infections (DAI) are associated with prolonged length of hospitalization, incremental health-care cost, and high morbidity and mortality rates. They are considered key indicators of both the patient safety and the quality of care.[2]

There are numerous studies from developed part of the world especially from the United States and European countries on the incidence of DAI. However, only limited studies pertaining to rate of DAIs are available from developing countries like India.

As per the available literature, DAI rates are reported to vary from country to country, region to region and as per the type of healthcare setup. DAI rates also vary within a particular healthcare setup as per the patient population.[3] DAIs are reported to be markedly higher in the intensive care units (ICUs) of developing countries. The severity of underlying comorbid conditions, invasive therapeutic and diagnostic interventions, non-compliance with sterilization and disinfection protocols, in addition to prevalence of resistant microorganisms are critical factors in the high rates of infections in ICUs.[3]

Catheter associated urinary tract infection (CAUTI), ventilator associated pneumonia (VAP) and catheter related blood stream infection (CRBSI) are common DAIs in ICU patients. [4]Studies focused on these infections have highlighted increased isolation of MDRO like Methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), and carbapenem resistant Enterobacterales (CRE). The present was conducted in a tertiary care teaching hospital with an aim to determine prevalence of MDRO in DAIs.

MATERIALAND METHODS.

A site-specific surveillance of DAIwas conducted in Medical Intensive Care Unit (MICU) for a period of 2 years. Based on the criteria of Centers for Disease Prevention and Control's National Health Safety Network (NHSN) samples received from three DAI i.e. CAUTI, VAP and CRBSI were included in the study.[5]

All the clinically relevant details of patients were collected and analyzed. For microbial analysis of VAP, deep tracheal aspirate from the endotracheal tube was accepted and processed. For CAUTI, urine samples, aseptically aspirated from the sampling port of the urinary catheter were considered to be relevant whereas for CRBSI, the peripheral blood sample, and the distal 5 cm of the catheter were accepted and processed.[5]

The samples were processed as per the standard microbiological protocol. Samples exhibiting microbial growth on blood agar or MacConkey agar were inoculated into specific identification cards of the automated VITEK® 2 system for identification. For Antimicrobial susceptibility testing of an isolate AST card of automated VITEK® 2 system was inoculated.

RESULTS

During the study period a total 3528 patients were admitted to Medical ICU. Out of these, 2668 (75.6%) had one or more indwelling medical devices. The type of indwelling medical devices is shown in table 1. Urinary catheter was the most common indwelling medical device. A total of 591 (16.8%) had all three (mechanical ventilator, central line and urinary catheter) devices.

Table 1.Types Of Indwelling Medical Devices.

Type of medical device	No. (frequency)
Urinary catheter	1821 (51.6)
Mechanical ventilator	936 (26.5)
Central line	792 (22.4)
Urinary catheter and Mechanical ventilator	648 (18.5)
Urinary catheter and Central line	451 (12.8)
Mechanical ventilator and central line	431 (12.2)
On all three medical devices	591 (16.8)

A total of 219 (6.2%) patients developed DAI. The rate of DAI is shown in the table.2. The rates of CAUTI, CR-BSI and VAP were 5.14/ 1000 catheter associated days, 4.74/1000 catheter associated days and 4.25/1000 ventilator associated days respectively.

Out of a total 1821 patients with urinary catheters, CAUTI was developed in 149 (8.2%) patients. A total of 36 (4.5%) patients with central line out of 792 developed CR-BSI. Out of a total 936 patients on mechanical ventilator, 34 (3.6%) developed VAP.

Table 2. Medical Device Associated Infections.

DAI	Total device days	Number of patients developing infection	Rate/1000 medical device associated days
CAUTI	28985	149	5.14
CR-BSI	7586	36	4.74
VAP	7987	34	4.25

The pathogen wise distribution of cases of DAIs is shown table. 3. Out of 219 isolates from DAI, 186 (84.9%) were bacteria and 33 (15.1%) were fungi. Enterobacterales were isolated from 139 (63.4%) cases. *Klebsiella* spp. (42.9)followed by *E. coli*(14.6%) and *Candida* spp. (12.8%). were common organisms isolated from DAI cases.*S. aureus* was isolated from 18 cases.*Candida* spp. and *Trichosporon* spp. were the fungal isolates from DAI. Fungi were not isolated from VAP cases. *Candida spp*. was the predominant fungal isolate,

Table 3.Pathogen wise distribution of cases of DAIs.

Pathogen	CA-UTI (%)	CR-BSI (%)	VAP (%)	Total (%)
Bacterial isolates				
Gram negative isolates				
*Klebsiella*spp	49(52.1)	22 (23.4)	23 (34.5)	94
E. coli	19 (59.4)	07 (21.9)	06 (18.8)	32
Pseudomonas spp.	06 (54.5)	01 (9.1)	04 (36.4)	11
*Serratia*spp.	03 (75)	01 (25)		04
*Acinetobacter*spp.	-	01 (20)	04 (80)	05
Proteus spp.	09 (8.4)	-	-	09
Total	86 (55.5)	32 (20.6)	37 (23.9)	155
Gram positive isolates				
Staphylococcus aureus	11 (61.1)	05 (27.8)	02 (11.1)	18
Coagulase negative *Staphylococci* (CONS)	04 (66.7)	02 (33.3)	-	06
Enterococcus spp.	06 (85.7)	01 (14.3)	-	07
Total	21 (67.8)	08 (25.8)	02 (6.4)	31
Fungal isolates				
Candida spp.	21 (75)	07 (25)	-	28
*Trichosporon*spp.	01 (20)	04 (80)	-	05
Total	22 (66.7)	11 (33.3)	-	33
Total number of isolates	**129 (40.3)**	**51 (23.3)**	**39 (17.8)**	**219**

The MDRO isolated from cases of DAIs are shown figure 1. In this study, a total of 52 (37.4%) Enterobacterales isolates were resistant to carbapenem (CRE). Out of 18 isolates of *S. aureus*, 7 (38.9%) were resistant to methicillin (MRSA) whereas 1 isolate of Enterococcus (n=7) was resistant to vancomycin (VRE).

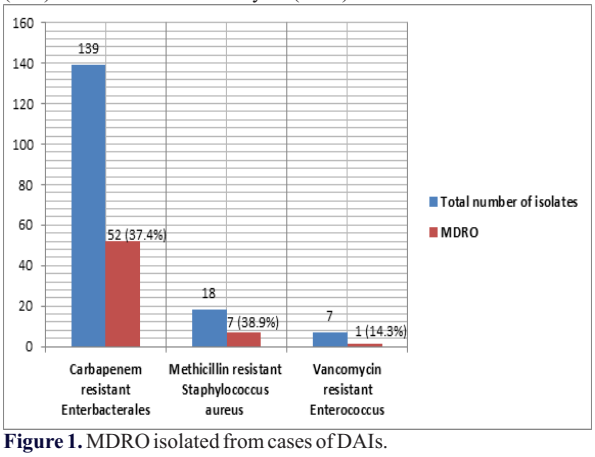

Figure 1. MDRO isolated from cases of DAIs.

Carbapenem resistant in Enterobacterales is shown in figure 2. Carbapenem resistance was high in *Klebsiella* spp. (39.4%).

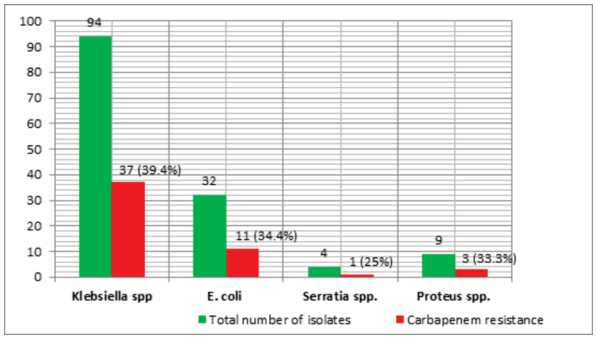

Figure 2. Carbapenem Resistant In Enterobacterales.

DAI wise distribution of MDRO is shown in table 4. MDRO like CRE, MRSA and VRE were isolated maximum from cases of CR-BSI. VRE were not isolated from cases of CA-UTI.

Table 4. DAI Wise Distribution Of MDRO.

MDRO	CA-UTI		CR-BSI		VAP	
	Total isolates	Resistant (frequency)	Total isolates	Resistant (frequency)	Total isolates	Resistant (frequency)
CRE	80	19 (23.8)	30	21 (70)	29	12 (41.4)
MRSA	11	03 (27.3)	05	03 (60)	02	01 (50)
VRE	06	-	01	01 (100)	-	-

DISCUSSION

The emergence of MDRO has become a universalpublic health problem. Itimposes an additional burden on medical care in patients admitted to the hospitals in general and ICU patients in particular. In ICUs, extensive use of antimicrobials creates a selective pressure that promotes the emergence of MDRO.[6]Other factors like underlying diseases or morbid conditions of patients, impaired immunity (acquired or induced) and presence multiple invasive devices add incrementally to the risk of acquiring HCAI. [7]

In this study, CA-UTI was the most common DAI, which was noted in 149 (8.2%) patients with indwelling urinary catheter. The rate of CA-UTI was 5.14/ 1000 catheter associated days. Various national and international researchers have also reported CA-UTI to be the common type of HAI.[8]Despite of remarkable advances in diagnosis, prevention and treatment, CAUTI still remains a severe burden on healthcareand antibiotic resistance rates are in this type of HAI are alarmingly high. [9] *Klebsiella* spp. was the most bacterial common isolate from CA-UTI cases. Similar findings were reported by other researchers. [10]

CA-UTI due to *Klebsiella* spp. is reported to be associated with high rates of antimicrobial resistance. In the present study, CRE was noted in 23.8% of CA-UTI cases and carbapenem resistance was high in *Klebsiella* spp. compared to other Enterobacterales. A total of 3 (27.3%) MRSA were isolated from cases of CA-UTI. MRSA is considered as an emerging cause of CA-UTI in recent years.[12]Additionally MRSA CA-UTI may further progress to more severe disseminated infections.

CR-BSI is one the most common, serious, lethal and costly complication of central line central venous catheterization. [13] In this study, a total of 36 (4.5%) patients who underwentcentral venous catheterization developed CR-BSI. The rate of CR-BSI was 4.74/1000 catheter associated days. In Indian hospitals, the proportion of Gram-negative CRBSI is reported to be much higher than that reported from western hospitals.[14] Similar observation was noted in this study, where the proportion of isolation Gram negative bacteria from CR-BSI was 80% whereas for Gram positive bacteria it was 20%.

In this study, CRE was reported 70% of Enterobacterales isolated from CRBSI. Similarly the rate of MRSA was also high. Similar finding was reported by Pandit*et al*. (2019).[15]VRE was noted only in the isolate from CR-BSI. *Enterococcus* isolates are increasingly reported from CR-BSI, often these isolates demonstrate resistant to vancomycin. However there is limited information regarding treatment of CR-BSI due to VRE. [16]

In critical illness, mechanical ventilator play is an important medical intervention. VAP is type of hospital acquired pneumonia that occurs

after 48 h of mechanical ventilation and associated with both high morbidity and mortality rates. [17,18]

In this study, a total of 34 (3.6%) on mechanical ventilatory support developed VAP. The rate of VAP was 4.25/1000 ventilator associated days. Although, the incidence of VAP and death due to VAP is reported to be declining in recent years, episodes due MDRO have significantly high mortality rates. In this study, the rates of isolation of CRE and MRSA from VAP cases were 41.4% and 50% respectively.

CONCLUSION.

Emergence of multidrug resistance as a cause of healthcare associated infections in general and device associated infection (DAI) in particular often complicates the treatment and hence the outcome of patients in critical care areas. As seen in the present study, multidrug resistant organisms (MDRO) are common cause of DAI. Therefore the present study highlights the importance of strict adherence to institutional and national antimicrobial policy along with implementation of infection prevention and control policies to prevent emergence of DAI due to MDRO.

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