Original Article

Incidence, microbiological profile of nosocomial infections, and their antibiotic resistance patterns in a high volume Cardiac Surgical Intensive Care Unit

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ABSTRACT

Background: Nosocomial infections (NIs) in the postoperative period not only increase morbidity and mortality, but also impose a significant economic burden on the health care infrastructure. This retrospective study was undertaken to (a) evaluate the incidence, characteristics, risk factors and outcomes of NIs and (b) identify common microorganisms responsible for infection and their antibiotic resistance profile in our Cardiac Surgical Intensive Care Unit (CSICU). **Patients and Methods:** After ethics committee approval, the CSICU records of all patients who underwent cardiovascular surgery between January 2013 and December 2014 were reviewed retrospectively. The incidence of NI, distribution of NI sites, types of microorganisms and their antibiotic resistance, length of CSICU stay, and patient-outcome were determined. **Results:** Three hundred and nineteen of 6864 patients (4.6%) developed NI after cardiac surgery. Lower respiratory tract infections (LRTIs) accounted for most of the infections (44.2%) followed by surgical-site infection (SSI, 11.6%), bloodstream infection (BSI, 7.5%), urinary tract infection (UTI, 6.9%) and infections from combined sources (29.8%). *Acinetobacter*, *Klebsiella*, *Escherichia coli*, and *Staphylococcus* were the most frequent pathogens isolated in patients with LRTI, BSI, UTI, and SSI, respectively. The Gram-negative bacteria isolated from different sources were found to be highly resistant to commonly used antibiotics. **Conclusion:** The incidence of NI and sepsis-related mortality, in our CSICU, was 4.6% and 1.9%, respectively. Lower respiratory tract was the most common site of infection and Gram-negative bacilli, the most common pathogens after cardiac surgery. Antibiotic resistance was maximum with *Acinetobacter* spp.

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INTRODUCTION

The Center for Disease Control and Prevention has defined nosocomial infection (NI) as a localized or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxins, without any evidence that the infection was present or incubating at the time of admission to the Intensive Care Unit (ICU).[1] NIs are more common in patients admitted in the surgical ICU because of immobility, surgical incisions, multiple invasive monitoring lines, urinary

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catheters, and mechanical ventilation. In Cardiac Surgical Intensive Care Unit (CSICU), in addition to the aforementioned issues, there are intercostal drainage tubes, long duration surgeries, hypothermia, poor nutrition, cardiac cachexia, and patients undergoing open chest management which increases the susceptibility of these patients for infections. NIs in the postoperative period not only increase morbidity and mortality, but also impose a significant economic burden on the health care infrastructure.[2] The other factors which can prolong the stay in CSICU, and predispose the patients for NI are low cardiac output syndrome, acute kidney injury, need for increased inotropic support, need for renal replacement therapy, coagulopathies, neurological injury, and cardiopulmonary bypass (CPB) induced systemic inflammatory response. On the basis of perioperative risk factors many models have been formulated to predict the occurrence of NI after cardiac surgery.[3]

The data on the incidence of NI among the CSICUs and the organism profiles together with the antibiotic resistance details in developing setups is scanty, more so from surgical ICUs. Such information is useful for medical audit as well as planning for preventive/corrective measures. We analyzed the incidence, risk factors, common sites, the pathogens responsible for NI and their antibiotic susceptibility profile in our cohort of cardiac surgical patients in a large CSICU.

PATIENTS AND METHODS

Study design, setting

This retrospective study was conducted in the CSICU of Cardiothoracic Vascular Surgery Department of the All India Institute of Medical Sciences, New Delhi. The CSICU has 42 beds including 8 for neonates.

Patient selection

All (neonates, infants, pediatric, and adult) patients admitted to the CSICU after elective cardiovascular surgery from January 2013 to December 2014 were studied. Detailed information was obtained from the records of all patients who developed microbiologically documented NI. In addition for comparative purposes, data on admitted patients who did not develop NI was collected for a 2-month period from November to December 2014. This was done mainly due to the consideration that data on patients admitted during a 2-month period in a high output center like ours would give enough statistical power for any comparison between infected and non-infected groups. Demographic data, intra- and post-operative information, time, and source and number of samples sent for microbiological investigations were collected. Patients with preoperative infection, on ventilator, on antibiotics before surgery, emergency operations, heart transplant recipients, and patients received on extracorporeal membrane oxygenator were excluded. Patients were categorized into valvular (valve repair/replacements), nonvalvular (coronary artery bypass grafting, aortic aneurysms, and dissections), cyanotic (all right to left shunts and univentricular hearts), acyanotic (all left to right shunts), and miscellaneous (all closed heart surgeries including patent ductus arteriosus ligation, coarctation of aorta repair, pericardiectomy, etc.).

Infection classification

NIs: Infections developed within 48 h of shifting the patients from ICU to the wards or patients who were readmitted to the ICU for infection before their hospital discharge. All infections were diagnosed on the basis of clinical suspiciousness, radiological information and were confirmed by biochemical criteria like positive cultures from different body secretions. Major infections such as lower respiratory infections (LRTIs), wound/surgical-site infections (SSIs), blood stream infections (BSIs), and urinary tract infections (UTIs) were defined as follows - LRTIs-infections involving lower respiratory tract including bronchitis, pneumonitis, and pneumonia; SSI-nonhealing wound with or without discharge involving the sternal wound and/or leg or arm (sites of graft harvesting) and culture proven pathogens from the discharge; BSI-culture proven pathogens in blood, sampled from one central, and one peripheral site; UTI – more than 10^5 colony forming bacterial units on culture.

All biological samples were collected and sent to the microbiology laboratory as per the standard procedures. The data on the positive culture reports from different sites, the microorganisms isolated and their susceptibility to commonly used antibiotics were collected from the microbiology reports.

Clinical antibiotic protocol

All patients in the postoperative CSICU were treated with antibiotics as per the standard protocol of the unit. Those were changed to the next level of broad spectrum antibiotics in case of suspiciousness of infection and/or according to the antimicrobial susceptibility results when available.

Approval was obtained from the medical research ethics committee of the hospital.

Data analysis

The overall incidence risk of NI was calculated along with 95% confidence interval (CI). Ventilation duration, length of ICU stay, and the mortality in the two groups with and without infection were compared using Student's t-test/Chi-square test as appropriate. A $P < 0.05$ was considered to be statistically significant. Analysis carried out using STATA version 12.1 (STATA corporation, Texas, USA).

RESULTS

During the period January 2013 to December 2014, a total of 7156 patients were admitted to the CSICU, out of which 6864 patients met the inclusion criteria. Review of the records of study patients indicated that NI was detected in 319 patients. Thus, the overall incidence of NI was 4.6% (95% CI: 4.2% 5.2%) during the study period. Medical data of all the 319 infected patients during the 2-year period along with the data of a comparable control pool of 572 patients during a 2-month period were analyzed. Age of the study patients varied from 1 month to 84 years. Majority (69%) were males.

Of the total 6864 patients during the 2-year period, 457 died giving an all-cause mortality during the study period as 6.7% (95% CI: 6.1–7.3%) while the mortality due to sepsis was 1.9% (95% CI: 1.5–2.2%). More than one-third (39.8%) of the patients acquiring NI died (95% CI: 34.4–45.4%) while the mortality among patients without NI was 5.0% (95% CI: 4.5–5.6%). The mortality risks were statistically significantly different between the groups with and without NI ($P < 0.001$).

Comparison of the patients with and without NI indicated that the duration of ventilation (14.8 ± 13.4 vs. 12.1 ± 14.1 h, $P < 0.001$) and also the length of ICU stay (13.6 ± 18.5 vs. 3.3 ± 3.1 days, $P < 0.001$) were significantly higher among the infected patients than noninfected patients. Infants (<1 year of age) and patients with cyanotic heart disease were more prone to NI. CPB time was also found to be significantly higher in the infected patients but the aortic cross clamp time was not statistically different between the two groups [Table 1].

Of the 319 patients who acquired NIs, only one microorganism was detected in 228 (71%) patients, two in 71 (22%), three in 16 (5%), and four organisms in four (1%) of patients. In all, 319 patients acquired a total of 434 infections.

Table 1: Distribution of study characteristics between patients with and without nosocomial infections

Characteristic	Infected (*n*=319)	Non-infected (*n*=572)	*P*
Age (years)			
Mean±SD	20.0±25.43	25.0±22.68	<0.01
<1 year	41.8	12.8	<0.001
1-5	11.9	15.3	
5-15	4.4	16.8	
15-40	16.0	25.6	
40-60	12.9	17.5	
>60	12.9	11.9	
CPB time# (min)	109.2±38.76	97.5±49.25	<0.001
Aortic clamp time* (min)	60.0±22.82	60.7±32.02	0.77
Ventilation (h)	14.8±13.38	12.1±14.08	<0.001
ICU stay (days)	13.6±18.52	3.3±3.05	<0.001
Patient category			
Nonvalvular	18.8	17.1	<0.001
Valvular	17.2	28.2	
Cyanotic	38.2	25.2	
Acyanotic	21.0	26.2	
Miscellaneous	4.7	3.3	
Cyanotic	38.2	25.2	
Other	61.8	74.8	<0.001

*Excluding surgeries without ACC, #Based on surgeries with CPB. Nonvalvular: CABG, Aortic aneurysms and dissections, Valvular: All valve repairs and replacements, Cyanotics: All right to left shunts and univentricular hearts, Acyanotics: All left to right shunts, Miscellaneous: All closed heart surgeries like PDA ligation, Coarctation repair and pericardiectomy, etc. ACC: Aortic cross clamp, CPB: Cardiopulmonary bypass, ICU: Intensive Care Unit, PDA: Patent ductus arteriosus, CABG: Coronary artery bypass grafting

LRTI was the most common among all infections, occurring in 141 (44.2%) of the 319 infected patients followed by SSI in 37 (11.6%), BSI in 24 (7.5%), and UTI in 22 (6.9%) patients [Figure 1]. In the rest 95 patients (29.8%), pathogens were isolated from other sources such as tissues/vegetations, chest drainage, central venous catheter tips, and/or multiple (>1 site) sources. There was considerable variation in the isolated organisms from different sources. The most commonly detected organisms from respiratory secretions were Gram-negative bacteria such as *Acinetobacter*, *Klebsiella*, and *Pseudomonas*. Similarly, *Escherichia coli* was maximally grown from urine, whereas wound discharge/pus samples yielded mainly the Gram-positive Staphylococci. *Klebsiella* and *Pseudomonas* were the leading Gram-negative bacteria isolated from blood cultures. Figures 2 and 3 depict the distribution of various organisms detected from each type of sample for the total 319 patients with NIs.

Antibiotic resistance patterns for the isolated microorganisms are shown in Table 2 and Figure 4.

DISCUSSION

In the present study, we observed NI incidence of 4.6% among patients undergoing cardiac surgery during a 2-year period. This is lower than that observed 6–31% in other series[4-9] of postoperative cardiac surgical patients. The Fowler *et al*. study[3] found that major infections occurred in 3.51% of coronary bypass patients. Our incidence is almost similar to a study by Michalopoulos *et al*.[10] where the microbiologically documented NI occurred in 107 of the 2122 (5.0%) adult patients undergoing open heart surgery. One of the largest studies comprising of both surgical and medical patients (European Prevalence of Infection in Intensive Care [EPIC] study) conducted across Europe documented an infection risk of 20.6%.[11]

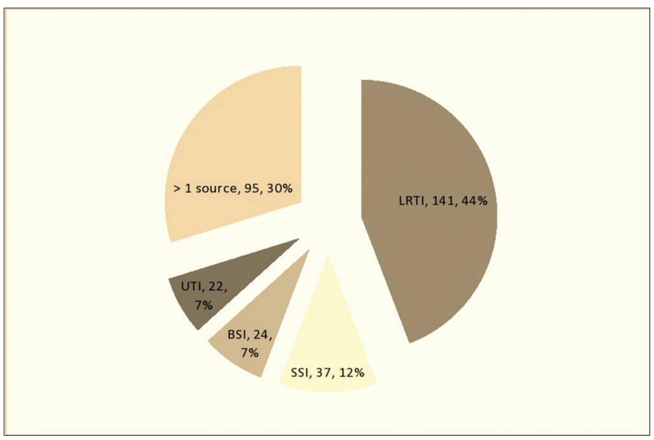

Figure 1: Depicts the source of infection in number of cases with percentage

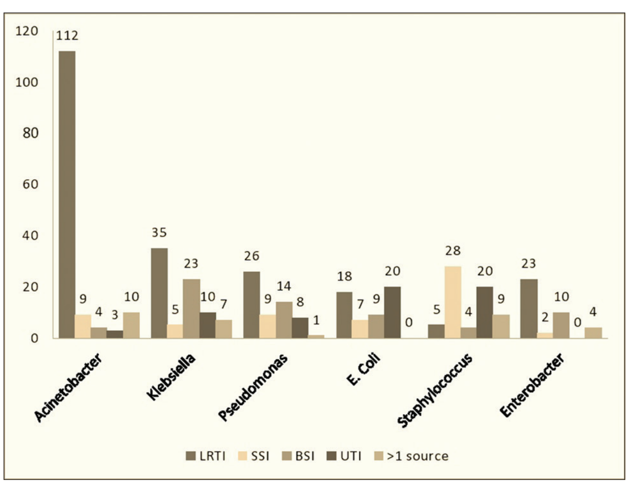

Figure 3: Causative microorganisms isolated from different sources

We observed a sepsis-related mortality rate as 1.9% and mortality among infected patients was 39.8%. Michalopoulos *et al*.[10] and Fowler *et al*.[3] documented mortality of 16.8% and 17.9%, respectively, in adult cardiac surgical patients having NI. Kelava *et al*.[9] documented a mortality rate of 1.5% for same day admission group of patients which is very much similar to our mortality risk.

In our study, LRTI was found to be the most common NI (44.2%) followed by SSI (11.6%), BSI (7.5%), and UTI (6.9%). The distribution of NI was more or less similar to that of Michalopoulos *et al*.[10] (respiratory infections 42% followed by central venous catheter-related infection 22.4%, SSI 16.8%, and UTI 7.5%). In the study conducted by Lola *et al*.,[7] BSI accounted for 30%, SSI for 26.7%, and LRTI for 13.3%. The predominance of respiratory tract infections is similar to the studies based on medical ICUs like EPIC II study (63.5%),[12] Chinese study (68.5%),[13] and Indian study (65.8%).[14] In our study, we found very small number of infections related to the central venous catheter (<1%) contrary

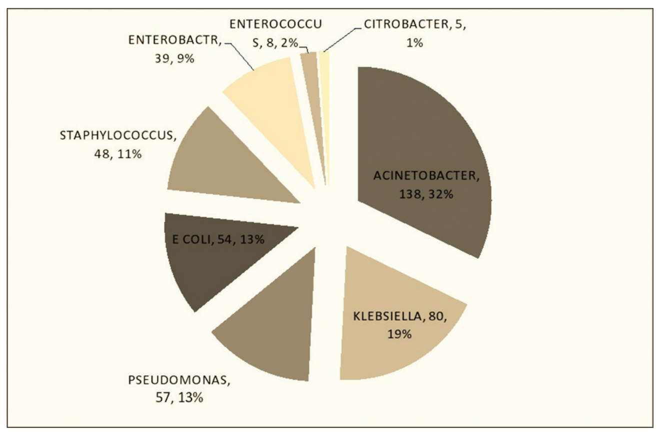

Figure 2: Depicts the causative microorganisms responsible for nosocomial infection and their frequency

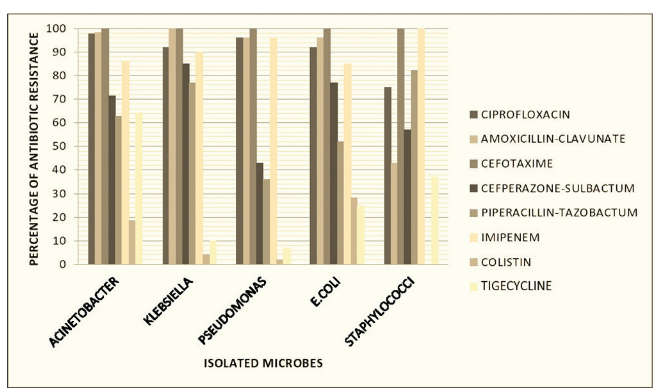

Figure 4: Antimicrobial resistance pattern among different microbes

Table 2: Antibiotic resistance profile *n* (%) of microorganisms

Drug	Organism					
	Acinetobacter Resistant (%) 95% CI	*Klebsiella* Resistant (%) 95% CI	*Pseudomonas* Resistant (%) 95% CI	*Escherichia coli* Resistant (%) 95% CI	*Enterobacter* Resistant (%) 95% CI	*Staphylococcus* Resistant (%) 95% CI
Colistin	23/126 (18.3) (11.4-25.1)	3/71 (4) (0.5-9)	1/48 (2) (2-6)	9/32 (28) (11-44)	4/33 (12) (0.3-23)	0/9 (0)
Tigecycline	68/106 (64.2) (54-73)	3/29 (10) (1-22)	1/14 (7) (8-22)	3/12 (25) (3-53)	3/15 (20) (2-42)	3/8 (37) (0-80)
Amikacin	98/121 (81.0) (73-88)	54/63 (86) (76-94)	38/45 (84) (73-95)	26/43 (60) (45-75)	22/33 (66) (49-83)	13/37 (35) (18-51)
Netilmicin	126/134 (94.0) (89-98)	69/73 (95) (89-99)	32/38 (84) (72-96)	40/47 (85) (74-95)	30/34 (88) (76-99)	39/46 (85) (73-95)
Ciprofloxacin	125/128 (97.7) (94-100)	70/76 (92) (85-98)	48/50 (96) (90-100)	48/52 (92) (84-99)	31/38 (82) (68-94)	42/46 (91) (82-99)
Levofoxacin	-	-	19/22 (86) (70-100)	30/32 (94) (84-102)	10/18 (55) (30-80)	3/4 (75) (0-100)
Ceftazidime	136/136 (100.0) (-)	78/78 (100) (-)	53/53 (100) (-)	53/53 (100) (-)	38/38 (100) (-)	17/17 (100) (-)
Cefotaxime	135/135 (100.0) (-)	77/77 (100) (-)	33/33 (100) (-)	51/51 (100) (1)	37/37 (100) (-)	17/17 (100) (-)
Cefoperazone-sulbactam	70/98 (71.4) (62-80)	53/62 (85) (76-94)	22/51 (43) (29-57)	33/43 (77) (63-89)	22/30 (73) (56-90)	8/14 (57) (27-86)
Piperacilin-tazobactum	73/116 (62.9) (54-71)	56/73 (77) (66-86)	15/41 (36) (21-51)	25/48 (52) (37-66)	24/37 (65) (48-81)	9/11 (82) (54-108)
Imipenum	118/137 (86.1) (80-91)	68/75 (90) (83-97)	53/55 (96) (91-100)	46/54 (85) (75-94)	37/38 (97) (92-102)	20/20 (100) (-)
Meropenem	104/127 (81.9) (75-88)	62/7 (86) (77-94)	43/51 (84) (73-94)	37/51 (72) (59-85)	29/35 (83) (69-95)	20/22 (90) (77-103)
Nitrofurantoin	-	-	31/32 (97) (90-100)	8/10 (80) (49-110)	4/4 (100) (-)	-
Amoxicillin-clavulinic acid	119/121 (98.4) (96-100)	15/15 (100) (-)	24/25 (96) (87-104)	47/49 (96) (90-101)	26/27 (96) (88-103)	17/39 (43) (27-59)
Vancomycin	-	-	-	-	-	0/12 (0)
Teicoplanin	-	-	-	-	-	1/31 (3) (0-9)
Linezolid	-	-	-	-	-	21/27 (77) (61-94)

to the other studies including that of Lex *et al*. (25%),[15] Michalopoulos *et al*. (22.4%),[10] and Lola *et al*. (16.7%).[7]

Our study documented a predominance of Gram-negative organisms in nosocomial ICU infections. Lola *et al*.[7] demonstrated equal frequencies of Gram-positive cocci and Gram-negative bacilli from the culture results, whereas Gram-positive organisms were noted predominantly in Michalopoulos *et al*. study.[10] Our profile was similar to what has been observed in the EPIC study[11] and the EPIC II study.[12]

In the present study, the most frequently isolated pathogens were *Acinetobacter* (32%) and *Klebsiella* (19%). *Staphylococcus* (60.6%) and *Enterobacter* species (10%) were the most common pathogens in the US report by Michalopoulos *et al*.[10] *Acinetobacter* was responsible for most LRTI (81%) in our cohort of patients whereas it was completely absent in the study by Michalopoulos *et al*.[10] *Acinetobacter* (26.7%) was found to be a most common Gram-negative pathogen in the cohort of patients studied by Lola *et al*.,[7] the same was observed in our study. *Klebsiella* was responsible for most of the BSIs (29%), and *Staphylococcus* was the most common pathogen for SSI (58%) in the present study [Figure 2] whereas Michalopoulos *et al*.[10] demonstrated that bacteremia was caused by Gram-positive organisms like Staphylococci and Gram-negative organisms like *Klebsiella* were responsible for LRTI. *E. coli* was the most common bacterial cause of nosocomial UTI in our study [37%, Figure 2] which was similar to that observed in other medical ICU in India[16] and China.[13]

The most common isolated *Acinetobacter* was found to be multidrug resistant with 86% resistance to imipenem, 62% resistance to piperacillin-tazobactam, and 18% resistance to colistin. Multidrug-resistant *Acinetobacter* isolates varying between 62% and 70% have been reported in other studies.[17,18] This Gram-negative bacterium was posing a major hurdle in our ICU as it was becoming very difficult to treat.

In the present study, *E. coli* was resistant to most of the commonly used antibiotics such as amoxicillin-clavulanate (96%), amikacin (60%), ciprofloxacin (92%), and cefotaxime (100%). In the Chinese study,[13] 22.2% of *E. coli* isolates were sensitive to the combination of amoxicillin-clavulanate, whereas 78.8% of *E. coli* isolates exhibited susceptibility to the combination in EPIC II study.[12] In addition, there was a high proportion (80%) of *E. coli* isolates resistant to ciprofloxacin, whereas the rate was <10% in the UK and the United States.[19,20] This shows that *E. coli* in our setup are far more resistant to antibiotics as compared to other countries. We also found that a considerable number of *Pseudomonas aeruginosa* isolates were resistant to fluoroquinolones (96% to ciprofloxacin and 86% to levofloxacin) which is much higher compared to Chinese (41.3–66.9%) and the USA (30%) reports.[13,21] *Staphylococcus* was found to be resistant to amoxicillin + clavulanate combination in 43% cases and to linezolid in 77% cases but was highly sensitive to vancomycin (same was observed by Ding *et al*.),[13] colistin and teicoplanin.

The risk of NI in the present study was comparatively less, probably because our CSICU being in the apex institute of the country follows good hand hygiene practices by the staff and doctors, stringent aseptic precautions, streamlined antibiotic policies, and infection control guidelines. A low rate of central venous catheter-related infection reflects a good aseptic care during insertion, handling in ICU, and their early removal. The high rate of LRTI in our ICU was because of risk factors such as long CPB time, longer duration of ventilation, and length of ICU stay. Moreover, our inclusion of all age group of patients in the study probably had an impact on the high rate of LRTI. NI was more common in neonates and infants having cyanotic congenital heart disease. Statistically significant difference in the CPB time and ventilation duration was observed between the groups with and without infection. There was also statistically significant increase in ICU stay and mortality in patients with NI compared to those without infection. Reduced duration of ICU stay in the uninfected group suggests the possibility of considerable savings in the hospital turnaround time, which can be used for increased services. The high mortality among the patients acquiring NI may or may not be directly due to the NIs, as it might depend on many other factors such as the underlying condition of the patient and other concomitant conditions/co-morbidities. Further specific studies on this aspect can answer whether NIs, *per se*, can be the cause for mortality in patients undergoing cardiac surgeries, if so their magnitude, etc. The high prevalence of antibiotic resistance is of great concern for both the clinicians and the patients, which suggests a fast assessment of the resistance profile of the NIs among the CSICU patients so that appropriate antibiotics could be administered for the early cure of NI and associated morbidities. This high resistance noted is also a pointer to the need for appropriate antibiotic policies for prescription, procurement, and usage.

Limitations of the study

The results of the present study were based on all cases with NIs during a 2-year period, but for comparison the cases without infections during a 2-month period only were taken. In view of this, limitations arising out of such comparison, if any, will be applicable for our results too.

CONCLUSION

We report the burden, characteristics of microbial flora, and resistance patterns of NIs in a postoperative cardiac surgical facility in the apex medical institute of India. Literature review did not indicate such a comprehensive attempt in any cardiac surgical ICU. The overall incidence of NI was 4.6% with a notably high mortality among the infected patients. LRT was found to be the most common site for NI and *Acinetobacter* was the most commonly detected organism, with high resistance. The outcome of cardiac surgery with NI might deteriorate further because of the fast emerging multidrug resistant pathogens (particularly the Gram-negative bacteria).

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Conflicts of interest

There are no conflicts of interest.

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