Cardiac Surgery And Associated Nosocomial Infections, A Systemic Review And Meta-Analysis

Cardiac surgery and nosocomial infection

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Abstract:

Objectives

We designed this systemic review meta-analysis based on all the reported scientific studies to conduct on cardiac patients and evaluate the prevalence of nosocomial infection, reported pathogens, related infections, MDR pathogens, associated risk factors, comorbidities, ICU stay, and mortality. Our outcome-focused was the prevalence of nosocomial infection in Cardiac patients from 2017-January 2021.

Methods

We performed an advanced search of PubMed and google scholar 2017 till up January 2021. The selected scientific articles were based on defined inclusion criteria and the selection was done according to the PRISMA guideline.

Results

A total of thirteen full-text scientific studies were selected based on inclusion criteria (n=30027 participants). 1653 (5.5%) prevalence of nosocomial infection among adult cardiac patients was calculated.

Conclusion

Nosocomial infection is global healthcare worrisome in an escalating manner and surgical patients are at great risk due increased possibility of infectious risk. Strict infection control and antibiotic policies should implement to reduce this hazard.

Keywords—Cardiac surgery, Nosocomial, Nosocomial infection, hospital acquired infection

Introduction:

Nosocomial Infections (NI) or Healthcare-associated infections (HAI) are one of the great challenges of every healthcare setup, especially for patients undergoing surgical procedures. These infections are not only associated with high mortality risk but also with increased cost and prolong length of stay (LOS) [1, 2]. Cardiac surgery is usually a low infectious rate surgery with a 6 - 24%infectin rate of NI, and about 4% of cardiac surgery patients die especially those who had a longer hospital stay [3-5]. The contributing factors of high mortality are due to longer hospital stay is unclear. However, NI and HAIs are always the strongly associated reason for high mortality [4, 5]. Cardiac intensive care units have reportedly high incidence of NIs and a high rate of antibiotics administration. The patient was highly prone to infections due to illness, surgical complexities, use of invasive devices like multiple catheters, and endotracheal tubes. Nosocomial infections (NI) are hospital-acquired infections (HAI) which acquired within and after 48 hours of hospital admission and discharge [6, 7]. World health organization reported that every 7 out of 100 patients reported for NI with approximately 99,000 deaths yearly in the United States [4, 8]. Associated comorbidities, age, and gender are additional risks for cardiac surgery patients and risk of NI [1]. The increased LOS in NI patients also generates a negative effect in the healthcare system and also burdens the cost [1, 9].

Another associated concern of cardiac surgery patients and NI is the escalating trend, an 18-year study reported NI prevalence 8% to 20% from 1995 to 2013 [10, 11]. This escalating trend is alarming for the healthcare sector due to the advancement and implementation of advanced infection control guidelines and antimicrobial stewardship practices [10]. Diagnosis of NI leads to several other difficulties in postoperative cardiac patients such as inflammation, systemic inflammatory response syndrome (SIRS), tissue damage [10]. Another worrisome with NI is multidrug-resistant organisms, which are difficult to treat and took a long time to eliminate [10, 12]. The trend of pre-operative antibiotic administration may be a contributing factor to microbial resistance [13]. Another high-risk factor is prolonged intensive care stay, studies proved the strong correlation between prolong ICU stay and NI epidemiology, with approximately 20% - 30% of the high possibility of acquiring NI [14, 15]. The most common site of NI is pneumonia, surgical site infections (SSI), Central line-associated bloodstream infection (CLABSI), and urinary tract infections (UTIs) [3, 4].

This systemic review was designed to investigate the cardiac surgery and its associated nosocomial infections, and reported microbes.

Inclusion Criteria

Scientific articles and abstracts based on reporting nosocomial or hospital-acquired infections in cardiac surgery patients. We included only adult patients in this study with no gender restriction.

Methods:

Search Strategy and Eligibility Criteria

We designed this systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for scientific literature search [16]. No language and gender restrictions were imposed. Age and year filter was used for "Adult" cardiac patients from 2017 – till January 2021. Keywords variation was used to avoid any data loss (eg, cardiac surgery, nosocomial OR eg, cardiac surgery, nosocomial infection OR eg, cardiac surgery, healthcare-associated infections OR eg, cardiac surgery, infection OR eg, cardiac surgery, NI OR eg, cardiac surgery, HAI). All the selected articles were manually downloaded for further screening. The references of selected articles were critically analyzed to pick out any relevant study.

Data Extraction

Data extraction was done with defined broad-spectrum search keywords to enfold the inclusion criteria. Pubmed and Google scholar was used for data extraction from 2017 till January 2021.

Quality assessment of extracted data

Cochrane Risk of bias assessment guidelines was followed for extraction of data, and extraction was done twice by using same keywords in different time frames [17, 18].

Outcome basis and assessment

The primary analyzed outcome was the prevalence of nosocomial infections among cardiac surgery adult patients.

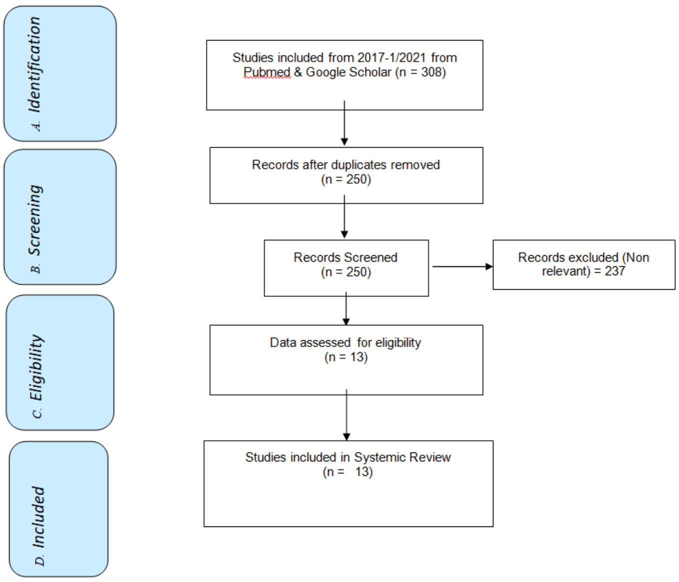
Patient and public involvement:

It's a systemic review and not required patient or public involvement in this study.

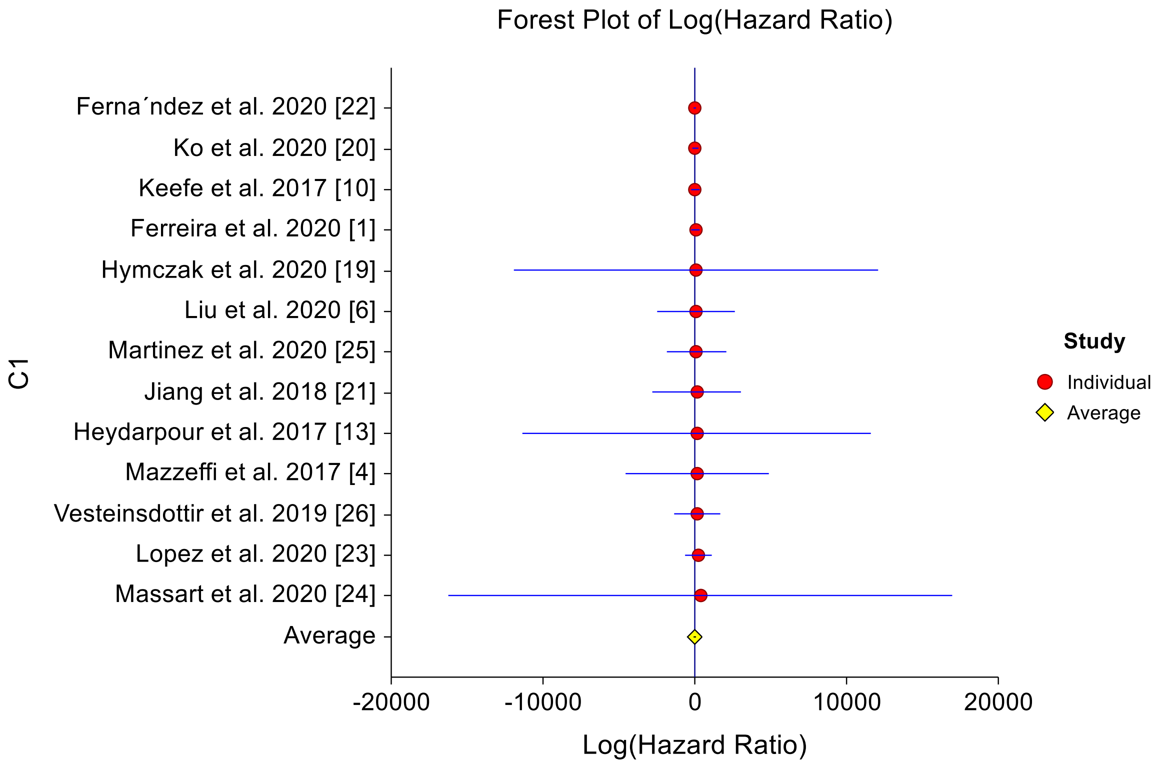
Data evaluation and statistical analysis

THE STATISTICAL ANALYSIS WAS PERFORMED BY USING NCSS STATISTICAL SOFTWARE. 95% CONFIDENCE INTERVAL (CIS) OF CONTINUOUS DATA WAS CALCULATED. THE P-VALUE <0.05 WAS STATISTICALLY SIGNIFICANT. THE POSSIBILITY OF PUBLICATION BIAS WAS ASSESSED BY BLAND ALTMAN ANALYSIS REPORT, AND EACH STUDY WAS EVALUATED WITH 0.999535 CORRELATION COEFFICIENT, FIGURE 3. A FOREST PLOT REPRESENTS THE HAZARD RATIO AND 95% CONFIDENCE INTERVAL, SEE FIGURE 2. T TEST P-VALUE ALSO REPORTED IN FIGURE 4.

FIGURE 1: Summary of Study Selection Process

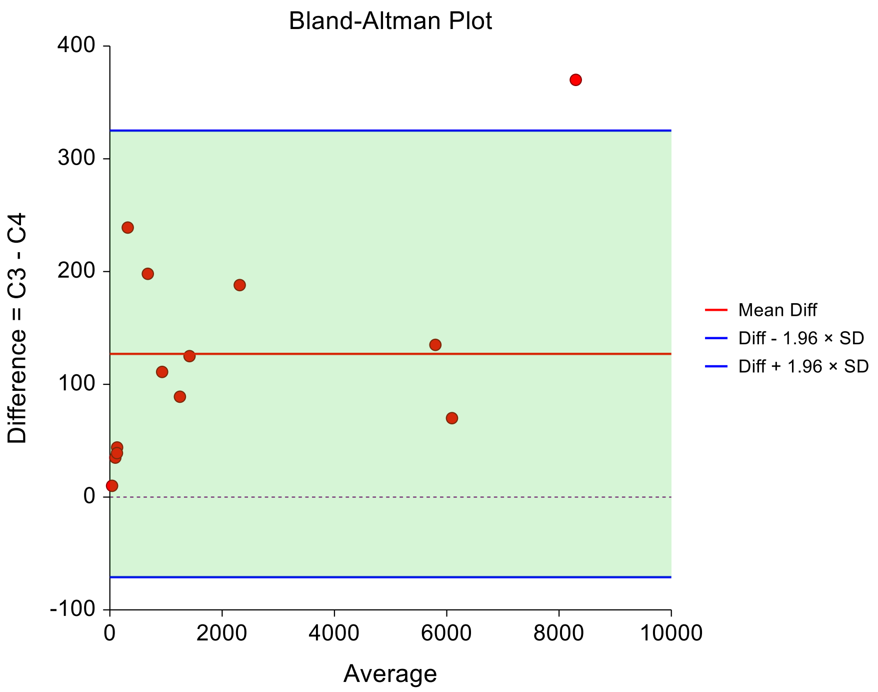


PRISMA flow diagram, Preferred Reporting Items for Systematic Review and Meta-Analysis
RCT: Randomized Control Trial
Data base: Cochrane Central Register of Controlled Trials (CENTRAL)



	Log Hazard Ratio	Standard Error	95.0% Lower Confidence Limit	95.0% Upper Confidence Limit	Percent Random Effects Weight
Ferreira et al. 2020 [1]	44.0000	151.0000	-251.9546	339.9546	6.3367
Ko et al. 2020 [20]	35.0000	115.0000	-190.3959	260.3959	10.9251
Jiang et al. 2018 [21]	125.0000	1481.0000	-2777.7067	3027.7067	0.0659
Liu et al. 2020 [6]	89.0000	1292.0000	-2443.2735	2621.2735	0.0866
Heydarpour et al. 2017 [13]	135.0000	5865.0000	-11360.1888	11630.1888	0.0042
Mazzeffi et al. 2017 [4]	188.0000	2407.0000	-4529.6333	4905.6333	0.0249
Keefe et al. 2017 [10]	39.0000	146.0000	-247.1547	325.1547	6.7782
Lopez et al. 2020 [23]	239.0000	438.0000	-619.4642	1097.4642	0.7531
Massart et al. 2020 [24]	370.0000	8483.0000	-16256.3745	16996.3745	0.0020
Martinez et al. 2020 [25]	111.0000	986.0000	-1821.5245	2043.5245	0.1486
Vesteinsdottir et al. 2019 [26]	198.0000	775.0000	-1320.9721	1716.9721	0.2406
Hymczak et al. 2020 [19]	70.0000	6128.0000	-11940.6593	12080.6593	0.0038
Ferna´ndez et al. 2020 [22]	10.0000	44.0000	-76.2384	96.2384	74.6302

Figure 2: Meta-Analysis of Hazard-Ratio Studies



Correlation Coefficient = 0.999535

Standard	95.0% LCL	95.0% UCL			
Parameter	Count	Value	Deviation	of Value	of Value
Bias (Difference)	13	127.1538	100.895	66.18359	188.1241
Lower Limit of Agreement	13	-70.60042	49.11731	-177.6178	36.417
Upper Limit of Agreement	13	324.9081	49.11731	217.8907	431.9255

Figure 3: Bland-Altman Analysis Report

Stage	t-Test P-Value	Efficacy Boundary	Information Proportion		
1		0.00000	0.2000		
2		0.00039	0.4000		
3		0.00368	0.6000		
4		0.01102	0.8000		
		5		0.02113	1.0000

Figure 4: P-Values and Boundaries at Stage 0

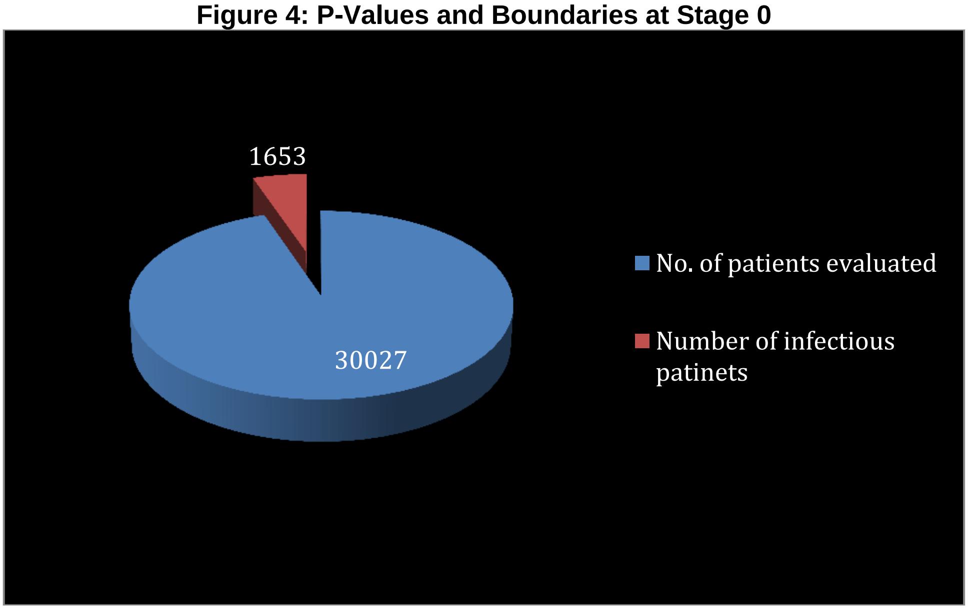


Figure 5: Frequency of nosocomial infections among selected studies

Table 1: Selected Studies of Nosocomial Infection among Cardiac Surgery Patients

First Author, year, and Reference Number	Duration	Country	No. of patients	Gender n (%)	Age, mean (SD), years (Infection group)	Infection type	Infectious organism (n)	Infection	
								Yes	No
Ferreira et al. 2020 [1]	January 2012 - January 2018	Brazil	195	Male: 114 (58.5), Female: 81 (41.5)	64.5±12.1 years	NR	NR	44	151
Hymczak et al. 2020 [19]	January 2014 -December 2016	Poland	6198	Male: 45 (64.3)	73.0 [64.0–78.0]	Clostridioides difficile infection (CDI)	*Clostridioides difficile*	70	6128
Ko et al. 2020 [20]	January 2010 -December 2018	Korea	213	Male: 23 (65.7)	67.0 [52.5–73.0]	Pneumonia, Urinary tract infection, Primary bacteremia, Catheter related bloodstream infection	NR	35	115
Jiang et al. 2018 [21]	2010-2015	China	1606	NR	57.6±8.9	SSI 0.7%, CVCRI 0.8%, UTI 1.1%, RTIP 5.2%	*Pseudomonas aeruginosa* 10, *Acinetobacter baumannii* 11, *Escherichia coli* 7, *Klebsiella pneumoniae* 6, *Burkholderia cepacia* 4, *Stenotrophomonas maltophilia* 4, *Citrobacter freundii* 3, *Haemophilus influenzae* 4, *Enterobacter aetogenes* 1, *Enterobacter cloacae* 2, *Proteus vulgaris* 1, *Staphylococcus aureus* 10, *Staphylococcus epidermidis* 9, *Staphylococcus saprophyticus* 2, *Staphylococcus citreus* 2, *Streptococcus pneumonia* 5, *Streptococcus viridans* 2, *Enterococcus faecium* 4, *Enterococcus faecalis* 2, *Enterococcus mundtii* 1, *Candida albicans* 17, *Candida tropicalis* 8, *Candida parapsilosis* 6, *Candida krusei* 2, *Candida glabrata* 1, *Aspergillns spp.* 1	125	1481
Liu et al. 2020 [6]	January 2018 - December 2018	China	1381	Male: 56 (62.9%)	67.90±11.76	Pneumonia, blood stream, SSI, urinary tract	*Acinetobacter baumannii* 50, *Klebsiella pneumoniae* 19, *Pseudomonas aeruginosa* 17, *Enterobacter cloacae* 8, *Escherichia coli* 6, *Staphylococcus epidermidis* 9, *Enterococcus faecium* 6, *Staphylococcus aureus* 3, *Candida* 8, *Aspergillus* 1	89	1292
Heydarpour et al. 2017 [13]	March 2011 to March 2014	Iran	6000	Female: 80, Male: 55	62.69±11.97	Respiratory tract, SSI, UTI, BSI	NR	135	5865
Mazzeffi et al. 2017 [4]	January 1, 2011, and December 31, 2013	Maryland	2,595	Male: 109 (58.0)	67 (56–75)	Pneumonia 35.0% Urinary tract infection 18.5%, CLABSI 53.6%, Surgical site infection 39.4%,	MRSA HAI 44.4% VRE HAI 40.0% Clostridium difficile 25.0%, MDR HAI 38.5%	188	2407
Keefe et al. 2017 [10]	May and June 2013	Canada	185	Male: 82%	64.4 ± 12.6 years	UTI 35.9% Pneumonia 30.8% Leg harvest site 23.1% SSI 20.5% Sepsis 7.7%	*Escherichia coli* 7	39	146
							Pseudomomas aeruginosa 2		
							Citrobacter youngae 1		
							Serratia marcescens 1		
							Candida albicans 1		
							Klebsiella pneumoniae 1		
							Morganella morganii 1		
							Haemophilus influenzae 3		
							Pseudomonas aeruginosa 2		
							Escherichia coli 1		
							Serratia marcescens 1		
							Staphylococcus aureus 1		
							Streptococcus pneumoniae 1		
							Proteus vulgaris 1		
							Enterobacter cloacae 1		
							Candida albicans 2		
							Coagulase-negative staphylococci 2		

Ferna´ndez et al. 2020 [22]	7-week	Spain	54	Male:6, Female:4	74.5 ± 10 years	Postoperative mediastinitis	*Serratia marcescens*	10	44
Lopez et al. 2020 [23]	1991 to 2015	Spain	677	_	Adult	Respiratory infections 33%, Urinary tract infections, 13.5% Bacteremia 12.1% Surgical site infections 7.2%, Abdominal focus 9.5%	*Enterobacteriaceae* 21.8% Gram-positive cocci 16.7%	239	438
Massart et al. 2020 [24]		France	8853	_	Adult	Bloodstream infection, Pneumonia	NR	370	8483
Martinez et al. 2020 [25]	January 2011 and January 2016	Spain	1097	_	Adult	Pneumonia 4.2%	NR	111	986
Vesteinsdottir et al. 2019 [26]	1 January 2013 to 31 December 2017	Iceland	973	_	Adult	Pneumonia 9.1%, Superficial surgical site 5.7%, Bloodstream 2.8%, Deep sternal wound 1.7%	*Klebsiella oxytoca* 22, *Pseudomonas aeruginosa* 10, *Enterococcus faecalis* 2	198	775

Not reported (NR), surgical site infections (SSI), urinary tract infection (UTI), Blood stream infection (BSI), Central line associated Blood Stream Infection (CLABSI), central venous catheter-related infection (CVCRI), respiratory tract infection and pneumonia (RTIP), Methicillin resistant *Staphylococcus aureus* (MRSA), Vancomycin resistant Enterococci (VRE)

Results & Discussion:

A total of 13 studies were selected based on inclusion criteria. PRISMA flow chart illustrates the details of data search, screening, and selection, see Figure 1. In this study, we reported the NI incidence of 5.5% among adult patients undergoing cardiac surgery in the last 3 years time, based on selected studies' outcomes. Individually, all selected studies have different NI incidence based on their analytical strategy and infection control practices of healthcare settings. The reported nosocomial infection among selected studies was Pneumonia, bloodstream, SSI, urinary tract, Sepsis. *Clostridioides difficile* infection (CDI) and Postoperative mediastinitis was also reported with *Clostridioides difficile* and *Serratia marcescens*, See Table 1. All included studies were retrospective except Ferreira et al. 2020, which was an observational cross-sectional study [1]. The age and gender reportedly was the predominant risk factor in NI with the increasing length of stay (LOS) [1]. Other associated risk factors duration of surgery, lung diseases, low cardiac output syndrome (LCOS), urinary catheter, suction continuous venovenous hemofiltration (CWH), artery or vein catheter, mechanical ventilation time, reintubation, tracheostomy, diabetes, hypertension, and intubation [6, 13].

Not all studies linked mortality with nosocomial infection. Ko et al. 2020 reported a very high 23.3% NI prevalence among cardiac arrest patients who underwent extracorporeal cardiopulmonary resuscitation. This study did not report any link between hospital mortality and nosocomial infection, Only MDR organisms associated with hospital mortality. It was reported that age, an autoimmune disorder, Neurological disorders, higher Sequential Organ Failure Assessment score, and extracorporeal membrane oxygenation (ECMO) duration were the strong NI predictors [21, 28, 29]. However, low BMI and flow rate, longer CPR was the strong predictors of HAI development reported in another study [20]. Jiang et al. and Liu et al. linked mortality with nosocomial infection; a high mortality rate of 16.8% was reported in NI patients. The prolonged hospitalization of two weeks was also linked with NI which increased the extra medical cost by 60% [6, 21].

Despite all the infection control awareness HAI remain increased reported by Centers for Disease Control's 2016 progress report [30]. Studies also identify RBC transfusion as the potential cause of risk, which was linked with pneumonia, Systemic Infections, and CLABSI [4]. Another interesting fact was reported for NI was the continuation of antimicrobial therapy even after negative microbiology culture report which was highly discouraged due to increased selective pressure for antibiotic-resistant bacteria [10].

Cardiac surgery and associated NI is a vast topic, some studies reported specifically one type of infection or organism. Hymczak et al. reported *Clostridioides difficile* infection (CDI) in Cardiac Surgery patients. This retrospective study was based on the only hospital-acquired diarrhea due to *Clostridioides difficile* infection. We included this study, reporting of hospital-acquired infection in cardiac patients [19]. Associated comorbidities were the major risk factor of this infection including Atherosclerosis, Dyslipidemia, Coronary disease, previous myocardial infarction, Atrial fibrillation, Diabetes mellitus, History of malignant neoplasms, Chronic kidney disease, Thyroid disease, Peptic ulcer disease, and COPD. The mortality rate was quite high which 21% was. Other studies also reported 2.5 to 27.7% CDI mortality [26, 27]. Fernandez et al. reported an outbreak of postoperative mediastinitis by *Serratia marcescens* in adult cardiac surgery patients. *Serratia marcescens* is an opportunistic organism and the use of an aqueous chlorhexidine solution was contaminated with *S. marcescens* responsible for an outbreak of postoperative wound infections [22].

Nosocomial infections in association with cardiac surgery contributes to increase mortality and healthcare cost. There are plenty of associated risk which needs to be identified before surgery and necessary cautions accordingly. The rate of NI is reportedly increasing despite all infection control practices, this need to be revising infection control protocol and its strict implementation.

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