

Epidemiology of healthcare acquired infection – An Indian perspective on surgical site infection and catheter related blood stream infection

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ABSTRACT

Healthcare acquired infections or hospital acquired infections (HAIs) are amongst the most common complications of hospital care, leading to high morbidity and mortality. While WHO estimates about 7-12% HAI burden in hospitalized patients globally, the figures from India are alarming, with an incidence rate varying from 11% to 83% for different kinds of HAIs. The article reviews literature and data for HAIs from India, with particular focus on surgical site infections (SSIs) and catheter related blood stream infection (CRBSI). The profile of SSIs and CRBSIs in India with a relative context to the relevant global data has been discussed.

Key words: Hospital acquired infection, Surgical site infection, Catheter related blood stream infection, pathogens

INTRODUCTION

Healthcare acquired infection, alternatively also called 'hospital acquired infection' (HAI), or 'nosocomial infection' refers to the infection occurring in patients after admission at the hospital for a reason other than that infection; an infection that was neither present nor incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility (1, 2, 3). As a general timeline, infections occurring more than 48 hours after admission are usually considered hospital acquired. The Hospital Infection Society of India (HISI) finds the latter justified in the Indian scenario, as most of the time it is difficult to

make out whether an infection was acquired outside the hospital or inside a specific healthcare set-up (4). The current clinical review highlights published literature on epidemiology of HAI, surgical site infection (SSI) and catheter related blood stream infection (CRBSI) in India. The literature search was performed using Medline database, PubMed website and general search engines. The citations published in last two decades, highlighting incidence rate, prevalence rate and economic burden were considered for the review. Total 18 studies were shortlisted for the review. Most of them were prospective observational studies and one study was single day point prevalence study.

HAI are likely to be the most common complication of hospital care. World Health Organization (WHO) estimates these infections to occur among 7-12% of the hospitalized patients globally, with more than 1.4 million people suffering from infectious complications acquired in the hospital at any time (1, 2, 5). A survey amongst 55 hospitals of 14 countries representing the 4 WHO regions (Europe, Eastern Mediterranean, South-East Asia and Western Pacific) showed that 8.7% of hospital patients had nosocomial infections (1). HAIs have highest prevalence in intensive care units (ICUs), and in acute surgical and orthopaedic wards (1). Moreover, the burden of HAIs is higher in developing countries (6). The estimated prevalence of HAIs in the United States (US) is 4.5% corresponding to 9.3 infections per 1000 patient-days; while that in Europe is reported to be 7.1% corresponding to a cumulative incidence of 17.0 episodes per 1000 patient-days (3). A Multicenter, prospective cohort surveillance of device-associated infection by the International Nosocomial Infection Control Consortium (INICC) in 55 ICUs of 8

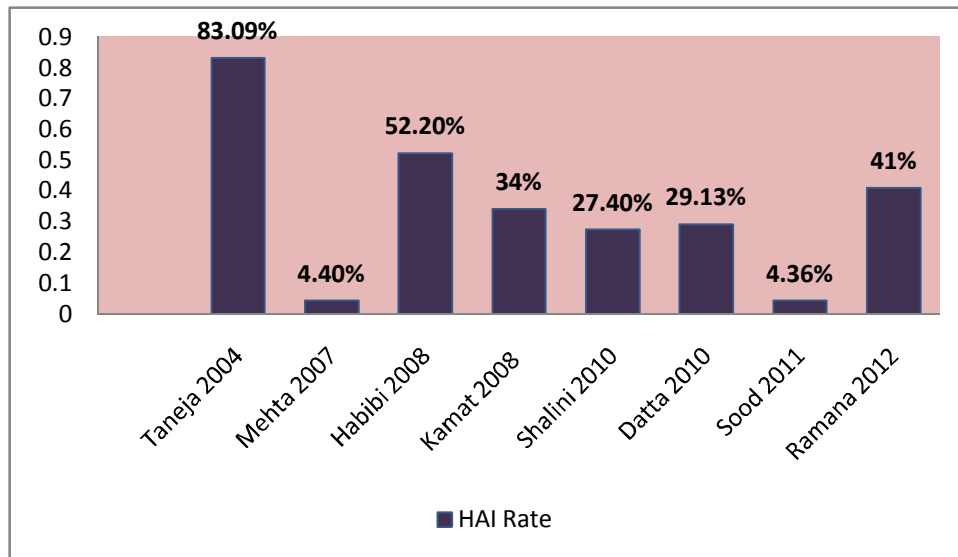
developing countries including India revealed an overall rate of 14.7% HAI corresponding to 22.5 infections per 1000 ICU days (7). In 2007, the INICC conducted a prospective surveillance in 7 Indian cities to determine the rate of HAI, microbiological profile, and related aspects in India. Data for a total of 10,835 patients hospitalized for a total of 52,518 days from 12 ICUs at 7 different hospitals were evaluated. This study benchmarks HAI rates in Indian ICUs against international standards. An overall HAI incidence rate of 4.4% corresponding to 9.06 infections per 1000 ICU-days was reported (9). Lately, there are increasing reports from different parts of the country revealing varying HAI incidence rates across various healthcare setups. In India, major health services are given by government hospitals. Unfortunately, very limited HAI data is available from government hospitals to assess the actual burden of HAI in India. Data on HAI prevalence in India over the last few years has been summarized in Table 1. The table also reflects an increasing trend in HAI incidence across India over the last decade.

Table 1: Incidence of Hospital acquired infections in India

| Source | Total Patients (N) | Patients with HAI (n) | HAI number of episodes | HAI rate [#] | Infections per 1000 patient days |
|-------------------|--------------------|-----------------------|------------------------|-----------------------|----------------------------------|
| Mehta 2007 (9) | 10,835 | <i>ns</i> | 476 | 4.4% | 9.06 |
| Taneja 2004 (14) | 71 | 71 | 59 | 83.09% | 36.2 |
| Habibi 2008 (15) | 182 | 62 | 95 | 52.2% | 28.6 |
| Kamat 2008 (16) | 498 | 103 | 169 | 34% | 40.66 |
| Shalini 2010(13) | 355 | 97 | <i>ns</i> | 27.4% | <i>Ns</i> |
| Datta 2010* (17) | 429 | 105 | 125 | 29.13% | <i>Ns</i> |
| Sood 2011* (18) | 435 | <i>Ns</i> | 19 | 4.36% | 6.16 |
| Ramana 2012* (19) | 642 | 266 | <i>ns</i> | 41% | <i>Ns</i> |

N = total number of patients in the study, n = number of patients with HAI, *ns* = not specified in the source, # where episodes of HAI are unavailable, this column presents HAI percentage, * only device associated infections included.

Figure 1: HAI rate reported in various Indian publications



HAI account for major causes of death, functional disability, emotional suffering and economic burden among the hospitalized patients (2, 3). The crude mortality rate in the INICC survey across developing countries including India ranged from 35.2% to 44.9% (7). The increased length of stay for infected patients is the greatest contributor to cost. It is suggested that the increased length of stay varies from 3 days for gynaecological procedures to 19.8 days for orthopaedic procedures. The increased use of drugs, the need for isolation, and the use of additional laboratory and other diagnostic studies also contribute to costs. There are also indirect costs due to loss of work (1, 3). In India, the extravagant use of antibiotics and antibiotic resistance adds to the expenditure as well as mortality following HAI (10). Additionally, In India, infections due to multi drug resistant organisms increase mortality and also warrant the use of high end antibiotics like Carbapenems and new generation Tetracyclines which increase the health care expenditure. In the US, assuming an incidence of 2 million nosocomial

infections per year, the estimated added healthcare expenditure is in excess of \$2 billion per year; while the direct medical cost of HAI ranged from \$28-45 billion (3). In the UK, a patient with HAI spends 2.5 times longer in hospital, incurring additional costs of £3000 more than an uninfected patient (11). A retrospective case-control, cost utility analysis in a tertiary care Indian hospital reported a significantly longer total hospital stay averaging to 22.9 days in patients with bacteraemia, accompanied with significantly longer ICU stay of 11.3 days and a significantly higher attributable mortality of 54%; all these costing significantly more (average US \$14,818) than the controls (12). An integrated infection control program can reduce the incidence of infection by as much as 30% and reduce the health care costs (13).

CLASSIFICATION OF HAIs AND INDIAN RELEVANCE

The most frequent and important HAIs are: 1) catheter associated urinary tract infection (CAUTI), 2) surgical site infection (SSI), 3) ventilator-

associated pneumonia (VAP), and 4) intravascular device or catheter related bloodstream infections (CRBSI).

Different organisms cause HAI, and the infecting organisms vary among different patient populations, health care settings, facilities, and countries. HAI can also be classified into organism specific (1). Gram-positive organisms commonly reported include *Staphylococcus aureus*, Coagulase-Negative Staphylococci (CoNS), Enterococci; while commonly reported gram-negative organisms include *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinobacter baumannii*, and *Escherichia coli* (1, 16, 20, 21, 22, 23, 24). *Clostridium difficile* is the major cause of nosocomial colitis in adults in developed countries (1). The implications of hospital acquired methicillin-resistant *Staphylococcus aureus* (MRSA) infections in nosocomial sepsis are an escalating concern in most of the hospitals globally as well as in India. In the INICC study, 87.5% of all *S. aureus* infections were caused by MRSA, revealing a high burden of MRSA in Indian ICUs (9). Additionally, there are increasing reports of community-acquired MRSA in India (25, 26). Apart from bacteria, fungi, especially *Candida* species is being recognized as an important cause of nosocomial blood stream infections in India (27).

In India, the challenges such as poor medical infrastructure, un-controlled use of antibiotics increased the risk of development of HAIs. SSIs and CRBSIs are considered to be the commonly reported HAIs in India. Hence, we decided to conduct systematic review of epidemiology SSIs and CRBSIs in India, which could help to ascertain the clinical and economic burden due to these HAIs in India and also to implement new or change of current patient management plan by adopting appropriate preventive

measures, thus reducing morbidity, mortality and the extra cost.

1) SURGICAL SITE INFECTIONS

Before the mid-19th century, surgical patients commonly developed post-operative “irritative fever,” followed by purulent drainage from their incisions, overwhelming sepsis, and often death. Post 1860s, introduction of the antiseptics principles substantially decreased the postoperative infectious morbidity. Nevertheless, SSI remained as one of the major nosocomial infections amongst hospitalized patients (28). WHO defines SSI clinically as: “a purulent discharge around the wound or the insertion site of the drain, or spreading cellulitis from the wound”. Infections of the surgical wound (whether above or below the aponeurosis), and deep infections of organs or organ spaces are identified separately. The US Centre of Disease Control and Prevention’s (CDC) National Nosocomial Infections Surveillance (NNIS) system classifies SSIs as being either incisional or organ/space, occurred within 30 days after the operation. Incisional SSIs are further divided into those involving only skin and subcutaneous tissue (superficial incisional SSI) and those involving deeper soft tissues of the incision (deep incisional SSI). Organ/space SSIs involve any part of the anatomy (e.g. organ or space) other than incised body wall layers that was opened or manipulated during an operation. The global data suggests the SSI incidence rate varies from 0.5 to 20% depending upon the type of operation and underlying patient status (28, 29). A recent surveillance by INICC across 82 hospitals of 66 cities in 30 limited-resource countries including India revealed an overall SSI rate of 2.9 as compared with the incidence rate of 2.0 for the US hospitals (30). For India, the overall incidence rate of SSI varies from 2 to 21% across recent reports. The

profile of SSI in India from various studies over the last decade has been summarized in the **Table 2**.

For an SSI, microbial contamination of the surgical site is a prerequisite. The risk of SSI is markedly

increased when a surgical site is contaminated with $>10^5$ microorganisms per gram.

Table 2: Profile of Surgical site infections (SSIs) in India

| Source | SSI | Microorganisms * | | Surgery |
|----------------------|------------------------|---|---|--|
| | <i>Incidence (n/N)</i> | <i>Gram-positive</i> | <i>Gram-negative</i> | <i>Type (%SSI)</i> |
| Bhatia 2003 (51) | 18.7% (116/615) | <u>S. Epidermis (42.24%)</u> MMSE (26.72%), MRSE (15.5%) <u>S.aureus (15.55%)</u> MRSA (12.06%), MSSA (3.2%) | <u>Total (12.06%)</u> E. coli, P.aeruginosa | CABG (ns) |
| Agarwal 2003 (53) | 1.6% (40/2558) | <u>S. aureus (57.5%)</u> MRSA 35%, MSSA 22.5% | P. aeruginosa (10%) E.coli (15%) | Neurosurgeries (1.6%) |
| Pawar 2005 (52) | 5.1% (7/136) | Staphylococcus sp. (10%) | - | Cardiac surgery with intraaortic balloon pulsation (5.1%) |
| Lilani 2005 (34) | 8.95% (17/190) | <u>S. aureus (35.3%)</u> MRSA (33%) | P. aeruginosa (4/17) E.coli (2/17) | Thoracotomy (44.44%) Gastrointestinal surgeries (variable upto 100%) |
| Sharma 2009 (54) | 2.5% (786/31927) | Staphylococcus sp. | - | Neurosurgeries (2.5%) |
| Joyce 2009 (35) | 12% (135/1125) | <u>S.aureus (33.3%)</u> MRSA (14.0%) <u>E faecalis (33.3%)</u> VRE (1.4%) | P. Aeruginosa (24.4%), E.coli (7.4%), Klebsiella spp(1.4%) | Gastrectomy (36.4%), Cholecystectomy (15.4%), Prostatectomy (15.2%), Hysterectomy (10.4%), Appendicectomy (3.4%) |
| Patel 2011 (2) | 12.72% (7/55) | S. aureus (42.86%) | Klebsiella sp. (ESBL) (57.14%) | Colon surgery (29.41%), Amputation (50%) |
| Sarma 2011 (36) | 21% (14/66) | <u>S. aureus</u> MRSA 67% MSSA 33% E.faecalis | <u>E coli</u> ESBL (43%), ESBL+ Amp-C hyperproducers (29%) Amp-C hyperproducers (14%) NDM-1 producer (14%) | (ns) Post-operative patients |

| | | | | |
|----------------------|----------------|--|--|---|
| | | | <u>K. Pneumoniae</u> ESBL (67%), NDM-1 (33%) Enterobacter cloacae - NDM-1 producer (100%) | |
| Reddy 2012 (55) | 3.63% (27/743) | Enterococcus species CoN S. epidermis S. aureus (MRSA) beta-hemolytic Streptococci | klebsiella sp., E.coli Enterobacter sp. | <u>general surgery; surgical</u> <u>gastroenterology</u> SSI in bowel resection (50%) Elective open hernia (<1%) |
| Patel S 2012 (32) | 16% (32/200) | CoNS (14.3%) S. aureus (7.1%) | E. coli (35.7%) Klebsiella sp. (21.4%) P. aeruginosa (14.3%) Proteus mirabilis (7.1%) | Appendicetomy (0-40%) Laparotomy (19.2-31.6%) Amputation (10-60%) Cholecystectomy (7.1- 28.6%) Nephrectomy (13.3-40%) |

N = total number of patients in the study, n = number of patients with SSI, *ns* = not specified in the source, * percentage of isolates specified in () if available from the source

However, when foreign material is already present at the site (i.e. 100 *Staphylococci* per gram of tissue introduced on silk sutures), the dose of contaminating microorganisms required to produce infection may be much lower. The endogenous flora of the patient's skin, mucous membranes, or hollow viscera is the source of pathogens for most SSIs. When mucous membrane or skin is incised, the exposed tissues are at risk for contamination with endogenous flora. Usually, these are aerobic gram-positive cocci (e.g. *Staphylococci*), but when incisions are made near the perineum or groin, these may also include faecal flora (e.g. anaerobic bacteria and gram-negative aerobes). Gram-negative bacilli (e.g. *Escherichia coli*), gram-positive organisms (e.g. *Enterococci*), and sometimes anaerobes (e.g. *Bacillus fragilis*) are the typical SSI isolates when a gastrointestinal organ is operated and is the source of pathogens. Apart from these endogenous sources, exogenous sources of SSI pathogens include surgical personnel (especially members of the surgical team), the operating room

environment (including air), and all tools, instruments, and materials brought to the sterile field during an operation. Exogenous flora are primarily aerobes, especially gram-positive organisms (e.g. *Staphylococci* and *Streptococci*). Rarely, fungi from endogenous and exogenous sources are reported as causative organisms for SSIs (28).

Globally, *S. aureus* continues to top the list of pathogens isolated from SSI, followed by *CoNS*, *Enterococcus* sp, *E.coli*, *P. aeruginosa*, and *Enterobacter* sp. Other pathogens involved include *Proteus mirabilis*, *K. pneumoniae*, *C. albicans*, and other *Streptococcus* sp. (28). Indian studies over the last decade also find *S. aureus* to be the most common gram-positive pathogen followed by *CoNS* and *E. faecalis*; while *E.coli*, *P. aeruginosa* and *K. pneumoniae* remain the commonest gram-negative culprits (**Table 2**). The infecting microorganisms are variable, depending on the type and location of surgery, and antimicrobials received by the patient. Other organisms like *Proteas mirabilis*,

Enterobacter, and *Mycobacterium fortuitum* are also identified in discrete reports (31, 32). A report also identified *Mycobacterium chelonae* as a causative pathogen from a series of laparoscopic port site infections (33).

The gradual increase in the emergence of antibiotic resistant microorganisms in surgical patients in India further complicates the management of SSIs (2, 34, 35) Upfront and indiscriminate use of antimicrobials as prophylaxis is a routine in India partly contributing to this resistance (2, 10). As expected, majority of the *S. aureus* isolated in Indian patients were found to be MRSA (Table 2). Moreover, 100% resistance of *S. aureus* to penicillin has been documented in one study, while resistance to oxacillin, cloxacillin, clindamycin, cephalosporins, ciprofloxacin, ampicillin, amoxicillin, tetracycline, and cotrimoxazole has also been found in other studies (2, 35). *S. aureus* strains positive for beta-lactamase have also been reported from Indian patients (34). *E. faecalis* strains were found to be resistant to penicillin, cloxacillin and clindamycin, cotrimoxazole, amikacin, gentamicin, and ciprofloxacin in varying extent (35). Among the gram-negative organisms, *P. aeruginosa* has exhibited 100% resistance to gentamycin (33), which was also one of the antibiotics used for antimicrobial prophylaxis in those patients. Resistance to third generation cephalosporins, cotrimoxazole, ciprofloxacin, gentamicin and amikacin has also been observed with *P. aeruginosa*, *E. coli*, as well as *Klebsiella sp.* (35). ESBL producers and Amp-C hyperproducers isolated from *Enterobacteriaceae* infections were resistant to multiple classes of antimicrobials - ampicillin, piperacillin, piperacillin-tazobactam, third generation cephalosporins, amikacin, gentamicin, tobramycin, ciprofloxacin. Metallo- β lactamase (MBL) producers were resistant

to all antimicrobials except colistin and tigecycline heralding an era of untreatable infections. Carbapenems are usually the choice of antimicrobials in infections caused by ESBL and Amp C producing enterobacteriaceae. However, there are increasing reports of carbapenem resistant strains across the globe. The New Delhi metallo- β -lactamase-1 (NDM-1) containing strains – a type of carbapenemase producer, has been isolated from different locations in India since 2006 (36, 37, 38, 39, 36). All these multidrug resistant strains have raised concerns about increasing carbapenem resistance amongst gram-negative bacteria in various infections over the last decade in India (40, 41, 42).

The incidence of SSI also varies more widely between surgical procedures suggesting the type of surgery to be an important determinant. The INICC comparison revealed that the SSI rates amongst hospitals in limited-resource countries including India were significantly higher after abdominal surgeries, cardiothoracic surgeries, and ventricular shunt when compared to those in the US hospitals (30). Reports exclusively from India also suggest a higher incidence for gastrointestinal and cardiothoracic surgeries; while a relatively lower one with neurosurgical procedures (Table 2). Moreover, while laparoscopic procedures are associated with lesser infections as compared to open surgeries, port site infections are a growing concern in patients undergoing laparoscopic procedures (43, 44, 45). Port-site mycobacterial infection following laparoscopy is also on a rise over last decade in India (46, 47, 48, 49). In most of these cases, the source of infection is attributed to the laparoscopic instruments and lack of their proper sterilization (50).

Various risk factors to develop SSIs are listed categorically; such as wound types (clean, clean-contaminated, contaminated, and dirty-infected), age

above 45 years, female gender, diabetic status, pre-hospital stay, the quality of surgical technique, presence of foreign bodies including drains, and the experience of the surgical team, and the pre-hospital stay (1, 2, 32, 34, 35). Indian data have shown an increased SSI incidence with the degree of contamination. SSI rates were low in elective surgeries compared to emergency procedures (2, 32; **Table 3**). Nevertheless, prolonged pre-operative hospital stay in elective surgery was associated with higher rate of infection. The duration of surgery was also an important risk factor for SSI; surgeries lasting 30 minutes to 1 hour were associated with lower rates as compared to higher duration of 1 to 2 hours (32, 34, 51). SSIs considerably impact the postoperative hospital stay and hospital costs, as well as mortality (1). Indian studies have shown that patients affected by SSI have longer stays in ICU as well as in wards, and receive multiple antibiotic regimes, which lead to increasing financial burdens (35, 52). Post-operative stay of infected patients was about 4 times longer than those without any infections. An average

increase in the cost of treatment of 3.8% for mild infections, 14.7% for moderate infections, and 29.4% for severe infections has been reported in patients with SSI (34, 51). A cost comparison in India revealed total expenses incurred by patients with SSIs was INR 29,000 (average) as compared to INR 16,000 (average) incurred by non-infected patients (35). The incidences of mortality were also higher in infected patients (12.8% to 19.9%) as compared to the controls (1.1% to 3.8%) (34, 51).

Despite advances in infection control practices, emergence of antimicrobial-resistant pathogens, increased elderly patients with a wide variety of chronic, debilitating, or immune-compromising underlying diseases continue to increase the burden of SSI. A systematic and preventive approach should be targeted towards awareness that the risk to SSI is influenced by characteristics of the patient, operation, personnel, and hospital. The risk factors considered to be predictor for the development of SSI are given in the Box 1.

Table 3: Type of Interventions and Wounds associated with SSIs in India

| Source | Overall SSI | SSI rate as per Wound Type | | | | SSI by Intervention type | |
|-------------------|-----------------|----------------------------|--------------------|--------------|-----------------|--------------------------|----------------|
| | | Incidence (n/N) | | | | Incidence (n/N) | |
| | Incidence (n/N) | Clean | Clean Contaminated | Contaminated | Dirty/ Infected | Elective | Emergency |
| Lilani 2005 (34) | 8.95% (17/190) | 3.03% (4/132) | 22.41% (13/58) | ns | ns | ns | ns |
| Patel D 2011 (2) | 12.72% (7/55) | 0 (0) | 15.38% (2/13) | 0% (0/2) | 23.81% (5/21) | 10.26 % (4/39) | 18.75% (3/16) |
| Sarma 2011 (36) | 21% (14/66) | 18% (7/39) | 10% (2/21) | Ns | 83% (5/6) | ns | Ns |
| Patel S 2012 (32) | 16% (32/200) | 3% (2/66) | 11.4% (8/70) | 20% (4/20) | 40.9% (18/44) | 12.68% (18/142) | 24.14% (14/58) |

n = number of infected patients, N = total number of patients in the category, ns = not specified in the source

| BOX 1: Risk factors considered as predictors of SSI development | |
|--|---|
| • Old age | • Prolonged operative procedures |
| • Immunocompromized status and underlying illness | • Complex procedures |
| • Obesity | • Inadequate preparation of skin |
| • Hypertension | • Increased pre-operative stay |
| • Smoking | • Wound type (contaminated or dirty wounds) |

2) CATHETER RELATED BLOODSTREAM INFECTIONS

Vascular access poses significant potential risks of iatrogenic complications in general, but in particular, of catheter related bloodstream infections (CRBSIs) (56). Insertion of central line, a very common procedure in critical care settings is associated with infectious complications such as local colonization of organisms eventually leading to bacteraemia and sepsis (57). The definitive diagnosis of catheter related infection can be made by using a combination of clinical signs and symptoms together with the quantitative culture techniques (58).

CRBSI and central line associated blood stream infection (CLABSI) were used interchangeably in various studies. For reporting purpose, the term “CRABSI” has been used for CLABSI.

CRBSI might occur as a result of the entry of pathogenic microorganisms to the bloodstream via four different routes: local insertion site colonization, catheter hub contamination, haematogenous seeding and infusion of contaminated fluids. The spread of infection from the insertion site has been widely recognized as the main cause of CRBSI. On the other hand, microorganism colonization may occur due to the contamination of the catheter hub, its lumen, and its guidewire during insertion, the catheter, and the connectors to the infusion lines when handling them, or the infusion administered through the catheter (59,

60, 61). Once the microorganism has access to the CVC, infection occurs as a result of the capacity of bacteria to adhere to the catheter surface, colonize and develop biofilm, which is formed when the microorganisms are irreversibly attached to the external or internal surface of the catheter and produce extracellular polymers that facilitate their adherence and form a structural matrix (60).

The majority of CRBSIs are associated with CVCs, and the relative risk for CRBSI is higher with CVCs than with peripheral venous catheters (58, 62). In developed countries such as US, France, Spain, Germany, Italy and the UK, it has been observed that the incidence of CRBSIs varies widely among different healthcare institutions, ranging from 1.12 to 4.2 per 1,000 catheter days (57). A recent systematic review across selected CVC studies revealed a CRBSI incidence of 0 - 4.9% with a mean of 1.01%, while that with PICCs ranged from 2.7 - 4% with a mean of 3.23% (63). In US, it has been estimated that approximately 31,000 deaths per year are attributable to bloodstream infections, representing an expenditure of about \$18,000 per CRBSI. A surveillance study by the INICC in 422 ICUs of 36 countries in Latin America, Asia, Africa, and Europe revealed a pooled rate of 6.8 CRBSI per 1000 central line-days. This was more than 3-fold higher than the 2.0 per 1,000 central line-days reported in comparable US ICUs. The medical, neurologic and

paediatric ICUs topped the list with an infection rate of >10 per 1000 central line-days as compared to other ICUs (64).

In another epidemiological survey by the INICC across developing countries, a total of 292 CRBSI in 36,857 catheter days were reported from the medical-surgical-neurosurgical ICUs of India. This corresponded to a CRBSI rate of 7.7 per 1000 catheter days for India; a rate too high when compared to the US medical-surgical ICUs that had a mean CLABSI rate of 1.5 cases per 1000 catheter days (56). There are very limited reports specifically on CLABSI from Indian setups. An account of available information on CRBSI available from

Indian studies is presented in **Table 4**. Over the last decade, CRBSI incidence in India has been varying from 0.2 to 27%, with a rate of 0.5 - 47 per 1000 catheter days. As with the global scenario, neonatal ICUs in India also have a higher CRBSI rate (27.02 per 1000 catheter days) when compared with other ICUs (65). The variability of CRBSI incidence is attributed to various risk factors like (57, 60, 62) listed in **Box 2**;

| BOX 2: Risk factors attributing to the variability of CRBSI incidence | |
|--|--|
| • Patient setting (e.g. ICU, hospital, or home), | • Length of hospitalization time, |
| • Insertion techniques, | • Long-term indwelling central venous catheter, |
| • Site of catheterization, | • Number of catheter lumens, |
| • Type of catheter used, | • Local and systemic antibiotic use, |
| • Type and frequency of dressing, | • Type of antiseptic solution use, |
| • Frequency of manipulation, | • Experience of the person in charge of catheter care, |
| • Duration of catheterization, | • Emergent versus elective placement, and |
| • Diagnostic criteria used for diagnosing catheter related infections | |

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Table 4: Profile of Catheter Related Bloodstream Infections (CRBSI) in India

| Source | % CLABSI (n/N) | CLABSI Rate <i>per 1,000 catheter days</i> | Gram-Positive Isolates (%) | Gram-negative Isolates (%) | Candida Isolates (%) |
|------------------------------|--------------------|--|---|--|----------------------------|
| Pawar 2004 (62) | 2.6% (35/1314) | 4.01 | <u>Staphylococcus (17.5%)</u> MRSA (11.7%), CONS sp(5.8%) | <u>Total 70.5%</u> E.coli (47%), Acinobacter (11.7%) Enterobactor sp (5.8%), Proteus sp (5.8) | 11.7% |
| Datta 2010 [#] (17) | 13.34% (55/412) | 13.86 | Enterococcus spp.(18%) Staphylococcus aureus (8.5%) | P.aeruginosa (32%), Acinetobacter sp. (31%), K. pneumoniae (20%), E. coli (11%) | 4% |
| Singh 2010 (21) | 0.16% | 0.48 | CoNS (67%) | K.pneumoniae (33%) | - |
| Chopdekar 2011 (65) | 7.6% (6/78) | 9.26 (General) 8.64 (PICU) 27.02 (NICU) | CoNS (50%) | K.pneumoniae P.aeruginosa | <i>Present</i> |
| Patil 2011 (58) | 27.77% (15/54). | 47.31 | <u>CoNS (65%):</u> S.epidemidis (45%) S. haemolyticus (15%) S. saprophyticus (5%) S. aureus (15%) | K.pneumoniae (10%) E coli (5%) | 5% |
| Parameswaran 2011* (71) | 10.7% (25/232) | 8.75 | <u>Total 64%</u> <u>S. aureus (40%)</u> MRSA-26.7%, ESBL -13.3% | <u>Total 36%</u> P. aeruginosa, E.coli, K. pneumonia | 16% |
| Kaur 2012 (68) | 1.67% (8/480) | 2.79 | S.aureus (16.6%) | Acinobacter sp. (59.5%) E.coli (43%) | - |

* patients with CVC (~75%) and midline catheters, # isolated pathogens refer to all device associated infections (CRBSI, CAUTI, VAP).

The prevalence of infection as it relates to the exit site is influenced by the density of skin flora, skin moisture, and body temperature in that area. For instance, CVCs inserted into the internal jugular or femoral veins carry more risk of infection than do CVCs inserted into a subclavian vein. The incidences

of infection are often higher in the ICUs than in the less acute inpatient or ambulatory setting. In the ICU, central venous access might be needed for extended periods of time; patients can be colonized with hospital acquired organisms; and the catheter can be manipulated multiple times per day for the

administration of fluids, drugs, and blood products. Further, some catheters can be inserted in urgent situations, during which optimal attention to aseptic technique might not be feasible (66). Recent data also suggest that a significant numbers of patients with central lines are in hospital units outside the ICU (e.g. patients on haematology–oncology wards), and many patients are discharged with central venous catheters in place where there is a substantial risk of CLABSI (61, 67). A univariate analysis from Indian study revealed that multi-lumen catheters were significantly associated with the CVC-BSI group (37.5% vs. 2.4% controls; $p < 0.001$). It was also shown that longer duration of catheterization was an independent predictor of CVC-BSI (62). Indian hospitals catering to a lower socioeconomic group, with overall poor hygiene of patients; more elderly patients with age above 60 years, and emergency catheterization were particularly associated with higher incidences of BSI (58, 61). A central line exceeding 7 days in situ has increased risks of BSI, as reported in Indian studies (58, 68). Internationally, CoNS, *S. aureus*, Enterococci and *Candida* sp. are considered the most commonly reported causative pathogens for CLABSI; while gram-negative bacilli account for about 20% of the infections (59). However, the microorganism profile in Indian patients depicts a different picture (Table 4). While CoNS and *Staphylococcus* species are common gram-positive microorganisms associated with CLABSI, gram-negative isolates including *Klebsiella* sp., *Enterobacter* sp., and *E. coli* seems to be predominating in Indian population with CLABSI over the last decade (17, 61, 62, 65, 68, 69). The occurrence of candidemia as a nosocomial blood stream infection has been increasing in India, and CVCs have been significantly related to the acquisition of candidemia (27, 58, 62). An isolated

case report of *Rhizobium radiobacter* BSI associated with a CVC has also been described in India (70).

Antimicrobial resistance is a problem for all common pathogens causing CLABSIs globally as well as in India, particularly in ICUs (59). *CoN S. epidermis* was resistant to oxacillin, but 100% susceptible to vancomycin. MRSA accounted for 26.7% of patients with CRBSI in a recent study at a tertiary care hospital in India. Additionally, 13.3% of the isolates were ESBL producing organisms (71). Multiple drug resistance has been found in gram-negative organisms as well. One study showed that *K. pneumoniae* isolates were resistant to all the antibiotics except amikacin and ciprofloxacin; similarly *E. coli* was resistant to all the antibiotics except amikacin and cefotaxime (58). In a retrospective review of VAP/CRBSI data over 8 years in a tertiary care hospital of India, ESBL strains of *Enterobacteriaceae* were isolated along with carbapenem resistant *Pseudomonas* and *Acinetobacter* strains (72). A strain of *A. baumannii* isolated from a patient with CRBSI was resistant to all routine and reserved drugs (71). The incidence of resistant device related infections predominantly caused by biofilm producing bacteria are also on a rise in India (65). Gram-negative pathogens were found to be predominant biofilm producing bacteria along with *Staphylococcus* at a tertiary care centre in northern India (73).

Internationally, approximately 5 million CVCs are inserted per year, and of these 3-8% lead to BSI. The attributed mortality rate is 10-25% making them the most deadly of all HAIs (61, 63, 74, 75). A much higher mortality rate varying from 20% to 33% has been reported from India (62, 65). CVC-BSI infections led to significant increases in the ICU stay and postoperative stay in a prospective study, which would significantly increase the hospital care cost

(62). Prevention is the cornerstone of catheter-related infections. The control of risk factors can reduce the incidence of CRBSI by 40% or greater (60). Because CRBSIs are due to multiple factors, there is no simple strategy to prevent infection. Prevention and control programs based on the proven technology to prevent CRBSIs should be widely used, and future research should focus on our understanding of the biologic forces that cause colonization so technology designs focus on products that prevent microorganisms from gaining entry.

The most of the studies were represented the HAI rate in tertiary care hospitals, where the standard operating procedures are followed to control the infection. Due to paucity of HAI data from government hospitals or from cities beyond metro towns, the currently available data would not give the correct incidence and prevalence of HAI in India. It would be highly advisable to conduct properly designed prospective observational studies to collect critical data on HAI.

SUMMARY

HAIs are a major public health problem throughout the world. The most likely complication of hospital care, HAIs, mainly SSI and CRBSIs significantly impacts the morbidity and mortality, and financial cost implications due to prolong hospital stay and related expenditure, thus adding to the overall healthcare cost for patients. The burden of HAIs is even higher in developing countries like India, as compared to developed countries. SSI and CRBSIs are the most preventable types of HAIs with proper prevention and control measures which not only help reducing the incidence of infection, but also decrease the related financial burden on the patient.

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