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REVIEW

Health care-associated infections – an overview

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Mainul Haque[1]
Massimo Sartelli[2]
Judy McKimm[3]
Muhamad Abu Bakar[1]

[1]Faculty of Medicine and Defence Health, Universiti Pertahanan Nasional Malaysia (National Defence University of Malaysia), Kem Sungai Besi, 57000 Kuala Lumpur, Malaysia; [2]Department of Surgery, Macerata Hospital, Via Santa Lucia 2, 62100 Macerata, Italy; [3]Swansea University School of Medicine, Swansea University, Singleton Park, Swansea, Wales SA2 8PP, UK

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Correspondence: Mainul Haque
Faculty of Medicine and Defence Health, Universiti Pertahanan Nasional Malaysia (National Defence University of Malaysia), Kem Sungai Besi, 57000 Kuala Lumpur, Malaysia
Mobile +60 10 926 5543
Email runurono@gmail.com

Abstract: Health care-associated infections (HCAIs) are infections that occur while receiving health care, developed in a hospital or other health care facility that first appear 48 hours or more after hospital admission, or within 30 days after having received health care. Multiple studies indicate that the common types of adverse events affecting hospitalized patients are adverse drug events, HCAIs, and surgical complications. The US Center for Disease Control and Prevention identifies that nearly 1.7 million hospitalized patients annually acquire HCAIs while being treated for other health issues and that more than 98,000 patients (one in 17) die due to these. Several studies suggest that simple infection-control procedures such as cleaning hands with an alcohol-based hand rub can help prevent HCAIs and save lives, reduce morbidity, and minimize health care costs. Routine educational interventions for health care professionals can help change their hand-washing practices to prevent the spread of infection. In support of this, the WHO has produced guidelines to promote hand-washing practices among member countries.

Keywords: health care-associated infections, central line-associated bloodstream infections, surgical site infections, catheter-associated urinary tract infections, ventilator-associated pneumonia

Background

Health care-associated infections (HCAIs) are those infections that patients acquire while receiving health care.[1] The term HCAIs initially referred to those infections linked with admission to an acute-care hospital (earlier called nosocomial infections), but the term now includes infections developed in various settings where patients obtain health care (eg, long-term care, family medicine clinics, home care, and ambulatory care). HCAIs are infections that first appear 48 hours or more after hospitalization or within 30 days after having received health care.[2] Multiple studies indicate that the most common types of adverse events affecting hospitalized patients are adverse drug events, HCAIs, and surgical complications.[3–7] The US Center for Disease Control and Prevention identifies that nearly 1.7 million hospitalized patients annually acquire HCAIs while being treated for other health issues and that more than 98,000 of these patients (one in 17) die due to HCAIs.[8] The Agency for Health care Research and Quality reported that HCAIs are the most common complications of hospital care and one of the top 10 leading causes of death in the USA.[9] Out of every 100 hospitalized patients, seven patients in advanced countries and ten patients in emerging countries acquire an HCAI.[10] Other studies conducted in high-income countries found that 5%–15% of the hospitalized patients acquire HCAIs which can affect from 9% to 37% of those admitted to intensive care units (ICUs).[11,12] Multiple research studies

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report that in Europe hospital-wide prevalence rates of HCAIs range from 4.6% to 9.3%.[13–21] The WHO reports however that HCAIs usually receive public attention only when there are epidemics.[22] HCAIs also have impact on critically ill patients with around 0.5 million episodes of HCAIs being diagnosed every year in ICUs alone.[7,14,23] ICU patients are often in a very critically ill, immuno-compromised status which increases their susceptibility to HCAIs.[24,25]

Brief history

There has been long-standing awareness that the practice of medicine can do harm as well as good. For example, Hippocrates, the father of modern medicine, stated more than 2,500 years ago that "I will use treatments for the benefit of the ill in accordance with my ability and my judgment, but from what is to their harm and injustice I will keep them."[26] It was also recognized (eg, by Semmelweis discussing puerperal fever) many years ago that coming into hospitals (in particular) can be dangerous.[27] In this century, the idea that medicine could cause harm, including death is described as "unintended physical injury resulting from or contributed to by medical care, including … [its] absence … that requires additional monitoring, treatment or hospitalization, or … results in death."[28,29] Offering another perspective, an American natural sciences writer noted that HCAIs are now killing around 100,000 people, many more than HIV/AIDS, cancer, or road traffic accidents.[30]

The Hungarian obstetrician Professor (Dr) Ignaz Phillip Semmelweis is largely considered as the medical doctor who realized that health care providers could communicate disease. His work identified the mode of communication and spread of puerperal sepsis while working at the Maternity Hospital in Vienna. In 1847, he observed higher rates of maternal mortality among patients treated by obstetricians and medical students than among those cared for by midwives. At that time, he also found that a pathologist had died of sepsis after wounding himself with a scalpel while carrying out an autopsy on a patient with puerperal sepsis. The pathologist's illness mirrored that of women with puerperal sepsis, and Semmelweis wrote that both a scalpel and a physicians' contaminated hands could transmit organisms to mothers during labor. He introduced chlorinated lime hand washing to the obstetric hospital staff, resulting in large improvements in maternal mortality rates.[31] However, Semmelweis' theories were dismissed by most of the medical establishment because of a lack of appropriate statistical analysis of the data. Nevertheless, after Koch's postulates were published in 1890, the germ theory of disease and Semmelweis' theory of transmission of disease from doctor to patient were found to be valid. Semmelweis was therefore the first to describe an HCAI and provide an intervention to avert its spread through hand hygiene.[32]

Prevalence and brief outline of HCAIs

A survey conducted in 183 US hospitals with 11,282 patients reported that 4% of patients had at least one HCAI with the most common microorganism being *Clostridium difficile*. Most infections were surgical site infections (SSIs), pneumonia, and gastrointestinal infections.[33] A study 2 years earlier by the same group found that 6% (51) of patients had suffered from HCAIs with the top 75.8% acquiring SSIs, urinary tract infections (UTIs), pneumonia, and bloodstream infections. *Staphylococcus aureus* was the most frequently detected microorganism.[34] The group conducted a comparative study between 2011 and 2015 and found a statistically significant ($P<0.05$) reduction of HCAIs in SSIs, UTIs, and central line infections, probably due to a national initiative.[35]

HCAIs are also problematic elsewhere in the world. For example, a study in Singapore reported 11.9% (646) patients with HCAIs, primarily undetermined clinical sepsis, and pneumonia caused mainly by *S. aureus* and *Pseudomonas aeruginosa*.[36] This study also reported that the *Acinetobacter* species and *P. aeruginosa* were extremely resistant to carbapenem.[36] A recent European study found that 2,609,911 new patients were identified as having HCAIs annually in the European Union and European Economic Area.[37] This study revealed that for every 20 patients hospitalized, at least one acquired an HCAI which was preventable.[37] *Klebsiella pneumoniae* and the *Acinetobacter* species were exceedingly resistant to multiple antimicrobials, and the lack of new antimicrobials increases the huge burden in Europe.[37] In Greece, the HCAI prevalence rate was 9.1%. The frequent types of HCAIs were lower respiratory tract infections (LRTIs), bloodstream infections, UTIs, SSIs, and systemic infections.[38] One systematic review and meta-analysis regarding HCAIs in Southeast Asian countries (Brunei, Myanmar, Cambodia, East Timor, Indonesia, Laos, Malaysia, the Philippines, Singapore, Thailand, and Vietnam) found an overall prevalence rate of 9.1% with the most common microorganisms being *P. aeruginosa*, the *Klebsiella* species, and *Acinetobacter baumannii*.[39]

A study conducted in eight university hospitals of Iran (ranging from 60 to 700 beds) reported an overall HCAI frequency of 9.4%, the most common HCAIs were bloodstream infections, SSIs, UTIs, and pneumonia.[40] A logistic regression analysis showed that the odds ratio (OR) for males as opposed to females acquiring infections was 1.56 (95% confidence interval [CI] 1.21–2.02). Additional risk factors for HCAIs include a central intravascular catheter, adjusted OR of 3.86 (95% CI 2.38–6.26), and with a urinary catheter, adjusted OR of 3.06 (95% CI 2.19–4.28). Being admitted to an ICU is not in itself a self-determining HCAI risk factor. The OR for all HCAIs of acquiring an infection was 3.24 (95% CI 2.34–4.47) in patients with hospital stays longer than 8 days.[33] Seventy-one percentage (71%) of the studied patients received antimicrobials, but 9.4% had at least one evidence of infection.[33] Another study revealed that the average number of microbes ranged from on (9.67×1011), working surfaces (1.64×1012), door handles (1.71×1012), and highest in taps (2.08×1012).[41] The highest number (23) of pathogens were isolated from door handles, and the peak variance of pathogens were on hospital floors (7). Among those microbes, those that were disease-producing were 46.14%, 53.86% were nonpathogenic, the most common was *S. aureus* at 14.42% and 45.2% of the total bacterial isolates comprised *Bacillus subtilis*. A study conducted in Ghana reported that gentamicin was the most effective antibiotic (100%) on both Gram-positive and Gram-negative organisms, but of the 12 antibiotics tested (ampicillin, cefuroxime, cotrimoxazole, cefotaxime, tetracycline, amikacin, gentamicin, chloramphenicol, cefixime, cloxacillin, and erythromycin), six were resistant to either Gram-positive or Gram-negative organisms.[41] Most of the HCAIs in the US are triggered by the ESKAPE group, comprising the antimicrobial-resistant Gram-negative microorganisms (*K. pneumoniae, A. baumannii, P. aeruginosa*, and *Enterobacter* spp.) and the Gram-positive species, *Enterococcus faecium* and *S. aureus*.[42–44] Multiple studies report that Gram-negative organisms are responsible for 10%,[45] 20%–40%,[46] of HCAIs and that antimicrobial resistance places a significant burden on the global health care system, particularly in low resource countries.[47,48] This problem is exacerbated as research and development into new antimicrobials targeting Gram-negative organisms has rapidly decreased in recent years.[48]

Among the newer aminoglycosides, plazomicin has been found to be active against the extended-spectrum beta-lactamase (ESBL) generating strains of *Enterobacter* spp., *Escherichia coli*, and *K. pneumoniae*[49] and more effective in laboratory experiments against *A. baumannii* than *gentamicin*, *tobramycin*, and *amikacin*.[50] Plazomicin has a better safety profile than other drugs, with no report of damage to the cochlea, auditory nerve, vestibular, and renal system in healthy volunteers, even with high and multiple doses.[51] Another study found that, in a comparison between HCAIs due to methicillin-sensitive *S. aureus* and methicillin-resistant *S. aureus* (MRSA), isolates were statistically significantly ($P<0.005$) more resistant to ciprofloxacin, clindamycin, trimethoprim/sulfamethoxazole, erythromycin, gentamicin, and tetracycline.[52] Hospital waste, especially contaminated surgical waste, often acts as a reservoir for pathogenic virulent microorganisms, and it suggested that 20%–25% of the waste produced by health care outlets is considered to have high potential to cause HCAIs, it therefore needs appropriate handling and disposal.[53,54]

Causative organisms

Around 12–17 microorganisms cause 80%–87% of HCAIs: *S. aureus*, *Enterococcus species* (eg, *faecalis*, *faecium*), *E. coli*, coagulase-negative *Staphylococci*, *Candida species* (eg, *albicans*, *glabrata*), *K. pneumoniae* and *Klebsiella oxytoca*, *P. aeruginosa*, *A. baumannii*, *Enterobacter* species, *Proteus* species, Yeast NOS, *Bacteroides* species, and other pathogens.[45,55,56] Among these pathogens, 16%–20% include multidrug-resistant (MDR) phenotypes: MRSA, vancomycin-resistant *E. faecium,* carbapenem-resistant *P. aeruginosa*, extended-spectrum cephalosporin-resistant *K. pneumoniae*, *K. oxytoca*, *E. coli*, and *Enterobacter species*, and carbapenem-resistant *P. aeruginosa*, *K. pneumoniae/K. oxytoca*, *E. coli*, *Enterobacter* species, and *A. baumannii*.[45,55] Some of these Gram-negative microorganisms have a much higher rate (20%–40%) of resistance than others[45] with the organisms isolated from device-associated HCAIs having the highest antimicrobial resistance phenotypes.[56] In the latter study, although similar to the percentage resistance for most phenotypes was that in an earlier research study,[45] an upsurge in the scale of the resistance fractions against *E. coli* pathogens was observed, especially with fluoroquinolones.[56] *Acinetobacter, Burkholderia spp.* and *Pseudomonas spp*. isolates were 100% were 92% resistant to cephalosporins respectively. *Burkholderia* spp. was again totally resistant to fluoroquinolones and *Acinetobacter* spp. and *Pseudomonas* spp. were 94.2% and 95.8% resistant, respectively. The same study reported that 86.4% *Acinetobacter* spp. and 62.5% *Pseudomonas* spp. showed a high resistance to carbapenems, the preferred drug regime in ICUs. Carbapenems were found more effective against *Burkholderia* spp. with 20% resistance.[57] In another study, *Enterobacteriaceae* community were found to be completely resistant to third-generation cephalosporins.[58] Over 80% of the *Klebsiella* spp. community were resistant to ciprofloxacin, gentamicin, piperacillin, tazobactam, and imipenem showing 48.6% resistance. *E. coli* was equally resistant although carbapenems were effective in almost

80% cases. Although *Citrobacter* spp.-related HCAIs are a relatively minor proportion, they also show resistance toward cephalosporins, fluoroquinolones, and aminoglycosides.[58] Another study reported that although the *Acinetobacter* spp. were 76.99%–92.01%, resistant to most antimicrobials, only 30% of *Acinetobacter* spp. isolated were susceptible.[59] It can be seen therefore that the causative pathogenic microorganisms differ from country to country as does patterns of resistance.

Types of HCAIs

Alongside infections due to cross-contamination between patients and health workers, patients being susceptible to common infections due to diminished immune responses, and infections at surgery sites (SSIs), many HCAIs are due to implants and prostheses. These include central line-associated bloodstream infections (CLABSIs), catheter-associated UTIs, and ventilator-associated pneumonia (VAP).[57,60,61]

CLABSIs

CLABSIs substantially increase morbidity, mortality, and health care costs, and great attention has been paid to addressing these.[62,63] As a consequence, in 2009, 25,000 fewer CLABSIs occurred in the ICUs of US hospitals than in 2001, a 58% reduction, with about 6,000 lives saved and estimated financial savings of US$414 million in potential excess health care costs, although the costs of reducing such infections is very high.[64] It is estimated that it costs ~$1.8 billion between 2001 and 2009 to save an additional 27,000 lives.[64] Despite this investment, a considerable number of CLABSIs still occur, especially in outpatient hemodialysis centers and inpatient wards.[64] Another study also reported the link between CLABSIs and considerable morbidity and mortality, although there is a wide variation in reported infection rates (from 20% to 62.5%) in emerging economies.[65] A study conducted in Taiwan reported the occurrence of CLABSIs as 3.93 per 1,000 central-catheter days.[66] The most common causative pathogens were Gram-negative (39.2%), Gram-positive (33.2%), and *Candida* spp. microorganisms (27.6%).[66] In this study, patients developed CLABSIs 8 days from the time of insertion of the central line catheter.[66] Multivariate analysis showed that a higher Pitt bacteremia score (OR 1.41; 95% Cl=1.18–1.68) and the prolonged interval between the onset of CLABSIs and catheter removal (OR 1.10; 95% CI=1.02–1.20) were associated with higher death rates.[66] Another similar study identified prolonged catheter in situ, pediatric ICU stay, and intravenous nutrition were significant prognosticators of peripherally inserted central catheter-related CLABSIs among hospitalized children.[67]

SSIs

SSIs (formerly termed "wound infections") are still one of the most common adverse events that occur in hospitalized patients undergoing surgery or in outpatient surgical measures, regardless of the advances in preventive procedures.[68] SSI is the most common complication in postoperative surgical patients, associated with significant morbidity, high death rates, and financial stress on national budgets and individual patients.[69–71] SSIs are defined as infections arising up to 30–90 days after surgery in patients receiving an organ, group of cells, or device and affecting both the incisional site and deeper tissues around the surgery location.[72,73]

The type of surgery determines the proportion of SSIs. Between 2% and 36% of patients may develop SSIs, with the highest risk for orthopedic followed by cardiac and intra-abdominal surgery.[14,72,74,75] The length of hospital stay for patients with SSIs increases from 4 to 32 days as compared with patients with no post-surgical infections.[76–78] Approximately 25% of patients with SSIs develop severe sepsis and shock and are moved to an ICU.[65] SSIs cause statistically significant morbidity, mortality, and financial burdens for individuals and for communities.[69–71,78]

HCAIs are common following cardiac surgery, with a reported incidence rate of between 5.0% and 21.7%,[79,80] often accompanied with multiple organ failure and prolonged hospital stays, leading to increased mortality rates.[79,80] The three most common locations for HCAIs after cardiac surgery are lungs, central venous catheters, and surgical sites.[69] SSIs followed by cardiac surgery classically present with localized cellulitis (erythema, warmth, and tenderness), purulent discharge, sternal instability, chest pain, and systemic upset with deep infections.[81–83] SSIs are devastating for orthopedic patients as it is very difficult to rid the bones and joints of the infection.[83] One Saudi Arabian study reported an incidence of SSIs in orthopedic patients of 2.55% (79 of 3,096 patients) with the most common pathogens being *Staphylococcus* species including MRSA (29.11%); *Acinetobacter* species (21.5%); *Pseudomonas* species (18.9%), and *Enterococcus* species (17.7%).[84] Surgical wound contamination potentials, patients' clinical conditions, type of surgery, and length of surgery were variables statistically significantly associated with SSIs and should be viewed as risk factors.[85] The movement and number of staff and the structural features of the operating theater also affect the incidence of SSIs.[85,86] One study found that 73.33% cases of SSIs following orthopedic surgery were culture positive, and a total of 35 bacterial strains were isolated, among which 65.72% were Gram-positive isolates and 34.28% were Gram-negative bacteria.[87]

About 68.6% of all bacterial isolates were resistant to cefuroxime used in the management of orthopedic SSIs. This study also found that diabetes mellitus, smoking, operations lasting more than 3 hours, the absence of antibiotic prophylaxis, and a history of previous surgery were positive risk factors associated with a significant upsurge in SSIs.[87]

SSIs comprise at least 14%–22.2% of all HCAIs for abdominal surgery[88–90] and often lead to extended hospitalization and higher antimicrobial costs.[71] The microorganisms generally involved in such SSIs include *S. aureus*, coagulase-negative *Staphylococci* and *Enterococcus* spp., and *E. coli*.[71] *S. aureus* has been known to be a major cause of HCAIs for over 100 years.[91] When first introduced, nearly all strains were susceptible to penicillin, but since its wide and often irrational use, *S. aureus* started to become resistant by producing β-lactamase enzyme.[91] By 1960, 95% hospital variants of *S. aureus* were resistant.[91,92] To help combat resistance, several new penicillins were developed to resist *Staphylococcal* β-lactamase, such as methicillin, oxacillin, cloxacillin, and flucloxacillin.[91] However, within 1 year of methicillin being marketed in 1960, the first MRSA strain of *S. aureus* was reported in England.[93] The MRSA strain represents 50% of HCAIs in the US and Europe and causes infections that are very difficult to manage because of their potential resistance to multiple antimicrobials.[94–96] In one study, the incidence of SSIs was after gastrectomy in 11.3%, after colorectal surgery in 15.5%, after hepatectomy in 11.3%, and after pancreaticoduodenectomy in 36.9%.[97] While the incidence of SSIs was higher in the absorbable stitching material than the silk group for all surgical procedures, the difference was not statistically significant. [97]A Japanese study on abdominal surgery reported an overall SSI rate of 14.4%. The SSI rates in the suture-less, Vicryl, and silk groups were 4.8%, 14.8%, and 16.4%,[88] respectively, again with no statistically significant differences between the groups. In colorectal surgery, the SSI rate in the polyglactin 910 (absorbable, synthetic, usually braided suture; Vicryl™) group was 13.9%, which was statistically significantly lower than that of the silk group (22.4%; *P*=0.034). The incidence of deeper SSIs in the Vicryl group, including deep incisional SSIs (ISSIs) and organ/space SSIs (OSIs), was statistically significantly lower than that in the silk group (*P*=0.04).[88] The SSI rates did not differ among the suture types overall in gastric surgery or in appendectomy.[98] A US study of pediatric patients found that while this was only 2.5% of the caseload, colorectal surgery contributed to 7.1% of the SSIs.[98] The SSI rates of all types of colorectal surgery were 5.9% (ISSIs: 3.2%; OSIs: 2.7%) with the uppermost being total abdominal colectomy (11.4%) trailed by partial colectomy (8.3%) and colostomy closure (5.0%).[98] Inflammatory bowel diseases caused the topmost health problems in a comparison of all colorectal diagnosed diseases (24.9%; ISSIs: 22%; OSIs: 28.6%). Hirschsprung's disease (14.2%; ISSIs: 15.4%; OSIs: 12.8%) and anorectal malformations (12.4%; ISSIs: 17.6%; OSIs: 6.4%) were the next major group in colorectal diseases.[98] Finally, a study utilizing univariate analysis defined 13 statistically significantly variables related to SSIs. Those were patients aged over 60 years, lower functional status, diabetes mellitus, congestive heart failure, immunocompromising disease, anticancer medications, immunosuppressive agents, impaired immune system, open cholecystectomy, laparotomy, an American Society of Anesthesiologists score above 2, drain insertion, and dirty wound.[99] Using multivariate regression analysis, this study also found that immunosuppressive agents (OR =2.5, 95%, CI =1.099–143.443), open cholecystectomy (OR =2.25, 95% CI =2.242–40.109), and contaminated wound (OR =2.179, 95% CI =3.80–20.551) were statistically significantly linked with SSIs.[99]

Catheter-associated urinary tract infections (CAUTIs)

Internationally, UTIs are the most common HCAIs and one of the top ranking microbial infections, representing around 40% of HCAIs, with significant consequences for morbidity and mortality and substantial financial implications.[14,99,100] Although CAUTIs are typically benign, some patients have potentially pathogenic virulent bacteria but are asymptomatic, and these patients were associated with a three-times higher mortality than in non-bacteriuric patients.[101,102] Multivariate analysis indicates the risk factors for CAUTIs including prolonging the duration of the catheter, female sex, older age, diabetes mellitus, the absence of systemic antibiotics, catheter insertion outside the operating room, and a breach in the closed system of catheter drainage.[101,103] The rate of CAUTIs has been estimated to be about 5% per day, regardless of the duration of the indwelling catheter, with *E. coli* being the main infecting pathogenic microorganism, although a wide spectrum of other microorganisms were identified, including eukaryotic fungus.[104,105] The repetitive inappropriate administration of antimicrobials often leads to greater bacterial resistance. CAUTIs habitually lead to biofilm formation on both the extraluminal and intraluminal portal catheter surface, largely from extraluminal microorganisms.[106–108] The biofilm defends microbes from both antimicrobials and host defense mechanisms.[109] Although morbidity from CAUTIs with short-term catheter use is limited if catheters are appropriately inserted and cleaned, in patients with long-term indwelling catheters, fever from CAUTIs is common with a frequency fluctuating from one per 100 to one per 1,000 catheter days.[105] Patients in institutional care with long-term indwelling catheters have a greater risk for the presence of pathogenic microorganisms and other urinary tract diseases than those without catheters.[105] One meta-analysis found that CAUTIs were linked with statistically significantly higher death rates (OR =1.99; 95% CI =1.72–2.31; $P<0.00001$; $I^2=54\%$; eight studies; 62,063 patients) and days in the ICU (weighted mean difference of +12 days; 95% CI =9–15; $P<0.00001$; $I^2=96\%$; seven studies; 13,011 patients) and hospital (mean difference +21 days; 95% CI =11–32; $P<0.0001$; $I^2=98\%$; five studies; 10,183 patients).[110] An Australian health care-associated urinary tract infection (HCAUTI) non-concurrent cohort study carried out for 4 consecutive years found that patients had an extra 4 days (95% CI =3.1–5.0 days) of hospitalization.[111] This study further reported that the infection rate was statistically significantly minimized utilizing a Cox regression model (HR =0.78; 95% CI =0.73–0.83) when patients were released from the hospital.[111] HCAUTIs very rarely cause death (HR =0.71; 95%CI =0.66–0.75), especially in large hospitals when compared to other health care institutes, even when compared with age and sex (HR =0.74; 95% CI =0.69–0.78), although elderly patients more often died (HR =1.40; 95% CI =1.38–1.43).[111]

VAP

The death risk for patients in the ICU is not only because of their original illness but often because of HCAIs.[2,54,112] Pneumonia is the second commonest HCAI in ICUs, affecting more than one-quarter of patients.[113,114] Around 86% of HCAIs are associated with motorized automatic ventilation and VAP.[113] Between 9% and 27% of patients with assisted ventilation develop this kind of pneumonia, and VAP has been identified internationally as a potential major cause of death.[114] The average critical time to develop VAP following endotracheal intubation and mechanical ventilation was 2–3 days.[115] Patients usually develop a fever, altered bronchial sounds, white blood cell counts reduced, changes in sputum, and causative organisms are often identified.[116–121] A US study found a range of VAP of between 1.2 and 8.5 per 1,000 ventilator days[122] although an international group reported a much higher occurrence of VAP of 13.6/1,000 ventilator days.[123] In Asian countries, a different picture of 3.5–46 infections/1,000 ventilator days emerges,[124] with a very high incidence rate in India of 40.1 per 1,000 ventilator days.[125] The initial 5 days of mechanical ventilation is the most critical time for the development of VAP, with a mean duration of 3.3 days between intubation and the development of VAP.[119–126] Another recent Indian study reported that non-fermentative Gram-negative bacilli[127] were the predominant organisms, followed by *Pseudomonas* and *Klebsiella* genus. In this study, *S. aureus* reduced in prevalence from 50% to 34.9% between 2011 and 2013, but between 2012 and 2013 vancomycin-resistant *Enterococci* increased from 4.3% to 8.3%, while methicillin resistance among *S. aureus* exceeded 50% in 2013. In addition, an upwavard trend in resistance by *Pseudomonas* genus was observed for piperacillin-tazobactam, amikacin, and imipenem. The incidence of non-fermenters' resistance continued to be very high except for amikacin and imipenem (33.1%) and polymyxin-B (2.4%).[127] A study at Chonnam National University Hospital in South Korea of the transtracheal aspirates or bronchoalveolar lavage of patients suffering from VAP found that *S. aureus* (44%) was the most frequently detected causative microorganism followed by *A. baumannii* (30%), *P. aeruginosa* (12%), *Stenotrophomonas maltophilia* (7%), *K. pneumoniae* (6%), and *Serratia marcescens* (2%).[128] In addition, *S. aureus* was found as MRSA and 69% of *Acinetobacter baumannii* were imipenem-resistant.[128] No statistically significant variance was observed in the imipenem-resistant *A. baumannii*[128] between the earlier and late VAP-related study groups (73% [8/11] vs 67% [14/21], $P=1.000$).[128] In this study, 67% of *K. pneumoniae* was ESBL-positive.[128] VAP was frequently linked with substantially increased morbidity, including prolonged ICU and hospitalization, and higher ventilator days and health care costs.[129]

In the UK and the Republic of Ireland, a European study of HCAIs connected with respiratory infection found a prevalence rate of 7.59%. Among these HCAIs, 15.7% were pneumonia, and 7% were lower respiratory tract infections other than pneumonia (LRTIOP).[130] Around 21% of patients in both the groups were having artificial ventilation, which was much higher when compared to the rest of the patients with HCAIs. MRSA was the principal invading microorganism for both pneumonia and LRTIOP. Although the patients with LRTIOP suffered more from *C. difficile*-induced diarrhea than pneumonia, this was not statistically significant.[130] A recent Chinese study reported that 14.94% (895) of inpatients acquired a LRTI which prolonged their hospital stay and increased the costs per individual case by US$2,853.93.[131] Another study revealed that 9.6% of patients developed HCAIs, of which respiratory tract infections were the highest at 65.8%.[132] The most frequently identified respiratory pathogen was Gram-negative *Acinetobacter* species (40.4%), and among these 21% were MDR.[132]

A significant number of patients develop pneumonia after surgery which includes both hospital-acquired pneumonia (pneumonia developing 48–72 hours after admission) and (as discussed above) VAP (pneumonia developing 48–72 hours after endotracheal intubation).[133] Postoperative pneumonia has been described as one of the leading consequences of all types of surgery with a high incidence of morbidity and mortality.[134] It increases hospital stays on an average of 7–9 days and increases health care costs from US$12,000 to US$40,000.[114,135,136]

HCAIs

HCAIs are a major safety concern for both health care providers and patients. They continue to escalate at an alarming rate, especially in emerging economies, with infection rates 3–20 times higher than in high-income countries.[1,2,137] HCAIs increase morbidity, mortality, length of hospital stays, and costs;[138–140] therefore, more research and changes in practice are needed to ensure hospital safety and prevent HCAIs.[32,141–143] The annual costs for HCAIs alone in the USA are between US$28 and US$45 billion, but with even this amount of spending, 90,000 lives are still lost per year: HCAIs are among the top five killers in the USA.[14,144–147] The WHO advocates that effective hand hygiene is the single most important practice to prevent and control HCAIs, which form colonies with MDR microbes.[1,2,148,149] Several studies report that a simple and straightforward process, taking only a few seconds to clean hands with an alcohol-based hand rub helps prevent HCAIs and save lives, reduce morbidity, and minimize health care costs.[150,151] However, factors such as the availability of alcohol-based hand rubs and up-to-date knowledge of the importance of hand washing hinder good practice in hand hygiene. For example, an Australian observational study of community nurses highlighted poor practices of hand hygiene in comparison with a standard protocol.[152]

The WHO promotes and advocates that all health care workers (HCWs) must wash their hands before touching a patient, before clean/aseptic procedures, after body fluid exposure/risk, after touching a patient, and after touching patient surroundings.[153] The Center for Disease Control and Prevention has developed a comprehensive plan and guidelines for the prevention of HCAIs which covers basic infection prevention and control (IPC); antibiotic resistance; device- and procedure-associated infections; disease/organism-specific infections; and guidance for health workers working in specific settings.[154] This guidance, like that of the WHO and the UK Royal College of Nursing (RCN) also emphasizes the importance of hand washing.[153–155] The RCN also promotes and advocates that all health care professionals must receive compulsory "infection control training as part of their induction and on an ongoing annual basis. It is particularly important that knowledge and skills are continually updated."[155] Multiple research studies indicate that policy changes and the adoption of novel multifactorial, multimodal, multidisciplinary strategies offer the greatest possibility of success in terms of hand hygiene improvement and the reduction of HCAIs.[156–167]

Instigating best practice in health care stems "from a response to factors that are outside a purely scientific understanding of infection and not simply understood as a deficit in knowledge."[168,169] Good practice for infection prevention among HCWs can be ensured through compliance to IPC guidelines.[168] Specific individuals acting as "change champions" can act as arbitrators or negotiators, contributing to changing behaviors and implementing best practice to ensure patient safety.[168–171] This calls for educational interventions that reflect the philosophies, principles, and community understanding of dirt and infection.[169] An educational intervention involving 4,345 health professionals in three public hospitals in the USA successfully improved hand hygiene immensely with the use of alcohol hand rub. Nurses, physicians, and allied HCWs improved from 14% to 34%, 4.3% to 51%, and 12% to 44%, respectively.[172] Other studies also highlight how behavior change around hand washing can result from educational interventions.[149,151,172] Health professionals must protect themselves with barriers for example, gloves, gowns, face masks, protective eyewear, and face shields,[173] to decrease the work-related transmission of microorganisms. Regular use of personal protective equipment (PPE)[173] devices protects both the professional and the patient from potentially infectious body fluids.[173] Nevertheless, the use of PPE does not confirm 100% protection,[174] for example, needlestick injury can breach PPE, and, in many occasions, issues might go unrecognized which might cause a dangerous health hazard including hepatitis B or HIV.[175]

Respiratory microorganisms, for example, influenza virus, *Bordetella pertussis*, *Haemophilus influenzae*, *Neisseria meningitidis*, and *Mycoplasma pneumoniae*, severe acute respiratory syndrome-associated coronavirus, Group A *Streptococcus*, adenovirus and rhinovirus, and tubercular bacilli[176] are easily dispersed through droplets (particles ≤5 μm in size) in closed health care settings and often cause endemics and epidemics.[176] PPE, vaccines, and drugs are the main measures to prevent and control such infections.[177] This includes national annual campaigns such as requiring all health professionals to have a flu vaccine. Multiple research studies have found that poor cleaning of hospital surfaces is a major source of HCAIs because of the transmission of many dangerous microorganisms such as MRSA, vancomycin-resistant *Enterococcus* spp. (VRE), *C. difficile*, *Acinetobacter* spp., and norovirus.[178–182] Meticulous cleaning of hospital surfaces is therefore vital to maintain standards and reduce the risk of HCAIs.[183] Several studies conclude that ultraviolet devices and hydrogen peroxide vapor technologies successfully eradicate potentially dangerous hospital microorganisms adhering to the surfaces in ward or patient rooms.[183–186] Furthermore, hydrogen peroxide vapor efficiently sterilizes and sanitizes all clinical areas where potentially dangerous microbial MDR microorganisms and spores were suspected to be present.[187]

Conclusion

In the early to mid-19th centuries in both Europe and USA, thousands of young women died from puerperal sepsis and fever, the diseases rampant in the charity maternity clinics of the time[188] and, due to the efforts of (among others) Dr Ignaz Phillip Semmelweis and Dr Oliver Wendell Holmes, the fight against puerperal fever was won and it was confirmed that HCAIs were transmitted via the hands of HCWs.[188–192] Despite the development of many hi-tech methods, hand washing with soap and water or alcohol rub is still the most important means of maintaining personal hygiene and preventing HCAIs.[192] However, due to the rise of antibiotic-resistant bacteria and a reluctance of some HCWs to implement best practice infection control, HCAIs remain one of the biggest causes of death in most countries. Therefore, it is essential that strategic, policy, and education initiatives continue to focus on managing and controlling such (predominantly needless) infections.

Limitations of the study

The topic of HCAIs is a very broad issue, and it has therefore not been possible to cover all aspects of HCAIs in one paper; hence, we have been selective in selecting key aspects of the current debate.

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Disclosure

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