

Healthcare - associated infections: A public health problem

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ABSTRACT

Disinfection and sterilization in hospitals, is of increasing concern. Nosocomial infections can be defined as those occurring within 48 hours of hospital admission, 3 days of discharge or 30 days of an operation. They affect 1 in 10 patients admitted to hospital. Nosocomial infections are associated with a great deal of morbidity, mortality, and increased financial burden

Key words: Infections, health problem, morbidity, hospitals

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INTRODUCTION

Nosocomial infections, otherwise known as hospital-acquired infections, are those infections acquired in hospital or healthcare service unit that first appear 48 h or more after hospital admission¹ or within 30 days after discharge following inpatient care. They are unrelated to the original illness that brings patients to the hospital and neither present nor incubating as at the time of admission. They are several reasons why nosocomial infections are even more alarming in the 21st century. These include hospitals housing large number of people who are sick and whose immune system are often in a weak end state, increased of outpatient treatment meaning that people who are in hospital are sicker on average, many medical procedures that bypass the body's natural protective barriers, medical staff move from patient to patient thus providing a way for pathogens to spread, inadequate sanitation protocols regarding uniforms equipment sterilization, washing and other preventive measures that may either be unheeded by hospital personnel or too lax to sufficiently isolate patients from infectious agents, and the routine use of anti-microbial agents in hospitals creates selection pressure for the emergence of the resistant strains of microorganisms.

Healthcare-associated infections occur in both adult and pediatric patients. Bloodstream infections, followed by

pneumonia and urinary tract infections are the most infections in children, urinary tract infections are the most common healthcare-associated infections in adults. Among pediatric patients, children younger than 1 year, babies with extremely low birth weight <1000g and children in either the PICU or NICU have higher rates of healthcare-associated infections.^{2,3} The most effective method of containment is disinfection – of instruments and especially hospital staff and visitors. The surgeons disinfection procedure- hand rubbing 3 min or hand scrubbing 5 min has to be repeated many times a day, with a number of negative side effects arising from the mechanical irritation, chemical and, possibly allergic stress for the skin, quite apart from the time required. For the hospital staff, the issue of the hand disinfection is equally daunting. Plasma sterilization of equipment is a well-established technology in medicine. It works at the atomic molecular level and therefore is able to reach all surfaces, including the interior of hollow needle injections and other regions not accessible to fluid disinfectants.

In addition to the presence of systemic signs and symptoms of infection (e.g. fever, tachycardia, tachypnea, skin rash, general malaise), the source of healthcare-associated infections may be suggested by the instrumentation used in various procedures. For example, an endotracheal tube may be associated with sinusitis, tracheitis, and pneumonia; an intravascular catheter may be the source of phlebitis or line infection; and a Foley catheter may be associated with a urinary tract infection.

Patients with pneumonia may have fever, cough, purulent sputum and abnormal chest auscultatory findings such as decreased breath sounds, crackles or wheezes.

Patients with urinary tract infection may present with or without fever. Patients with cystitis can have suprapubic tenderness while those with pyelonephritis can have

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10.4103/0300-1652.103543

costovertebral tenderness. Upon inspection, their urine can be cloudy and foul-smelling.

Neonates on the other hand usually do not present with any of the above findings and may have very subtle and nonspecific signs of infection. Fever may or may not be present. Signs of infection can include temperature and/or blood pressure instability, apnea, bradycardia, lethargy, fussiness, and feeding intolerance.

Laboratory investigations should be guided by the results of a detailed physical examination and review of systems.

Caution should be taken when interpreting laboratory results because not all bacterial or fungal growth on a culture are pathogenic. Growth on cultures may reflect simple microbial colonization. Consider the following:

- Clinical presentation of the patient
- Reason for obtaining the test
- The process by which the specimen was obtained (e.g. a urine culture obtained through a newly placed Foley catheter is less likely to be contaminated by microbial colonization)
- The presence of other supporting evidence of infection (e.g. the significance of bacterial growth on tracheal aspirate culture is strengthened by the presence of radiographic changes and clinical signs compatible with pneumonia)

Among the different methods used to establish the catheter as the source of bloodstream infections (catheter-associated bloodstream infection), the differential time to positivity of paired blood cultures is the simplest.⁴ The catheter is confirmed as the source of bloodstream infection if the blood culture from the catheter showed microbial growth 2 h or more earlier than a peripheral blood culture obtained at the same time. The other methods include quantitative cultures of blood obtained from the catheter and peripheral vein and also, quantitative culture of catheter segment. Unfortunately, quantitative culture is not readily available in most laboratories and culture of the catheter requires pulling out the device.

Multiple blood cultures over 24 h and appropriate volume of blood sample may increase the yield in cases of intermittent or low-inoculum bacteremia. Fungal cultures should be obtained if fungal infection is suspected. The laboratory should incubate cultures longer for fungus detection than for other pathogens.

Imaging studies such as echocardiography should be considered if thrombosis or vegetations is a concern. Candidate patients include those who have prolonged or persistent bacteremia or fungemia despite antimicrobial therapy or in patients with a new-onset murmur.

In immunocompromised patients, special studies are occasionally requested, such as cultures for nocardia

and atypical mycobacteria, cytomegalovirus, and cytomegalovirus antigenemia detection. Special imaging techniques (e.g. ultrasonography, CT scan, MRI) may be helpful in evaluating obscure-site infections.

PATHOPHYSIOLOGY

We have witnessed a cyclical parade of pathogens in hospitals. In Semmelweis's era, Group A *streptococci* created most nosocomial problems. For the next 50 to 60 years, gram-positive cocci, particularly *streptococci* and *Staphylococcus aureus*, were the hospital pathogens of major concern. These problems culminated in the pandemic of 1940 to 1950, when *S. aureus* phage type 94/96 caused major nosocomial problems. In the 1970s, gram-negative bacilli, particularly *Pseudomonas aeruginosa* and *Enterobacteriaceae*, became synonymous with nosocomial infection. By the late 1980s and early 1990s, several different classes of antimicrobial drugs effective against gram-negative bacilli provided a brief respite. During this time, methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant enterococci (VRE) emerged, signaling the return of the "blue bugs." In 1990 to 1996, the three most common gram-positive pathogens—*S. aureus*, coagulase-negative staphylococci, and enterococci—accounted for 34% of nosocomial infections, and the four most common gram-negative pathogens—*Escherichia coli*, *P. aeruginosa*, *Enterobacter* spp., and *Klebsiella pneumoniae*—accounted for 32%.⁵ However, tracking nosocomial infections by site has become difficult in the last few years because of shorter inpatient stays. For example, the average postoperative stay of approximately 5 days now is usually shorter than the 5- to 7-day incubation period for *S. aureus* surgical wound infections. Acquired antimicrobial resistance is the major anticipated problem in hospitals. VRE and MRSA are the major gram-positive pathogens of concern.^{6,7} *P. aeruginosa*, *Klebsiella*, and *Enterobacter* that harbour chromosomal or plasmid-mediated beta-lactamase enzymes are the major resistant gram-negative pathogens. Devices have more bloodstream infections due to coagulase-negative *staphylococci*. In fact, most cases of occult bacteremia in ICU patients are probably due to vascular access-related infections. Fungal urinary tract infections have also increased in ICU patients, presumably because of extensive exposure to broad-spectrum antibiotics. In the National nosocomial infections Surveillance system, *Candida* spp. are the main cause of nosocomial urinary infections in ICUs.⁸

ANTIBIOTICS

Appropriate use of antibiotics is important. Up to 30 of ventilator associated pneumonias are treated inadequately. There is increasing evidence to suggest that the use of appropriate and early antibiotics improves morbidity and mortality. Antibiotics should be administered at the

right dose and for the appropriate duration.⁹ Daily ICU ward rounds with the microbiologist can lead to rational use of antibiotics tailored to benefit individual patients. Antibiotic-resistant bacteria prolong hospitalization, increase the risk of death, and require treatment with toxic and expensive antibiotics. Empirical use of antibiotic is often necessary as laboratory results are often not available for 48 h after the samples are sent to the laboratory for culture. Appropriate specimens include blood, urine, sputum, bronchoalveolar lavage, pus and wound swabs. Blood cultures are only positive for pathogen in a third of cases. Once the antibiotic profile is available, a narrow-spectrum antibiotic can be commenced. Indicators of response to treatment include temperature, leucocytes count and C-reactive protein CRP levels. Procalcitonin is secreted by macrophages in response to septic shock and is an early and a more specific marker of bacterial infection than CRP.

DE-ESCALATION

De-escalation involves early initiation of broad-spectrum antibiotic therapy in patients with suspected sepsis without the availability of microbiology results. The increase in antibiotic resistant pathogens such as MRSA has led some investigators to suggest broader antibiotic coverage by adding a glycopeptide to carbapenem as the initial empirical therapy. This aggressive empirical regimen is continued for 24–48 h by which time laboratory tests have confirmed the causative organisms and sensitivities. This allows for de-escalation of antibiotic therapy.

This regimen should be reserved for selected patients on ICU who are seriously ill, with an extended antibiotic history and evidence of colonization by multi-resistant organisms. Unnecessary continuation of this regime will increase the risk of colonization with resistant bacteria.

ROTATIONAL ANTIBIOTIC THERAPY

Rotational antibiotic therapy is a strategy to reduce antibiotic resistance by withdrawing an antibiotic, or class of antibiotics, from ICU for a short period, to allow resistance rates to decrease or remain stable. The persistent use of one class of antibiotics leads to the emergence of resistant strains of bacteria; this is known as selective pressure. Rotational regimens are thought to reduce this selective pressure. There is growing support for this regimen. Kollef and colleagues¹⁰ demonstrated a statistical decrease in nosocomial pneumonia in a large ICU after the introduction of an antibiotic rotation policy.

Restrictive antibiotic policies are less flexible and, to a certain extent binding, with respect to prescribing. They require the prescriber to give written justification for any deviation from the policy. Automatic stop orders restrict prolonged antibiotic administration. In the general hospital

setting, these measures have had some success with significant reductions in antibiotic resistance. However, the overall survival in ICU was unchanged.

The concept that commensals within the bowel may provide a protective role against more virulent organisms is called colonization resistance. Translocation of Gram-negative bacteria across the intestinal wall is thought to be a major cause of nosocomial infections. SDD aims to eliminate Gram-negative aerobic bacteria by decontamination of the oral cavity and intestinal tract. There are several variations of the SDD regimen. One such regimen is non-absorbable polymyxin E, tobramycin, and amphotericin B for gastrointestinal decontamination and cefotaxime for systemic prophylaxis. Cephalosporins are usually given as prophylaxis as they act on commensal respiratory flora such as *Streptococcus pneumoniae*, *Hemophilus influenzae* and *S. aureus*. Meta-analysis has demonstrated that SDD regimens decrease the incidence of nosocomial pneumonia but overall survival or duration of intensive care treatment is unchanged. The cost effectiveness of SDD has not been evaluated.

EPIDEMIOLOGY

Healthcare-associated infections are most commonly caused by viral, bacterial, and fungal pathogens. These pathogens should be investigated in all febrile patients who are admitted for a nonfebrile illness or those who develop clinical deterioration unexplained by the initial diagnosis. Most patients who have healthcare-associated infections caused by bacterial and fungal pathogens have a predisposition to infection caused by invasive supportive measures such as endotracheal intubation and the placement of intravascular lines and urinary catheters. Ninety-one of bloodstream infections were in patients with central intravenous lines CVL, 95 of pneumonia cases were in patients undergoing mechanical ventilation and 77 of urinary tract infections were in patients with urinary tract catheters.

Risk factors for the development of catheter-associated bloodstream infections in neonates include catheter hub colonization, exit site colonization, catheter insertion after the first week of life, duration of parenteral nutrition, and extremely low birth weight (< 1000g) at the time of catheter insertion.¹¹ In patients in the PICU risks, for catheter-associated bloodstream infections increase with neutropenia, prolonged catheter dwell time 7d, use of percutaneously placed CVL higher than tunneled or implanted devices, and frequent manipulation of lines.¹²

Candida spp are increasingly important pathogens in the NICU. Risk factors for the development of candidemia in neonates include gestational age less than 32 weeks, 5 min Apgar scores of less than 5, shock disseminated

intravascular coagulopathy, prior use of intralipids, parenteral nutrition administration, CVL use, H2 Blocker administration, intubation, or length of stay longer than 7 days.¹³ Risk factors for the development of ventilator-associated pneumonia (VAP) in pediatric patients include reintubation, genetic syndromes, immunodeficiency, and immunosuppression.¹⁴ In neonates, a prior episode of blood stream infection is a risk factor for the development of VAP.¹⁵

Risk factors for the development of healthcare associated urinary tract infection in pediatric patients include bladder catheterization, prior antibiotic therapy, and cerebral palsy.

Both developed and resource-poor countries are faced with the burden of healthcare-associated infections. In a world health organization (WHO) cooperative study (55 hospitals in 14 countries from four WHO regions), about 8.7% of hospitalized patients had nosocomial infections.¹⁶

A six year surveillance study from 2002-2007 involving intensive care units (ICUs) in Latin America, Asia, Africa, and Europe, using CDC's NNIS definitions, revealed higher rates of central-line associated blood stream infections (BSI), ventilator associated pneumonias (VAP), and catheter-associated urinary tract infections than those of comparable United States ICUs.¹⁷ The survey also reported higher frequencies of methicillin-resistant *Staphylococcus aureus* (MRSA), Enterobacter species resistance to ceftriaxone, and Pseudomonas aeruginosa resistance to fluoroquinolones.

With increasing recognition of burden from healthcare-associated infections, national surveillance systems have been developed in various countries; these have shown that nationwide healthcare-associated infection surveillance systems are effective in reducing healthcare-associated infections.¹⁸

Healthcare-associated infections result in excess length of stay, mortality and healthcare costs. In 2002, an estimated 1.7 million healthcare-associated infections occurred in the United States, resulting in 99,000 deaths.¹⁹ In March 2009, the CDC released a report estimating overall annual direct medical costs of healthcare-associated infections that ranged from \$28-45 billion.²⁰

A report from the CDC showed that among the intensive care units in the United States, the year 2009 had 25,000 fewer central line-associated bloodstream infections (CLABSI) than in 2001, representing a 58% reduction. Between 2001 and 2009, an estimated 27,000 lives were saved and potential \$1.8 billion cumulative excess health-care costs were prevented. Coordinated efforts from state and federal agencies, professional societies, and healthcare personnel in implementing best practices for insertion of central lines were thought to play a role in this achievement.²¹

Healthcare-associated infections do not have a discernible sex predilection.

Healthcare-associated infections occur in both adult and pediatric patients. Bloodstream infections, followed by pneumonia and urinary tract infections are the most common healthcare-associated infections in children; urinary tract infections are the most common healthcare-associated infections in adults.²² Among pediatric patients, children younger than 1 year, babies with extremely low birth weight (≤ 1000 g) and children in either the PICU or NICU have higher rates of healthcare-associated infections.²²⁻²⁵

PREVENTION

The European prevalence of infection in intensive care study identified several factors predisposing a patient to nosocomial infections. Poor hand hygiene is responsible for 40% of infections²⁶ transmitted in hospitals. Surveys have shown that the improvement in compliance with hand washing reduces nosocomial infection.

Accessibility of the hand washing stations and the use of alcohol gels improves compliance with hand washing. Alcohol gel dries quickly, and is bactericidal, fungicidal and virucidal. Numerous studies have shown that doctors wash their hands less frequently than nurses and backs of hands, tips of fingers, web spaces and thumb are commonly missed areas.

Infection control can be very cost-effective. Approximately one third of nosocomial infections are preventable. To meet and exceed this level of prevention, we need to pursue several strategies simultaneously²⁷

First, we need to continue to improve national surveillance of nosocomial infections so that we have more representative data. We must assess the sensitivity and specificity of our surveillance and of our case definitions, particularly for difficult-to-diagnose infections like ventilator-associated pneumonia. We also need to develop systems for surveillance of "nosocomial" infections that occur out of the hospital, where much health care is now given.

Second, we need to ensure that surveillance uses are valid. The Joint Commission on Accreditation of Healthcare Organization's ORYX initiative for monitoring health-care processes and outcomes will lead to core indicators and sentinel event monitoring. This initiative will be followed by increased outpatient surveillance, which ultimately may lead to systemwide realtime surveillance and reporting. Because, we want to use nosocomial infection rates as a core indicator of quality of care, we need to improve our ability to "risk adjust" infection rates so that we know our inter-provider and hospital comparisons are valid. Risk stratification will ultimately depend on

organic-based computer systems that will mimic biologic events.

Third, many of our successes in controlling nosocomial infections have come from improving the design of invasive devices. This is particularly important given the marked increase in frequency of vascular access-associated bloodstream infections, particularly in ICU patients. Given the choice of changing human behavior (e.g. improving aseptic technique) or designing a better device, the device will always be more successful. Of particular importance is the development of noninvasive monitoring devices and minimally invasive surgical techniques that avoid the high risk associated with bypassing normal host defence barriers (e.g. the skin and mucous membranes).

Fourth, forestalling the post-antibiotic era will require aggressive antibiotic control programs;²⁸ these may become mandated for hospitals that receive federal reimbursements, as happened in the past with infection control programs. Risks for antibiotic-resistant strains also may be reduced in the future by controlling colonization through use of immunization or competing flora.

Fifth, antimicrobial resistance problems and the advent of xenotransplantation emphasize the importance of newer microbiologic methods. For investigation of outbreaks of multidrug-resistant pathogens, pulsed-field gel electrophoresis has become a routine epidemiologic tool.²⁹ Molecular epidemiologic analysis also may help us better understand the factors that lead to the emergence of resistant strains. For diagnosis of syndromes caused by unusual pathogens, representational difference analysis and speciation by use of the pathogen's phylogenetic r-RNA "clock" may become routine.

Sixth, control of tuberculosis (TB) in hospitals is an excellent example of the successful collaboration of the infection control community, CDC, and regulatory agencies. But, we can anticipate that the Occupational Safety and Health Administration may have many new employee health issues-beyond TB and bloodborne pathogens- to evaluate in hospitals, such as health problems related to exposure to magnetic fields, to new polymers, and to medications that contaminate the environment. Problems of mental stress due to unrelenting exposure to pagers, faxes, e-mail, holograms, and telephonic implanted communicators will require special attention.

INFECTION CONTROL IN DEVELOPING COUNTRIES WITH PARTICULAR EMPHASIS OF SOUTH AFRICA

Healthcare-associated infections HAIs area cause of significant morbidity and mortality in patients receiving healthcare, and the costs direct and indirect of these

infections deplete the already limited financial resources allocated to healthcare delivery.

Approximately one in seven patients entering South African hospitals are at risk of acquiring an HAI.

Lower respiratory tract infections, urinary tract infections, bloodstream infections and post-surgical infections account for the majority of HAIs.

Indiscriminate and inappropriate use of antibiotics leads to the selection of antimicrobial-resistant organisms.

Bi-directional flow of resistance from hospitals into communities and vice versa makes it difficult to distinguish community-acquired multidrug-resistant pathogens from those that are nosocomial.

To counter the emergence and spread of multidrug-resistant pathogens the only feasible strategy is the implementation of an effective and integrated program that involves antimicrobial resistance surveillance, a rational antimicrobial-use program, and infection control.

Infection control activities on their own are primarily centered around the goal of decreasing or preventing the transmission of nosocomial healthcare -associated pathogens to patients and staff, irrespective of whether these organisms are multidrug-resistant or not.

To further reduce and control the emergence of antimicrobial resistance it is therefore essential that infection control activities be coupled with an optimized, effective and highly restrictive antimicrobial-use program.

Most importantly, such a program must be realistic, adaptable, and take cognizance of the severe limitation of resources characteristic of many developing countries.

CONCLUSION

Intensive care is a risk factor for the emergence of antibiotic resistant bacteria. Gram-positive bacteria have overtaken Gram-negative organisms as the predominant cause of nosocomial infections. Inadequate antibiotic therapy is associated with poor outcome and particularly with bacterial resistance. Infection control measures are important for the effective control, prevention and treatment of infection. Shorter duration of treatment and correct dosage of antibiotic therapy is recommended to reduce the selection pressure for resistant isolates. Hand washing is the single most important measure to prevent nosocomial infections. Gloves must not be used as a substitute for hand washing; they must be washed on glove removal.

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How to cite this article: Revelas A. Healthcare - associated infections: A public health problem. *Niger Med J* 2012;53:59-64.

Source of Support: Nil, **Conflict of Interest:** None declared.