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Review Article

NOSOCOMIAL INFECTIONS: AN OVERVIEW

Maazuddin Mohammed[1]*, Arshad H. Mohammed[2], Misba Ali B. Mirza[3], Azizullah Ghori[3]
[1]Pharm. D, Department of Hospital and Clinical Pharmacy Practice, Deccan School of Pharmacy, Hyderabad, AP, India
[2]Pharm.D, Department of Hospital and Clinical Pharmacy Practice, Asst. Professor, Deccan School of Pharmacy, Hyderabad, AP, India
[3]M. Pharm, Department of Hospital and Clinical Pharmacy Practice, Asst. Professor, Deccan School of Pharmacy, Hyderabad, AP, India
*Corresponding Author Email: dr.maazkhateeb@gmail.com

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ABSTRACT
Nosocomial infections (NI) are one of the major complications for the healthcare professionals to tackle. It is a major source of morbidity, mortality, and also monetary burden on patients. The main risk factors for NI's are related to both hospitals and patients. Maximum number of NI's is known to be caused by *Staphylococcus aureus* including MRSA and VRSA, *Pseudomonas aeruginosa, Acinetobacter baumannii, Coagulase negative staphylococci* to name but few. Similarly the major sites of infections are respiratory tract, urinary tract, surgical site and blood stream. Certain strategies are needed to be followed by the hospital authority to reduce the incidence of NI's, such as better surveillance system and infection control, proper use of antibiotics, hand hygiene and many more. The treatment options for NI's vary depending upon the site of infection and severity which includes combination antibiotic therapy. Although NI's are hazardous they can be resolved by following the prevention and treatment strategies.
Keywords: nosocomial infection, causes, prevention strategies, treatment options.

INTRODUCTION

According to world health organisation (WHO) a nosocomial infection (NI) is defined as "An infection occurring in a patient in a hospital or other healthcare facility in whom the infection was not present or 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] NI's are a major source of morbidity, mortality and also monetary burden on patients.[2,3] Immuno compromised patients are at threat of NI's when they undergo surgery or have any underlying disease. They are worse affected when admitted in intensive care unit (ICU) as the rate of NI's were almost three times higher than any other departments of hospital.[4] The epidemiology of NI's includes the understanding and causes of these infections, patients characteristics and the rate of occurrence of such infections.[2] According to a survey conducted by WHO in 4 Regions (Europe, Eastern Mediterranean, South-East Asia and Western Pacific) reveals that 8.7 % of patients prevailed with NI's. The survey also showed that the sites at which NI's are more prone to attack are infections of surgical wounds, urinary tract infections and lower respiratory tract infections. The NI's are caused by both gram positive, gram negative, and also by other microorganisms like fungi and viruses. NI's are also usually being caused by resistant strains of bacteria like MRSA, VRSA, and VRE. Various pathogens and their site of infection are shown in Table 1.

Causes of NI's

In the litreature three major causes of NI's are documented. First is antimicrobials use, long-term and irrational use of antimicrobials leads to the development of resistant strains of pathogens. Second the leniency of hospital staff and infection control committee in maintaining sterility conditions. And lastly the patient itself is prone to NI's due to low immunity and unhygienic conditions around themselves. Apart from these major factors some other precipitating factors may also add up the cause of NI's.

Sites of NI's

The 4 most frequent types of NI's which possess a big challenge for health care professionals to tackle are:

Respiratory tract

The bacteria causing respiratory tract infections (RTI) becomes resistant in the nasopharynx which is the ecological niche where evolution towards resistance occurs.[6] These resistant bacteria are able to cause NI's in the respiratory failure patients, as the Patients with acute respiratory failure are predisposed to acquire nosocomial infection primarily because they may need ventilatory support, usually invasive mechanical ventilation.[7] The most frequent type of pathogen causing hospital acquired pneumonia belongs to gram negative type (65.9 %).[8] The two most important clinical problems in pulmonology department is nosocomial and ventilator-associated pneumonia with more mortality and morbidity.[9] The patients admitted with acute respiratory failure undergoing mechanical ventilation are prone to NI's by two factors. First is the endotracheal tube which create glitches in defence mechanism of the respiratory tract and second, the risk of cross transmission of pathogens while handling and manipulating the ventilator associated devices.

Bloodstream

Bloodstream infections (BSI) are second most common type of NI's after hospital acquired pneumonia. BSI represents the failure of immune system by which dissemination of pathogens occurs. It is the major NI causing mortality and morbidity.[10,11] in united states annually 250,000 cases of nosocomial BSI are reported. Among these numbers 35 %

attribute to mortality. Remaining 65 % survivors stay at hospital increases up to 24 days, this in turn increase monetary loss up to 40,000$. The data is nearly similar in other countries; both gram positive and negative bacteria responsible for nosocomial BSI. In a study it is approximated that 52 % cases were caused by gram-negative *bacilli* and 42 % were caused by gram-positive *cocci* %). It is estimated that gram positive cocci is more responsible than gram negative isolates in case of BSI, only 4.6 %-3.4 % of *E. coli* was reported among gram negatives. %).[8] In addition, the gram positive *cocci* have notable antimicrobial resistance making them more difficult to tackle.[11]

Surgical site infections

Surgical site infections (SSI) are one of the most common type of NI's in all around the globe.[12] The pathogens involved in this are usually *Acinetobacter* isolates apart from *E. coli* and *Enterobacter* isolates. During the dressing of wounds cross transmission occurs either by the hands of personnel or by contaminated instruments. SSI also depends upon the type of surgery and wound. For example SSI rates were reduced drastically in a laparoscopic procedure[13], whereas the open surgery site is more prone to the infection.

Urinary tract

A urinary tract infection (UTI) when acquired in any healthcare setup due to cross transmission of pathogens is referred to as nosocomial UTI (NUTI).[14] Among all other sites of NI's UTI approximately accounts for 40 % of NI's.[15] In more than two thirds of the cases patient's flora is responsible for origin of infection. Usually the common aetiology of NUTI is due to catheter. The main mechanism of infection in non catheterized patients is the ascending way and in the catheterized patients the mechanism is of four types. Acquisition on insertion of the urinary catheter, Acquisition through the endoluminal way, Acquisition through the extra luminal or periurethral way, acquisition through the lymphatic or haematogenous way; among gram negative bacteria *E. coli* was the most commonly reported gram-negative pathogen, followed by *Pseudomonas aeruginosa.* other strains isolated was *K. pneumoniae* and *Acinetobacter* species.[8]

Table 1: Common pathogens and sites of infections

Site of infection	Common pathogens	Less common pathogens
Blood stream	*coagulase-negative staphylococci* (CNS) *S. aureus* *P. aeruginosa* *Candida* sp	*Enterococci* *Klebsiella* sp *Serratia marcescens* *Enterobacter* sp *Malassezia* sp
Pneumonia	CNS *S. aureus* *P. aeruginosa* Respiratory syncytial virus	*Enterococci* *Klebsiella* sp *Serratia marcescens* *Influenza*
Skin/soft tissue/surgical site	CNS *S. aureus*	*Enterococci* *Serratia marcescens* *Aspergillus* sp
Gastrointestinal tract	Rotavirus	Anaerobic bacteria coronavirus
Conjunctivitis/occular	CNS *P. aeruginosa*	*Serratia marcescens*
Urinary tract	Gram-negative bacilli *Enterococci*	*Candida* sp
Endocarditis	CNS *S. aureus*	*Candida* sp
Central nervous system	CNS *S. aureus*	*Candida* sp *Serratia marcescens* *Enterobacter* sp
Osteoarthritis	*S. aureus* Group B *streptococci*	*Candida* sp Gram-negative bacilli[5]

Table 2: Distribution of major infection sites in teaching and non teaching hospital setups

	% of cases				
Infection type	**All hospitals (n = 62, 214)**	**Non teaching hospitals, < 200 beds (n = 1.994)**	**Non teaching hospitals, ≥ 200 beds (n = 12, 086)**	**Teaching hospitals, < 500 beds (n = 29, 062)**	**Teaching hospitals, ≥ 500 beds (n = 19, 072)**
UTI	33.1	35.9	37.6	32.0	31.5
Pneumonia	15.5	20.4	16.8	14.8	15.4
SSI	14.8	15.2	16.0	14.9	13.9
BSI	13.1	9.6	8.4	12.8	16.9
Other	23.5	18.9	21.2	25.5	22.2[2]

Pathogens

The major pathogens involved in most of the cases of NI's belong to gram negative class of bacteria. Some frequently isolated strains are discussed hereafter.

Acinetobacter baumannii

A gram negative bacterium which is usually present in human dermal flora; it is a healthcare-associated pathogen that tends to cause NI's such as UTI, bacteraemia, septicaemia, pneumonia, secondary meningitis, SSI, BSI. Nowadays it is increasingly reported as the cause of nosocomial infections.[16,17] *A. baumannii* strains which are resistant to much antibiotic class are now a big concern for both prevention and treatment of NI's caused by this resistant strains.[17] *A. baumannii* is vastly present in respiratory infections and can cause opportunistic infections like pneumonia. As in respiratory department mechanical ventilators are used and chances of colonization of pathogens

increases leading to NI's. In surgical department as the superficial dermal layers are involved, *A. baumannii* can colonize in the surgical site and disseminate from there. In some studies it is been noted that this pathogen is very much isolated from the surgical wound infections.[16] The resistance to antibiotics are usually gained by combination of chromosomally associated β-lactamases and porin protein mutations. To tackle the colonization of this pathogen certain initiatives must be taken for eradication and lessen the cases of NI's in ICU's.[18]

Escherichia coli

Escherichia coli is the leading cause of BSI's among all other gram-negative pathogens, and is the fifth leading pathogen for causing BSI in the United States. *E. coli* associated NI's are associated with around 22 % of mortality. A study shows that Extended-spectrum-β-lactamases producing *E. coli* colonization in patients increase the duration of hospital stay and sometimes lands them into ICU.[19] *E. coli* is less common in SSI. But can colonize in the surgical wounds and disseminate into bloodstream causing BSI. In a study it was concluded that *E. coli* is the most common agent found in nosocomial diarrhoea.[20]

Coagulase negative staphylococci

The *coagulase-negative staphylococci* (CNS) species are widely causing NI's specifically bacteraemia in patients who are immune comprimised and also in patients with prosthetic implants and catheters. Among the CNS species most common are *Staphylococcus epidermidis* and *S. haemolyticus.*[21] During the present days CNS has appeared as a notable pathogen in catheter-related BSI.[22] The three most widely isolated pathogens tends to cause BSI's are (in descending order) were coagulase-negative *staphylococci*, *S. aureus,* and *Enterococci*. In a study it was calculated that the number of isolates increases from 9 % to 31 % in an around 10 years, and their counts were almost double when compared to *S. aureus* and *Enterococcus* species. It usually takes approximately 19 days for CNS to cause bacteraemia after hospitalisation. Despite of the fact that CNS are the most recurrent pathogen involved in genesis of BSI's, the mortality rate is lesser than that of other common pathogens.[11] The main reason for CNS colonization is antimicrobial resistance. More than half of CNS isolates are resistant to methicillin, oxacillin, or nafcillin.[2]

Pseudomonas aeruginosa

P. aeruginosa is a gram-negative organism known to cause majority of nosocomial pneumonia and BSI's cases. 1 in 10 cases of infections contains *P. aeruginosa* strains affecting all major sites except bloodstream as it is not often found there. In a 3 years study *P. aeruginosa* was isolated in 18 % of cases of nosocomial pneumonia making it the most frequent pathogen it this type of NI.[23] *P. aeruginosa* grabbed third place with 11 % isolates in a 3 years study. Many contemporary studies show that antibiotic resistance among gram-negative bacteria is increasing especially in *P. aeruginosa*. As they have the ability to express certain resistance phenotypes, they pose threat to the treatment approach and increase in the incidence of NI's when compared to other nosocomial pathogens. In 18 years study it was noted that rates of resistance to ceftazidime and imipenem among *P. aeruginosa* isolates were increased dramatically. The resistance to imipenem was very common in teaching hospitals and the isolates obtained from respiratory tract.[2] In a study it was identified that resistance is acquired by multiple clones and this was revealed by four different typing methods.[24] There was a notable growth in the mortality rate associated with *P. aeruginosa* especially in immune compromised patients. This is due to improper usage of empirical therapy.[23]

Staphylococcus aureus

It is a gram-positive organism which is known to be a leading cause of bacterial infections in humans around the globe. The incidence of nosocomial BSI's is more known to be caused by *S. aureas*.[2,25] *S. aureus* is rarely isolated from UTI.[2] Most of the infections are caused by methicillin-resistant *S. aureus* (MRSA) isolates. Over the last decade isolation of MRSA has been continuously increasing.[25,26] Nosocomial infections may occur during the hospital stay by *streptococci* and *Staphylococci* species when compared to gram-negative bacteria. The average duration of onset of infection during the hospitalization period may be within 2 weeks[11]; apart from MRSA the emergence of vancomycin resistant *S. aureus* (VRSA) may result in more severe and complicated infections. According to the litreature, the eradication of MRSA can be done as similar as or more effectively than vancomycin by linezolid in the treatment of BSI's and community acquired pneumonia.[26]

Prevention Strategies

It is estimated that approximately one third of NI's are preventable, but for this certain strategies have to be followed.

Surveillance of nosocomial infections

Surveillance is defined as "the ongoing, systematic collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know". Generally the nosocomial infection surveillance is categorized into sentinel event based or population based or both.[2] Development and improvement of nosocomial infections surveillance system may helps in detection and assessment of outbreaks of infection or antimicrobial resistance patterns.[4] In a Study on the Efficacy of Nosocomial Infection Control (SENIC) conducted at hospitals in the United States to calculate infection rates, it was found that hospitals which had strong surveillance and prevention/control programs shows lowest nosocomial infection rates.[13] in a study done on computer-assisted, laboratory-based surveillance, it was found that it can play an important role in the identification and control of NI's which was governed by the evidence that three clusters of nosocomial bacteraemia were detected by this procedure.[27]

Validity of surveillance

Validation of the surveillance is essential for comparison of the data from the inter-provider and inter-hospitals regarding the rate of NI's. According to the Joint Commission on Accreditation of Healthcare Organization's (ORYX) initiative for monitoring health-care processes and outcomes, core indicators and sentinel event monitoring are essential for initiating the surveillance validation.[4] For reliable validation, surveillance system must contain: trained personnel, criteria for nosocomial infections, risk factors, and other outcomes, sources of data for identifying infections, accurate and

complete data, confidentiality of the data, strategies for identifying infected patients, to name but few.

Development of non invasive monitoring devices

Invasive devices bypass normal first line of defence (e.g., the skin and mucous membranes) by developing non invasive devices and minimally invasive surgical techniques may helps in maintaining aseptic condition of the patient and to diminish the chances of BSI's, especially in the intensive care patients.[4] Evidence suggest that use of non-invasive ventilation warrant the reduction in the incidence of nosocomial infections and should be used whenever possible.[7] In case of nosocomial UTI's prevention can be done by using non-invasive bladder monitoring devices or procedure such as portable ultrasound bladder volume technology.[15]

Proper antibiotic usage and antimicrobial resistance

Most of the NI's are caused by the resistant pathogens and is estimated that emergence of these bacterial strains are due to improper or irrational use of antibiotics. To monitor and control the use certain antibiotic control programs have to be initialise.[1,4] This programs can be backed by federal reimbursements as in case of infection control programs. The Antimicrobial Use Committee in the hospitals will classify antimicrobial agents into the following categories: unrestricted, restricted or reserved, excluded. The antibiotic usage monitoring can be done in pharmacy department and should be reported to the Antimicrobial Use Committee in timely manner. This control programs in turn reduces the antibiotic resistance problems which is a big threat for the hospitals.[2] Now a days, for estimating the incidence of resistance strains causing NI's are investigated by pulsed-field gel electrophoresis technique. Molecular epidemiologic analysis may also helps researchers in understanding the factors for resistance.[4] Role of microbiology laboratory has proved to be worthy in tackling antimicrobial resistance problem. Some of the roles are: Performing antibiotic susceptibility testing, monitor and report trends, provide microbiological support for investigations of resistant pathogens, notify infection control committee in case of unusual antimicrobial resistance patterns, participate in activities of the Antimicrobial Use Committee.

Infection control committee

An Infection Control Committee is a board which deals about the prevention of NI's. It involves multidisciplinary personals, to start with, physicians, pharmacists, clinical microbiologists, to name but few. This committee works on input, co-operation, and information sharing principle. It has following tasks to perform for preventing and eradication of NI's: to review and approve surveillance procedures on a yearly basis or when needed, to review the surveillance data, validation check and intervention areas, to examine and encourage infection control practices, to provide proper staff training in infection control and safety, to assess the new devices used in the hospital for their risk in violating infection control strategies if any so, to communicate and co-operate with other hospitals infection control committees for information dissemination.[1] In a study, according to infection control committee statistics, the nosocomial bacteraemia rate were increased from 13.8 to 22.1 per 1000 catheter-days.[28] Therefore infection control committee plays a key role in preventing NI's.

Hand hygiene

In usual practice, hygiene is an important and crucial point where the chances of disseminating of infection may occur. To reduce the risk of cross transmission from patients to patients by healthcare personnel, better hygiene practices should be implemented.[4,7,29] Around 40 % of the NI's are caused by poor hand hygiene.[30] Hand washing only with soap and water may not be enough for decontamination, along with this germicidal liquids should be used for proper sterilization of hands. Generally alcohol based liquids warrants the effective degerming properties.[15] According to WHO, procedure for hand hygiene are categorized in the Table 3.

Table 3: Procedure for hand hygiene

Routine care (minimal)	Antiseptic hand cleaning (moderate) aseptic care of infected patients:	Surgical scrub (surgical care):
Hand washing with non-antiseptic soap	Hygienic hand washing with antiseptic soap following manufacturer's instructions (e.g. one minute)	Surgical hand and forearm washing with antiseptic soap and sufficient time and duration of contact (3–5 minutes)
Quick hygienic hand disinfection (by rubbing) with alcoholic solution	Quick hygienic hand disinfection: as previously	Surgical hand and forearm disinfection: simple hand wash and drying followed by two applications of hand disinfectant, then rub to dry for the duration of contact defined by the product. [1]

Treatment Regimens

Although the first step to counter NI's is prevention and minimising the incidence of NI's, various treatment options are available for the treatment including, vaccines as second step; for all the types of NI's empirical antimicrobial treatment should be initiated. After the identification of the causative organism specific treatment must be started at the earliest. Central line removal has to be considered, when no longer needed, in case of blood stream and post operative patients.

Pneumonia

For nosocomial pneumonia there is a probability that multidrug resistant organisms may manifest. Therefore high-end antibiotics must be considered in an empirical therapy. The administration of medications can also play a role in the treatment as in a study it was concluded that administration of antibiotics by the respiratory tract may help in treating nosocomial pneumonia.[9]

Urinary tract infections

As urinary catheters are the major source of nosocomial UTI's, their removal should be considered whenever possible.[15] However removal may result in spontaneous bacteriuria or asymptomatic cystitis. Alternative methods should be considered for the bladder management such as external catheters, absorbent products and intermittent catheterization for secure treatment from NI's.[15] Both antibiotic and antifungal therapy should be started to abstain

the complications like pyelonephritis and renal damage to name but two.

Treatment of resistant pathogens

Generally MRSA and multidrug resistant *Pseudomonas aeruginosa, Acinetobacter* species are known to cause difficulties in the treatment strategies. For the effective eradication of such pathogens can be done by specific high-end antibiotics. Many studies have been done on successful elimination of resistant organisms. Among all other drugs colistin, vancomycin, linezolid and doripenem have given satisfactory results. In a study doripenem appears to provide advantageous results by showing broad-spectrum coverage and antipseudomonal activity in high risk patients and MDR pathogens.[31] Colistin therapy in cases of MDR *A. baumannii* and *P. aeruginosa* shown promising results. It is a better treatment option for the eradication of MDR *A. baumannii* and *P. aeruginosa*.[18,24] In another research it was found that linezolid is as effective as vancomycin for treating NI's caused by MRSA.[26] Various immunisations have been developed against NI's caused by *staphylococcal* species, *C. difficile, P. aeruginosa* which can be administered through mucosal route.[32]

CONCLUSION

To put into a nutshell, NI's are the foremost aspect that needed to be tackled carefully and efficiently by the healthcare professionals for the betterment of patients who are hospitalised. By following stringent strategies to control and eradicate the complicated culprit (i.e. NI) hospital staff will be able to maintain the safety of patients and themselves with an ease. Further, more efficient procedures have to be constructed in future as the pathogens may develop more resistant patterns that lead to severe complications for treatment. Researchers can do many studies regarding the pathogens their mechanism of resistance, incidence and prevalence of such organisms, prevention and treatment strategies, newer antibiotics and their proficient use, to name but few.

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