



An In-Depth Analysis of Microorganisms Linked to Various Forms of Hospital-Acquired Infections: A Systematic Review

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Abstract

Nosocomial infections (NIs) represent one of the serious public health concerns worldwide that are linked with healthcare-associated infections. The present study reviewed the microorganisms associated with various types of NIs. The data search strategy was guided by the PRISMA-P protocol with the utilization of various search engine databases (PubMed, Springer Link, Science Direct, and Google Scholar) and pre-determined keywords. The search retrieved 504 articles from 2014 to 2019. Based on the inclusion and exclusion criteria stated, only a total of 63 articles have been discussed further in this study. The signatures of NIs can be described by microorganisms associated with the transmission route groups (Nosocomial bloodstream infections-BSI, Hospital Acquired Pneumonia-HAP, Catheter-Associated Urinary Tract Infection-CAUTI, Surgical Site Infection-SSI). BSI is the major cause of morbidity and mortality in hospitals. HAP is the most frequently reported case including Ventilator-associated Pneumonia-VAP. Microorganisms such as *Acinetobacter Baumannii* spp., *Escherichia* spp., *Streptococcus* spp., *Staphylococcus aureus* spp., and *Pseudomonas* spp. pathogens are commonly associated

with NIs. Recently, the healthcare challenge is also associated with Multi-Drug Resistant (MDR) related strains that contribute to a significantly high mortality rate, especially in immune-compromised patients. Hence, the emergence of various nosocomial infections marked the relevant steps and measures that need to be taken with effective precautions.

Keywords: Nosocomial infection, Communicable disease, Hospital-acquired infection, Disease, Health, Multi-drug resistant

1. Introduction

Nosocomial infection (NIs) or also known as a hospital-acquired infection is a type of infection acquired in hospitals or any healthcare-related. It represents a serious concern especially in developing countries (75%) due to the prolonged hospital stay, disability, and high financial losses (Khan et al., 2015). NIs also cause ultimate risk for immunocompromised patients which increased the death rate of patients. During hospitalization or treatment procedures, patients are exposed to various types of pathogens from different sources such as healthcare workers, specialists, and visitors (Khan et al., 2015).

Transmission of these infections can occur through direct contact from the staff, inadequately sterilized medical instruments, surgery, or air droplets from other patients. The emergence of NIs mainly associated with microorganisms such as Gram-positive

Significance | The study aims to provide a detailed understanding of the microorganisms involved in different types of HAIs, such as surgical site infections, urinary tract infections, bloodstream infections, and respiratory tract infections.

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bacteria, Gram-negative bacteria, and fungi. NIs often associated with morbidity and severe infection resulting in mortality among patients. Broad research reports have documented that there is quite a striking result of the prevalence of NIs among patients and health care related especially in the hospital. This systematic review focused on microorganisms associated with different types of NIs transmission groups which are known as Nosocomial bloodstream infections (BSI), Hospital-Acquired Pneumonia (HAP), Catheter-Associated UTI (CAUTI), and Surgical site infection (SSI) (Irek et al., 2018).

Materials and Methods

Search Strategy

The predetermined keywords, PRISMA-P guidelines, and Boolean strategy were followed using several database engines such as Science Direct, Springer Link, Pub Med, and Google Scholar. The databases used in this research provide reliable information in nosocomial infections and related topics. The predetermined keywords used in this research are (nosocomial infections) and (microorganisms associated), (microorganisms related) and (nosocomial infections), (nosocomial infections), (microorganisms) and (nosocomial), (hospital-acquired infection) and (microorganism), (nosocomial) and (bacteria), (nosocomial) and (fungi), (nosocomial infections) and (pathogenic microorganisms), (virus) and (nosocomial infections), (hospital-acquired infections).

Study selection

The published peer-reviewed English-based journals between January 1, 2014 and January 31, 2019 were included. The inclusion criteria were: 1) only the research conducted in hospitals or healthcare facilities, 2) types of microorganisms and 3) types of NIs. The exclusion factors were: 1) research conducted outside of the hospitals, 2) viruses and terms related to them and 3) research conducted in hospitals but not related to NIs.

Data analysis

The data collected from the studies were sorted, concluded respectively, and compared to ascertain the strength of the study. Results from the microorganisms associated with NIs were pooled, sorted, extrapolated, and descriptively analyzed. All the materials that had been retrieved underwent further screening and filtering. First, all the materials from databases are collected. Any duplication has been omitted then the next step is to look for the title. The unrelated and irrelevant titles were also omitted. After that, the abstracts were screened. The abstract was read and any unrelated abstract will be excluded. Then, the materials left are screened for the whole content. At this phase, the exclusion and inclusion factors are involved. Finally, the definite number of articles taken is decided.

Results

In total, 504 articles were identified by indexed in PubMed, Springer Link, Science Direct, and the general search engine Google Scholar. The search identified 500 articles. These articles were screened by abstract and title (Figure 1 shows the PRISMA flowchart). Of these, 380 articles were excluded during the title and abstract screening. Fifty-seven articles were excluded during the full-text review. Therefore, only 63 articles were included in the systematic review.

Based on the data regression and synthesis, there are a few types of microorganisms that are associated with NIs. Few types of common microorganisms are recorded. Those microorganisms are pathogenic and lethal to human health. However, there are also, rare types of pathogenic microorganisms recorded though it is very small in frequency. These microorganisms caused various types of NIs.

Types of microorganisms associated with NIs

Table 1 represents the frequencies for 19 groups of pathogenic microorganisms. Out of the 19 groups, only one group is identified as fungus or yeast. The other groups are bacteria including the “others” group. *Staphylococcus* spp. made up the biggest finding with 38 cases recorded, whereas *Pseudomonas* spp. was found with 27 cases. While bacteria influenza and non-influenza viruses are also present and with moderate frequencies. These are the common pathogenic isolated from patients who are having NIs. Figure 2 shows the frequencies of microorganisms collected from the articles. The highest microorganism and mostly found is *Staphylococcus* spp. In addition, Table 2 represents all the microorganisms that are associated with NIs.

Each group of microorganisms is made up of different species of microorganisms and some are only identified at the genus level. The list of tables below shows the different species of microorganisms according to their group. Table 2 shows the types of microorganisms and their frequencies. Table 3 shows the Gram-positive bacteria and their frequencies based on the cases recorded. While table 4 shows the multi-resistant bacteria (MSB) and their frequencies same as in table 5 which represents the gram negatives bacteria and their frequencies. Table 6 below is the types of fungi together with the frequencies and Table 7 recorded the number of viruses with the frequencies. All the collected data in the tables are based on their frequencies.

Types of NIs

Figure 3 (pie chart) below showed the types of NIs and their frequencies. Pneumonia-associated NIs is the most frequent with 18 cases. The Pneumonia included VAP, Non-VAP, and HAP. While BSI at second place with a frequency of 17. BSI also included CLABSI, HABSI, and other related infections. While UTI, RTI, Neonatal associated NIs, viral influenza, SSI, and dead

Table 1. The Group of Microorganisms and Their Frequencies (cases recorded)

Microorganisms	Frequencies (n)
<i>Staphylococcus</i> spp.	38
<i>Escherichia coli</i> spp.	17
<i>Pseudomonas</i> spp.	27
<i>Acinetobacter</i> spp.	14
<i>Enterococcus</i> spp.	17
<i>Streptococcus</i> spp.	8
<i>Clostridium difficile</i> spp.	2
<i>Ralstonia</i> spp.	2
<i>Serratia</i> spp.	5
<i>Enterobacter</i> spp.	10
<i>Proteus</i> spp.	6
<i>Citrobacter</i> spp.	3
<i>Klebsiella</i> spp.	18
<i>Candida</i> spp.	23
Hepatitis B	1
Influenza viruses	10
Non-Influenza viruses	13
<i>Sarcoptes scabiei</i> spp.	1
Others	7
TOTAL	222

Table 3. Gram-Positive Bacteria and Their Frequencies (cases recorded)

Microorganisms	Frequencies (n)
Bacteria	
Gram Positive	
<i>Streptococcus</i>	
<i>Streptococcus</i> spp.	4
<i>S. pneumonia</i>	4
<i>Staphylococcus</i>	
<i>Staphylococcus</i> spp.	2
<i>S. aureus</i>	16
<i>S. maltophilia</i>	1
<i>S. epidermis</i>	3
<i>S. Hominis</i>	1
Coagulase “-” <i>Staphylococcus</i>	5
<i>Enterococcus</i>	
<i>Enterococcus</i> spp.	9
<i>E. faecium</i>	4
<i>E. faecalis</i>	2
<i>E. cloacae</i>	2
<i>Clostridium difficile</i>	2
<i>Corynebacterium</i> spp.	1
<i>Cutibacterium</i> spp.	1
TOTAL	57

Table 1. Types of Microorganisms and Their Frequencies (cases recorded)

Microorganisms	Frequencies (n)	Microorganisms	Frequencies (n)
Staphylococcus		Pseudomonas (-)	
<i>Staphylococcus</i> spp. (+)	2	<i>Pseudomonas</i> spp.	7
<i>S. aureus</i> (+)	16	<i>P. aeruginosa</i>	17
<i>S. maltophilia</i> (+)	1		
<i>S. epidermis</i> (+)	3	Acinetobacter (-)	
<i>S. Hominis</i> (+)	1	<i>Acinetobacter</i> spp.	6
Coagulase “-” <i>Staphylococcus</i>	5	<i>A.baumannii</i>	7
MRSA	6		
MSSA	2	Enterococcus (+)	
		<i>Enterococcus</i> spp.	9
Klebsiella (-)		<i>E. faecium</i>	4
<i>Klebsiella</i> spp.	8	<i>E. faecalis</i>	2
<i>K. pneumonia</i>	8	<i>E. cloacae</i>	2
<i>K. oxytoca</i>	1		
		Clostridium difficile (+)	2
Streptococcus (+)			
<i>Streptococcus</i> spp.	4	Ralstonia (-)	
<i>S. pneumonia</i>	4	<i>Ralstonia</i> spp.	1
		<i>R. mannitolilytica</i>	1
Escherichia coli (-)	17		
		Candida	
Serratia(-)		<i>Camdida</i> spp.	7
<i>Serratia</i> spp.	1	<i>C. albicans</i>	6
<i>S. marcescns</i>	4	<i>C. glabarata</i>	4
		<i>C. tropicalis</i>	2
Enterobacter spp. (-)	10	<i>C. dubliniensis</i>	1
		<i>C. parapsilosis</i>	3
Others			6
<i>Achromobacterdentificans</i> (-)	1	Proteus spp. (-)	
<i>Sphirgomonas paucimobiles</i> (-)	1		
<i>Corynebacterium</i> spp. (+)	1	Citrobacter(-)	
<i>Cutibacterium</i> spp.(+)	1	<i>Citrobacter</i> spp.	2
<i>Bacteroides</i> spp.(-)	1	<i>C. koseri</i>	1
<i>Cryptococcus</i> spp. (fungi)	1		2
MDR	1		3
<i>Sarcoptei scaibei</i>	1	Non-Influenza viruses	
		Parainfluenza	2
Influenza viruses		Rhinovirus	2
<i>Influenza A (H1N1) pdmo9</i>	2	Bocarivirus	1
<i>Influenza A (H1N1)</i>	2	Coronavirus	1
<i>Influenza A</i>	1	Paravirus	
<i>Influenza B</i>	3	Norovirus	
<i>Haemophillus influenza</i>	1	Metapneurovirus	
<i>Influenza</i>	1	Hepatitis Virus B	1
		Human T Cell Lymphotropic Virus	

Table 4. Multi-Resistant Bacteria and Their Frequencies (cases recorded)

Microorganisms	Frequencies (n)
Multi Resistant Bacteria	
MRSA	6
MSSA	2
MDR	1
TOTAL	9

Table 5: Gram Negatives Bacteria and Their Frequencies (cases recorded)

Microorganisms	Frequencies (n)
Bacteria	
Gram Negative	
<i>Klebsiella</i>	
<i>Klebsiella spp.</i>	8
<i>K. pneumonia</i>	8
<i>K. oxytoca</i>	1
<i>Escherichia coli</i>	17
<i>Serratia</i>	
<i>Serratia spp.</i>	1
<i>S. marcescens</i>	4
<i>Enterobacter spp.</i>	10
<i>Achromobacter dentificans</i>	1
<i>Sphingomonas paucimobiles</i>	1
<i>Bacteroides spp.</i>	1
<i>Pseudomonas</i>	
<i>Pseudomonas spp.</i>	7
<i>P. aeruginosa</i>	17
<i>Acinetobacter</i>	
<i>Acinetobacter spp.</i>	6
<i>A. baumannii</i>	7
<i>Ralstonia</i>	
<i>Ralstonia spp.</i>	1
<i>R. mannitolilytica</i>	1
<i>Proteus spp.</i>	6
<i>Citrobacter</i>	
<i>Citrobacter spp.</i>	2
<i>C. koseri.</i>	1
TOTAL	100

Table 6: Fungi and Their Frequencies (cases recorded)

Microorganisms	Frequencies (n)
Fungi	
<i>Cryptococcus spp.</i>	1
<i>Candida</i>	
<i>Candida spp.</i>	7
<i>C. albicans</i>	6
<i>C. glabrata</i>	4
<i>C. tropicalis</i>	2
<i>C. dubliniensis</i>	1
<i>C. parapsilosis</i>	3
TOTAL	24

Table 7. Viruses and Their Frequencies (cases recorded)

Microorganisms	Frequencies (n)
Viruses	
Influenza viruses	
Influenza A (H ₁ N ₁) pdmo9	2
Influenza A (H ₁ N ₁)	2
Influenza A	1
Influenza B	3
Haemophilus influenza	1
Influenza	1
Non-Influenza viruses	
Parainfluenza	2
Rhinovirus	3
Bocavirus	2
Coronavirus	2
Paravirus	1
Norovirus	1
Metapneumovirus	1
Human T Cell Lymphotropic Virus	1
Hepatitis B Virus	1
TOTAL	24

also make up the portion with few cases. Other NIs included Bacteremia, cancer-related NIs, diarrhoea, haematology, hepatitis and clinical sepsis. One case of Norwegian Scabies caused by an ectoparasite was also recorded. The NIs and their respective associated microorganisms are fully listed in Supplementary A.

Discussion

Further understanding of the types of microorganisms in NIs can be described by the transmission route groups such as BSI, HAP, CAUTI, SSI (Liang and Marschall, 2011; Khan et al., 2017; Azar et al., 2019; Edwardson and Cairns, 2019).

Nosocomial bloodstream infections (BSI)

BSI is the major cause of morbidity and mortality in hospitals. BSI was placed as the 10th leading cause of death as reported by the CDC United States of America (USA). BSI can be divided into Central Line-Associated Bloodstream infections (CLABSI) and Hemodialysis-associated bloodstream infections (HABSI). CLABSI is one of the deadly NIs. The incidence rate of CLABSI is between 12% to 25% (Liang and Marschall, 2011; Khan et al., 2017). Coagulase-negative *Staphylococcus* spp. is the main cause for CLABSI. Other bacteria included *Enterococcus* spp., *S. aureus* spp., *Klebsiella* spp., *Enterobacter* spp., *Pseudomonas* spp., *E. coli* spp., and *Acinetobacter* spp. *Candida* spp. is the main yeast that causes this infection (Chavan and Kelkar, 2017). In (Gnass et al., 2014) report, there are five common types of microorganisms associated with HABSI such as *Candida albicans* spp., *Escherichia coli* spp., *Enterococcus faecalis* spp., *Enterobacteriaceae* spp. and *Staphylococcus* spp. *Staphylococcus* spp. is also included the coagulase-negative, *S. aureus* spp., Methicillin Resistant *Staphylococcus aureus* spp. (MRSA) and stimulant.

Among other microorganisms isolated in BSI related to ICU are *Serratia* spp., *Salmonella* spp., *Acinetobacter* spp., and yeast (Šuljagić et al., 2005). Meanwhile, for the catheter-related BSI, the distribution of causative pathogens is coagulase-negative *Staphylococcus* spp., *Staphylococcus aureus* spp., family *Enterobacteriaceae* spp., and *Candida* spp. *Candida* spp. is further divided into *Candida albicans* spp., *Candida parapsilosis* spp., *Candida glabrata* spp., *Candida tropicalis* spp., and others (Nagao, 2013). Thus, the significant six major pathogens could be associated with BSI are *Staphylococcus aureus* spp., *Enterococcus* spp., *Escherichia coli* spp., *Klebsiella* spp., *Pseudomonas aeruginosa* spp., and *Candida* spp., as supported by (Nagao, 2013) case study conducted on hospitalized patient blood samples (2,491 subjects) in the Japanese university hospital (from 2008 to 2011).

Hospital Acquired Pneumonia (HAP)

HAP or nosocomial pneumonia is a lower respiratory infection. It was not incubated during the hospital admission and presents clinically after two or more of hospitalization. The causal factor of HAP is bacterial infections. It is usually prevalent in the medical

and surgical intensive care units (ICUs). Patients who are possessed HAP will have few symptoms such as fever, and shortness of breath (Zuo et al., 2018). Among the microorganism that can be the causal factor for lower respiratory infection is *Acinetobacter Baumannii* spp (Jain et al., 2019). In a case study of nosocomial pneumonia infections among patients undergoing continuous renal replacement therapy (CRRT), about four to five microorganisms are isolated. *S. aureus* spp. made up the biggest portion with numbers of isolation is 41 (58.78%) followed by *Pseudomonas aeruginosa* spp. with isolation of 12 (17.14%). *Escherichia* spp. and *Chlamydia* spp. are respectively with 9 (12.86%) and 5 (7.14%) (Zuo et al., 2018).

Ventilator Acquired Pneumonia (VAP) is a subset of HAP and also a significant cause of morbidity and mortality in ICU. It occurs in those who undergo invasive mechanical ventilation via an endotracheal tube or known as tracheostomy. The early onset of VAP which occurred within the first 3-4 days of mechanical ventilation usually are caused by bacteria: *Haemophilus* spp., and *Streptococcus* spp. While the VAP that developed after five days is caused by the MDR bacteria such as *P. aeruginosa* spp (Ciofi degli Atti et al., 2014).

Catheter-Associated UTI (CAUTI)

CAUTI on the other hand only happened when the patient is inserted with the catheter and infections occurred. Thus, the catheter must be inserted properly and taken out when it is not used. *E. coli* spp. is the most frequent microorganism that causes CAUTI. Infection also occurs under the exposure of MDR bacteria such as the Vancomycin-resistant Enterococci (VRE) (WHO).

According to (Greene et al, 2019), UTI is the most frequent NI in geriatric units. Bacteria are one of the major factors for infections. Vernier et al. (2015), stated that *Pseudomonas aeruginosa* spp. is the causal factor of nosocomial UTI in the ICU. Kang et al. in their research, listed five microorganisms that are associated with nosocomial UTI. All of the microorganisms listed are gram-negative bacilli spp. which are *E. coli* spp., *K. pneumonia* spp., *P. aeruginosa* spp., *Enterobacter* spp. and others.

Surgical site infection (SSI)

In USA, there are about 157,500 SSI occurs, and an estimated of 8,205 deaths each year. While 11% of all caused deaths in ICU are also associated with SSI (CDC, 2018). SSI is mainly caused by *S. aureus* spp. which also resulted in prolonged hospitalization and death (Khan et al., 2017). As with other NIs, SSI happened because of pathogenic microorganisms. The most common microorganism include the bacteria *Staphylococcus* spp., *Streptococcus* spp., and *Pseudomonas* spp. Pathogenic microorganisms can infect a surgical wound through various forms of contact, such as from the touch of a contaminated caregiver or surgical instrument, microorganisms in the air, and also microorganisms that are already in our body.

However, the degree of SSI is varied with the type of surgery. The surgical wounds are divided into clean wounds, clean-contaminated wounds, contaminated wounds, and dirty wounds. Among the risk factors of SSI is surgery that is conducted more than 2 hours, being overweight, smoking, having diabetes, weak immune system, and other medical problems or diseases (Johns Hopkins Medicine, 2019).

Other related issues

Multi-drug resistance (MDR) microorganisms

The emergence of MDR microorganisms marks that more precautions and prevention need to be taken. However, this also proved that it is quite difficult as critically ill patients will display a different spectrum of colonization of the bacteria. After 72 hours of admission, MDR infections can occur. Microorganisms will have higher rates of drug resistance. The microorganisms or bacteria evolve rapidly due to the selective pressure from regular antibiotics. MRSA, VRE, and MSSA are among the most common resistant bacteria (Edwardson and Cairns, 2019). Besides, the study by Bayode et al. (2021) highlighted the prevalence of antibiotic-resistant genes in healthcare settings.

Cross infections

The trend of cross-infections is also shown as there are infections that occur as a result of other NIs. Urinary tract-related Bloodstream Infection (UT-BSI) happened as a result of the urinary tract that later infected the patient's bloodstream. Greene et al., 2019, listed seven bacteria that can cause UT-BSI which are *E. coli* spp, *Staphylococcus* spp. and *Pseudomonas* spp. *Candida* spp. is the main yeast group that caused this cross-infection. Olalemi et al. (2021), highlighted the potential health risks associated with hospital wastewaters (Md. Robeul et al. 2024).

Conclusion

This systematic review provides an overview signature of microorganisms associated with the respective types of NIs. MDR-related and cross infections-NIs are more lethal and dangerous, especially to immune-compromised patients. Knowledge from this study could contribute to the development of relevant steps, measures, or effective precautions in tackling NIs issues in the healthcare system.

Author contribution

N.Y., R.B.S.M.N.M., C.S., N.H.H., S.S.N. developed the idea, study design, wrote, reviewed, edited the paper.

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None declared

Competing financial interests

The authors have no conflict of interest.

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