Original article

Hospital-Acquired Infections, Bacterial Causative Agents And Antibiotic Resistance Pattern In Intensive Care Units At Teaching Hospitals In North Of Iran

Farhang Babamahmoodi[1], Fatemeh Ahangarkani[1], Alireza Davoudi[1*]

1- Antimicrobial Resistance Research Center, Department of Infectious Diseases, Mazandaran University of Medical Sciences, Sari, Iran

Corresponding author: Alireza Davoudi

Email:eiy_iran@yahoo.com

Tel/fax:+981142316319

Abstract

aim: HAIs (Hospital-Acquired Infections) remain a major problem in ICUs. The purpose of this study is survey of HAIs and antibiotic susceptibility patterns of causative agent among patients admitted in ICUs.

Methods: A retrospective study was conducted in three teaching hospitals related to Mazandaran University of Medical Sciences in 2012-2014. The incidence, clinical presentation, risk factors, causative agents and antibiotic resistance pattern of bacteria analyzed by SPSS (ver. 16) and Descriptive statistics were used.

Results: The incidences of HAIs were 4.13%. The most common HAIs were respiratory infection 49.1%, wound infection 26.3%, UTI 16.7%, and blood Infection 7.9%. *P. aeruginosa 42.1%, Acinetobacter spp. 21.05%, Enterobacteriaceae* 19.29% and *S.* aureus 12.28% were the most bacteria isolated. We found that 35% ESBL and 14.58% carbapenemase-producer *Pseudomonas* spp. Also 60% of *Acinetobacter* spp were MDR and 14.28% of S.aureus was resistant to Vancomycin.

Conclusion: This article suggests that the prevalence of HAIs in ICUs of teaching hospitals in northern Iran is false low. Diagnosing of NI in our area focused on physician diagnosis and clinical criteria for reporting HAIs, The rate of inappropriate administration of antibiotics is very high in our region also significant resistance in organisms such as *Acinetobacter* spp, *P. aeruginosa, Enterobacteriaceae, S. aureus* to the most commonly used antibiotics has been increasing. Infection control procedures must be implemented carefully and Antibiotic resistance patterns of organisms causing HAIs should be checked periodically to guide empirical antibiotic therapy.

Keywords: Hospital-Acquired Infection, ICUs, Antibiotic resistance

Introduction

HAIs (Hospital-Acquired Infections) lead to high mortality and remain a major problem in health care centres in the world. The highest rates of HAIs are observed in ICUs (intensive care units), which are also the ward in that the most severely ill patients are treated. 1 Long-term hospitalization, use of invasive devices and a variety of vascular catheters caused increase of HAIs in this ward. The Centres for

Disease Control and Prevention estimates that 1.7 million HAIs occurred in the United States in 2002 and ICUs had the highest rates of infection, at 13 per 1,000 patient- days. The most common ICU infections are pneumonia, UTI (urinary tract infection), BSI (bloodstream infections) and are usually device related .2, 3 Organisms such as gram-negative bacilli, coagulase-negative Staphylococci, coagulase-positive staphylococci, Pseudomonas spp. and Streptococcus are cause of HAIs. Common problem in the treatment of HAIs is increasing antibiotic-resistant organisms. Limited data exist on the epidemiology of ICU-acquired infections in Iran, there is not any reported of HAIs in north of Iran. A surveillance activity, as part of infection prevention and control programs in health care facilities, contributes to meeting the program's overall goals. Surveillance activities are an essential component of effective clinical programs designed to reduce the frequency of adverse events such as infection. 4

Objective

The purpose of this study is survey of HAIs and antibiotic susceptibility patterns of causative agent among patients admitted in ICU in three teaching hospitals related to Mazandaran University of Medical Sciences in order to help the physicians choosing the better sort of antibiotics in the start of empiric therapy.

Methods

This is cross sectional-retrospective study. The location of study is ICU ward of three teaching hospitals of Mazandaran university of medical sciences (in north of Iran) included of Razi, Emam khomeyni and Bu Ali Sina hospitals. This study was approved by the (Code No: 9134, Date: July 11, 2012) Ethics Committee of Mazandaran University of Medical Sciences. Census method was performed for sampling. The study populations were patients hospitalized in ICU at these hospitals during 2012-2014, who had symptoms of HAIs. HAIs definition was based on National Directory of Nosocomial Infections Surveillance System 5, defined as: UTI: The patient must have at least one of these symptoms such as fever, dysuria, frequency, flunk pain, supra pubic pain, nausea and vomiting plus positive urine culture or at least must have two symptoms such as fever, dysuria, frequency, flunk pain, supra pubic pain, nausea and vomiting plus pyuria.Wound Infection: Superficial surgical site infection is identified with at least one of the following characteristics: purulent discharge from the wound, organisms isolated from the fluid or superficial surgical tissue that be prepared aseptic, at least one of the symptoms like pain, swelling, redness or warmness, or diagnosis of the wound infection by the doctor.Respiratory Infection: Hearing the crackles on lung examination or radiographic findings plus at least one of the following, purulent sputum or positive blood culture or positive culture of tracheal aspirate sample.Blood Infection : Blood culture grew a pathogenic organism, condition that is not related to the location of a localized infection or having fever, chills, decreasing of blood pressure plus existing infections related to the skin in at least two blood culture (like diphteroids, bacillus species, propionic bacterium or coagulase negative staph). Identification of organisms was performed according to standard microbiological procedures. 6, 7 Antimicrobial susceptibility testing method, Disk diffusion (Kirby-Bauer) was performed according to standard Clinical Laboratory Standard Institute. 8 We provided an information form included demographic and clinical characteristics, risk factors, medical history, main diagnosis, type of HAIs, sort of culture and then we took out the lists of the patients with HAIs. Collected data was analyzed by SPSS (ver. 16) and descriptive statistics were used.

Results

Of total 2760 hospitalized patients in ICUs, 114(4.13%) had HAIs which 60(52.06%) were female and 54(47.4%) male. The average age was 67.62±15.41 years. The average duration of hospitalization was 10.39±6.023 days. The prevalence of types of HAIs was respiratory infection (49.1%), wound infection (26.3%), UTI (16.7%) and blood Infection (7.9%). The demographic feature, clinical characteristics and risk factors of every infection have been described in table 1.The incidence causative agent of HAIs are in table 2.Antibiotic resistance pattern of the bacteria that cause HAIs are given in 3 and 4 Tables.

Table 1: demographic feature, Symptoms and risk factors of infection

		Respiratory Infection No. (%)	Wound infection No. (%)	Urinary tract Infection No. (%)	Blood Infection No. (%)	Total No. (%)
Gender	Female	28(50)	20(66.7)	11(57.9)	1(11.1)	60(52.6)
	Male	28(50)	10(33.3)	8(42.1)	8(88.9)	54(47.4)
Age	Year	69.12±13.40	69.06±11	61.84±20.66	65.66±24.08	67.62±15.41
Average duration of hospitalization	day	10.75±6.86	11.03±5.97	9.42±5.83	8.11±3.01	10.39±6.023
Risk factor	Diabetes	24(42.9)	3(10)	11(57.9)	7(77.8)	45(39.47)
	HTN	20(35.7)	5(16.7)	7(36.8)	7(77.8)	39(34.21)
	Cardiovascular disease	17(30.4)	9(30)	5(26.3)	5(55.6)	36(31.57)
	Urine catheter	6(10.7)	-	13(68.4)	-	19(16.66)
	IV. lines	-	-	-	9(100)	9(7.89)
	Mechanical intubation	50(89.28)	-	-	-	50(43.85)
	Steroid therapy	18(32.1)	9(30)	5(26.3)	6(66.7)	38(33.33)
	Lung diseases	24(42.9)	-	1(5.3)	-	25(21.92)
	Liver Cirrhosis	5(8.9)	-	1(5.3)	-	6(5.26)
	Renal failure	11(19.6)	1(3.3)	4(21.1)	-	16(14.03)
	Malignancy	11(19.6)	-	2(10.5)	-	13(11.40)
	Chemotherapy	11(19.6)	-	2(10.5)	-	13(11.40)
	Transplantation	2(3.6)	2(6.7)	-	-	4(3.50)
Symptoms	Fever	53(94.6)	10(33.3)	18(94.7)	9(100)	90(78.94)
	Dysuria	-	-	15(78.9)	-	15(13.15)
	Frequent urination	-	-	11(57.9)	-	11(9.64)
	Flank pain	-	-	4(21.1)	-	4(3.50)
	Suprapobic pain	-	-	9(47.4)	-	9(7.89)
	Nausea	27(48.2)	-	-	8(88.9)	35(30.70)
	Vomiting	21(37.5)	-	-	6(66.7)	27(23.68)
	Chest pain	25(44.6)	-	-	6(66.7)	31(27.19)
	Cough	45(80.4)	-	-	2(22.2)	47(41.22)
	Increase of sputum	54(96.4)	-	-	2(22.2)	56(49.12)
	dyspnea	42(75)	-	-	4(44.4)	46(40.35)
	Wound erythema	-	30(100)	-	-	30(26.31)
	Wound oozing	-	30(100)	-	-	30(26.31)
	Suture openings	-	19(63.3)	-	-	19(16.66)

Table 2: Causative agent of infection

Causative agent	No.(%) episodes of infection by site				
	Wound Infection (N=30)	Respiratory Infection (N=56)	Urinary Tract Infection (N=19)	Blood Infection (N=9)	Total (N=114)
P. aeruginosa	14(46.7)	26(46.4)	1(5.3)	7(77.8)	48(42.10)
Acinetobacter.spp	6(20)	15(26.8)	3(15.8)	0	24(21.05)
E.coli	0	0	6(31.6)	0	6(5.26)
C. freundii	0	1(1.8)	2(10.5)	0	3(2.63)
Enterobacter .spp	0	3(5.4)	3(15.8)	0	6(5.26)
Klebsiella.spp	0	4(7.1)	3(15.8)	0	7(6.14)
S. aureus	10(33.33)	1(1.8)	1(5.3)	2(22.2)	14(12.28)
S. epidermidis	0	3(5.4)	0	0	3(2.63)
S. pyogenes	0	3(5.4)	0	0	3(2.63)

Table 3: Antibiotic resistance pattern of gram negative bacteria isolated from infection

Antibiotics	*P.aeurogi nosa* No.(%)	Acinetoba cter.spp No.(%)	E.coli No.(%)	C. freundii No.(%)	Enterobac ter .spp No.(%)	Klebsiella .spp No.(%)
Ceftriaxone	38(79.16)	28(100)	6(100)	0	2(33.33)	0
Ceftizoxime	27(56.25)	28(100)	3(50)	0	3(50)	0
Ceftazidime	21(43.75)	27(96.43)	3(50)	0	2(33.33)	6(85.7)
Cefixime	14(29.16)	27(96.43)	0	3(100)	4(66.66)	0
Carbenicillin	31(64.58)	28(100)	3(50)	0	0	0
Ciprofloxacin	28(58.33)	28(100)	4(66.66)	1(33.33)	5(83.33)	0
Nalidixic Acid	11(22.91)	28(100)	6(100)	3(100)	2(33.33)	6(85.7)
Gentamicin	31(64.58)	21(75)	6(100)	1(33.33)	5(83.33)	7(100)
Amikacin	37(77.08)	18(64.28)	3(50)	1(33.33)	4(66.66)	0
Imipenem	7(14.58)	17(60.71)	2(33.33)	0	1(16.66)	0
Co – trimoxazole	38(79.16)	28(100)	6(100)	3(100)	4(66.66)	6(85.7)
Tetracycline	17(35.14)	28(100)	0	0	0	0

Table 4: Antibiotic resistance of gram positive bacteria isolated from infection

antibiotics	*S.aureus* NO.(%)	*s.epiderm idis* NO.(%)	*S. pyogenes* NO.(%)
Ampicillin	12(85.71)	3(100)	0
Carbenicillin	7(50)	2(66.6)	0
Penicilin	12(85.71)	3(100)	0
Oxacillin	10(71.42)	3(100)	1(33.3)
Cefazolie	13(92.85)	3(100)	1(33.3)
Ceftriaxone	7(50)	2(66.6)	2(66.6)
Ceftizoxime	11(78.57)	1(33.33)	3(100)
Ciprofloxacin	10(71.42)	3(100)	3(100)
Vancomycin	2(14.28)	0	0
Clindamycin	10(71.42)	2(66.6)	1(33.3)
Erythromycin	7(50)	3(100)	1(33.3)
Co - trimoxazole	13(92.85)	3(100)	3(100)
Tetracycline	8(57.14)	2(66.6)	3(100)

Discussion

In this study 4.13% of patients in ICU had HAIs which were lower than the rate (14.7%) observed in 55 ICUs of developing countries. 9 Also our result is close to HAIs in ICUs in many industrialized countries where the rates from 7.7- 16.5%. 10, 11 Young children, the elderly and immunocompromised patients are more susceptible to HAIs. Approximately 71% of our patients were age >60 years (P<02). Other risk factor for HAIs is a long hospital stay. 12, 13 The average duration of hospitalization of patients' in our study was 10.39±6.023 (p<008)was consistent with report of Sohrabi et al. 14 We observed that most risk factors were Diabetes mellitus(MD) 39.47% and steroid therapy 33.33%. Patients with MD are more susceptible to many types of infection, including HAIs, it has been observed in findings of Yamashita et al and Vardakas et al.15, 16 Accurate control for diabetic patients during hospitalization can reduce the HAIs. Also Rojas et al had mentioned steroid therapy and is as a risk factor for HAIS.17In our study incidence of renal failure, malignancy and chemotherapy, liver cirrhosis and, transplant patients were 14.03%, 11.40%, 5.26% and 3.5%, respectively. HAIs cause substantial morbidity and mortality in patients who are immunosuppressed. 18 Respiratory infections were the most type of HAIs in our study. Nearly 89.25% of these patients used Mechanical intubation.VAP (Ventilator-associated pneumonia) is the most common cause of HAIS among patients admitted in ICUs. 19 Studies in many western countries have suggested that Hospital-Acquired Lower respiratory tract infections are mainly due to mechanical ventilation. 20, 21 For reducing HAIs, we should try to have at least intubation or Non-invasive method. Nearly half of patients with respiratory infection had chronic lung diseases. In Ding et al study in China, respiratory tract infections in ICU accounted for most of the infections (68.4%) similar to our findings. 22 Consistent with the Ding et al findings, the most common bacteria isolated from respiratory sample in our study were Pseudomonas spp. and Acinetobacter spp.,in other hands P. aeruginosa and S. aureus were the most common pathogens in the US report (21). Close to our findings, Huang et al found that 14.7% of Acinetobacter spp. was isolated from sputum/endotracheal aspirates. 23 Wound infections occur in 3% to 12.7% of ICUs patients. 24, 25 Wound infection was second HAIs (26.3%) in our

study consistent with Zahraei et al findings. 26 Ding reported incidence of wound infections about .9%. 22 It seems prevalence of wound infection is high in our study comparing other studies, in other hand 33.33% of pathogen isolated wound samples are S. aureus. Although UTI accounts for almost 40% of all nosocomial infections worldwide, UTI incidence in our study was 16.7%. Most hospital-acquired UTIs are associated with urinary catheters. Up to 25% of hospitalized patients have a urinary catheter placed during their stay. 27-29Around 70% of patients with UTI in our study used catheter. The use of external urinary collection device is more comfortable than an indwelling catheter and can reducing UTI. 30E.coli was the most pathogen isolated from UTI. E. coli was the most common bacterial cause of nosocomial UTIs similar to Ding et al study and also many studies in Iran. 22, 31, 32The forth ranked group HAIs in our survey was blood infections with incidence 7.9%.P. aeruginosa 77.8% and S.aureus 22.2% were the causative agents of infection. During the recent studies gram posistive bacteria agents of nosocomial blood infections are increasing, but still gram negative bacteria are in first ranking of causing bloodstream infection. 33-35Our study showed gram-negative bacilli continue to be associated with HAIs in ICUs. Eighty percent of isolated bacteria were gram-nagative including pseudomonas spp. 42.10%, Acinetobacter spp. 21.05%, Enterobacteriaceae 19.29% followed by S.aureus 12.28%, S.epidermidis 2.63%, S. pyogenes 2.63%. Mylotte et al reported the most common pathogens isolated nosocomial infection sample were S. aureus and gram-negative such as pseudomonas. 36 The most common pathogens in Ott et al study were E. coli, coagulase-negative staphylococci. Also the most common pathogens isolated in Azim et al study were P. aeruginosa and A. baumannii consistent with our results. 37 At least 60% Acinetobacter spp. isolated in our study were multidrug-resistant. Prevalence of multi-drug resistance Acinetobacter spp. in countries of the Atlantic have been reported 29.3 %.38,39 Similar to our resuls, Vahdani et al reported incidence of multidrug-resistant Acinetobacter spp., between 58%- 96% in their study.40 We observed that 35% of Pseudomonas spp. was extended-spectrum β-lactamase. In other hand 14.58% were Carbapenemase-producing. Mohanty et al reported 40% P. aeruginosa are Carbapenemase-producer.41 Enterobacteriaceae species in our study have been shown a high antibiotic resistance. E. coli, Enterobacter spp., Klebsiella spp. and C. freundii, had an average 45% and 33.75% resistance to Fluoroquinolones and third generation cephalosporin. Antimicrobial resistance for S. aureus to Oxacillin, Clindamycin, Co – trimoxazole, cefazolin and vancomycin was 71.42%, 71.42%, 92.85%, 92.85% and 14.28%, respectively. Other gram positive such as s.epidermidis and S. pyogenes showed different but high range of resistance to antibiotics. It seems that the incidence of antibiotic resistance in Enterobacteriaceae ,s.epidermidis and S. pyogenes in our study is not valid due to the low number of these organisms. This article suggests that the prevalence of HAIs in ICUs of teaching hospitals in northern Iran is false low. These are needed attention that HAIs detection was based on clinical grounds in most of our cases; possibly missing patients with subclinical infections also because of laboratory reports might contain many false-negative results42. Absence of facilities for culture of anaerobic bacteria in north of Iran, low HAIs reporting from wards, consequently the rate of HAIs shows false low. However, significant resistance in organisms such as Acinetobacter spp, P. aeruginosa, Enterobacteriaceae, S. aureus to the most commonly used antibiotics has been increasing. It is necessary Infection control procedures must be implemented carefully and Antibiotic resistance patterns of organisms causing HAIs should be checked periodically to guide empirical antibiotic therapy.

Financial Disclosure: None declared

Funding/Support: This study was supported in part by grant 9134 from Vice-Chancellor for research at Mazandaran University of Medical Sciences.

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