Health Care Associated Infection and Trend of Antimicrobial Resistance in Tertiary Care Hospital -A Study in Low Income Setting

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ABSTRACT

Background

Antimicrobial resistance (AMR) and healthcare-associated infections (HAIs) are among the most serious public health problems and overall estimate indicates that at any point, over 1.4 million people are suffering from health care associated infection globally. According to the WHO report, the frequency of nosocomial infection is 10% in South East Asia where as 7% in developed countries. The increasing trend of AMR in pathogenic bacteria leads to complication to treat HAIs and failure in treatment and rise in mortality.

Objective

The study was conducted with the objective of to explore the incidence of different types of HAIs and AMR pattern in the patients admitted in a tertiary care hospital.

Method

The cross-sectional study was conducted at the tertiary care hospital and the patient who are one year or older and admitted for more than 48 hours were included in this study. The criteria for classification of HAIs were adapted from Centers for Disease Control. All the samples were collected then antibiotic sensitivity testing was conducted according to CLSI standards. Data were collected using a structured data collection form. Data were entered in EpiData software and analyzed using SPSS version 22.

Result

Among 2326 patients, female was slightly higher than male patients, where 77 (3.3%) patients experienced at least one episode of HAIs. The surgical site infection (71.42%) is the most common infection followed by Catheter Associated Urinary Tract Infection (18.18%) and Health Care Associated Pneumonia (6.49%). Mean hospitalization days is higher with HAI (14.5 days) compared to non-HAI (6.6 days). Out of 909 specimens, urine, sputum and blood were higher in numbers, where 217 bacterial isolates were isolated with Escherichia coli (83 isolates) was the most common bacteria. It is found that Escherichia coli bacterial isolates were resistance to most common antibiotics.

Conclusion

The study concludes that surgical site infection is the most common healthcare-associated infection and Escherichia coli is the most common bacteria responsible for HAIs. Further, surgical site infection being the most common infection, there is an urgent need to take effective infection prevention and control prevention.

KEY WORDS

Antimicrobial resistance, Healthcare-associated infections, Surgical site infection

INTRODUCTION

Antimicrobial resistance (AMR) and healthcare-associated infections (HAIs) are among the most serious public health problems, globally and in Asia.[1] The issue of HAI and AMR overlaps closely, but they are not the same. A nosocomial infection, also known as "Hospital Acquired Infection" or "Health Care Associated Infection" can be defined as: an infection acquired in hospital by a patient who was admitted for a reason other than that infection. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility.[2] With the increasing use of antibiotics, the problem of AMR is becoming more and more prominent. According to World Health Organization (WHO), AMR is defined as "that microorganisms are resistant to the antimicrobial drugs that are on originally to be effective on the treatment of infections caused by the microorganisms".[3] Overall estimate indicate that at any point, over 1.4 million people are suffering from health care acquired infection worldwide.[4] HAIs are considered as the most common complication in hospital settings both in developed and developing countries. In developed countries 5% to 10% of patients admitted to modern hospitals acquire one or more infections.[5,6] In some developing countries, the proportion of patients affected by a health care associated infection can exceed 25% and the risk is 2 to 20 times higher than in developed countries.[5] In addition to that, out of 100 hospitalized patients at any time, 7 in developed and 10 in developing countries will acquire HAIs.[4] According to the WHO report, the frequency of nosocomial infection is 10% in South East Asia where as 7% in developed countries.[7,8]

There has been an increasing concern that patient safety and quality is a serious aspect of universal health care coverage. HAIs has a significant impact that leads to longer hospital stay, long term disability, increased resistance to antimicrobials, high financial burden to patients and families and increased death.[6,9,10] The risk of HAI increases with the increase in duration of placement of invasive devices and prolonged hospitalization of patient.[7,11,12] The condition is considered to be serious when it is accompanying with AMR, which might need more diagnostic and laboratory test costing higher expenditure. The increasing trend of AMR in pathogenic bacteria leads to complication to treat HAIs and failure in treatment and rise in mortality.[13] Further, as Nepal is one of the developing countries with low GDP, where the total per capita health expenditure in 2014 was $ 137 and health expenditure accounted for 5.8% of GDP.[14] The health care cost estimates to be second largest expenditure after expenses for food. HAI being a major problem for patient safety, its surveillance and prevention should be first and foremost priority for healthcare settings committed to making safe health care.[9]

AMR is becoming the serious global threat to the public health worldwide. AMR has been also declared a public health threat by WHO and insisted countries to develop an action plan to combat the problem from everyone's side.[15] Tertiary care hospital is one of the major sources of antibiotics prescription and can play a crucial role in rational use of antibiotics. AMR surveillance helps to provide the insights of causative agents and susceptibility pattern which will eventually help to select the appropriate antibiotics. Although many studies are available in developed countries there are very few studies in developing countries like Nepal. From the review of WHO in 2014 in Nepal, it was observed that out of 140 isolates, 64% of *Escherichia coli* were resistant to fluoroquinolones and 38 % were resistant to third-generation cephalosporin. In addition, smaller data sets showed resistance rates of *S. aureus* to methicillin ranging from 2 to 69%. *Klebsiella pneumonia* showed resistance to third-generation cephalosporins of 0 to 48%, while no resistance to carbapenems was detected.[15] In Nepal, AMR surveillance program was first started in 1999 with the financial support of United States Agency for International Development (USAID) and technical support of International Center for Diarrheal Disease Research/ Bangladesh (icddr,b). Since 2004, National Public Health Laboratory (NPHL), as a national coordinating laboratory, continued this program financially supported by WHO. But as in many countries, a surveillance system for tracking antimicrobial resistance rates or documenting antibiotic use is not adequate in Nepal, resulting in obtaining the accurate report.[16]

The study was conducted with the objective of to explore the incidence of different types of HAI's and AMR pattern in the patients admitted in a tertiary care hospital. It may provide the necessary information to formulate the antibiotic policy in a tertiary care hospital and similar settings in developing countries.

METHODS

Study Design and Setting

This is a cross-sectional study conducted in Dhulikhel Hospital, Kathmandu University Hospital (DH, KUH) from December 2017 for six months after acquiring ethical approval from the Kathmandu University School of Medical Sciences, Institutional Review Committee. The patients one year or older and being admitted for more than 48 hours were included in this study. Those patients who had incomplete information regarding demographic and clinical outcomes were excluded from this study.

Healthcare Associated Infection

HAIs are defined as infection acquired after 48 hours of admission and were not present or incubating at the time of admission.[17] The criteria for classification of HAI's were adapted from Centers for Disease Control.[18]

Sample Collection and Antimicrobial Susceptibility Test

Samples were collected by aseptic technique and sent to the hospital laboratory. The culture was done on Nutrient

Agar, Blood Agar, MacConkey Agar, Chocoloate Agar and Cysteine Lactose Electrolyte Deficient Agar plates whereas all the blood samples were first inoculated in Bactec bottles followed by sub-culture on solid media. Suspicious colonies were sub cultured for purity and identified by colony morphology and biochemical tests. Antimicrobial susceptibility testing to various drugs molecule was done on Mueller-Hinton (Oxoid) agar plates by Kirby-Bauer disk diffusion technique. The diameter (in mm) of Zone of inhibition around the specified drug discs, for various isolates were read according to CLSI standards.[19]

Data collection and Management

Data were collected using a structured data collection form. Trained data collector visited different departments of the hospital to collect the data which includes demographic information, details of HAI's and laboratory information from electronic and paper-based data from relevant sources. In addition, the data collector directly observed patients to record the data on use of Foley's, drain, DJ stent, Foley's SPC and mechanical ventilator. For the quality measure, data were double checked after the completion of filled form to avoid missing data.

Statistical Analysis

Data were entered in EpiData software (version 3.1, EpiData association, Odense, Denmark) and analyzed using Microsoft excel and SPSS (version 22). The general characteristics of the participants were summarized in mean (standard deviation) for the continuous variables and proportion for categorical variables. Pattern of microorganism and susceptibility patterns were analyzed and expressed as percentages.

RESULTS

In the present study, a total of 2326 patients were included. The mean age of the patients was 39.87±20.45 years with more than 50% of them were female. The patients admitted was higher in medical ward followed by gynecology, surgical and orthopedics (Table 1).

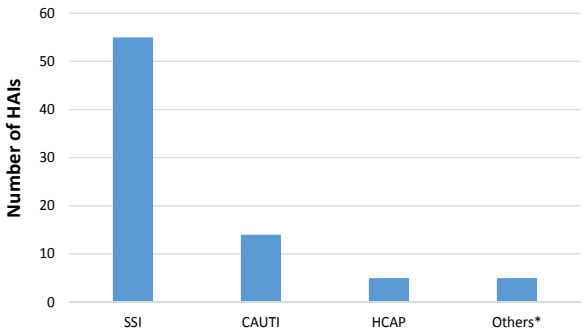
Healthcare Associated Infections

During the study period, 3.3% patients experienced at least one episode of HAI with SSI being the most common (71.42%) followed by 18.18% of Catheter-associated Urinary tract infection (CAUTI) and 6.5% of Healthcare associated pneumonia (HCAP) as shown in the figure 1. Further, it is observed that, mean hospitalization days is higher with HAI (14.5 ± 1.16 days) compared to non-HAI (6.6 ± 0.83 days).

Among 79 HAI's as shown in the Figure 2, orthopedics ward (27.3%) had the highest percentage of HAIs followed by surgical ward (26.0%) and gynecology ward (16.9%).

Table 1. Characteristics of the study population

	Frequency (%) n=2326
Age (years), mean (SD)	39.87 (20.45)
Sex	
Female	1298 (55.8)
Male	1028 (44.2)
Admitted Ward	
Pediatric Ward	99 (4.3)
Intensive Care Unit	25 (1.1)
Surgical Ward	463 (19.9)
Orthopedic Ward	446 (19.2)
Medical Ward	805 (34.6)
Gynecology Ward	488 (21)
Hospitalization days, mean(SD)	6.89 (4.53)



*Pin site infection, VAP, DJ stent infection

Figure 1. Different types of HAI.

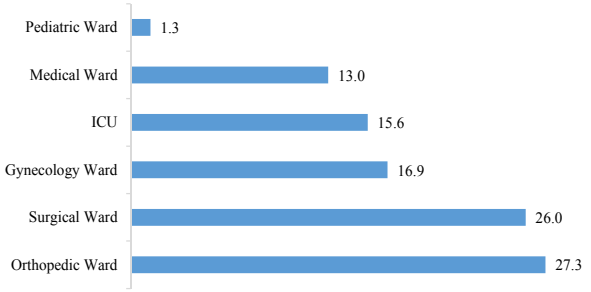
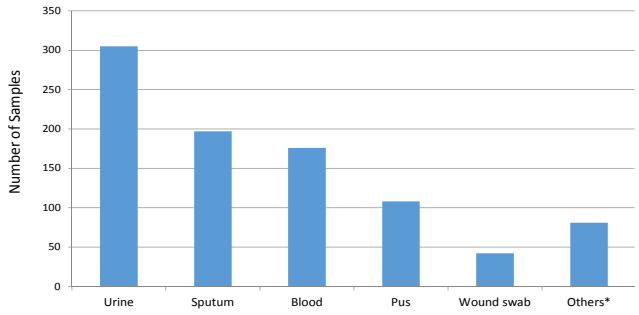


Figure 2. Distribution of HAI as per the different ward

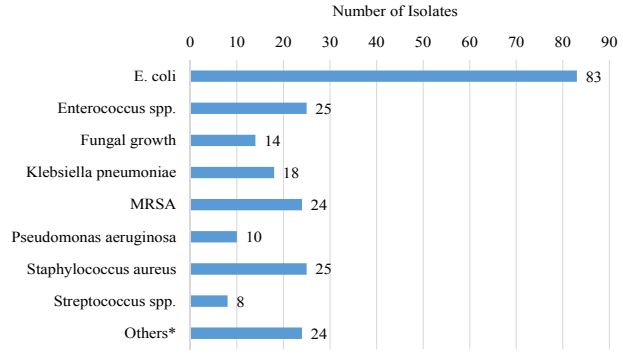
Clinical Samples and Microorganism Isolated

During the study period, 909 specimens were collected and analyzed. The maximum sample obtained was urine (n=305) which was followed by sputum and blood (fig. 3). Similarly, two hundred and seventeen bacterial isolates were isolated (fig. 4) where *Escherichia coli* (83 isolates) was the most common bacteria followed by Enterococcus spp. (25 isolates), *Staphylococcus aureus* (25 isolates) and 24 isolated of *Methicillin-Resistant Staphylococcus aureus (MRSA)*.



*Ascitic fluid, CSF, Bile, Stool, Tracheal aspirates

Figure 3. Distribution of Samples Collected



***Acinetobactor spp, Aspergillus fumigatus, Coagulase negative Staphylococcus aureus, Gonococcal bacilli, Klebsiella oxytoca, Proteus spp., Pseudomonas, Salmonella parathphi, Salmonella thphi, Shigella spp.*

Figure 4. Distribution of causative agents

Antibiotic Susceptibility Pattern

Escherichia coli bacterial isolates showed resistance to the most common antibiotics like *Azithromycin* (100%), *Amoxycillin+clavulanic acid* (100%), *Cefuroxime* (80%), *Cefotaxime* (78.6%), *Ceftriaxone* (66.7). Similarly, isolates of *Klebsiella pneumonia* were resistance to *Cefotaxime* (100%), *Ceftriaxone* (81.8%), *Cefixime* (87.5%), and *Cotrimoxazole* (81.8%). In addition, MRSA isolates showed resistance to *Cefixime* (100%), *Cotrimoxazole* (100%), *Cloxacillin* (100%), *Cefuroxime* (71.4%), *Ceftriaxone* (66.7%) and *Ciprofloxacin* (85.7%). Moreover, *Cefixime* (82.35%) and *Amoxicillin+clavulanic* acid (100%) were resistance to Staphylococcus aureus isolates as shown in figure 5.

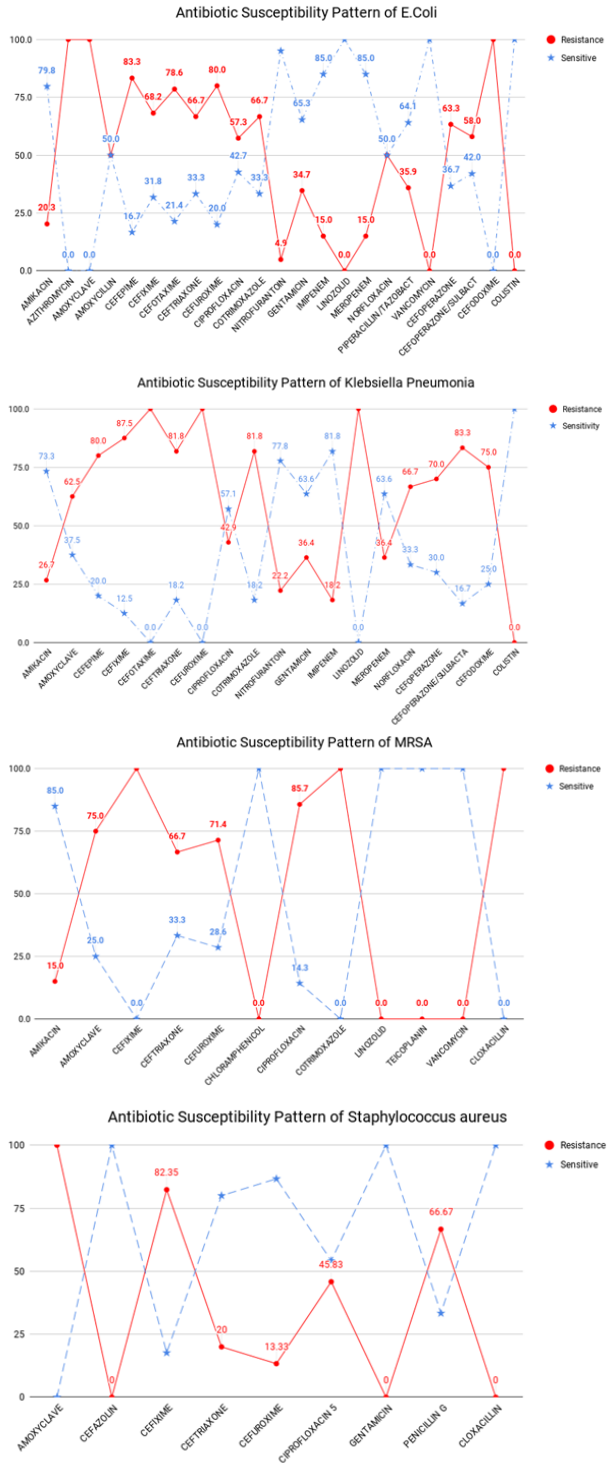


Figure 5. Antibiotic Susceptibility Pattern of different micro-organism.

DISCUSSION

The current study aimed to find out the incidence of various HAIs and AMR pattern in the patients admitted in the tertiary care centre. The various demographic parameters have been collected and compared with HAIs and AMR pattern.

In the study, female patients were found to be higher than male (55.8% vs. 44.2%). This finding is supported by the previous similar studies which also suggested to have more HAIs among female populations.[10,20,21] In this study, the higher number of female patients might be due to the inclusion of Obstetrics and Gynaecology department (21%). Further, female populations are more prone to the infections due to the anatomical structure as well, which is related to short urethra and the distance from anus to urethra.[22-25] This could be the one of the major reason to have more number of female populations than male in the current study as well. Further, the current study shows the most common HAI is SSI which is fivefold lower than the previous study.[19] The previous meta-analysis report of the developing countries showed much higher than the

current study and three fold lower than the meat-analysis from Southeast Asia.[20] The proportion is also lower than that studied in Ethiopia in 2016 which is 19.41%.[10] The study conducted in general ward of hospital in 2014 in India found the prevalence to be 11.7% higher than our study whereas study conducted in Bangladesh in 2013 observed HAI (9.4%) higher than our study.[26-27] While comparing with other similar studies done in Nepal, the findings is much lower than reports from study conducted in TUTH (34.4%) and critical unit in National Trauma Centre in 2017 (11.83%).[20,28] This could be due to difference in the study period, patient load, improper handling, substandard aseptic procedures during handling of insertion and removal of medical devices, patient's medical condition layout of hospitals and different definition adopted in the studies.[10] This might have also been observed due to the nature of the study involving different departments and medical conditions of the patients. The study being the first of its kind in this hospital, and the research team did not include the clinicians, the detection of the HAI might has resulted lower than other studies.

In current study, the most frequently observed HAI was in SSI (71.42%) followed by UTI (18.18%). The finding is similar to other studies where UTI and SSI being the most common ones study conducted in Ethiopia where UTI (68.71%) was most common followed by SSI (28.72%).[10,29,30] In addition to other related factors, HAI is often associated to surgical wounds and presence of indwelling devices such as catheterization.[10,31] Whereas the systematic review and meta-analysis in low and middle income countries showed SSI (29.1%) to be most frequent infection in developing countries followed by UTI (24%), BSI (19%) and HCAP (15%) which is similar but much higher in our study.[31] Similar to our study, systematic review chose studies on epidemiology of HAI focusing on common infections. There are few studies that have been conducted in the same setting on surgical site infection. One of the studies conducted among women who has undergone caesarean section for delivery found 12.6% infection rate and another study conducted among all patients undergone elective and emergency surgeries showed infection of 2.66%.[32,33] The higher proportion of SSI in the hospital may be attributed to less effective disinfection of the operating rooms, sterilization of instruments and establish operational procedure facility. In the meantime, the proportion is higher as the identification is much easier according to the clinical criteria.[34] Moreover, the previous studies have already been conducted on SSI in this hospital, which might lead to proper surveillance and identification of the cases. The distribution of the patients with HAI is higher in orthopaedics ward followed by surgical ward, gynaecology ward like in other studies.[10] The study site is a tertiary care center and also the referral center for surgical cases therefore, the higher number of surgical cases seemed to be normal in the current study.

In the study among 909 samples analyzed in overall, the bacterial culture positive was 23.87% (217/909). Of which most common bacteria was *Escherichia coli* (38.24%) followed by *Enterococcus spp.* and *Staphylococcus aureus* (11.52%) and MRSA (11.05%), which is similar to the previous study which also had shown the most common micro-organism as *Escherichia coli* followed by *Enterococcus species*, coagulase negative *Staphylococci species* and *Staphylococcus aureus* and Escherichia coli being the most common pathogen in the study conducted in the pediatric department of the same setting.[33,35] Various studies have also revealed that the most common bacterial isolates were Escherichia coli.[10,20,28,36]

Escherichia coli bacterial isolates were resistance to most common antibiotics like *Azithromycin* (100%), *Amoxycillin+clavulanic acid* (100%), *Cefuroxime* (80%), *Cefotaxime* (78.6%), *Ceftriaxone* (66.7). The trend for various antibiotics such as *Amoxycillin, Cefixime, Nalidixic acid, Ceftazidime, Ciprofloxacin, Cotrimoxazole, Norfloxacin, Ofloxacin,* and *Cefotaxime* were above 50% and in the verse of increased trend of resistance in the year 2006 to 2010.[37] Similarly, isolates of *Klebsiella pneumonia* were resistance to *Cefotaxime* (100%), *Ceftriaxone* (81.8%), *Cefixime* (87.5%), and *Cotrimoxazole* (81.8%) which has similar to the resistance pattern shown in studies in Nepal.[36,38] *Cotrimoxazole* (100%), *Amoxicillin+clavulanic acid* (75%), *Cloxacillin* (100%), *Cefuroxime* (71.4%), *Ceftriaxone* (66.7%), and *Ciprofloxacin* (85.7%) were resistance to *MRSA* isolates, which indicates the similar pattern in other studies conducted in Nepal.[39,40] In the developing countries like Nepal, the empirical treatment with the antibiotics has been more common in all healthcare sectors leading to the inappropriate antibiotic treatment. Moreover, antibiotics are widely sold as over the counter drugs although classified as prescription only drugs. Self-medication with antibiotics from community pharmacies is also common practice in Nepal, which leads to the antibiotic resistance. In addition to that, promotional activities from pharmaceutical companies plays a key role of antibiotic sales as top selling antibiotics seems to have high promotional activities.[41] The above mentioned factors are some of the key factors leading to inappropriate antibiotic use leading to antibiotic resistance. The overall resistance pattern indicates the phenotype of the bacterial isolates. It is an utmost importance to further isolate the genotype of the bacterial pathogens. Considering the pattern of resistance, there are few similarities and differences, which might vary according to the co-morbidities, geographical location etc.

CONCLUSION

The current study concludes that the Surgical Site Infection is the most common type of HAIs and is very common

among female. Further, *E. coli* is found to be the most common cause of HAIs and has shown resistant to the most antibiotics including third generation antibiotics. Our study also showed that *MRSA* is also one of the causative agents for HAIs. However, this is a mono-centered study at the semi-urban area, it might not represent the status of urban area and rural part. The incidence of HAIs in those areas may vary as per the treatment modality and healthcare facility.

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