Prevalence, Risk factors and Antibigram analysis of Nosocomial Infection in Tertiary Care Hospital of Rawalpindi, Pakistan

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Abstract

Background

Nosocomial infections are a global health problem, affecting 1.4 million people in treatment centers, responsible for 80,000 estimated annual deaths. The current study aimed to assess the factor influencing nosocomial infections and to choose the best antibiotic for its treatment through culture analysis.

Methodology

The current study was conducted in a tertiary care hospital Rawalpindi. A total of 120 patients with at least one nosocomial episode were included. Blood, urine, and wound swab sample were collected for hematology, biochemistry, electrolyte, and microbial analysis. Multivariate regression analysis through SPSS (ver. 16.0) were done, p-value of ≤ 0.05 was considered statistically significant.

Result

The prevalence of culture-confirmed nosocomial infection was 25%, among which age groups ($P = 0.00$, 95% CI, $-.382-.271$) were significantly correlated. Hematological analysis shows that 73.3% have lymphopenia ($P = 0.00$, 95% CI $.567-1.175$), 73.3% have Neutrocytosis ($P = 0.00$, 95% CI $.553-1.122$) and anemia (26.7%) ($P = 0.002$, 95% CI $.097-.404$) were statistically significant. Raised level of ALT (60%), Bilirubin (26.7%) and ALP (13.3%) among liver functional tests ($P = 0.68$, 95% CI $.686-.280$) found insignificant however abnormal level of urea (33.3%) and creatinine (46.7%) ($P = 0.00$, 95% CI $-1.227-.392$) were significantly correlated with nosocomial infections. Electrolytes profile shows that Hyponatremia (26.7%) ($P = 0.000$, 95% CI $-.491-.227$) were strongly correlated. Culture analysis isolated six bacterial agents, comprising 83.3%:16.6% ratio of gram-negative and gram-positive isolates. *Klebsiella pneumonia* was frequently isolated gram-negative, while *Methicillin-Resistant Staphylococcus aureus* was the only gram-positive isolate collected. Urinary tract infection (UTI) (36.6%) was frequently found, followed by bloodstream infection (26.6%) (BSI). The majority of the gram-negative isolates were sensitive to Imipenem while resistant to Amoxicillin + Clavulanic acid, Trimethoprim/sulfamethoxazole, cefoxitin, Levofloxacin, Norfloxacin, and linezolid antibiotics. *Methicillin-resistant staphylococcus aureus* was found sensitive against Trimethoprim/sulfamethoxazole while resistant towards linezolid, Imipenem, and Cefotaxime.

Conclusion

The current study revealed that nosocomial infection is still prevalent in our hospital environment and the leading cause of drug resistance and dysfunctions of various factors like WBCs, LFTs, RFTs, electrolytes, coagulation factors and anemia, which can lead to morbidity and mortality.

Introduction

Nosocomial Infections (NIs) or Hospital-acquired infection (HAIs), or Healthcare-associated infections (HCAIs) are those infections that occur within 48 hours of hospitalization or during 30 days after taking treatment from a hospital (1, 2). A worldwide survey conducted by WHO shows that 1.4 million peoples remain infected from Nosocomial infection at any time, responsible for 80,000 deaths per year (3, 4). The developing countries are 2 to 20 times more susceptible to NIs, accounts for 10% infections than developed countries having 7% of us (5, 6). Various negative impacts of NIs includes an excess amount of financial loss for the patients and their family due to treatment difficulties and prolonged hospital stay, increasing antimicrobial resistance, long-term disabilities, and increase death ratio (7). Diagnosis of us is still a global problem because it relies on multiple criteria, not on a single diagnostic test, and a lack of attention of national systems of continuous surveillance. Nosocomial Infections are founds in every setting, from ambulatory to long term hospital care, an alternative problem that no institution or country can claim to have solved yet (7). NIs is a global health-care problem; however, the global burden is unknown due to a lack of reliable diagnostic data (7). NIs are 2–5 times more prominent inside the intensive care unit (ICU) than in the general population (8) responsible for inducing morbidity and mortality, which is a matter of grave concern today (9).

Various Bacterial, viral and fungal pathogens are involved in Nosocomial infections(5); however, most of them are caused by bacteria, including normal flora (cause infection only in immune-compromised/immunosuppressed individuals (10). In the majority (80 to 87%) of NIs, 12 to 17 various pathogens, including *Bacteroides species*, *Candida species* (e.g., *Albicans*, *glabrata*), *Yeast NOS*, *Proteus species*, *Enterobacter species*, *A. baumannii*, *P. aeruginosa*, *Klebsiella oxytoca*, and *K. pneumonia*, *coagulase-negative Staphylococci*, *E. coli*, *Enterococcus species* (e.g., *faecium* and *faecalis*), *S. aureus*, and other pathogens are involved (11–13). These pathogens consist of 16–20% Multidrug-resistant isolates like carbapenem-resistant *A. baumannii*, *Enterobacter species*, *E. coli*, *K. oxytoca*, *P. aeruginosa*, extended-spectrum cephalosporin-resistant *Enterobacter species*, *E. coli*, *K. oxytoca*, *K. pneumonia*, vancomycin-resistant *E. faecium*, and Methicillin resistant *Staphylococcus aureus* (MRSA)(11, 12).

Various factors such as immune status of the patients, the bacterial population at the infection site, mechanism of action of antibiotics, the quantity of antibacterial reach to the bacterial community (14–17), induce usage of invasive materials, substandard infection control strategies, the congested environment of the hospitals and over the counter antibiotic use leads to the development of high antimicrobial resistance, especially in developing countries (18). According to a large surveillance study, around 70% of the ICU admitted patients are using antibiotics either as prophylaxis or for treatment purposes(19). In the recent era, most of the antibiotics become non-effective against bacterial infections leads to the failure of routine treatment (20), induces patient morbidity, mortality, and healthcare-related expenses(21, 22). Keeping the above literature in view, the present study was designed to analyze the various hematological, physiological changes, and antimicrobial profiles among ICU-admitted hospital-acquired infection patients.

Methodology

Ethics Statement and Informed Consent

The ethical review committee of Rawalpindi Medical University approved the current study (S/No. 12-13/RMU-2019). The patients were informed about the research study before sample collection. A written consent form consists of name, age, gender, date of admission, clinical settings, the reason for hospitalization, type of pathology, type of infection, and the number of days spent in the hospital before admission into ICU and start of the first nosocomial infection were filled appropriately.

Study design

The current study was carried out between 1st February 2019, and 31st January 2020 at District headquarter Hospital affiliated with Rawalpindi Medical University, Rawalpindi, Pakistan. During this study, we included all the patients admitted for more than 48 hours to the Intensive Care Unit (ICU), with no signs of bacterial colonization at the time of admission. Those patients who don't fulfill the above criteria were excluded from the study. The suspected patients of nosocomial infection were clinically examined by physicians to exclude community-acquired infection.

Sample Collection and Processing

A total of 120 patients were studied who were admitted to the ICU of the hospital, among which 30/120 (25%) patients developed at least one nosocomial episode. Various samples, including 5cc of blood, wound swab, and 10-20ml of urine in a sterile, dry, wide-necked, leak-proof container were collected using standard procedures described by Horan et al.(23). The specimens were labeled with the patient's identification, packed and transported within 30 minutes of the collection in a cold box to the pathology and microbiology Laboratory for further analysis.

Hematological Analysis

Analysis of the samples' various hematological assessments, including complete blood count (CBC) and hemoglobin, was carried out on unique automated analyzer **SYSMEX XP 100** (19 Jln Tukang, Singapore 619257). Different biochemical tests such as Serum Creatinine, Serum Bilirubin, Alanine transaminase (ALT), Aspartate transaminase (AST), Alkaline phosphatase (ALP), Prothrombin time (PT), and Urea were evaluated through AU480 Chemistry Analyzer (Bakman colter 400). Electrolytes (Sodium, Potassium, and Chlorides) analysis was performed through the EasyLyte analyzer (Medica Corporation, 5 Oak Park Drive, Bedford, MA 01730, USA).

Microbial analysis and Phenotypic Characterization of the Isolates

Samples were inoculated on Blood agar (Oxoid, UK), MacConkey agar (Oxoid, UK), and of Cystine Lactose-Electrolyte-Deficient Agar (CLED) agar followed by incubation of the plate aerobically at 35–37 °C for 24 hours. The entire bacterial isolates were phenotypically characterized through their culture uniqueness and biochemical tests as earlier by Cheesbrough, (2006). Briefly, various differential and selective culture media (Oxoid, Ltd., UK), like Blood agar, Chocolate (heated blood) agar, and MacConkey agar, were used for inoculation and investigation of bacterial isolates. Various bacterial isolates were characterized through their cellular morphology, the morphology of their colony, and colonial pigmentation. Bacterial Species were characterized through various biochemical tests like catalase, oxidase, coagulase, urease, and motility tests. After overnight incubation at 37°C, the reading of the culture were performed by two senior medical microbiologists.

Antibiogram Analysis

In vitro antibiogram analysis was performed according to the Kirby Bauer disk diffusion method based upon the criteria of Clinical and Laboratory Standards Institute criteria (CLSI, 2015). In brief, standard inoculum adjusted to 0.5 McFarland standard turbidity was uniformly distributed over Mueller Hinton agar (Oxoid, Ltd., UK). Antimicrobial disks, including (Oxoid, Ltd., UK), Cefixime (5 µg), Cefoxitin (10 µg), Erythromycin (5 µg), Ciprofloxacin (5 µg), Linezolid (30 µg), Meropenem (10 µg), Imipenem (10 µg), Cefoperazone/Sulbactam (30 µg), Ceftazidime (30 µg), Amikacin (30 µg), Vancomycin (30 µg), Chloramphenicol (30 µg), Gentamicin (10 µg), Tobramycin (10 µg), and Erythromycin (15 µg) were applied with the help of automatic disk dispenser on Mueller Hinton agar plates and incubated overnight at 37°C. The sensitive, intermediate sensitive, and resistant isolates were investigated by measuring their respective inhibition zone as per standard criteria (24). Any bacterial isolate found resistant to at least one antimicrobial in three or more antibiotics having different structural categories was considered multidrug-resistant (MDR) isolate(25).

Statistical Analysis

For statistical logistic multivariate regression analysis, SPSS for Windows version 16.0 (SPSS Inc., Chicago, IL, USA) was used. *P* values < 0.05 were considered significant.

Results

Distribution of Initial Diagnosis

The entire studied patients were admitted due to various complications, like (25%) RTA, 18.3% EXP, 10% FAI, 6.67% Head Injury, 5% spinal injury, and a Stab wound. Dengue infection and acute SDH, and Gynae consist of 3.3% each, while 1.6% each of ICB, SOL, Poisoning, DKA, EVD/Meningitis, Nephrotic disease, Trauma, Gastric Ulcer, Parietal EDH, Post Nephrectomy, Pneumonia, Gangrene and Pelvic Injury each respectively.

Age and Gender-Wise Distribution of Nosocomial Infections

Among the 120 patients studied male and female were in 86.7:13.3 ratio non-significant ($P=0.83$, 95% CI -.139-.171, $R=0.538$) respectively. They were divided into five age groups, and the effect of Nosocomial Infection was significantly correlated ($P=0.00$, 95% CI, -.382-.271, $R=0.538$), as shown in table 3.1.

Table 3.1. Age and Gender-Wise Distribution of Nosocomial Infections

Variable	Groups	Frequency	t-value	P-value	95% Confidence Interval		R-Square
Age	5-20 Years	16/120 (13.3%)	-11.613	.000	-.382	-.271	0.538
	21-35 Years	32/120 (26.7%)					
	36-50 Years	44/120 (36.7%)					
	>50 years	28/120 (23.3%)					
Gender	Male	104/120 (86.7%)	.208	.835	-.139	.171	
	Female	16/120 (13.3%)					

Hematological Analysis:

Hematological analysis performed for NIs are given below;

Total Leukocytes count

Among the 30 confirmed patients with nosocomial infection , 73.3% have lymphopenia (P=0.00, 95% CI .567-1.175, R=0.226) and 73.3% have Neutrocytosis (P=0.00, 95% CI .553-1.122, R=0.226) significantly correlated with nosocomial infection as shown in the table 3.2.

Table 3.2. Total Leukocyte count in culture-positive Nosocomial Infection

Characteristic	T-value	P-value	95% Confidence Interval		R-square
			Lower Boundries	Upper Boundries	
Leukocytosis	-.716	.475	-.249	.117	0.226
Thrombocytopenia	-.637	.525	-.225	.116	
Lymphopenia	5.667	.000	.567	1.175	
Neutrocytosis	5.834	.000	.553	1.122	
Erythrocytopenia	-1.311	.192	-.254	.052	

Coagulation Profile and Anemia

Among nosocomial patients, 33.3% have thrombocytosis (P= 0.75, 95% CI -.201-.145, R=0.012) were in-significant however 26.7% were found anemic (P=0.002, 95% CI .097-.404, R=0.092) were found statistically significant as shown in the table 3.3.

Table. 3.3 Coagulation Profile and Anemia among Culture-confirmed Nosocomial Infection

Characteristic	T-value	P-value	95% Confidence Interval		R-square
			Lower Boundries	Upper Boundries	
Platelets	-.318	.751	-.201	.145	0.012
PT	1.209	.229	-.177	.733	
APTT	1.171	.244	-.179	.696	
Anemia	3.227	.002	.097	.404	0.092

Biochemical Analysis:**Liver function test**

Among the Nosocomial Infection, 60% of the patients have raised ALT level, increased bilirubin (26.7%), while 13.3% have raised ALP; however, a non-significant correlation was observed, as shown in table 3.4.

Table 3.4. Liver Functional test in culture-confirmed Nosocomial Infection

Characteristics	T-value	P-value	95% Confidence interval		R-Square
			Lower Boundries	Upper Boundries	
Total Billirubin	.406	.686	-.185	.280	0.006
ALT	.497	.620	-.142	.237	
ALP	-.513	.609	-.370	.218	

Renal functional test

The renal functional test analysis of culture-confirmed nosocomial patient's shows abnormal level of urea (33.3%) (P=0.002, 95% CI .255-1.120, R=0.119) while (46.7%) Creatinine (P=0.00, 95% CI -1.227-.392, R=0.119) both were statistically significant as shown in the table 3.5.

Table 3.5. Correlation of Renal functional tests with Nosocomial Infection

Characteristics	T-value	P-value	95% Confidence interval		R-square
			Lower Boundries	Upper Boundries	
Urea	3.149	.002	.255	1.120	0.119
Creatinin	-3.843	.000	-1.227	-.392	

Electrolytes Analysis

Among the electrolytes analysis, Hyponatremia (26.7%) (P=0.000, 95% CI-.491--.227, R=0.703) were significant, while hyperchloremia (20%) and Hypokalemia (6.7%) were in-significant as shown in table 3.6.

Table 3.6. Electrolytes Analysis of culture-confirmed Nosocomial Infection patients

Characteristics	T-value	P-value	95% Confidence Interval		R-Square
			Lower boundries	Upper boundries	
Hypokalemia	.582	.562	-.190	.348	0.703
Hyperchloremia	-.546	.586	-.248	.141	
Hyponatremia	-.315	.753	-.576	.418	
Hypochloremia	.682	.497	-.174	.356	
Hyponatremia	-5.375	.000	-.491	-.227	

Microbial analysis and prevalence of nosocomial Infection

A total of 30/120 (25%) of all ICU admitted nosocomial-suspected patients were culture-confirmed, and 06 bacterial pathogens were isolated, consisting of 5/6 (83.3%) gram-negative bacteria. UTI was more frequently found (36.6%), followed by bloodstream (26.6%). Among gram-negative isolates, Klebsiella Pneumonia (40%) was most commonly isolated, followed by *Klebsiella oxytoca* (13.3%); however, MRSA (16.6%) were the only gram-positive isolate.

MRSA (50%) was the most frequent isolate followed by *Pauroginosa* (25%) found in surgical site infection, while *Klebsiella oxytoca* (27.7%) followed by 18.18% of *Serratia liquefaciens* and *Serratia marcescens* each was isolated from UTI. *Klebsiella pneumonia* (100%) was the only bacterial isolate found in respiratory tract infection. Among bloodstream infections, *Klebsiella pneumonia* (37.5%) was the most frequent isolate, followed by 25% of *Pauroginosa* and *S.aureus* each, as shown in the table 3.7.

Table 3.7. Distribution of bacterial isolates collected from patients of Nosocomial infection admitted to ICU of District Headquarter Hospital Rawalpindi, Pakistan, January 2019 to December 2020

Bacterial isolates	Surgical site no. (%)	Urinary tract no. (%)	Respiratory tract no. (%)	Bloodstream no. (%)	Total (%)
<i>Klebsiella pneumonia</i>	1 (25%)	1 (9.09%)	7 (100%)	3/8 (37.5%)	12 (40%)
<i>Klebsiella oxytoca</i>	0 (0)	3 (27.27%)	0 (0)	1 (12.5%)	4 (13.3%)
<i>Serratia liquefaciens</i>	0 (0)	2 (18.18%)	0 (0)	0/8 (0)	2 (6.6%)
<i>Pseudomonase auroginosa</i>	1 (25%)	0 (0)	0 (0)	2/8 (25%)	3 (10%)
<i>Serratia marcescens</i>	0 (0)	2 (18.18%)	0 (0)	0/8 (0)	2 (6.6%)
<i>Proteus spp</i>	0 (0)	2 (18.18%)	0 (0)	0 (0)	2 (6.6%)
<i>S. aureus</i>	2 (50%)	1 (9.09%)	0 (0)	2 (25%)	5 (16.6%)
Total	4 (13.3%)	11 (36.6%)	7 (23.3%)	8 (26.6%)	30 (100%)

Antimicrobial Susceptibility Pattern.

Out of all collected isolates, 100% sensitivity towards imipenem was observed by *Klebsiella pneumonia*, *Serratia liquefaciens*, *Proteus spp*, while 75% by *K. oxytoca*. Besides imipenem, the sensitivity of *Serratia marcescens* towards ceftriaxone and amikacin were also observed. 100% of *Serratia marcescens* isolates showed sensitivity towards ceftriaxone and amikacin. *Proteus spp* were found sensitive towards amikacin and gentamycin. The majority of the gram-negative isolates were found resistant towards Amoxicillin + Clavulanic acid, Trimethoprim/sulfamethoxazole, cefoxitin, Levofloxacin, Norfloxacin, and linezolid, as shown in table 3.8. [Supplementary Figures 3.1, 3.2, 3.3]

Table 3.8. Antibigram analysis of the entire bacterial agents isolated from Nosocomial Patients at District Headquarter Hospital Rawalpindi, Pakistan, January 2019 to December 2020.

Microbial isolates	Positive	Pattern	Antimicrobial susceptibility no (%)										
			AUG3+AMC30	CTX	CAZ	CFM	CRO	FOX	ZOX	VA	AK	CN	T
K. pneumoniae	12	R	12 (100)	12(1000)	12(100)	9(75)	11(91.6)	12(100)	10(85)	10(85)	10(85)	10(85)	1
		S	0	0	0	0	1(8.3)	0	2(15)	2(15)	2(15)	2(15)	2
		I	0		0	3(25)	0	0	0	0	0	0	0
K. oxytoca	4	R	4(100)	4(100)	3(75)	4(100)	4(100)	4(100)	4(100)	4(100)	2(50)	3(75)	3
		S	0	0	0	0	0	0	0	0	2(50)	1(25)	1
		I	0	0	1(25)	0	0	0	0	0	0	0	0
Serratia liquefaciens	2	R	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	0	1(50)	2
		S	0	0	0	0	0	0	0	0	2(100)	0	0
		I	0	0	0	0	0	0	0	0	0	1(50)	0
P. aurigonosa	3	R	3(100)	3(100)	3(100)	3(100)	2(66.6)	3(100)	3(100)	1(33.3)	1(33.3)	2(66.6))	3
		S	0	0	0	0	1 (33.3)	0	0	2(66.6)	2 (66.6)	0	0
		I	0	0	0	0	0	0	0	0	0	1(33.3)	0
MRSA	5	R	4(80)	5(100)	5(100)	4(80)	3(60)	5(100)	4(80)	3(80)	2(40)	4(80)	5
		S	0	0	0	0	2(40)	0	0	2(40)	2(40)	0	0
		I	1(20)	0	0	1(20)	0	0	1(20)	0	1(20)	1(20)	0
Serratia marcescens	2	R	2(100)	2(100)	2(100)	2(100)	0	2(100)	1(50)	1(50)	0	2(100)	1
		S	0	0	0	0	2(100)	0	0	1(50)	2(100)	0	1
		I	0	0	0	0	0	0	1(50)	0	0	0	0
Proteus spp	2	R	1(50)	2(100)	2(100)	2(100)	0	0	2(100)	2(100)	0	0	2
		S	0	0	0	0	1(50)	0	0	0	2(100)	2(100)	0
		I	1(50)	0	0	0	1(50)	2(100)	0	0	0	0	0
Total	30												

S: sensitive; R: resistance; I: Intermediate; CIP: ciprofloxacin; CRO: ceftriaxone; CAZ: ceftazidime; IPM: imipenem; LZD: linezolid; FOX: Cefoxitin; CFM: Cefixime; CTX: Cefotaxime; AK: Amikacin; CN: Gentamicin; TOB: Tobramycin; VA: Vancomycin; Lev: Levofloxacin; Ofx: Ofloxacin; Nor: Norfloxacin; Sxt: Trimethoprim/sulfamethoxazole; MXF: Moxifloxacin; AUG3+AMC30: Amoxicillin + Clavulanic acid; ZOX: ceftizoxime

Trimethoprim/sulfamethoxazole was a highly effective antibiotic against the gram-positive isolates (MRSA); however, all of them were resistant towards linezolid, imipenem, and Cefotaxime, etc. as shown in table 3.8. [Supplementary Figures 3.4].

Discussion

Nosocomial Infections (NCIs) or Hospital Acquired Infections (HAIs) are the leading cause of public health issues worldwide with variation in prevalence rates (26). The main strategies for managing these infections are the source and understanding of the conditions, the pathogens involved in HAI, and its risk factors (27).

The majority of the ICU patients experiences nosocomial bloodstream infections, total leukocytes count (TLC) and C-reactive protein (CRP) play a pivotal role in the diagnosis of these infections (28–31). The current study observed that 60% of the nosocomial patients have leukocytosis that describes the possible important role of leukocytosis in nosocomial infection, as describes earlier (28–31). Lymphopenia and risk of infection are poorly studied; however, according to a report, there is a 2.4-fold increased risk of lower respiratory tract infection and urinary tract infection with lymphopenia (32). So for another study at ICU reports that lymphopenia at admittance was associated with a 1.6-fold increased risk of infection(33). Similarly, in the general population, lymphopenia was associated with an increased risk of hospitalization due to conditions like sepsis, endocarditis, diarrheal disease, pneumonia, urinary tract infection, and skin infection (34). In the literature (35–37), it is well established that, in many cases, febrile neutropenic patients have bacteremia without any specific focus (37). Although most infections of neutropenic patients' are only clinically documented (37–39). The above-mentioned reports assist our current study, where we found 73.3% of the nosocomial patients with lymphopenia. However, discrepancies between the findings in the present and former studies (32, 40, 41) may be due to our study design that includes only nosocomial patients. The current study found Neutrocytosis in 73.3% of nosocomial infected patients as Neutrocytosis is frequently observed in the circulation and tissues during bacterial or fungal infections (42). The Neutrocytosis in the current study may be due to their important role during fungal and extracellular bacterial infections where they promote bacterial clearance through phagocytosis, production of reactive oxygen and nitrogen species (ROS/RNS), neutrophil extracellular trap (NET) formation, and production of pro-inflammatory cytokin(43, 44).

According to the current study, 33.3% of the nosocomial patients have thrombocytopenia, 12% have abnormal PT. In comparison, 8% have abnormal APTT; likewise, prolonged PT of 63.3% was observed in neonatal septicemia during nosocomial infection, more frequently among gram-negative infected patients (45). The deviation of our results may be because of different pathogenic microbes in the study may complicate infections by consumption coagulopathy (46), as well as the difference in the exposure to endotoxins, which may be attributed to the direct action of the endotoxins on endothelial cells or maybe an indirect result of the production of interleukin1 or tumor necrosis factor (47, 48).

The liver is one of the vital organs exposed to both hepatotropic and non-hepatotropic viruses and bacteria through the portal and systemic circulation and causes liver injury, either direct invasion or indirect cytokines and toxin production (49, 50). However, patients of Pneumococcal pneumonia and lobar pneumonia caused by one of the bacteria among *S. pneumonia*, *P. aeruginosa*, *S. aureus*, or *Haemophilus influenza* sometimes show elevated concentrations of bilirubin and Serum glutamic pyruvic transaminase/serum aminotransferases (SGPT/ALT) (51). Similar reports of elevated ALT/SGPT and bilirubin have been reported in typhoid fever caused by *Salmonella typhi* and gastroenteritis caused by nontyphoidal *Salmonella* (most commonly *S. enteritidis* and *S. Typhimurium*) (52). Consistently in the current study, an elevated level of SGPT/ALT, Bilirubin, and ALP among 60%, 26.7%, and 13.3% were found respectively among nosocomial patients. The changes in liver function tests in case of nosocomial infection are may be due to hepatic injury caused by nosocomial pathogens. So for in case of liver dysfunction during systemic disease, proper microbial examination, and sufficient knowledge about non-hepatotropic agents are necessary (49).

The said study finds that among nosocomial patients, 33.3% have an abnormal level of Urea. In comparison, 46.7% have an uncommon level of Creatinine; however, to our knowledge, there are no data to suggest whether or not the association of renal function test and nosocomial infection. Some previous studies report the higher risk of disease caused by MDROs, MRSA and VRE, in patients undergoing hemodialysis (53, 54). The renal function test increase may be due to the kidneys complication, either direct kidney injuries or immune-mediated injuries caused by all viruses, bacteria, mycobacteria, fungus, and protozoa (55) founds in nosocomial infections.

The current study reports that upon electrolytes analysis of nosocomial patients, 26.7% have Hyponatremia, 20% have hyperchloremia, while 6.7% have Hypokalemia. The change in various electrolytes might be due to the excessive use of antibiotics, which are directly proportional to NIs. Their adverse effects may be responsible for electrolyte abnormalities such as aminoglycosides, amphotericin B, trimethoprim, and tetracycline cause electrolyte disturbance (56–58).

The prevalence of culture-confirmed nosocomial infection in the current study was 25%, which is lower than other reports of 29.13% by Shaikh et al. (59), 27.03% by Noor *et al.*(60) from Pakistan, 35.8% from Ethiopia (61), however higher than that of Rabat, Morocco (10.3%) by (62), 6.9% in Eastern Ethiopia by (26), 0.3% from ambarene, Gabon by (63), and 1.03% from Mazandaran, India (64). The results may be due to many factors, like the difference in patient selection criteria, the case mix, ICU type, length of stay, device utilization rate, and discharge criteria (65, 66). The current study shows that the ratio of gram-negative vs. gram-positive isolates was 83.3%:16.6%, similar to other studies that most nosocomial infections occurring in the ICU are due to Gram-negative bacteria (19, 67). The precise pattern of causative organisms, whether bacterial or fungal, varies across countries and between ICUs according to patient case mix, infection site, antibiotic protocols, infection control practice, and local ecology and resistance patterns (28).

The current study shows that SSI contributes 13.3% of all infections, which was higher compared to the survey from Ethiopia (10.9%) (68), Iran (8.6%) (69) while lower as compared to (31.5%) reported by Tolera *et al.*(26). The prevalence of BSIs (26.6%) in this study was relatively comparable with the findings of (22.7%) by Shaikh et al. (59) from Pakistan and Ethiopia (20.8%) (61) while much higher compared with the study performed at Bahirdar (2.4%) (68). The current study reported 36.6% of the nosocomial infection was UTI which is higher than 9.03% and 9.4% reported by (70, 71) respectively. The discrepancy in the results may be due to the difference in the frequency of NSI in various developed and developing countries (72).

The current study found that the most frequent bacteria causing NIs were *K. pneumonia* (40%) and *S. aureus* (16.6%), consistent with other findings (61, 64, 73). The current study shows that imipenem was the most effective antibiotic against gram-negative isolates of *Klebsiella pneumonia*, *K. oxytoca*, *Proteus spp*, *Serratia liquefaciens* *Serratia marcescens*. Simultaneously, the majority of the resistance was found against Amoxicillin + Clavulanic acid, Trimethoprim/sulfamethoxazole, cefoxitin, Levofloxacin, Norfloxacin, and linezolid. Similar supporting results of sensitivity for *Klebsiella pneumonia* and *Klebsiella oxytoca* were reported (74–76). According to a study, *K.pneumoniae* was found resistant to all β -lactams and meropenem however susceptible to imipenem by (77) and resistance to all β -lactams, including meropenem except imipenem was found by (78–80). A similar consistent result of sensitivity against *Proteus spp* was found elsewhere (81, 82). Meropenem and imipenem were the potent antimicrobials against *Proteus spp*. (83, 84), in contrast to the resistance against imipenem and aztreonam by (85). Resistance rates were noted highest against ceftriaxone, ceftazidime, and piperacillin/tazobactam (86). According to a study, the isolated *Serratia* strain was sensitive towards imipenem, cefotetan, gentamicin, etc. (87), supporting the reported result of susceptibility to imipenem, meropenem, and amikacin, etc. (88). The sensitivity of *S. marcescens* was detected for imipenem, meropenem, and ceftazidime, etc. (89). The resistance of *S. marcescens* towards fluoroquinolones and third-generation cephalosporins was found by (88, 90–97).

Methicillin-Resistant *Staphylococcus aureus* (MRSA) was the only gram-positive isolate found in the study, highly sensitive towards Trimethoprim/sulfamethoxazole while resistant towards linezolid, Imipenem, and Cefotaxime, etc. Consistently similar reports from various countries show that around 90% of *S. aureus* isolated from nosocomial infections and community remain sensitive to Trimethoprim/sulfamethoxazole from the USA (98–100), Europe, Israel, and Turkey (101–103), Japan (104), Canada (105–108). A study reports higher susceptibility to amoxicillin + clavulanic acid, Doxycycline and Gentamicin, etc. (109). In contrast to the above reports, 30% of hospital-acquired MRSA in Australia, 19% in sub-Saharan Africa (110), and 85% from India (111, 112) were resistant towards Trimethoprim/sulfamethoxazole. Various reports observed resistance of *s.aureus* towards ampicillin and penicillin, rifampicin and clindamycin, oxacillin and erythromycin (108), Azithromycin, Ceftriaxone, Cefixime and Penicillin (109), Gentamycin, Erythromycin, Levofloxacin and Tetracycline (113). The divergence in the findings could be attributed to the mechanism of resistance like the permeability barrier, efflux pumps, mutational or recombinational changes in the target enzymes and acquired resistance by drug-resistant target enzymes in various antibiotics and alteration of the target with decreased affinity for the antibiotics (114).

Conclusion

The current study revealed that nosocomial infection is still prevalent in our hospital environment and the leading cause of drug resistance and dysfunctions of various factors like WBCs, LFTs, RFTs, electrolytes, coagulation factors and anemia, which can lead to morbidity and mortality.

Abbreviations

Nosocomial Infections, HCAI: Health care Associated Infections, WBCs: White Blood cells, UTI: Urinary tract infection, MRSA: Methicilin Resistant *Staphylococcus aureus*

Declarations

On behalf of all the co-authors, I am submitting the enclosed manuscript for potential publication only in Journal of Antimicrobial Resistance and Infection Control. I attest that this paper has not been published in whole elsewhere and is prepared following the instructions to authors. All authors have contributed to this manuscript, reviewed and approved the current form of the manuscript to be submitted.

- Ethics approval and consent to participate

The ethical review committee of Rawalpindi Medical University approved the current study (S/No. 12-13/RMU-2019). The patients were informed about the research study before sample collection. A written consent form was filled from the entire patients.

- Consent for publication

All the patients were informed for the publication of the current study

- Availability of data and materials

The corresponding author will provide the data and information on the currents study on reasonable requests.

- Competing interests

JK, IA, NB, AK, AS, SA, MS, ANK, IA, SS, AA, HK, and IA declare that they have no competing interests.

- Funding

Not applicable

- Authors' contributions

All authors have read and approved the manuscript. JK, NB designed the study. IA experimented. AK, SA, AS, SS, IA were major contributors in the writing of the manuscript. SA, ANK performed the statistical analysis and figure of the schoolroom. AA, HK, IA reviewed the final manuscript.

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