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Assessment of Nosocomial Pneumonia Antibiotic Susceptibility Patterns among Patients in Intensive Care Units

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ABSTRACT

Background: In intensive care units (ICUs), nosocomial pneumonia is by far the most frequent nosocomial disease seen. Severe infections, complications, prolonged hospital admissions, and higher mortality rates are all brought on by the rise in antibiotic resistance.

Objective: To identify the microbial causes of hospital-acquired pneumonia (HAP) and their antibiotic resistance pattern among ICU patients in Internal Medicine Department of Zagazig University Hospitals.

Subjects and methods: In a cross-sectional study the sample size assigned was 72 patients. All of those who were adults had signs and symptoms of pneumonia started at least 48 hours after admission to the ICU and that occurs more than 48 to 72 hours after tracheal intubation.

Results: The Most frequent organisms isolated were K. pneumonia, Acinetobacter baumannii complex and E. coli (42.9%, 18.6% and 14.3%, respectively). The most frequent sensitive drugs were colistin (48.6%) followed by imipenem, amikacin (both 18.6%). Most frequent intermediate drug was gentamycin (5.7%). Finally, most frequent resistant drugs were cefepime, ciprofloxacin and piperacillin (65.7%, 62.9% and 57.1%, respectively). There was a highly statistically significant increase in APACHE II score and mortality among dead compared to survived cases.

Conclusion: HAP and ventilator-associated pneumonia (VAP) ICUs patients were mostly affected by K. pneumonia, Acinetobacter baumannii complex and E. coli, K. pneumonia was the most frequent organism. Most of the cases were resistant to cefepime, ciprofloxacin and piperacillin, most probably due to its cheap cost and easy availability.

Keywords: Nosocomial Pneumonia, Antibiotic Susceptibility, Intensive Care Units.

INTRODUCTION

An infection of the pulmonary parenchyma that develops in a patient at least 48 h after hospital admission or within 14 days of hospital discharge is considered nosocomial pneumonia or hospital-acquired pneumonia (HAP) [(1)].

Ten percent to twenty percent of patients who require mechanical ventilation for more than 48 hours are thought to develop ventilator-associated pneumonia (VAP). VAP is defined as pneumonia that develops more than forty-eight to seventy-two hours after tracheal intubation. HAP is less dangerous than VAP [(2)].

About half of HAP patients, especially those admitted to the intensive care unit, develop serious consequences like empyema, septic shock, and multiorgan failure [(3)].

Aerobic Gram-negative bacilli are frequent causes of HAP and VAP (like Enterobacter spp, Klebsiella pneumoniae, Acinetobacter spp, Escherichia coli, as well as Pseudomonas aeruginosa) as well as gram-positive cocci (like Staphylococcus aureus, which includes strains of S. aureus and Streptococcus that are resistant to methicillin) [(4)]. Patients who required mechanical ventilation had an estimated 9-27% VAP incidence rate [(5)].

The abuse of antibiotics has contributed to a widespread public health problem: antimicrobial resistance. Severe infections, complications, prolonged hospitalizations, and higher mortality rates are all brought on by the rise in antibiotic resistance. The danger of antibiotic side effects increases when they are overused [(6)].

The geographical pattern of antimicrobial susceptibility, the number of underlying diseases, their severity, and the severity of the current illness are the four characteristics that should guide the choice and timing of antimicrobial medicines utilized [(7-9)].

We aimed at this work to identify the microbial causes of HAP and their antibiotic resistance pattern among ICU patients in Internal Medicine Department of Zagazig University Hospitals, and therefore antibiotic susceptibility.

PATIENTS AND METHODS

We carried out a cross-sectional study in the Internal Medicine ICUs of Zagazig University Hospitals and the Clinical Pathology Department of Zagazig University.

Inclusion criteria:

1. Adult patients of both sexes.
2. Patients stay in ICU for at least 48 hrs.

Exclusion criteria:

1. Patients treated with antibiotics within the preceding 2 weeks.
2. Age below 18 years.
3. pregnant women
4. Immunocompromised and cancer patient.

The designated sample size was 72 individuals. Each adult patient developed pneumonia symptoms more than 48-72 hours after tracheal intubation and was admitted to the intensive care unit. We excluded individuals with a history of antibiotic treatment of equal to or less than 2 weeks, pregnant females, and

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patients who were immunocompromised.

Patients who met the inclusion criteria but not the exclusion criteria had sputum samples obtained. Each sputum sample, containing at least 10 cc, was collected in a numbered, screw-capped wide-mouth container and delivered to the Clinical Pathology Department first thing in the morning. The samples were then inoculated with calibrated loops onto plates of blood agar, mannitol salt agar, and MacConkey agar. They spent the night in an incubator set between 35 and 37 degrees Celsius.

Once the cause was identified, antibiotic treatment could begin. Treatment with antibiotics followed CDC guidelines, both in terms of types and dosages (CDC). After that, the distance from the antibiotic discs was measured and compared to CLSI's 28th edition of the Journal's requirements. When all is said and done, they were classified as either resistant, intermediate, or sensitive.

Most patients in the intensive care unit have had a comprehensive medical history recorded, had their blood pressure checked, and had access to a CT scan of the chest. Furthermore, CBC, ABG, D-dimer, CRP, serum creatinine, NA level and serum procalcitonin level were done.

APATCHEII was calculated for all patients in this study for prediction of morbidity and mortality rate. Higher scores correspond to more severe disease and a higher risk of death.

Antibiotic Susceptibility Testing:

Isolated bacteria or fungus from sputum samples were diluted in saline and swabbed onto minimal inhibitory concentration (MIC) panels to determine their susceptibility to the antibiotics. Dish diffusion involves spreading antibiotics of varying concentrations across agar plates that have been swabbed for germs. 16–18 hours of incubation at 35 degrees C is typical for panels or plates. Manufacturer specifications dictate how to interpret the MIC panel, which measures the lowest effective concentration of antibiotic in preventing microbial growth. The findings are then shared.

Ethical approval:

The Zagazig Medical Ethics Committee of the Zagazig Faculty of Medicine gave its approval to this study. All participants gave written consent after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

SPSS version 24 was used to tabulate and analyse the data (SPSS Inc, Chicago, ILL Company). Quantitative data were presented as mean, standard deviation (Sd), and range. Qualitative data were presented as frequency and percentage. Categorical data were compared using the Chi-square test (X^2). We utilised the student t-test to compare normally distributed variables between 2 groups, and the Mann-Whitney U-test to compare non-parametric variables. In this study, a probability of less than 0.05 was considered significant.

RESULTS

This table shows that age of the studied cases ranged from 23 to 91 years with mean 60 years. Regarding sex 63.8% were female.

Table (1): Demographic and clinical data of the studied cases

Variable		(n=72)	
Age: (years)	Mean ± Sd	60±16.08	
	Range	23-91	
Variable		**No**	**%**
Sex:	Female	46	63.9
	Male	26	36.1
A: Associated condition	No	17	23.6
	Yes	55	76.4
	Addiction	3	4.1
	CKD	7	9.7
	GBS	7	9.7
	ICH	5	6.9
	Sepsis	3	4.1
	Stroke	28	38.8
	TTP	2	2.7
Acute kidney injury:	No	62	86.1
	Yes	10	13.9

Sd: Standard deviation CKD: chronic kidney injury GBS: Guillain-Barré syndrome
ICH: Intracerebral hemorrhage TTP: Thrombotic Thrombocytopenic Purpura.

This table shows the vital signs and arterial blood gases of the studied cases.

Table (2): Vital signs and arterial blood gases of the studied cases

Variable		(n=72)
GCS:	Mean ± Sd	9.07±2.23
Temperature: (degree)	Mean ± Sd	37.66±0.89
MAP: (mmHg)	Mean ± Sd	56.24±8.17
HR: (BPM)	Mean ± Sd	96.23±23.95
RR: (breath/min)	Mean ± Sd	17.4±4.31
FIO_2: (%)	Mean ± Sd	58.57±14.4
PaO_2:	Mean ± Sd	85.47±21.1
$PaCO_3$: (%)	Mean ± Sd	38.91±9.66
HCO_3: (%)	Mean ± Sd	21.99±5.44
pH:	Mean ± Sd	7.36±0.08

Sd: Standard deviation GCS: Glasgow Coma Scale MAP: mean arterial blood pressure
HR: heart rate RR: respiratory rate PH: Potential of Hydrogen.

Only 1.4% of the cases had no growth. Most frequent organisms isolated were K. pneumonia, Acinetobacter baumannii complex and E. coli (44.4%, 18% and 13.8% respectively) (Figure 1).

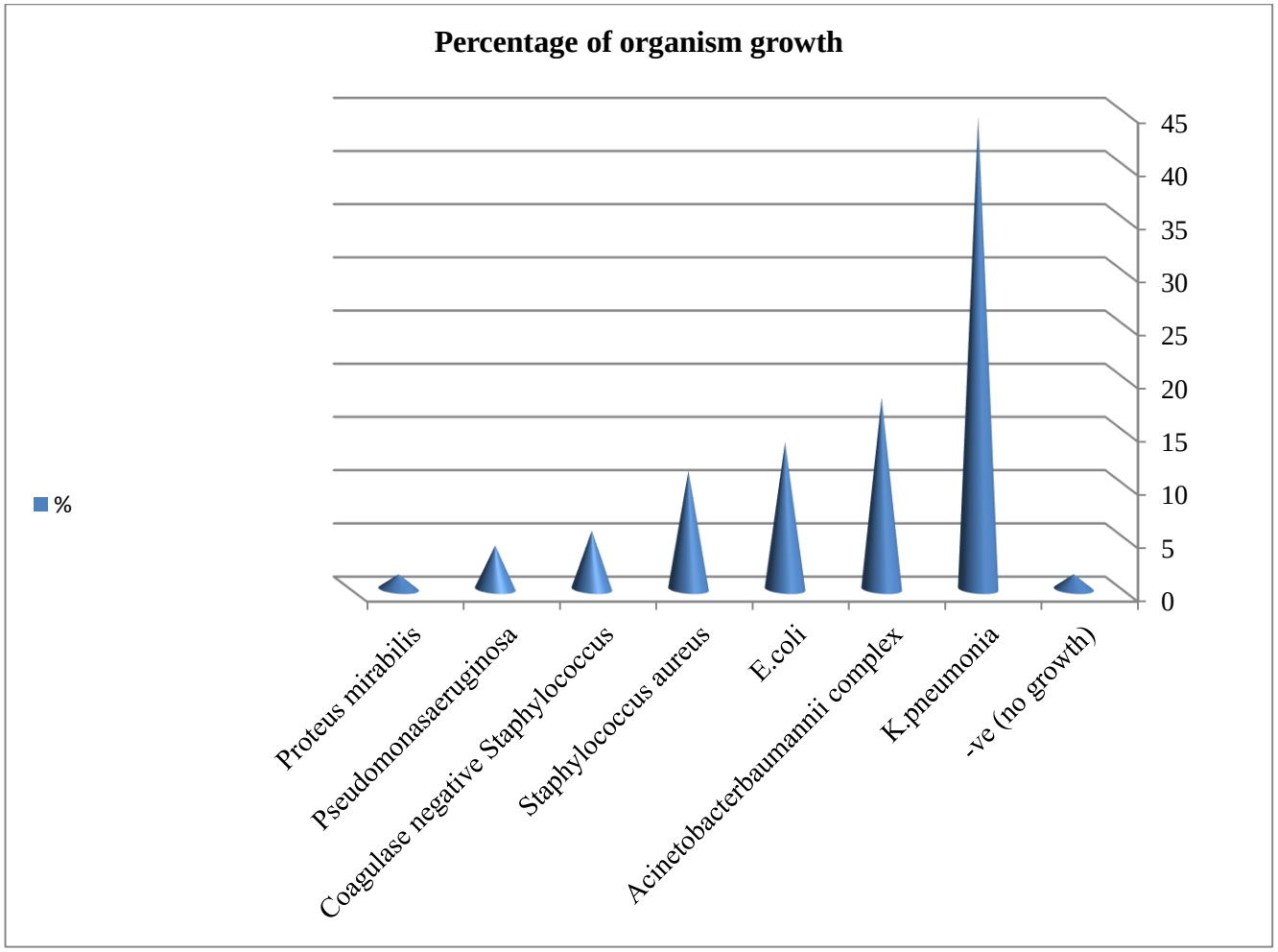

Figure (1): Isolated organisms among the studied cases

This table shows that most frequent sensitive drug was colistin, most frequent intermediate drug was gentamycin, and most frequent resistant drug was cefepime.

Table (3): Antibiotic sensitivity pattern of the studied cases

Antibiotic	(n=72)					
	Sensitive		Intermediate		Resistant	
	No	%	No	%	No	%
Amikacin	14	19.4	---	----	13	18
Amoxicillin	2	2.7	---	----	16	22.2
Ampicillin	---	----	---	----	24	33.3
Avibactam	5	6.9	---	----	---	----
Axetil	---	----	---	----	2	2.7
Azithromycin	---	----	---	----	1	1.4
Aztreonam	2	2.7	---	----	16	22.2
Ceftazidime	5	6.9	1	1.4	---	----
Cefepime	4	5.4	2	2.7	46	63.8
Cefixime	1	1.4	---	----	2	2.7
Cefotaxime	---	----	---	----	16	22.2
Cefoxitin	1	1.4	1	1.4	---	----
cefuroxime	---	----	1	1.4	4	5.4
Ceftaroline	3	4.1	---	----	---	----
Ceftazidime	4	5.4	---	----	29	40.2
Ceftriaxone	1	1.4	---	----	11	15.2
Chloramphenicol	---	----	1	1.4	2	2.7
Ciprofloxacin	6	8.3	2	2.7	44	61.1
Clavulanic Acid	3	4.1	3	4.1	28	38.8
Clindamycin	3	4.1	---	----	9	12.5
Colistin	34	47.2	2	2.7	1	1.4
Dalfopristin	6	8.3	---	----	---	----
Doxycycline	1	1.4	2	2.7	---	----
Erythromycin	1	1.4	1	1.4	8	11.1
Fosfomycine	3	4.1	---	----	6	8.3
Gentamicin	12	16.6	4	5.4	29	40.2
Imipenem	13	18	---	----	35	48.6
Levofloxacin	3	4.3	---	----	17	23.6
Linezolid	9	12.5	---	----	---	----
Meropenem.	9	12.4	---	----	44	61.1
Minocycline	4	5.4	3	4.1	8	11.1
Moxifloxacin	1	1.4	1	1.4	4	5.4
Nitrofurantoin	8	11.1	4	5.4	15	20.8
Oxacillin	---	----	---	----	6	8.3
Pefloxacin	---	----	---	----	3	4.3
Piperacillin	3	4.1	---	----	40	55.5
Polymynx b	1	1.4	---	----	---	----
Quinupristin	6	8.3	---	----	---	----
Rifampicin	5	6.9	1	1.4	2	2.7
Sulbactam	---	----	---	----	3	4.1
Sulfamethoxazole	10	13.8	1	1.4	25	34.7
Tazobactam	5	6.9	---	----	20	27.7
Temocillin	---	----	---	----	3	4.1
Tetracycline	4	5.7	---	----	2	2.7
Ticarcillin	1	1.4	3	4.1	35	48.6
Tigecycline	11	15.2	---	----	2	2.7
Tobramycin	8	11.1	1	1.4	14	19.4
Trimethoprim	12	16.6	1	1.4	24	33.3
Vancomycin	11	15.2	---	----	---	----

This table shows that there were no statistically significant differences between dead and survived in all CBC parameters, CRP, procalcitonin, K or creatinine, but there was a statistically significant increase in D Dimer and decrease in Na level among dead compared to survived cases

Table (4): Comparison between dead and survived in laboratory findings

Variable	Survived (n=23)	Dead (n=49)	t/MW	P
	Mean ± Sd	Mean ± Sd		
WBCs: (x10^3/mm^3)	14.1±3.4	13.52±3.2	0.10	0.92 NS
Neutrophil:	11.39±2.7	11.15±2.6	0.54	0.59 NS
Hb: (gm/dl)	11.36±2.13	10.64±2.18	1.3	0.20 NS
Hematocrit: (%)	34.64±6.66	34.12±7.07	0.29	0.77 NS
Platelets: (x10^3/mm^3)	216.09±53.81	202.19±48.82	1.15	0.25 NS
CRP: (mg/dl)	128.64±31.52	128.22±30.33	0.08	0.94 NS
Procalcitonin: (ng/ml)	3.98±0.71	1.82±0.44	0.15	0.88 NS
D. Dimer: (gm/L)	1.93±0.46	2.79±0.66	**1.96**	**0.05***
Na: (mmol/L)	146.73±9.21	141.25±8.37	**2.40**	**0.02***
K: (mEq/L)	4.11±0.80	3.9±0.85	0.97	0.33 NS
Creatinine: (mg/dl)	1.45±0.35	1.61±0.39	0.51	0.61 NS

SD: Standard deviation, t: Independent t test, MW: Mann Whitney test, NS: Non significant, *: Significant, **: Highly significant, WBC: white blood cell, Hb: Hemoglobin, CRP: C-reactive protein

This table shows that there was a highly statistically significant increase in score and mortality among dead compared to survived cases (increase score associated with increase mortality).

Table (5): Comparison between dead and survived in score

Variable	Survived (n=23)	Dead (n=49)	T	P
	Mean ± Sd	Mean ± Sd		
Score	15.14±4.4	23.42±4.85	**6.82**	**<0.001****
Mortality	22.85±12.11	47.34±15.68	**6.49**	**<0.001****

This table shows that score at cut off <17.5 had sensitivity 91.7%, specificity 81.8% and accuracy 82.9% in prediction of mortality among the studied cases.

Table (6): Validity of score in prediction of mortality among the studied cases

Variable	Cut off	AUC (CI 95%)	Sensitivity	Specificity	PPV	NPV	Accuracy	p
Score	>17.5	0.91 (0.83-0.99)	91.7	81.8	91.7	81.8	82.9	**<0.001****

AUC: Area under curve, CI: Confidence interval, PPV:+ve predicted value, NPV:-ve predicted value, **:Highly significant

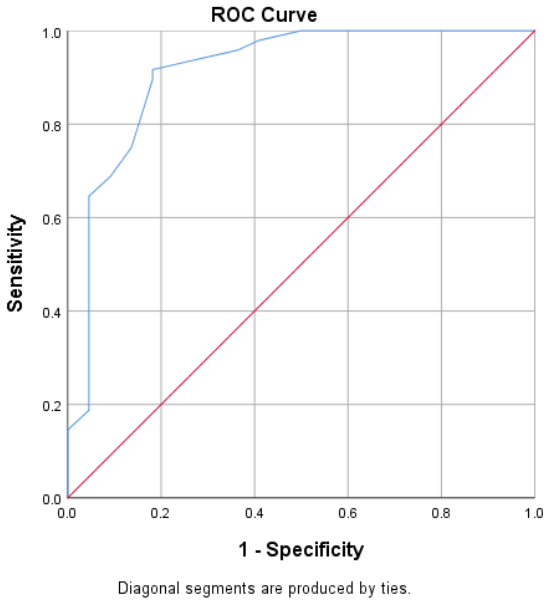

Figure (2): ROC curve for validity of score in prediction of mortality among the studied cases

DISCUSSION

One of the most frequent types of hospital-acquired infections, HAP and VAP are associated with a high rate of morbidity and mortality. The rising prevalence of ABR among the main bacterial pathogens associated with HAP and VAP, particularly among Enterobacterales and nonfermenting Gram-negative bacteria, has complicated the selection of empiric treatment for these illnesses. Poorer clinical outcomes have been linked to failure of first empiric therapy to cover the causal agents associated with HAP and VAP [(10)].

In this study, we have tried to detect the distribution of various bacteria causing HAP and VAP among the ICU patients in Zagazig Hospital and their antibiotic susceptibility pattern.

This study isolates the most common causative organisms and provides an overview of antibiotics that have been approved for the treatment of HAP and VAP. The approved antibiotics include the most sensitive, which are colistin followed by imipenem and amikacin, and most frequent intermediate drug, which is gentamycin. Finally, most frequent resistant drugs are cefepime, ciprofloxacin and piperacillin. Their major advantages include their high activity against MDR pathogens.

The present study revealed that most frequent organisms isolated were K. pneumonia, Acinetobacter baumannii complex, E. coli, Staphylococcus aureus, Coagulase negative Staphylococcus, Pseudomonas aeruginosa, and Proteus mirabilis coli (42.9%, 18.6%, 14.3%, 11.4%, 5.8%, 4.1%, and 1.4% respectively) and that most frequent sensitive drugs were colistin (48.6%) followed by imipenem, amikacin (both 18.6%). Most frequent intermediate drug was gentamycin (5.7%). Finally, most frequent resistant drugs were cefepime, ciprofloxacin and piperacillin (65.7%, 62.9% and 57.1%, respectively).

APATCHEII was calculated for all patients in this study for prediction of morbidity and mortality rate, in this study the validity of APACHEII score in the prediction of mortality among these studied cases had a sensitivity of 91.7%, specificity of 81.8% and accuracy of 82.9% in prediction of mortality among the studied cases.

These findings are similar to others [(1, 8-10)], which indicate that Gram-negative bacterium, particularly K. Pneumonia, remains the commonest pathogen isolated in patients with VAP in ICU.

Another study containing 194 patients of VAP was undertaken in Shanghai. Two hundred and twelve bacterial strains were among the respiratory pathogens found in these patients. Acinetobacter baumannii (33.96%), Klebsiella pneumonia (23.58%), Escherichia coli (19.81%), and Staphylococcus aureus (1.81%) were the most common causative agents of infection (7.08 percent). Carbapenems (21.64%), fluoroquinolones (20.10%), -lactam/-lactamase inhibitor combos (15.46%), third-generation cephalosporins (14.95%), and second-generation cephalosporins (5.63%) were the most commonly utilised antimicrobial agents (7.73 percent). Carbapenems (77.32%), fluoroquinolones (32.47%), -lactam/-lactamase inhibitor combos (31.44%), glycopeptides (30.41%), and third-generation cephalosporins (3.33%) were the most commonly administered antimicrobials following a diagnosis of VAP (24.22 percent) [(1)].

In another 511-person study conducted in China, antibiotic susceptibility profiles of the causative agents showed that K. pneumonia was present in 34.6% of cases, Pseudomonas aeruginosa in 25.0%, and Escherichia coli in 18.2%. Results showed that ceftolozane/tazobactam was effective against 87.0% of isolates and 93.33% of isolates were susceptible to meropenem [(11)].

In a study by **Llor and Bjerrum** [(12)], resistance to meropenem was not observed in K. pneumonia, E. coli, or Acinetobacter, but was 25% in Streptococcus spp. Resistance to amikacin was low (3%) among E. coli strains, nonexistent among Acinetobacter and Klebsiella pneumoniae strains, and particularly intriguing among Streptococcus species strains (75%). Acinetobacter showed no resistance to gentamicin, but E. coli, K. pneumoniae, and Streptococcus spp. showed 26, 9, and 87.5 percent resistance, respectively. That's why nitrofurantoin was more effective against resistance. Among E. coli and Streptococcus species, resistance was 12.5% and 11.9%, respectively. Acinetobacter and Klebsiella pneumoniae were particularly resistant to nitrofurantoin (100 percent, 50 percent respectively). The resistance to cephalosporins was moderate, but the resistance to amoxicillin and ciprofloxacin was consistently strong.

In our study, K. pneumonia-affected patients were 100% resistant to ceftriaxone, cefepime, ciprofloxacin and piperacillin.

In a study by **Weiss *et al.*** [(13)] eighty percent of HAP cases were caused by just six different pathogens: S. aureus, P. aeruginosa, Klebsiella spp., E. coli, Acinetobacter spp., and Enterobacter spp. A secondary study of data from 485 HAP patients who were intubated. Treatment of gram-negative HAP and VBP with imipenem/cilastatin/sulbactam is warranted, even in severely unwell high-risk patients [(13)].

The current results disagreed with **Luyt *et al.*** [(14)] in Paris, who revealed that the causative microorganisms for HAP/VAP vary by region, patient demographics, length of hospital/ICU stay preceding disease onset, and MDR pathogen risk factors. Many of the respiratory infections in this environment are caused by Gram-negative bacilli (GNB), the study found, with few differences between HAP and VAP.

Additionally, research on HAP was conducted in Japan's Multicenters. Most of the patients in the study fell into the category requiring intensive combination antibiotic treatment as empiric therapy covering a wide spectrum; this group included Staphylococcus aureus

(including methicillin-resistant S. aureus [MRSA]) (25.5%), Pseudomonas aeruginosa (18.3%), and Klebsiella pneumoniae (8.2%). Acinetobacter spp. was isolated from only 0.7% of the time [(15)].

Patients with HAP and VAP infections are often treated empirically, with culture and susceptibility testing being requested only if they do not show improvement after receiving antibiotic treatment. This pattern promotes the development of drug resistance in infections [(11)].

The K. pneumonia, Acinetobacter, and Enterococcus that are often to blame are notoriously skilled at adapting to new treatments[(13)].

Unfortunately, multidrug resistance is a growing concern, and careless use of broad-spectrum antibiotics is typically blamed as the root cause. Programs are established to reduce the occurrence of drug-resistant organisms with the goal of reducing the improper use of antibiotics.

In addition, the spread of drug-resistant pathogens can be mitigated by strictly adhering to treatment protocols[(15)].

CONCLUSION

HAP and VAP ICUs patients were mostly affected by K. pneumonia, Acinetobacter baumannii complex and E. coli. K. pneumonia was the most frequent organism. Most of the cases were resistant to cefepime, ciprofloxacin and piperacillin, most probably due to its cheap cost and easy availability. The most frequent sensitive drugs were colistin (48.6%) followed by imipenem and amikacin.

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