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Antibiotic Susceptibility Pattern of Bacterial Isolated from Lower Respiratory Tract Infections at Respiratory Intensive Care Unit

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ABSTRACT

Background: The control of infections in intensive care units (ICUs) is becoming more difficult. Antibiotics utilization Recent antibiotic overuse has prompted the emergence resistance to antibiotics, which poses a threat to healthcare, especially in developing nations without access to antibiogram in most ICUs.

Objectives: This study aimed to present antibiotic susceptibility pattern of microbial infections and describe some antibiotic use features.

Patients and method: This is a cross sectional study included 53 patients with lower respiratory tract infections admitted in respiratory ICU chest department, University Hospitals of Zagazig in the period from September 2018 to September 2019, we collected the following data: past history, length of hospital stay and comorbidities. The following parameters were assessed: clinical pulmonary infection score (CPIS), general and local examination, radiological and routine laboratory investigation, arterial blood gases (ABG) and microbiological results of isolated microbes and their susceptibility pattern using (blood and sputum culture).

Result: Among studied patients one patient died during the study and excluded, mean age was 56.48±15.73**,** 53.8% were males and 46.2% were females. 36 (69.23%) were improved, 16 (30.77%) were complicated. Blood and sputum culture were done for all patients most organism detected in sputum culture was *Klebsiella pneumonie*, in blood culture was *Staphylococcus aures*. According to culture towards Klebsiella, highest sensitivity was levofloxacin (93.33%), *Streptococcus pneumoniae* highest sensitivity was levofloxacin (83.33%), *Staphylococcus aureus* highest sensitivity was linezolid (85%), *Pseudomonas aeruginosa*. highest sensitivity was meropenem (83.33%), Acinetobacter highest sensitivity was imepenem (58%).

Conclusion: Combined clinical, laboratory, radiological and microbiological findings help in diagnosis and treatment of LRTI.

Keywords: LRTI, Antibiogram, Antibiotic, Utilization.

INTRODUCTION

Significant morbidity, death, and healthcare-related costs are attributable to respiratory infections in patients hospitalised to the ICU. Worldwide, respiratory infections are responsible for 3.5 million fatalities and 79 million years of lost productivity due to disability **(1)**.

The most common cause of pneumonia is a bacterial infection, which is treated with an antibiotic prescription. Antibiotic overprescribing carries a number of concerns, including exposing patients to side effects needlessly while failing to speed up their recovery, raising the chance of contracting an infection with an antibiotic-resistant bacterium, and lengthening the time, expense, and workload associated with patient recovery. On the other hand, under prescribing antibiotics can raise the chance of developing a serious pneumonia**(2)**.

The majority of currently known biomarkers target the host inflammatory response and are therefore notoriously less accurate for making a diagnosis in critically sick patients with several additional causes of inflammation or compromised immune function. Biomarkers can help with antibiotic monitoring as well. Nevertheless, in critically sick patients with a range of infections, a consistent pattern of safely reducing the length of antibiotic treatments based on a noticeable improvement or normalisation of biomarkers, such as procalcitonin and C-reactive protein, has been shown**(3)**.

The importance of identifying risk factors in clinical settings for multi-drug resistance bacteria (MDRB), before the results of the culture are available, the (MDRB) infection is to guide empirical therapy, or the pathogen identification and testing for antibiotic susceptibility. The intricate interactions between the host, environment, and pathogen preclude the use of a single algorithm to forecast an MDRB infection, necessitating the adoption of an individualised probabilistic method for the selection of empirical medications. It is not necessary to consider documented carriage as a specific need when selecting an empirical therapy. Patients who have experienced prior antibiotic exposure, protracted hospital stays, invasive surgeries, and advanced co-morbid conditions are at an elevated risk of MDRB infections**(4)**.

Antibiotic resistance has lately evolved as a result of antibiotic abuse and poses a threat to the healthcare system, particularly in developing nations where the majority of ICUs lack antimicrobial stewardship programmes **(5)**.

Therapeutic Drug Monitoring (TDM) is defined by the World Health Organisation (WHO) as ensuring that patients receive the right drugs for their clinical needs, for the shortest time possible, and at the least expensive possible price for them and their community. Since many factors that are crucial for the best possible antimicrobial therapy have previously been identified,

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these general principles are plainly applicable to the use of antimicrobials in general as well as to the administration of antibiotics in the critical care context[6].

Initial Gram stain and semi-quantitative cultures of endotracheal aspirates or sputum are used to identify the origin of the pneumonia. A culture without possible pathogens and a smear without inflammatory cells have extremely strong negative predictive values[7].

AIM OF THE STUDY

To present the antibiotic susceptibility pattern of microbial infections, and describe some antibiotic use features.

PATIENTS AND METHODS

This cross sectional research was carried out in respiratory ICU from September 2018 to September 2019.

The study included all the patients who meet the following criteria: admission to respiratory intensive care unit with lower respiratory tract infections in the form of:

- Acute Exacerbation of chronic obstructive pulmonary disease (COPD).
- Acute Exacerbation of bronchiectasis
- Pneumonia as hospital acquired pneumonia (HAP), and ventilatory associated pneumonia (VAP).
- Ventilator associated tracheobronchitis.
- Data collection: This was done by a predesigned sheet.

The following items were included:

I-Clinical assessment:

History taking: Previous history of (smoking, previous history of respiratory infections indicated ICU admission, mechanical ventilation), length of hospital stay, comorbiditie (DM, HTN), Prior antibiotic usage before admission and assessment score CPIS (clinical pulmonary infection score).

Full clinical examination: General and Local examination.

Radiological study: plain chest X-ray and CT scan of the chest.

Laboratory investigations: Complete blood counts, kidney function tests, liver function tests, CRP, procalcitonin level and arterial blood gases.

Record of Antibiotic prescription pattern (Antimicrobial assessment): In the form of documentation of the following: Name of group of antibiotics received by the patients, antibiotic and duration (0-5 days — 5-10 days — >10 days).

Reassessment of patients in the form of:

Days of hospital stay, Resistance and or change of antibiotic according to culture and sensitivity and de-escalation, Progression or regression of symptoms according to clinical evaluation and laboratory investigations, complications and mortality, Laboratory assessment (ABGs, CBC, Procalcitonin), and radiological assessment (CXR).

II-Microbiological work up:

Sputum culture and sensitivity and blood culture.

Antibiotic susceptibility testing of isolated bacteria:

This was done using the modified Kirby-Bauer disc diffusion technique on Muller Hinton agar (MHA) for a few antibiotics. Plates were incubated at 37°C for 16–18 hours. MHA supplemented with 5% sheep blood and Haemophilus test medium (HTM) were used, respectively, for the incubation of streptococci and *Haemophilus influenzae*. Screening for beta-lactam resistance in *Streptococcus pneumoniae* was done with the oxacillin 1 µg disc; isolates with oxacillin 1 µg disc zone diameter ≥20 mm are considered susceptible to piperacillin (without and with beta-lactamase inhibitor), ceftriaxone in addition to all carbapenems, while isolates with oxacillin 1 µg disc zone diameter <20 mm were further tested for MIC determination of these β-lactams.

Ethical approval:

The Institutional Review Board of Zagazig University approved this experiment. Patients who agreed to participate in the trial gave written informed consent. When conducting this study on humans, the Helsinki Declaration and the World Medical Association's Code of Ethics were adhered to.

Statistical analysis

The Statistical programme of Social Service (IBM SPSS) software programme, version 24.0 (Armonk, NY: IBM Corp.), was used to input the data and analyse them. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR).

Categorical qualitative variables were expressed as absolute frequencies (number) and relative frequencies (percentage). Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation).

Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). When the statistically significant probability was less than 0.05 (P0.05), the findings were deemed to be significant. P-values below 0.05 were deemed statistically insignificant, whereas those over 0.001 were deemed highly statistically significant (HS).

RESULTS

This cross-sectional study included 53 patients with lower respiratory tract infections admitted to ICU, their mean age was 56.48±15.73. 53.8% were males and 46.2% were females, one patient died during the study and was excluded, most of the studied participants were not addicts, 48.1% were smokers, 42.3% were diabetic, 28.8% were hypertensive and 28.8% were bird breeders. 36 (69.23%) of patients were improved and 16 (30.77%) were complicated in the form of; 9.6% underwent mechanical ventilation, 7.7%, 7.7%, 13.5% and 1.9% suffered from hemoptysis, pneumothorax, pleural effusion and pulmonary embolism, respectively.

Out of 52 patients included in this study. Regarding history of chronic medical diseases 7.7% were HCV, only one patient had parkinsonism, 5.8% epileptic patients ,and the same percent had rheumatoid arthritis, 7.7% suffered from chronic renal failure, 34.6% were previously admitted to ICU and 21.2% were mechanically ventilated (Table 1).

Table (1): Basic characteristics of the studied patients.

Characteristics		**n =52**	**%=100**
Age (yrs)	mean±SD	56.48±15.732	
	Range	30-82	
Gender	Male	28	53.8
	Female	24	46.2
Special Habits	Addict	7	13.5
	Smoking	25	48.1
	Bird breeder	15	28.8
Comorbidities	Diabetes Mellitus	22	42.3
	Hypertension	15	28.8
	HCV	4	7.7
	Parkinsonism	1	1.9
	Epilepsy	3	5.8
	Rheumatoid arthritis	3	5.8
	Renal failure	4	7.7
Past history of ICU admission		18	34.6
Past history of MV		11	21.2

Figure (1) shows positive results of blood culture for 30 (57.69%) of the studied patients, 11(36.67%) of the patients had *Staphylococcus aures*, 6(20%) had *Klebsiella pneumoniae* and 5 (16.67%) pseudomonas organism. 4(13.33%) revealed streptococcus and the same percentage for *H. influenza*.

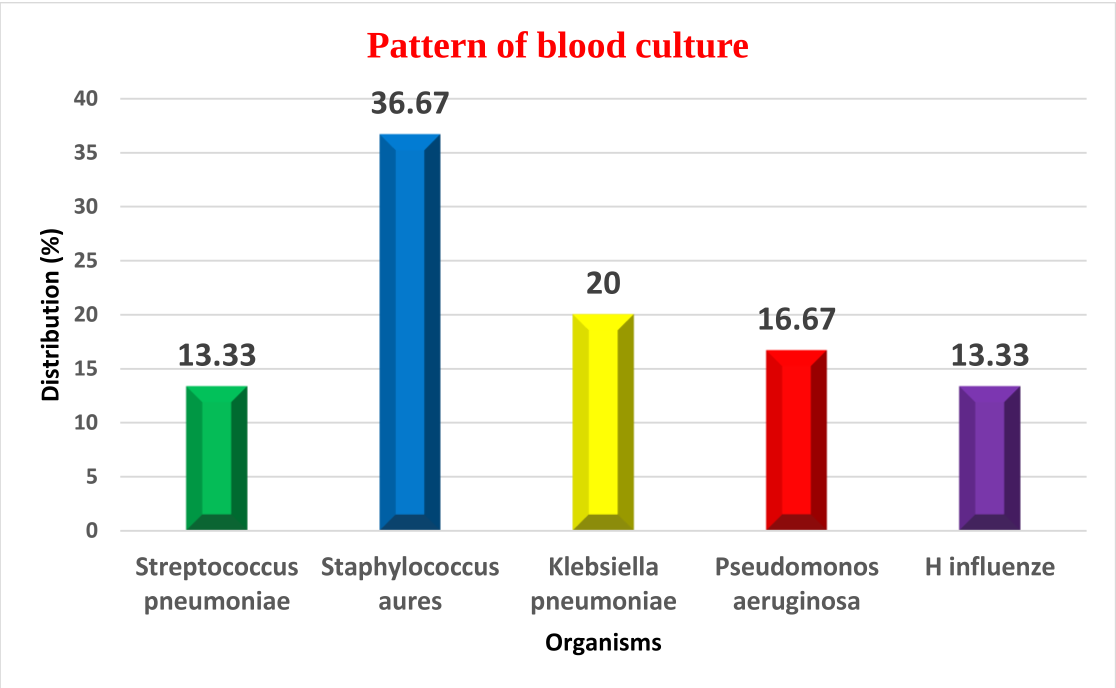

Figure (1): Bacteria isolated from the blood cultures of 30 patients.

Figure (2) shows sputum culture which had been performed for all participants, 23 (44.2%) of the patients had Klebsiella organism, 11 (21.2%) of sputum culture revealed *Streptococcus pneumoniae*, 6 (11.5%) had pseudomonas organism and *Staphylococcus aures*, while 4 (7.7%) acinetobacter organism and 2 (3.8%) of patients were suffering from *H. influenza*.

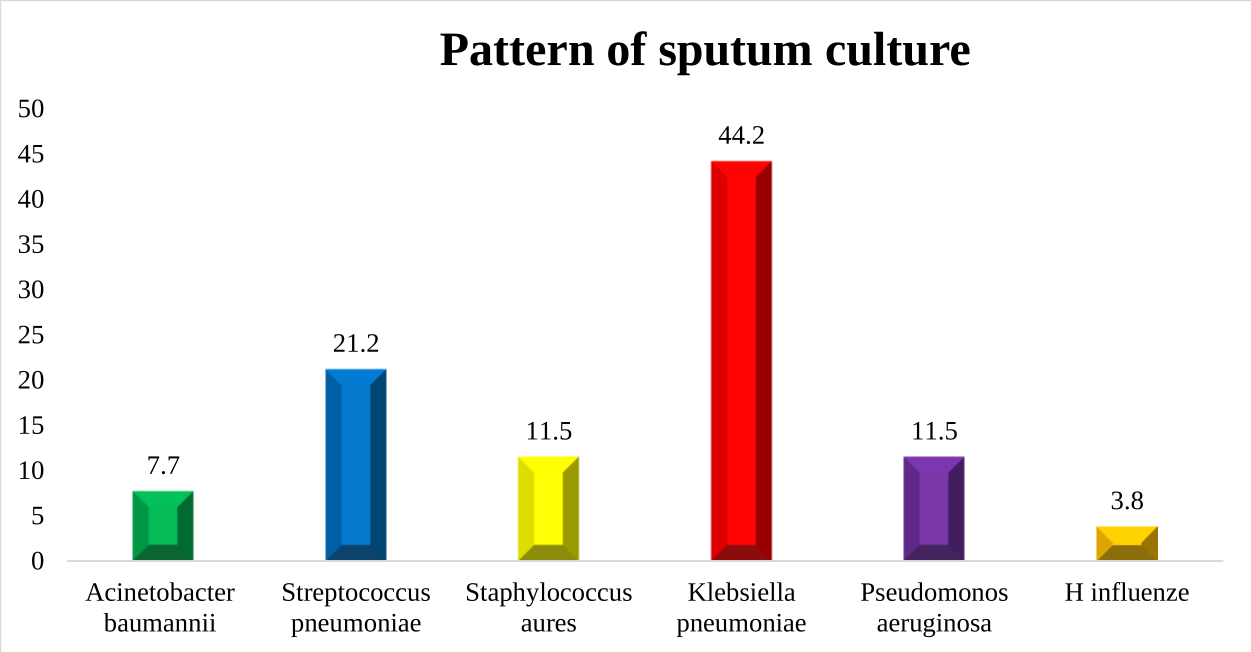

Figure (2): Bacteria isolated from the sputum cultures of 52 patients.

Figure (3) shows the spectrum of antibiotic sensitivity and resistance towards Klebsiella. The highest sensitivity was toward levofloxacin (93.33%) followed by meropenem and ciprofloxacin (76.67%). It had 45% sensitivity towards ceftazidime. Towards pipracillin/Tazobactam, amikacin and ampicillin/sulbactam, it had 23.33% sensitivity. The least sensitive antibiotics were linezolid and ceftriaxone (7.12 and 6.67% respectively).

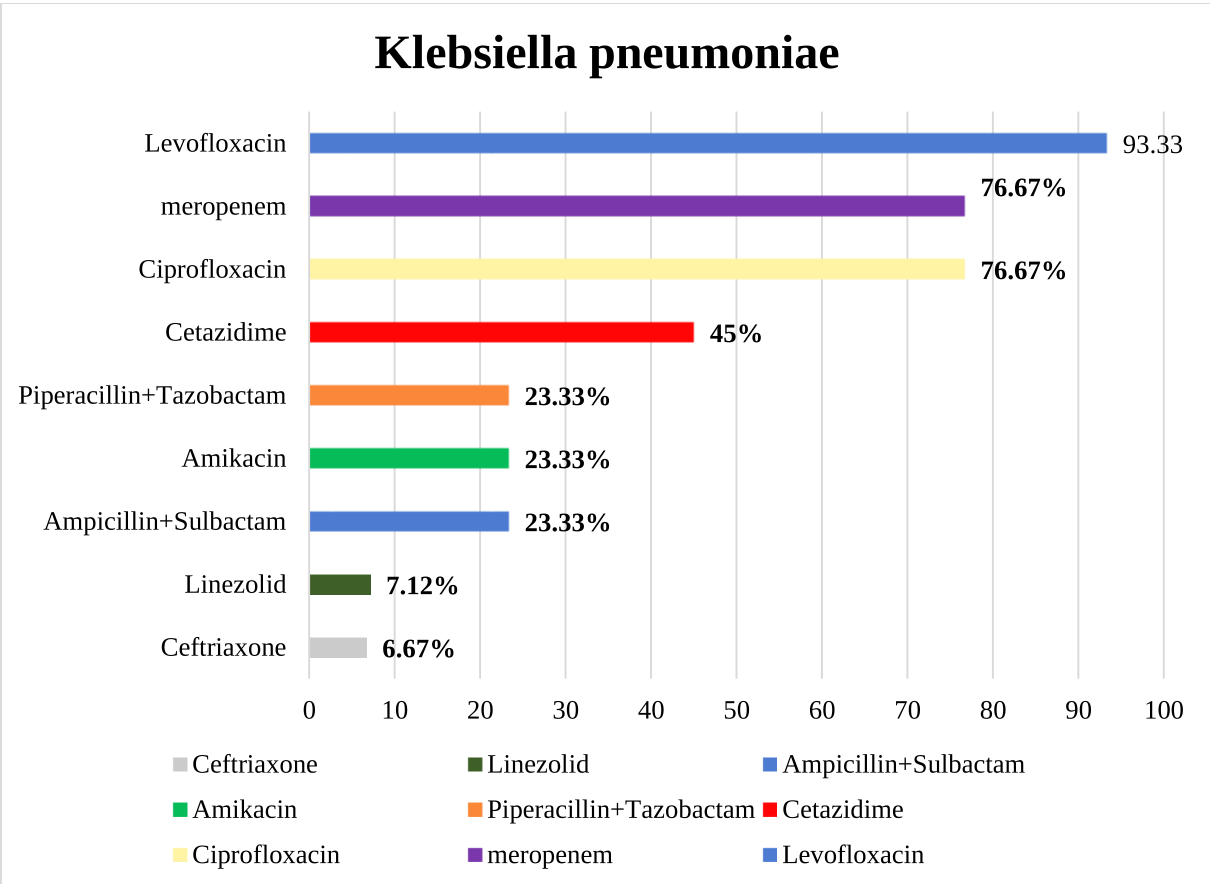

Figure (3): Antibiotic susceptibility pattern of *Klebsiella pneumoniae* isolates from 23 sputum and 6 blood cultures.

Figure (4) shows the spectrum of antibiotic sensitivity and resistance towards Streptococcus pneumoniae. The highest sensitivity was toward levofloxacin (83.33%) followed by clindamycin (57.3%) then ciprofloxacin (45.2%). Ceftazidime, ceftriaxone and ampicillin/sulbactam had 18.2% sensitivity. The least sensitive antibiotics were meropenem, pipracillin/tazobactam and amikacin (9, 8.2 and 6.4% respectively).

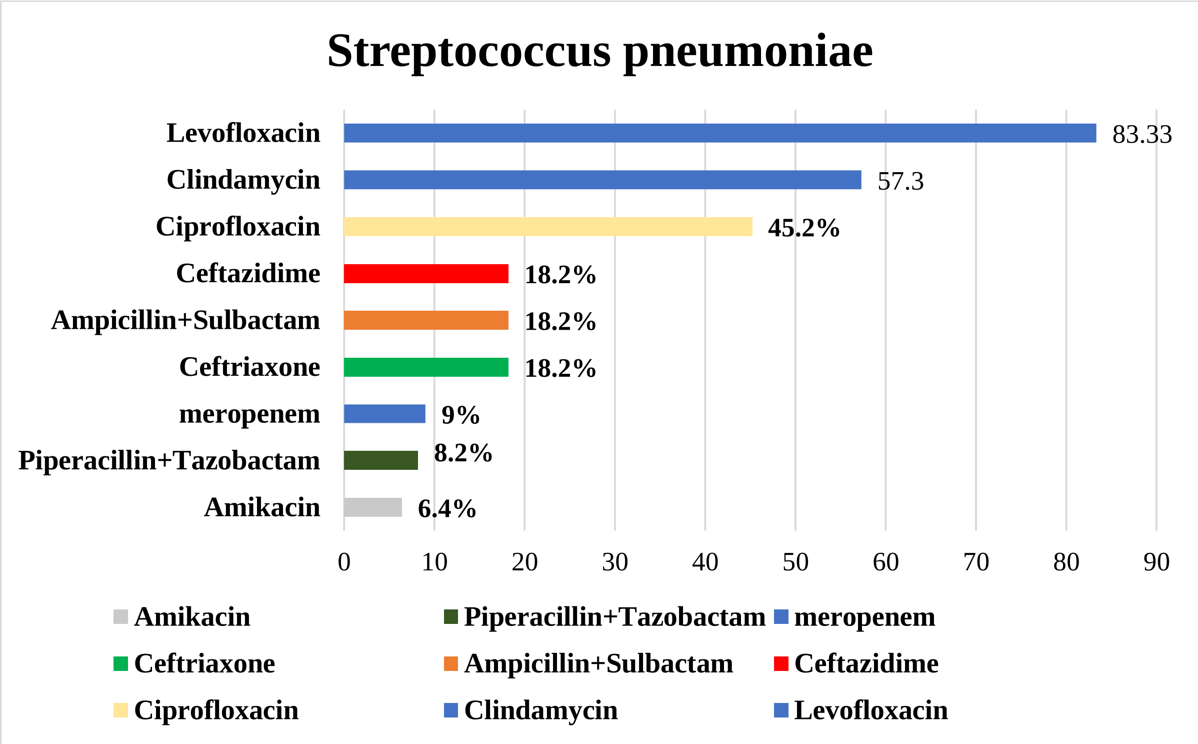

Figure (4): Antibiotic susceptibility pattern of towards *Streptococcus pneumoniae* (sputum (11) and blood (4) culture).

Figure (5) showed the spectrum of antibiotic sensitivity and resistance towards *Staphylococcus aureus*. The highest sensitivity was toward linezolid (85%) followed by clindamycin (54.2%) then ciprofloxacin and amikacin (36.67%). Cefipime had 16.67% sensitivity. The least sensitive antibiotics were ceftriaxone (6.3%).

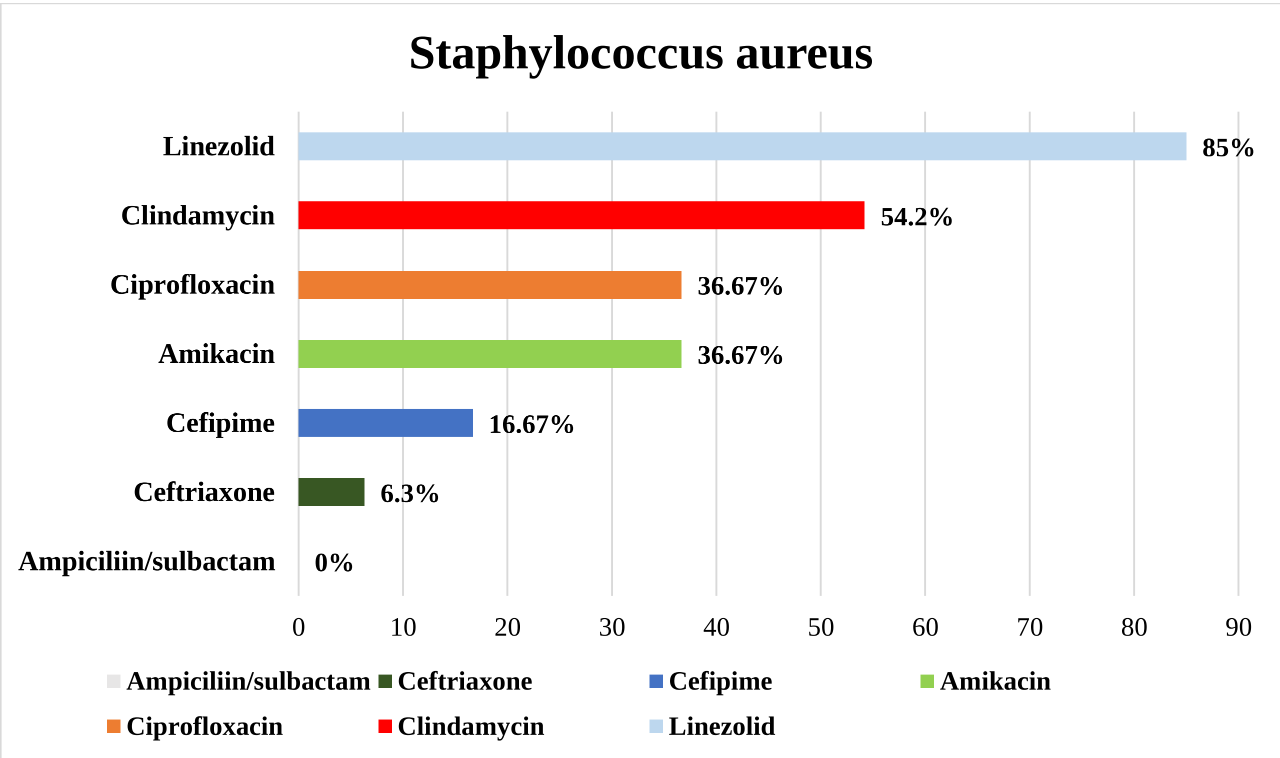

Figure (5): Antibiotic susceptibility pattern of towards *Staph. aureus* (sputum (6) and blood (11) culture).

DISCUSSION

Overuse of antimicrobial drugs occurs globally in both community and clinical settings. Antibiotic misuse can result in a number of negative outcomes, including the development of antimicrobial resistance and increased healthcare costs [8].

The use of therapeutic or preventative antibiotics that is not acceptable is known as inappropriate antimicrobial usage. Use of antibiotics when there is no sign of infection, giving antibiotics to patients who are colonized with an organism, giving antibiotics to treat infections brought on by microorganisms those that resist those antibiotics, giving multiple antibiotics with redundant spectrums, giving antibiotics that are insufficient for the microorganisms that cause the disease [9].

In this study there were 48.1% of patients smoker which can explained as smoking is associated with higher rates of viral and bacterial respiratory infections. Smokers are at a 2- to 4-fold increased risk of invasive pneumococcal disease [10].

In this study the most comorbid presented in patients with respiratory tract infections were diabetes mellitus that explain the effect of diabetes as alternations in host defense mechanism in entire body is the primary pathogenic factor in people with DM who also have lower respiratory tract infections (LRTI). Other contributing causes include compromised ciliary motility and compromised respiratory epithelium function [11].

In this study the most cases were COPD with lower respiratory tract infection that may explained by many factors as airway obstruction, low body mass index (BMI), older age, use of psychoanaleptics, presence of gastroesophageal reflux disease, increased blood neutrophil counts, and use of inhaled corticosteroids (ICS) [12].

In agreement with this study **El-Assal *et al.***[13], showed more than half of the patients were diagnosed as having acute exacerbation of COPD (52%), either alone or associated with other secondary diagnosis, 27% were diagnosed as having interstitial lung disease (ILD), 18% were diagnosed as having pneumonia, and 3% as having bronchiectasis.

According to **Stolza *et al.*** [14] final diagnosis were 87 acute COPD exacerbations, 60 community-acquired pneumonia cases, 59 cases of acute bronchitis, 13 cases of acute asthma exacerbations, and 24 cases of miscellaneous diagnoses. A total of 8 patients passed away, and 13 were unfollowable.

Blood culture had been performed for all patients only 30 (57.69%) of the studied patients were positive for organisms which were 36.67% of the patients had *staphylococcus aureus*, 20% *klebsiella pneumonia* and 16.67% pseudomonas. 13.33% revealed streptococcus and the same percentage for *H. influenza*.

In agreement with this study **Sahoo *et al.*** [15] among 26 out of the 100 study participants who had an organism growing in their blood culture. 11 were *Staphylococcus aureus*, 6 7 *Klebsiella pneumonia*, 2 *Acinetobacter baumannii*, and Escherichia coli. The remaining 74 patients' blood cultures did not exhibit any growth.

Alam *et al.*.[16] revealed that Coagulase-negative staphylococci made up 63.5% of the most frequently found Gram-positive bacteria, followed by Staphylococcus aureus (23.1%), enterococci (5.6%), and alpha-haemolytic streptococci (5.8%). Acinetobacter species (31%), Salmonella typhi (24.1%), Escherichia coli (23.3%), and Pseudomonas aeruginosa (13.8%) were the Gram-negative bacteria that were found most frequently.

In contrary to this study **Stolza *et al.***[14] revealed microorganisms were cultured from the blood stream in 16 cases (11 *Streptococcus pneumoniae*, 3 *Escherichia coli*, *Pseudomonas spp*. and *Klebsiella spp*. 1 case each).

Sputum culture had been performed for all studied participants, 23 (44.2%) of the patients had Klebsiella organism, 11 (21.2%) of sputum culture revealed streptococcus, 6 (11.5%) had pseudomonas organism and staphylococcus, while 2 (3.8%) of patients were suffering from H. influenza and 4 (7.7%) acinetobacter organism.

In agreement with this study **Negm *et al.*** [17] regarding the sputum culture, the most common pathogens isolated was *Klebsiella pneumonia (K. pneumoniae)* with an incidence of 33.51%, confirmed that Gram-negative bacteria accounted for the majority of the pathogens that were identified (74.41%), which may be related to the high incidence of these bacteria in hospitals. Additionally, their regular antibiotic resistance may contribute to their persistence and spread. With the exception of the coronary care unit (CCU), K. pneumoniae was the most frequently found Gram-negative bacterium across the board in the Zagazig hospital.

This is consistent with this study in **Hidron *et al.***[18] revealing that at than 30% of hospital acquired illnesses are caused by Gram-negative bacteria. **El-Sokkary *et al.***[19] showed agreement with current study which revealed the most frequent bacterium was *Klebsiella pneumoniae*, which was followed by *Streptococcus pneumoniae* and *P. aeruginosa* (7.78% each).

Agmy *et al.*[20] addressed the issue of HAP in 75 instances of ICU patients at Assiut University Hospital, with *S. aureus* (32%), *P. aeruginosa* (30%), and *S. pneumoniae* being the most common infections. (15%).which is differ from current study.

Also, in contrary to this study **Elkolaly *et al.***[21] revealed *Pseudomonas* (37.5%), *Klebsiella* (25%), *Staphylococcus* (20.8%), and methicillin-resistant bacteria were the isolated organisms *A. Staphylococcus* (4.2%).

In this study, sensitivity and resistance of isolated organisms to different antibiotics was evaluated. Regarding pattern of sensitivity and resistance of *klebsiella*, which was the most isolated organism from sputum of our patients (44.2%) and the second organism isolated from blood (20%), towards different antibiotics revealed that the highest sensitivity was toward levofloxacin (93.33%) followed by meropenem and ciprofloxacin (76.67%). The least sensitive antibiotics were linezolid and ceftriaxone (7.12 and 6.67% respectively).

This is in accordance with **Agmy *et al.*** [(20)] revealed that *klebsiella pneumonia*, which when the second most bacteria found in patients with HAP, was mostly sensitive to levofloxacin in community acquired pneumonia (CAP) and acute exacerbation chronic obstructive pulmonary disease (AECOPD) patients and to ciprofloxacin in patients with HAP. It also had the least sensitivity towards cephalosporins in all studied patients.

Near similar results reported by **Saied *et al.*** [(22)] who reported that *klebsiella spp* were the most common (43.2%) bacteria isolated which showed highest susceptibility to imipenem followed by ciprofloxacin. The lowest susceptibility was towards ceftriaxone.

Different results were recorded by **Negm *et al.***[(17)] the most prevalent isolated bacteria in their study was *Klebsiella*, shown a significant level of carbapenem resistance (81% meropenem and 80.5 imipenem). But similar to this study, a significant trend of resistance to third-generation cephalosporins was observed.

The second frequent sputum isolated orgnism was sterptococcus pneumoniae (21.2%) which showed the highest sensitivity towards levofloxacin (83.33%) followed by clindamycin (57.3%) then ciprofloxacin (45.2%). The least sensitive antibiotics were meropenem, pipracillin/tazobactam and amikacin (9, 8.2 and 6.4% respectively). It had low sensitivity towards ceftazidime, ceftriaxone and ampicillin/sulbactam (18.2%).

Near similar results reported by **Agmy *et al.***[(20)] who reported that S.pneumoniae was the most predominant organism isolated in patients with CAP and the second organism isolated in patients with AECOPD but not isolated in patients with HAP. It showed the highest sensitivity towards quinolones (moxifloxacin and levofloxacin) followed by macrolides. Also, According to their research, doxycycline, cephalosporins, and -lactam-lactamase inhibitors all had high rates of resistance. These results are consistent with the rising global, regional, and Egyptian prevalence of S. pneumoniae resistance to certain antibiotic classes.

Most of pneumonic patients included in this study were COPD patients (28.8%) and asthmatic (19.2%). This explains the cause of high percentage of sputum isolated streptococcus pneumonia in this results.

Regarding *staphylococcus aureus* in this study, it was the most isolated organism from blood (36.67%) and the third isolated organism from sputum (11.5%). The highest sensitivity of *S. aureus* was toward linezolid (85%) followed by clindamycin (54.2%) then ciprofloxacin and amikacin (36.67%). The least sensitivity was toward ceftriaxone (6.3%) with no sensitivity toward ampicillin/sulbactam.

These results were in consistence with **Negm *et al.*** [(17)] who recorded that MRSA showed sensitivity linezolid (100%), and to vancomycin (76.8%). **Saied *et al.*** [(22)] in their study reported that all *staphylococcus* isolates were sensitive to vancomycin followed by rifampicin then macrolides and ciprofloxacin and the least sensitivity was toward ceftriaxone. In addition, none of the *S. aureus* isolates were sensitive to penicillin.

CONCLUSION

(1) Combined clinical, laboratory, radiological and microbiological findings help in prompt diagnosis and treatment of LRTI and for identification of the causative organism for providing a local antibiogram that helps in appropriate management of LRTI.

(2) To conserve the potential of the current antimicrobial drugs, this local prevalence analysis will help build an efficient antimicrobial stewardship, and creating a new challenge to clinicians as it adds to the burden of the antibiotic resistance pattern.

DECLARATIONS

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Conflicts of interest: The authors of this study failed to disclose any conflicts of interest.

Information and resources are accessible; upon reasonable request, the corresponding author will grant access to the database utilised for this study.

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