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Research Article

Bacteriological Profile and Antibiotic Sensitivity Patterns among Hospitalized Patients with COVID Infection: A Retrospective Study

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Abstract

Background and Objectives: The COVID pandemic not only increased the global healthcare burden, but also escalated the risk of pneumonia and acute respiratory distress syndrome (ADRS) among the hospitalized individuals. Hence, we planned this study to determine the bacterial sources of infection among the hospitalized COVID patients. We also gauged the sensitivity patterns observed among the participants.

Methods: In this retrospective study, we screened all the bacterial culture-positive samples of patients diagnosed with COVID-19 infection and hospitalized between April 2020 and August 2021. Of them, we analyzed only the culture reports of adult patients with pneumonia and/or acute respiratory distress syndrome (ARDS) due to a single causative microorganism. The bacteria identification and susceptibility testing were performed with VITEK 2. We assessed the diagnosis and outcome of female and male participants. Moreover, we analyzed the antimicrobial susceptibility of the participants with forty antibiotics. R software (version 4.4.1) was leveraged for the data analysis.

Results: We analyzed the data of 1980 eligible patients. Of them, 1114 (56.3%) were females. The median age of the study population was 48.0 (38.0-62.0) years. The most common causative bacteria were *Staphylococcus aureus* (517, 26.1%), followed by *E. coli* (332, 16.8%), *Acinetobacter baumannii* (260, 13.1%), *Klebsiella pneumoniae* (159, 8.0%), *Pseudomonas aeruginosa* (146, 7.4%), *Streptococcus spp.* (118, 6.0%), and *Enterobacter spp.* (110, 5.6%). The majority of our study participants (1341, 67.7%) were diagnosed with pneumonia. The cure rate was 87.5% in the study population. The culture sensitivity patterns were similar across the gender.

Conclusion: Our study showed that middle-aged individuals were more affected with respiratory infections. We noted multiple microorganisms as cause of those infections. The antimicrobial susceptibility findings were similar among females and males. Moreover, the cure rate was considerably high.

Keywords: *COVID Pandemic; Pneumonia; Respiratory Distress; Bacterial Infection; Culture and Sensitivity; Antibiotics*

Abbreviations

ADRS: Acute Respiratory Distress Syndrome; AIDS: Acquired Immunodeficiency Syndrome; AMB: Amphotericin B; AMI: Acute Myocardial Infarction; AMK: Amikacin; AMP: Ampicillin; AMX: Amoxicillin; BNZP: Benzylpenicillin; CFP: Cefepime; CFPS: Cefepime-sulbactam; CFRX: Cefuroxime; CFTX: Ceftriaxone; CFTZ: Ceftazidime; CIP: Ciprofloxacin; CLND: Clindamycin; COL: Colistin; COVID: Corona Virus Disease; CSPF: Caspofungin; CTMX: Cotrimoxazole; CVA: Cerebrovascular Accident; DPT: Daptomycin; DRP: Doripenem; ERTM: Erythromycin; ETP: Ertapenem; FCT: Flucytosine; FCZ: Fluconazole; FSM: Fosfomycin; GNTM: Gentamicin; HIV: Human Immunodeficiency Virus; ICU: Intensive Care Unit; ID & AST: Bacterial Identification and Antimicrobial Sensitivity Testing; IMI: Imipenem; IQR: Interquartile Range; LAMA: Left against Medical Advice; LFX: Levofloxacin; LNZ: Linezolid; MCF: Micafungin; MNC: Minocycline; MRP: Meropenem; NDX: Nalidixic Acid; NTF: Nitrofurantoin; NTM: Netilmicin; OXC: Oxacillin; PTZ: Piperacillin-Tazobactam; RFP: Rifampicin; RT-qPCR: Reverse Transcription-Quantitative Polymerase Chain Reaction; SRMA: Systematic Review and Meta-Analysis; TB: Tuberculosis; TCN: Tetracycline; TCP: Teicoplanin; TGC: Tigecycline; VAP: Ventilator-Associated Pneumonia; VCZ: Voriconazole; VNC: Vancomycin

Introduction

Since December 2019, the global dominance of coronavirus has shifted our perspectives, thoughts, and visions. It had a significant impact on billions of people globally, affecting their physical, emotional, social, and economic well-being. COVID infection may cause mild pneumonia or ARDS. Throughout the COVID pandemic, a large proportion of patients necessitated admittance to intensive care unit (ICU) for either respiratory failure or pneumonia [1,2].

The lung microbiome is an extremely complex and dynamic ecology that is unique to each individual. Ventilator-associated pneumonia (VAP) is a major issue in hospitalized patients, but determining its cause can be daunting due to limitations in standard diagnostics. The oral microbiome is important in the development of VAP, particularly by microaspiration of microbes during mechanical ventilation [3].

ARDS differentiates itself by lung inflammation and damage, which are triggered by a profusion of inflammatory cells and cytokines [4,5]. Individuals having ARDS have poorer clinical outcomes, longer hospital stays, increased healthcare costs, and higher mortality and morbidity [5]. ARDS cases surged enormously during the COVID pandemic [4,6]. With its wide range of facades, levels of severity, and upsurge in occurrence and public awareness caused by the COVID pandemic, ARDS has become a tricky condition to discern and cure [7,8].

Regardless of geography, *Staphylococcus aureus* and *K. pneumoniae* continue to be the most common pathogens for respiratory infections in people of any demographic [9]. *Acinetobacter baumannii* and *Pseudomonas aeruginosa* are other organisms responsible for a significant portion of lung infections. Some bacterial pathogens (e.g. *Pseudomonas*, *Enterobacteriaceae*, methicillin-resistant *S. aureus*) are resistant to a multitude antimicrobial drug [9,10].

A recent Systematic review and meta-analysis (SRMA) revealed a significant pooled prevalence of bacterial isolates as well as multidrug resistance in patients with respiratory infections. Because of the pertinent prevalence of antibiotic resistance, initial empirical treatment for these patients remains challenging [11]. Therefore, we mapped this study to determine the bacteriological profile and antibiotic susceptibility patterns among the hospitalized COVID patients.

Materials and Methods

This retrospective study was conducted from April 2020 to September 2021 at Kalinga Institute of Medical Sciences, India. Before commencing the study, we obtained the ethics approval from the concerned authority (KIIT/KIMS/IEC/750/2021 dated 12/10/2021). Our study included hospitalized COVID patients of either gender, with single bacterial isolates evidenced through culture reports. We excluded the patients with multiple isolates. We also excluded the admitted patients who had HIV/AIDS, pulmonary TB, cerebrovascular accident (CVA), acute myocardial infarction (AMI), organ transplantation.

For this study, we collected data from the hospital records. COVID infection was detected in all participants using a reverse transcription-quantitative polymerase chain reaction (RT-qPCR) assay. Multiple one-step quantitative RT-PCR techniques were utilized to test nasopharyngeal samples from suspected COVID patients. A clinically significant positive bacterial culture within 48 hours of admission indicated a possible bacterial coinfection. The bacterial identification and antimicrobial sensitivity testing (ID & AST) data were obtained directly from electronic health records. Two of our researchers analyzed the results of all participants with single bacterial isolates evidenced through culture reports.

All samples had been grown in the laboratory for aerobic bacterial identification and antibiotic sensitivity testing with the VITEK-2 instrument. Blood and all body fluids, apart from urine, were processed for five days in an automated blood culture system, BacTAlert, Biomeriux. When the bottles produced a positive flag signal, they were withdrawn from the device and plated in blood and MacConkey agar. Chocolate agar served as an enhanced medium for CSF samples. Pus, sputum, and other swabs were directly plated on blood agar and MacConkey agar, then incubated at 37 degrees Celsius in a 5% carbon dioxide incubator. The material was also grown in Tryptic soya broth for subculture purposes. Urine samples were treated with CLED agar. All plates were incubated overnight at 37 degrees Celsius in a 5% carbon dioxide incubator. Following incubation, colony features and Gram stain were used to identify the colonies. Catalase and oxidase assays were used for preliminary identification. VITEK-2 identified individuals using commercially accessible gram-positive and gram-negative cards. The VITEK-2 device utilized various AST cards.

For this retrospective study, we adopted convenience sampling. We used the Shapiro-Wilk test to ensure that the collected data were normally distributed. For categorical variables, frequency and proportion were used as summary statistics. We used Pearson's chi-square test to compare categorical data. The continuous data was presented using the median and interquartile range (IQR). We employed the Wilcoxon test to gauge the quantitative data. For data analysis, we used R software (version 4.4.1) [12]. All the statistical tests were two-tailed. The p-values less than 0.05 were interpreted as statistically significant.

Results

For the retrospective study, we screened a total of 2724 COVID patients hospitalized during the stipulated period. Seven-hundred thirty-eight had multiple bacterial isolates. Six others had pulmonary TB. The remaining 1980 (72.7%) subjects met the eligibility criteria. Of them, 1114 (56.3%) were females. The sociodemographic traits have been elucidated in table 1. The median age of the study population was 48.0 (38.0-62.0) years [female: 48.0 (38.3-62.8) years; male: 48.0 (38.0-61.8) years; p = 0.73]. A total of 365 participants (216 females and 149 males) were aged above 65 years. A total of 868 (43.8%) participants were admitted to ICU for assisted ventilation. The median hospital stay was 8.0 (5.0-14.0) days.

Parameter	Total (n = 1980)	Female (n = 1114)	Male (n = 866)	p-value
Age (years)	48.0 (38.0-62.0)	48.0 (38.3-62.8)	48.0 (38.0-61.8)	0.73
Age > 65 years	365 (18.4%)	216 (19.4%)	149 (17.2%)	0.03
Socioeconomic status				
Lower	322 (16.3%)	178 (16.0%)	144 (16.6%)	0.01
Lower-middle	828 (41.8%)	503 (45.2%)	325 (37.6%)	
Upper-middle	556 (28.1%)	289 (25.9%)	267 (30.8%)	
Upper	274 (13.8%)	144 (12.9%)	130 (15.0%)	
ICU requirement	868 (43.8%)	533 (47.8%)	335 (38.7%)	0.02
Hospital stay duration	8.0 (5.0-14.0)	8.0 (6.0-14.8)	8.0 (4.5-13.3)	0.62

Table 1: *The sociodemographic traits of the study population.*

The continuous and categorical variables are expressed as median (IQR) and frequency (proportion), respectively.

The age distribution of the study participants and common pathogenic bacteria are illustrated in figure 1. The most common bacteria were *Staphylococcus aureus*, *E. coli*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Streptococcus spp.*, and *Enterobacter spp.* Other pathogenic bacteria included *Burkholderia cepacia*, *Staph. haemolyticus*, *Staph. saprophyticus*, *Elizabethkingia meningoseptica*. The median age of affected individuals spanned from 40-55 years. It indicated the higher susceptibility of middle-aged individuals for the nosocomial infections.

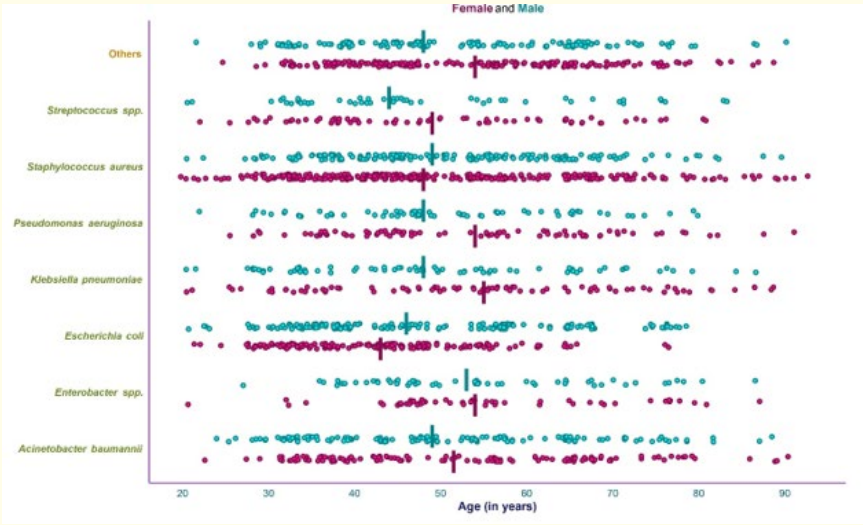

Figure 1: *Age distribution of the participants and common pathogens.*

The jitter plots demonstrate the age of the female and male participants and their pathogenic bacteria. The solid lines represent the median age of the participants.

Figure 2 showcases the bacteriological profile of the female and male participants. The most common causative bacteria in the entire study population were *Staphylococcus aureus* (517, 26.1%), followed by *E. coli* (332, 16.8%), *Acinetobacter baumannii* (260, 13.1%), *Klebsiella pneumoniae* (159, 8.0%), *Pseudomonas aeruginosa* (146, 7.4%), *Streptococcus spp.* (118, 6.0%), and *Enterobacter spp.* (110, 5.6%). The intragroup analysis yielded statistically significant difference only for *Staphylococcus aureus* ($p < 0.001$). The lowered p-value from the analysis of other bacteria could be attributed to the collective assessment of the less common bacteria. The remaining bacterial infections did not show any significant differences across the gender. Nonetheless, the intergroup analysis displayed statistically significant difference ($p < 0.001$).

The stacked bar plots demonstrate the frequency and proportions of the female and male participants with various bacterial infections. We adopted the Pearson's chi-square test for the analysis.

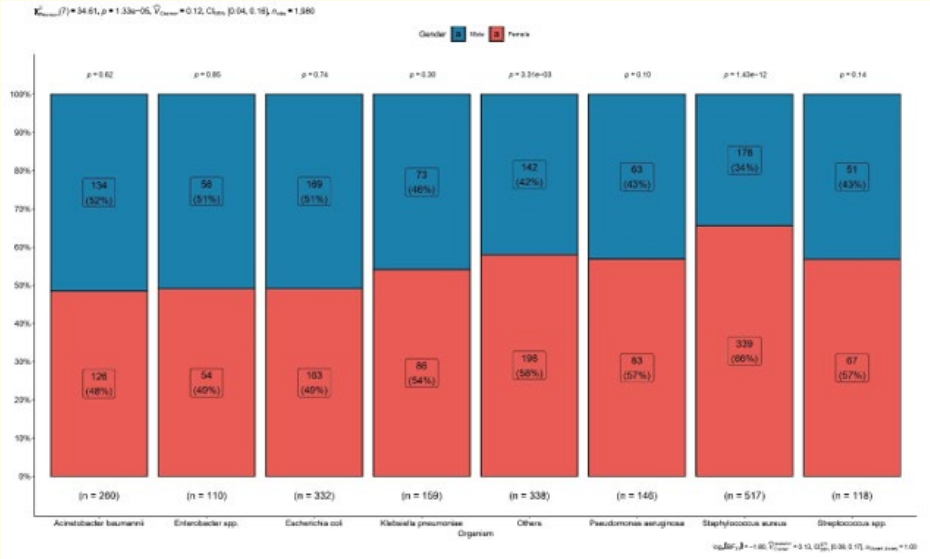

Figure 2: *Bacteriological profile of the participants.*

Figure 3 displays the incidences of pneumonia and ARDS in the study population. The majority of the participants (1341, 67.7%) had pneumonia. Of them, the highest number of cases were due to *E. coli* (270, 20%), *Staphylococcus aureus* (268, 20%), *Acinetobacter baumannii* (183, 14%). *Staphylococcus* and *Acinetobacter* also caused the maximum cases of ARDS and pneumonia-ARDS. Both intragroup and intergroup analyses yielded statistically significant differences ($p < 0.001$).

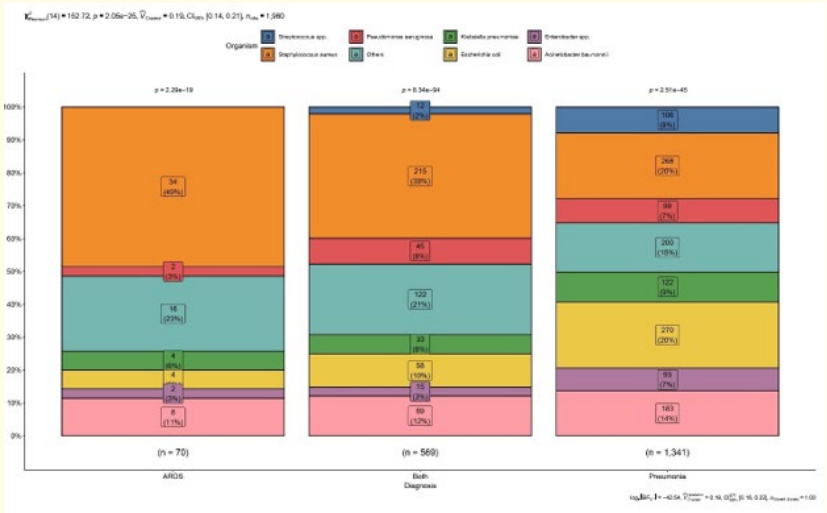

Figure 3: *Pneumonia and ARDS by various pathogenic bacteria.*

The stacked bar plots demonstrate the frequency and proportions of the study population with pneumonia and ARDS. We adopted the Pearson's chi-square test for the analysis.

Figure 4 shows the outcomes of the respiratory illnesses in the study population. The majority of the participants (1733, 87.5%) were cured with or without the requirement of ICU and ventilatory support. Hundred thirty-nine (7.0%) patients succumbed to death pertaining to their infections. The remaining 108 (5.5%) subjects left against medical advice (LAMA). *Staphylococcus*, *Acinetobacter*, and *Pseudomonas* were the most common pathogens causing mortality in the study population. Both intragroup and intergroup analyses yielded statistically significant differences ($p < 0.001$).

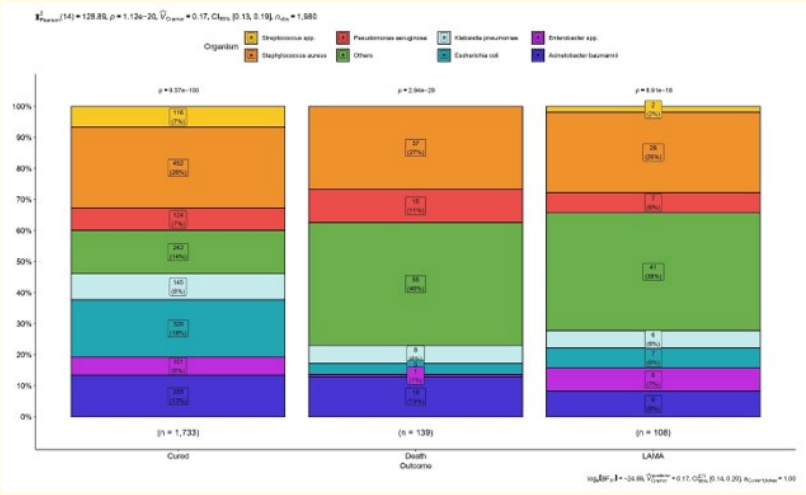

Figure 4: *Outcome of the respiratory illnesses.*

The stacked bar plots demonstrate the frequency and proportions of the study population with various outcomes. We adopted the Pearson's chi-square test for the analysis.

We assessed the antimicrobial susceptibility of the pathogens with forty common pharmaceutical agents. For the ease of assessment, we considered every drug-patient as a single unit. Hence, we analyzed a total of 79200 drug-patient combination with 1980 patients and 40 drugs. Figure 5 portrays the antimicrobial susceptibility among the study population. The reports were denoted as sensitive, resistant, intermediate, or not applicable. The most common sensitive drugs were tigecycline, gentamicin, cotrimoxazole, amikacin, cefepime, and piperacillin-tazobactam. Resistance was maximally observed with ciprofloxacin, cefuroxime, and levofloxacin. Both intragroup and intergroup analyses displayed statistically significant difference ($p < 0.001$). Figure 6 illustrates the subgroup analysis (based on gender) of the antimicrobial susceptibility among the study participants. Considering 866 males and 1114 females, we analyzed 34,640 drug-male patient combinations and 44,560 drug-female patient combinations in Figures 6a and 6b respectively. The patterns were similar irrespective of gender. We found both intragroup and intergroup analyses as statistically significant ($p < 0.001$).

The pie diagrams in plots a and b demonstrate the antibiotic susceptibility patterns in the male and female participants, respectively. We adopted the Pearson's chi-square test for the analysis.

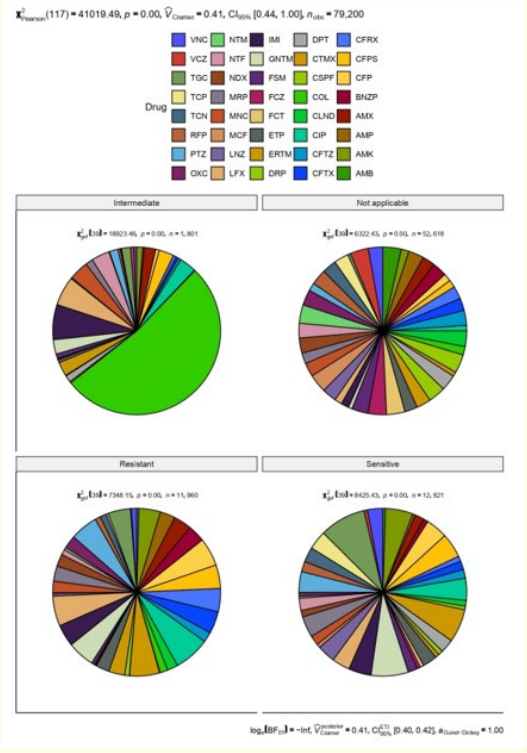

Figure 5: *Antimicrobial susceptibility pattern in the study population.*

The pie diagrams demonstrate the antibiotic susceptibility patterns in the study population. We adopted the Pearson's chi-square test for the analysis.

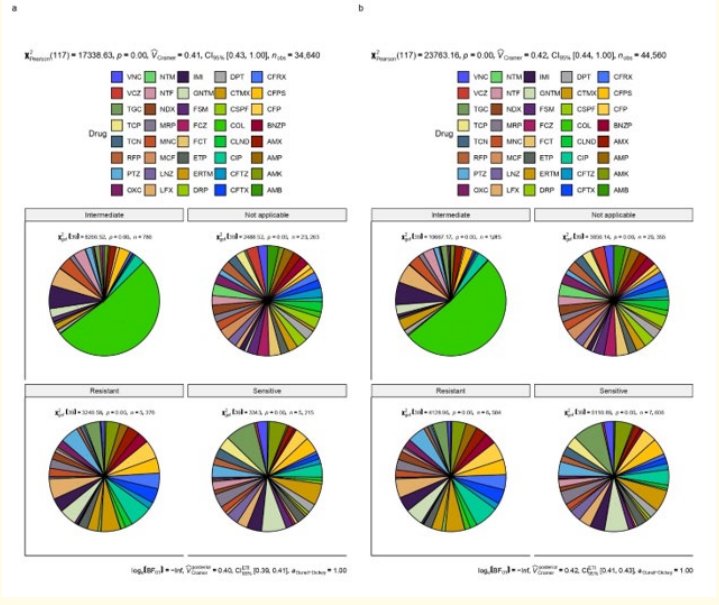

Figure 6: *Antimicrobial susceptibility patterns among male and female participants.*

Discussion

In this retrospective study, we determined the common pathogenic bacteria among the female and male patients hospitalized with COVID infection. Additionally, we analyzed the antimicrobial susceptibility patterns in the study population.

We found a slightly higher female preponderance in our study population. We also noted that middle-aged individuals were predominant in the study population. The most common causative bacteria in the entire study population were *Staphylococcus aureus* (517, 26.1%), followed by *E. coli* (332, 16.8%), *Acinetobacter baumannii* (260, 13.1%), *Klebsiella pneumoniae* (159, 8.0%), *Pseudomonas aeruginosa* (146, 7.4%), *Streptococcus spp.* (118, 6.0%), and *Enterobacter spp.* (110, 5.6%). Other pathogenic bacteria included *Burkholderia cepacia*, *Staph. haemolyticus*, *Staph. saprophyticus*, *Elizabethkingia meningoseptica*. Our study findings concorded with some recent studies [13-16].

The major chunk of our study population was cured and discharged. Nonetheless, 139 (7.0%) subjects succumbed to death. *Staphylococcus*, *Acinetobacter*, and *Pseudomonas* were the most common pathogens causing mortality in the study population. Recently published articles [17-19] supported our study findings. The average duration of hospitalization was 1-2 weeks. This finding matched with that of a lately conducted research [2]. Our observations regarding the antimicrobial susceptibility patterns were backed by the studies by Santella., *et al*. [20] and Chung., *et al*. [21].

Our study could have been improved in some ways. First, the sample size was small as excluded the patients with multiple bacterial isolates. Second, we did not analyze the duration of hospitalization, treatment history, and comorbidities. Third, our study findings lack generalizability as we focused only on respiratory illnesses of bacterial origin. Fourth, we did not evaluate any other clinical parameters of the participants with the antimicrobial susceptibility.

Conclusion

Respiratory ailments pertaining to pathogenic bacteria affected middle-aged people. The most common culprits were *Staphylococcus aureus*, *E. coli*, *Acinetobacter baumannii*, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa*. Less common pathogenic bacteria were *Burkholderia cepacia*, *Staph. haemolyticus*, *Staph. saprophyticus*, *Elizabethkingia meningoseptica*. *Staphylococcus*, *Acinetobacter*, and *Pseudomonas* contributed maximum towards the mortality in the study population. The most common sensitive drugs were tigecycline, gentamicin, cotrimoxazole, amikacin, cefepime, and piperacillin-tazobactam. Resistance was maximally observed with ciprofloxacin, cefuroxime, and levofloxacin. We suggest prospective studies with larger sample sizes and longer study durations to generalize our study findings.

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Conflict of Interest

The authors declare that there is no conflict of interest.

Funding Source

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