Original Article

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Antibiotic Resistance Pattern in Respiratory Tract Infection during COVID-19 Era

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Abstract

Background: Respiratory Tract Infection (RTI) is a very common disease in our country. Bacterial infections in the respiratory tract causing significant morbidity andmortality in hospitalized patients. Information on the prevalence of bacterial infection in RTI in our health care settings is lacking. Moreover, the injudicious use of antibiotics often leads to antibiotic resistance which is an emerging problem. The objective of this study was to determine the prevalence of bacterial infections and antibiotic resistance patterns in pathogens isolated from the sputum samples of admitted patients suffering from RTI in a tertiary care teaching hospital in the Coronavirus Disease (COVID-19) era.

Materials and methods: In this cross-sectional study 104 patients who were admitted to the Medicine Department of Chittagong Medical College Hospital with a diagnosis of RTI from February 2021 to June 2021 were included. Bacterial isolates from the sputum culture were confirmed by the standard microbiological methods. Antibiotic resistance was determined by using the disk diffusion method.

Results: Out of 104 processed sputum samples 92 (88.5%) cases had established bacterial etiology. Klebsiella (45.2%) was the most common organism followed by Pseudomonas (17.2%) and Acinetobacter (14.4%). In antimicrobial susceptibility testing, Imipenem and meropenem were sensitive against Klebsiella. Ciprofloxacin, levofloxacin, imipenem, meropenem and piperacillin were sensitive against Pseudomonas. Acinetobacter was highly resistant to ceftriaxone.

Conclusions: The resistance pattern varied for different organisms. Therefore, appropriate identification of the causative organisms and their antibiotic resistance is crucial for the right choice of antibiotic therapy in LRTIs.

Key words: Antibiotic resistance; Bacterial isolates; Lower respiratory tract infection.

Introduction

There is no question that Antimicrobial Resistance (AMR) poses a significant public health threat on a national and global scale. COVID-19 has made the most serious public health emergency in our lifetime. As these two threats intersect, there are early indications of antibiotics that the COVID-19 pandemic may intensify antibiotic resistance.[1] Empirically use of a huge number of antibiotics will lead to the development and spreading of AMR, which is a serious health issue whole over the world. One of the vital recommendations to overcome this mess is to optimize antibiotic use by guiding that the prescribed antibiotic is administered at the precise dose, for the appropriate duration and in such a way that ensures the best outcome and minimizes side effects and antimicrobial resistance. These are the crucial measures of antimicrobial stewardship programs.[2]

According to the WHO, Globally, up to 11 February 2021, there have been 106,797,721 confirmed cases of COVID-19, including 2,341,145 deaths, reported to WHO.[3] In Bangladesh Coronavirus cases 539531, death 8248, recovered 485971 up to 11 Feb 2021.[4] t is easy to understand that what a devastating situation is going on in our health sector and throughout the world. Influenza-like illness, dry cough, sore throat, malaise, myalgia, arthralgia, nasal congestion, sneezing and runny nose are the most common presenting features in COVID-19. Although some unusual presentations also reported including abdominal pain, loss of appetite, vomiting, diarrhea, altered taste sensation and ageusia, bilateral pneumonia, radiological lung consolidation, altered liver function, acute kidney injury, neurological manifestations, and vascular (venous and arterial) thrombosis.[5-7]

Over 80% of hospitalized COVID-19 patients have been treated in general medical wards. A very small number of patients with more severe

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disease who has developed ARDS require additional non-invasive or invasive ventilatory support. They are required to be admitted in high dependency or Intensive Care Units (ICUs).[8]

During the pandemic, clinical uncertainty around the management and treatment of COVID-19 has contributed to the inappropriate prescription of antibiotics. The disease often presents itself like bacterial pneumonia, in the case of severe COVID disease different types of injectable antibiotics have been prescribing according tothe national guideline or physician's experience.[2,8]

Antibiotic resistance has been recognized as increasingly inappropriate use of antibiotics causing alarming global health threats, the current pipeline of antibiotics in development is dwindling.[9] More investment in research and development is needed to ensure those novel antibiotics are brought to market to meet current and future patient needs. Given a decline in novel antibiotics, it is even more critical to ensure that we are using the life-saving drugs appropriately or not in the COVID era especially in the respiratory tract infection.[10]

This cross-sectional study was organized to assess the antibiotic resistance pattern of sputum culture-positive bacterial isolates that were tested in different laboratories of Chattogram city including the Microbiology Department of Chittagong Medical College. We aimed to assess bacterial growth in sputum, to identify the spectrum of organisms responsible for infection in our geographical area, and to evaluate the pattern of antibiotic susceptibility of those organisms.

Materials and methods

This cross-sectional study was conducted in the Department of Medicine of Chittagong Medical College Hospital (CMCH) in Chattogram city, Bangladesh from February 2021 to June 2021. One hundred and four adult patients hospitalized with RTI into the CMCH during the study period diagnosed on the basis of presenting symptoms, laboratory parameters and radiological findings were included in the study. COVID-19 cases were not included in this study. Unconscious patients unable to give sputum and patients who refused to participate in the study were excluded. Ethical approval was taken from the Ethical Review Committee of Chittagong Medical College. Written consent was obtained from the patients after explaining the detailed study procedure.

Data on socio-demographic characteristics, clinical features, risk factors, and comorbid conditions were collected through a structured case record form. Variables are age, sex, The sputum samples were collected and processed for culture and sensitivity testing in the Department of Microbiology. The cultured plates were examined after 24 hours and the reports of culture and sensitivity testing of the samples were collected. The results were interpreted according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI). Antibiotic susceptibility of the isolates was determined by the modified Kirby-Bauer disc diffusion method, according to CLSI recommendations. The zones of inhibition were measured and the organisms identified as sensitive or resistant based on standard criteria.[11] Organisms were identified by their colonial morphology, Gram staining, and appropriate biochemical tests using standard techniques. [11]

Data were entered in a Microsoft Excel Sheet. Results were expressed as frequency and percentages. Appropriate graphs and Tables were used to present the results.

Inclusion criteria:

i) Hospitalized RTI patients who can give sputum.
ii) Age≥18 years of age.

Exclusion criteria:

i) Who will not give the consent for collection of sputum
ii) Who is unable to give the sputum including unconscious patients
iii) Age below 18 years of age.

Results

Out of 104 included patients about one-third (33.7%) were in the geriatric age group. The majority were male and came from rural areas. The socio-demographic characteristics of the patients are shown in Table I.

Table I Sociodemographic characteristics of the patients (n=104)

Variables		Frequency	Percentage (%)
Age	≤60 years	69	66.3
	>60 years	35	33.7
Sex	Male	59	56.7
	Female	45	43.3
Residence	Rural	68	65.4
	Urban	36	34.6
Socioeconomic class	Upper lower	74	71.2
	Lower middle	21	20.2
	Upper middle	9	8.7

Out of 104 patients, 18 (17.3%) were malnourished and another 32 (30.8%) were obese. One-fourth of the patients reported smoking in the past and 17.3% were current smokers. The most common comorbid condition was hypertension (36.6%) followed by chronic obstructive pulmonary diseases or asthma (32.6%), diabetes mellitus (28.8%) and ischemic heart disease (13.8%) (Table II).

Table II Risk factors and comorbidity pattern of the patients (n=104)

Variables	Frequency	Percentage (%)
Malnourished[a]	18	17.3
Obese[b]	32	30.8
Ex-smoker	26	25.0
Current smoker	18	17.3
Any comorbidity[c]	72	69.2
Hypertension	38	36.6
Diabetes mellitus	30	28.8
COPD/Asthma	37	35.6
Ischaemic heart disease	14	13.8
Chronic kidney disease	4	3.8
Malignancy	6	5.8
Tuberculosis	9	8.7

[a]Body mass index <18.5 kg/m^2; [b]Body mass index ≥25.0 kg/m^2, [c]Reported by the patients.

Out of 104 samples majority of the sample (92/104, 88.6%) yield positive growth in sputum culture (Figure 1).

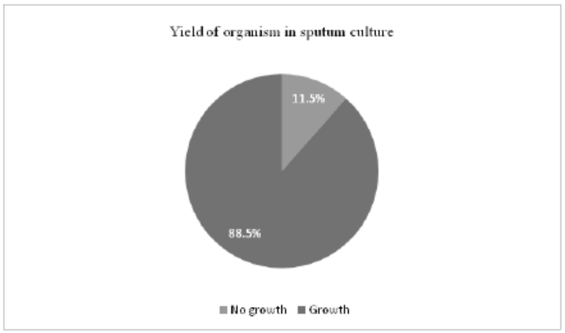

Fig 1 Yield of an organism in sputum culture (n=104)

Klebsiella (45.2%) was the most frequently isolated bacteria, followed by Pseudomonas (17.3%) and Acinetobacter (14.4%) and. The common pathogens that were isolated from the sputum sample are shown in Table III.

Table III Common pathogens in sputum samples (n=104)

Organisms	Frequency	Percent (%)
Klebsiella	47	45.2
Pseudomonas	18	17.3
Acinebacter	15	14.4
Enterobacter	5	4.8
E. coli	3	2.9
MRSA	2	1.9
Seratia mercescens	2	1.9

The antibiotic sensitivity pattern of Klebsiella is shown in Table IV. Out of 47 sputum samples with Klebsiella, ciprofloxacin was given in all samples. Among those samples, the majority (74.5%) were resistant to ciprofloxacin. Amoxiclav, cefuroxime, ceftriaxone and meropenem were given in 44 sputum samples. Among those only meropenem showed good sensitivity (80.9%) against klebsiella. Other than meropenem, only imipenem had good sensitivity against Klebsiella (80%). Isolated Klebsiella organisms were mostly resistant to cefuroxime, ceftriaxone, amoxicillin, cefixime, levofloxacin, doxycycline, tetracycline and azithromycin.

Table IV Sensitivity pattern of Klebsiella (n=47)

Drug's Name	Total sputum sample	Resistance	Sensitive	Intermediate
Ciprofloxacin	47	35 (74.5)	7 (14.9)	5 (10.6)
Amoxi-clav	44	30 (68.2)	6 (13.6)	8 (18.2)
Cefuroxime	44	38 (86.4)	3 (6.8)	3 (6.8)
Ceftriaxone	44	30 (68.2)	13 (29.5)	1 (2.1)
Meropenem	44	4 (9.1)	38 (80.9)	2 (4.5)
Amoxicillin	42	29 (69.1)	5 (11.9)	8 (19.0)
Piperacillin	7	4 (57.1)	3 (42.9)	0 (0)
Cefixime	6	6 (100.0)	0 (0)	0 (0)
Imipenem	5	0 (0)	4 (80.0)	1 (20.0)
Levofloxacin	5	4 (80.0)	0 (0)	1 (20.0)
Doxicycline	4	3 (75.0)	1 (25.0)	0 (0)
Tetracycline	3	3 (100.0)	0 (0)	0 (0)
Nitrofurantoin	2	2 (100.0)	0 (0)	0 (0)
Azithromycin	2	0 (0)	0 (0)	2 (100.0)

The antibiotic sensitivity pattern of Pseudomonas is shown in Table V. Out of 18 sputum samples with Klebsiella, ciprofloxacin, levofloxacin, imipenem, meropenem, and piperacillin were given in 17 samples. Among those samples, the majority showed good sensitivity (>75%) against pseudomonas. Though tested in a few samples, pseudomonas was highly sensitive to amoxiclav, amoxicillin, azithromycin, cefuroxime, and cefixime.

Table V Sensitivity pattern of Pseudomonas (n=18)

Drug's Name	Total sputum sample	Resistance	Sensitive	Intermediate
Ciprofloxacin	17	3 (17.6)	13 (76.5)	1 (5.9)
Levofloxacin	17	3 (17.6)	14 (82.4)	0 (0)
Imipenem	17	3 (17.6)	13 (76.5)	1 (5.9)
Meropenem	17	3 (17.6)	13 (76.5)	1 (5.9)
Piperacillin	17	3 (16.7)	14 (77.8)	0 (0)
Amoxi-clav	5	1 (20.0)	4 (80.0)	0 (0)
Ceftriaxone	2	1 (50.0)	1 (50.0)	0 (0)
Amoxicillin	1	0 (0)	1 (100.0)	0 (0)
Azithromycin	1	0 (0)	1 (100.0)	0 (0)
Cefuroxime	1	0 (0)	1 (100.0)	0 (0)
Cefixime	1	0 (0)	1 (100.0)	0 (0)

Discussion

A lot of antibiotics has been used empirically in hospitalized and community-based COVID patient whole over the country. In COVID, the primary target organ is lungs and upper airway, there could be a strong chance of antibiotic resistance in RTI. We wanted to see bacterial infections and antibiotic resistance in our RTI patients which would reduce drug burden and will help to select an appropriate antibiotic in respiratory tract infection in the COVID era.

The present study showed the types of bacterial pathogens and the antibiotic sensitivity pattern of these pathogens isolated from sputum samples of admitted patients suffering from RTI. Klebsiella was the predominant microorganism isolated from these samples (45.2%). Klebsiella was also found as a predominant organism in studies done by Debnath et al, Ahmed et al, Promite et al and Manikandan et al showing 52.3%, 59.7%, 42.5%, and 28.4% frequency respectively.[12-15] Another previous study which was conducted in the same institution two years before also reported that Klebsiella was the most commonly isolated organism from the sputum samples of hospitalized patients with community-acquired pneumonia.[16]

In this study, the other common isolated pathogens were Pseudomonas (17.3%) and Acinetobacter (14.4%). This finding correlates with the findings of Mohammad et al showing the prevalence of pseudomonas to be 10.3%. Debnath et al showing prevalence of Acinetobacter (13.49%) and Pseudomonas were 13.5% and 13.2% respectively.[16,12] Ali et al showing the prevalence of Acinetobacter and Pseudomonas to be 13.69% and 35.35% respectively.[17] Agarwal et al also found Acinetobacter and Pseudomonas as commonly encountered pathogens and the prevalence was 34.8% and 23.9% respectively.[18]

Mythri et al reported that the most common pathogen was Klebsiella spp followed by S. pneumoniae and P. aeruginosa.[19] These findings indicate that RTI by Gram-negative organisms constitutes a significant burden in our locale and the spectrum of organisms is subject to geographical alternations.

Gram-positive organisms were less commonly isolated in the present study and only 2 (1.9%) samples yield growth of MRSA. Our finding was in agreement with the findings of Mohammad et al but disagreed with an earlier study conducted in Dhaka, Bangladesh.[16,20] Among 64 bacterial isolates, six different types of bacteria were recognized. A greater number of the isolates were gram-positive cocci, i.e 89.06% and 10.93% were Gram-Negative Bacilli (GNB) in their study.[20] This indicated that microorganism pattern varies from time to time and from place to place. So, constant surveillance is mandatory to promptly identify any changing pattern.

In this study, Klebsiella was highly sensitive to meropenem and imipenem. Similarly, Mohammad et al also observed isolated Klebsiella strain was mostly resistant to commonly used antibiotics for community-acquired pneumonia-likeAmoxicillin-Clavulanate, Cefixime, Cefuroxime, clarithromycin and Ceftazidime Ullah et al also reported Klebsiella spp was mostly resistant to ceftriaxone, ceftazidime and amoxicillin (100%).[16,20] On the other hand isolated Klebsiella organisms were mostly resistant to ciprofloxacin, cefuroxime, ceftriaxone, amoxicillin, cefixime, levofloxacin, doxycycline, tetracycline and azithromycin. In contrast, a recent study from India reported that Klebsiella was sensitive to amikacin, imipenem, gentamycin, gatifloxacin, levofloxacin, ciprofloxacin, piperacillin/tazobactam and cefuroxime.[12] These findings in our setting were alarming, as meropenem and imipenem are costly and also not recommended for lower respiratory tract infections.[21]

Regarding the sensitivity pattern of Pseudomonas, present study indicated that ciprofloxacin, levofloxacin, imipenem, meropenem and piperacillin showed good sensitivity against pseudomonas. Though tested in a few samples, pseudomonas was highly sensitive to amoxiclav, amoxicillin, azithromycin, cefuroxime, and cefixime. In contrast, Mohammad et al observed pseudomonas were highly resistant to Amoxicillin-Clavulanate, Cefixime, Cefuroxime and clarithromycin.[16] Ullah et al stated that for pseudomonas isolates azithromycin, cotrimoxazole, gentamycin were the most effective (100% sensitivity) antibiotics and amoxicillin was the least effective one (0% sensitivity).[20] Similarly, in the study of Debnath et al Pseudomonas was found to be sensitive to imipenem (83.72%), piperacillin/tazobactam (83.72%), gentamycin (84.85%) ceftazidime/clavulanic acid (79.41%) ceftazidime (67.44%) and ticarcillin/clavulanic acid (61.54%).[12]

The antibiotic sensitivity pattern of the Acinetobacter was variable in the present study. none of the tested antibiotics showed good sensitivity against acinetobacter in the current study, 60%of the Acinetobacter were sensitive to levofloxacin and 53.3% were sensitive to ciprofloxacin and imipenem. All of them were resistant to ceftriaxone. Debnath et al reported acinetobacter was sensitive to many antibiotics e.g imipenem, piperacillin/tazobactam, cefuroxime but the association was not significant. Rather, ceftriaxone was found to be resistant to 76.47% of samples of Acinetobacter which was statistically significant.[12] Nepal et al in their study also found that Acinetobacter to be resistant to multidrug like amoxicillin, cefixime, ciprofloxacin, azithromycin.[22] Whereas ceftazidime, cefepime, gentamicin, etc. were found to be resistant to Acinetobacter by Thomas et al.[23]

Many bacterial and viral pathogens causing RTI have been identified in different studies. Incidence and prevalence data differ between studies for several reasons. First, the true incidence of the various pathogens can vary according to the geographical setting or the population included. Secondly, the recovering rate of specific pathogens is influenced by the specific diagnostic means that were used. This study was conducted over a short period. A larger multicentre study will need to be carried out to obtain accurate information on the epidemiology of RTI in this area of Bangladesh.

Limitation

The study population was selected from a single center. So, The results of the study does not reflect the exact picture of the country.The Sample size was small. A large sample size could give us more generalizability of the findings.

Conclusions

The study was conducted to analyze the antimicrobial sensitivity pattern of bacteria isolated from the sputum samples in a tertiary hospital of Chattogram. The commonest pathogens isolated from the sputum samples were Klebsiella followed by Pseudomonas, and Acinetobacter Imipenem and meropenem were sensitive against Klebsiella. Ciprofloxacin, levofloxacin, imipenem, meropenem, and piperacillin were sensitive against Pseudomonas. Acinetobacter was highly resistant to ceftriaxone.

Recommendation

Large scale multi centered studies can be carried out over prolong period of time involving large number populations of different socioeconomic background may provide more precise information.

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Contribution of authors

MAS-Acquisation of data, interpretation of data, drafting and final approval.

RB- Design, Acquisation of data, analysis, critical revision of content and final approval.

EH-Conception, drafting and final approval.

EEU- Design, interpretation of data, critical revision and final approval.

MHA- Interpretation of data, drafting of article and final approval.

MNK-Design, interpretation of data, critical revision and final approval.

MC-Conception , drafting and final approval.

MASC- Acquisationof data, drafting the article, critical revision of content and final approval.

Disclosure

All the authors declare no competing interest.

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