Original Article

Bacterial Infections in Covid-19 Patients Admitted in Intensive Care Units of a Tertiary Care Hospital

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Abstract

Objective: To detect presence of bacterial infections in RT-PCR confirmed Covid-19 patients.

Methods: This is a retrospective study of the data from 246 RT-PCR confirmed Covid-19 patients, admitted to ICUs of Mayo Hospital, Lahore from 1st April 2020 to 30th September 2020 and conducted in the department of Pathology, King Edward Medical University, Lahore. Bacterial infections were determined by characteristic clinical features and positive bacterial cultures. The data was extracted from the record of ICUs of Mayo hospital and Microbiology laboratory record with a standardized data collection form. The ethical approval was obtained from institutional review board of King Edward Medical University, Lahore.

Results: Bacterial infections were detected in 32.5% patients. Tracheal secretions were the most frequent source, representing 51.3% of all the infections, followed by pus 16.2%, urine 13.5%, blood 12.1%, pleural fluid 4%, sputum and cerebrospinal fluid (CSF) constituting 1.3% Klebsiella pneumoniae was the most frequently isolated organism (28.4%), followed by Pseudomonas 24.4%, Eschericia coli 22.9%, Staphylococcus aureus 8.1% and Acinetobacter baumanii 8.1%, Citrobacter freundii 6.8%, Salmonella typhi 1.3%. Bacterial infections were frequent in age group 60-70 years.

Conclusion: Bacterial infections in patients of Covid-19 are not uncommon. These can lead to increased morbidity and mortality.

Keywords: Bacterial infections, COVID-19, Severe acute respiratory syndrome (SARS), Intensive care units (ICUs).

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Introduction

Severe acute respiratory syndrome corona virus-2 (Covid-19) is a newly emerged viral infection. Viral-bacterial co-infections are one of the key medical concerns, leading to increased morbidity and mortality rates.[1] Secondary and co-bacterial infections particularly with Streptococcus pneumonia were responsible for most of the fatalities during the influenza outbreak of 1918. The increased mortality in the 2009 H1N1 Influenza pandemic was also associated with bacterial co-infections. 20-30% of patients presenting with influenza have superimposed bacterial infections.[2] Similarly, children suffering from respiratory syncytial virus infections are more prone to superimposed bacterial pneumonia in more than 30% of the cases.[3] The importance of bacterial co-infections in the severity of respiratory diseases is well established but despite that their association and outcomes are not well studied during large outbreaks of respiratory viral infections.[4]

Langford et al. differentiated bacterial co existing infections from secondary infections. Variable results

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were reported in a meta-analysis of 3448 hospitalized patients from 28 studies in Asia. Eight (8) studies described secondary bacterial infections developed during hospitalization while 20 studies showed bacterial co-infections.[5] Klebsiella pneumoniae. Eschericia.coli, Pseudomonas, Acinetobacter, Hemophilus influenzae, Serratia, Enterobacter cloacae, Methicillin resistant Staphylococcus aureus (MRSA), Methicillin sensitive Staphylococcal aureus (MSSA) were the isolated organism according to a study.[6]

There are certain important limitations of the studies investigating bacterial infections in Covid-19 patients. Existing data available on bacterial infections in Covid-19 patients is scanty both geographically and temporally all over the world. This fact highlights the importance of more data analysis on coexisting bacterial infections to highlight their significance in Covid-19 mortality and morbidity.[7]

As no comprehensive data is available on the subject in our set up too and this knowledge gap has important implications, so the present study was conducted to get an estimate of bacterial infections in patients admitted in ICUs of Mayo hospital, Lahore.

Methods

A retrospective analysis of all the PCR confirmed patients of Covid-19, admitted in ICUs of Mayo Hospital, Lahore from 01.04.2020 - 30.09.2020 conducted at Department of Pathology, King Edward Medical University/Mayo hospital Lahore. Patients of all ages and both genders with symptoms of respiratory and non-respiratory bacterial infections were included. Suspected cases of Covid-19 and patients admitted in ICUs for non-Covid-19 conditions were excluded.

Data was obtained and extracted by one reviewer and was cross checked by another reviewer. The patient's identification done by using the admission record of all patients with Covid-19 infection, admitted to Mayo hospital ICUs. Demographic factors including age, gender, and clinical factors, including comorbid conditions like hypertension, diabetes, asthma, chronic obstructive pulmonary disease was noted from medical records of ICUs.

Laboratory data was extracted from Microbiology laboratory record with a data collection form especially designed proforma for this purpose. The ethical approval was obtained from institutional review board of King Edward Medical University, Lahore.

Statistical analysis

Categorical variables like gender, comorbid conditions, sample type and bacterial growth were expressed as percentages. Continuous variables like age, were analyzed and expressed as mean. Categorical variables like gender, comorbid conditions (like diabetes, hypertension, and asthma), sample type (source of sample) and bacterial growth were compared by using chi-square ($\chi2$) test. The 95% confidence interval with a p-value of < 0.05 was considered statistically significant. The SPSS software version 23.0 for windows was used for statistical analysis.

Results

Total 339 patients tested positive via RT PCR for Covid-19 were evaluated. We included total 246 patients after excluding the 93 patients with incomplete record. The patient age ranged from 32 -74 years. The mean age $\pm$ SD was 5.83 ± 11.84. Male to female ratio was 2:1. The comorbid conditions recorded were diabetes, hypertension, chronic obstructive disease, and asthma. One hundred twenty three covid-19 patients (50%) had Diabetes mellitus and hypertension was found in 175 Covid-19 patients (70%). Chronic obstructive disease and asthma were seen in 15 of the 246 Covid-19 patients (21%). The concomitant bacterial infection was seen in 74 Covid-19 patients (32.5%).

Respiratory secretions were the most frequent source, representing 52.3% of all the co-infections, followed by pus 16.8%, urine 13.5%, blood 12.1%, pleural fluid 4% and last of all sputum and CSF constituting 1.3%. The most frequent organism isolated was Klebsiella pneumoniae 28.3%, followed by Pseudomonas aeruginosa 24.3%, Escherichia coli, 22.9, Staphylococcus aureus 8.5% and Acinetobacter baumanii 8.0%, Citrobacter freundii 6.7%, Salmonella typhi 1.3%. In present study bacterial coinfections were found to be more prevalent in age group 60-70 years.

Discussion

This single center study analyzing the data retrospectively determined that coexisting bacterial infections in patients with Covid-19 is not uncommon especially in patients admitted in ICUs. Currently, there is inadequate data about bacterial co-infections in Covid-19 across the world.

In our study the rate of bacterial co-infection was found in 74 patients out of 246(32%). The results of study conducted in Washington revealed that bacterial co-

infection was present in 4.8% of the patients.[8] This is relatively lower to the coinfection rate calculated in our study (32.5%). Most of the studies from China and Spain shown equally lower coinfection rates.[9,10,11,12] In another metanalysis, only 7% admitted patients in intensive care units and non-intensive care units' Covid-19 patients showed bacterial concurrent infection.[13] The most suitable explanation for this difference in bacterial co-infections is a comparatively sicker patient population with hypertension and diabetes mellitus. Half of the (50%) patients had diabetes and 70% showed hypertension while 21% were having chronic obstructive disease and asthma in our study. Patients with cardiorespiratory and metabolic comorbidities are predisposed to bacterial co-infections while suffering from viral infections, due to a dysfunctional and dys-regulated immune response. It is a well-known fact that Diabetes mellitus itself down regulate effective T cell and neutrophil reaction.[14] As a result, ineffective chemo taxis, decreased bactericidal activity of neutrophils/ macrophages and defective phagocytosis leads to diminished innate immune response, causing suscep-tibility to secondary bacterial infection.[15]

Respiratory bacterial co-infections were the most fre-quently observed infections in COVID-19 patients admitted in ICUs in our study. Our study identified Klebsiella pneumoniae as the most frequent respiratory pathogen, followed by Pseudomonas, Escherichia coli, Staphylococcus aureus, Citrobacter and Acinetobacter as the less commonly isolated respiratory pathogens.

While other studies reported Haemophilus influenzae, Mycoplasma pneumoniae and Pseudomonas aeruginosa.[16] Skin Infections were the 2nd common bacterial infec-tions in Covid-19 ICU admitted patients constituting 16.2% with bacterial profile of Pseudomonas aerugi-nosa, Klebsiella pneumoniea, Eschericia coli, Acine-tobacter, Staphyloccocus Aureus. UTIs constituted 13.5% of all the infections with Eschericia coli as the most common organism. Rest of the spectrum comprised of Klebsiella pneumoniae and Pseudomonas aeruginosa.

The organisms isolated in UTIs can be due to a variety of conditions varying from asymptomatic bacteriuria, lower urinary tract infections to acute pyelonephritis. It has been studied that predisposition to such infections can point toward a malfunctioning primary mucosal immune system with subsequent inability to discrimi-nate and build a response to commensal bacteria.[17] Relatively higher incidence of diabetes mellitus in our study may be another probable justification for increased

rates of urinary tract infections in the studied popula-tion. Furthermore, it was observed in our study that patients who had bacterial infections were relatively older. The elderly population is known to have amplified proinflammatory cytokines and reduced anti-infla-mmatory cytokines. Other age-related pathophysio-logical processes providing explanation to our results are modification of angiotensin converting enzyme-2(ACE-2) receptors' expression, altered autophagy and increased production of reactive oxygen species.[18]
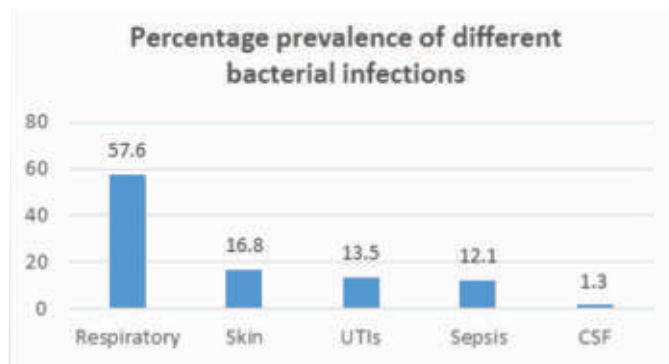

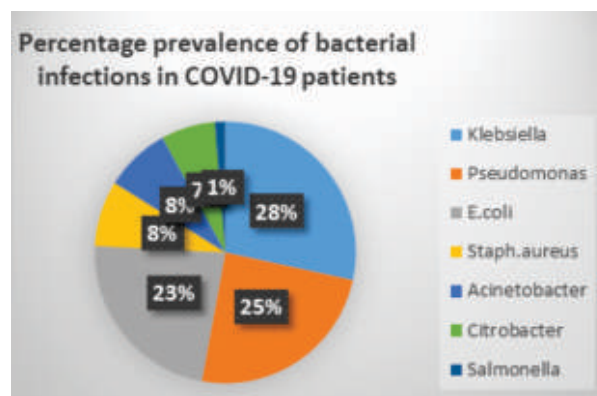**Figure.1** *Percentage Prevalence of different Bacterial Infections in Covid-19 Patients.*

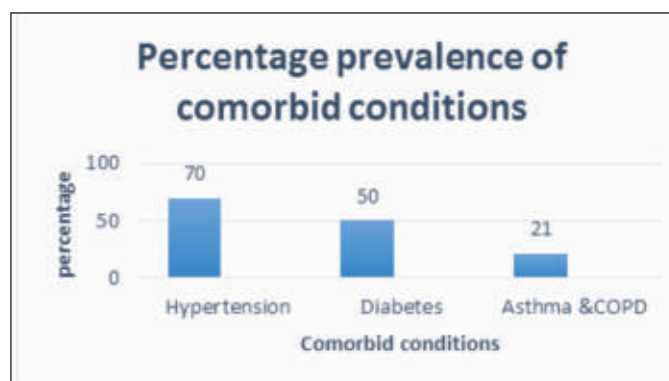**Figure.2** *Percentage Prevalence of Bacterial Infec-tions in Covid-19 Patients*

Figure.3 *Percentage Prevalence of Comorbid Conditions*

Limitation of the study

Though this study was conducted in a big tertiary care hospital, but it was a single center study limiting the sample size. The studied population was predominantly from Lahore and only patients admitted in ICUs were included in study, thus limiting the generalizability of the data.

Conclusion

Concomitant bacterial infections in patients with COVID-19 are not uncommon among the Covid-19 patients admitted in intensive care units.

Strengths of the study and recommendations

As the study determined that concomitant bacterial infections are common especially among Covid-19 patients admitted in ICUs, this finding highlighted the importance of the culture surveillance of such bacterial infections. Therefore, it is recommended that suspected cases must be confirmed through bacterial culture surveillance so that patients can be managed timely and appropriately for bacterial infections.

More prospective multicenter studies with large sample size, including all the admitted Covid-19 patients in hospital can be conducted to get further clarity on the topic.

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Authors Contribution

Q.U.I.: Conceptualization of Project,
Q.U.I, R.S, S.A.: Data Collection, Review
Q.U.I, S.A.: Literature Search
Q.U.I, S.A, R.D.: Statistical Analysis, Review
Q.U.I.: Writing of Manuscript