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Prevalence of Bacterial Co-infections among Patients admitted with COVID-19

Hina Sabir[1]✉**, Syed Ali Abbas**[2]**, Wania Shahid**[1]**, Amna Khalid**[1]

[1]Department of Internal Medicine, Ziauddin University Hospital North Campus, Karachi – Pakistan [2]Department of Respiratory Medicine and Critical Care, Ziauddin University Hospital North Campus, Karachi – Pakistan

Corresponding Author:
Hina Sabir
Department of Internal Medicine,
Ziauddin University Hospital North Campus,
Karachi – Pakistan
Email: drhinaimran281@gmail.com

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ABSTRACT

Background: A respiratory disease with variant SARS-CoV-2, which was later names as corona virus was first detected in city of China, Wuhan in the end of the year 2019 that rapidly transmitted across the world. The disease could turn into a serious condition in some of the patients who requires hospital care with mechanical ventilation support in nearly 5-15%. Approximately 10% of the infected patients required hospital admission due to thrombotic events, developing pneumonia or co-infections.

Objective: To ascertain the pattern of bacterial co-infection in patients admitted with COVID-19 in a tertiary care hospital in Karachi, Pakistan.

Methodology: This was Prospective, observational study conducted at Ziauudin Hospital Karachi during April 2021-June 2022. This study included COVID-19 patients those were admitted with COVID-19 in a tertiary care hospital in Karachi, Pakistan. All of the patients were investigated after confirmation of COVID-19 through real-time polymerase chain reaction test. Detailed history including comorbidity, smoking status and presenting symptoms was noted at the time of hospital admission. Blood and urine specimens were taken according to the hospital protocol.

Results: Total 99 patients were studied with mean age of 60.7 ± 15 years. Majority of the admitted patients were males (43.5%), non-smokers (85.9%) and had comorbidity (76.8%). More than half of the patients had co-infections (77.8%) with total 116 detected microorganisms. Out of 77.8% patients having infections other than SARS-CoV-2, the most frequent organisms isolated were, Candida albicans (44.2%), Escherichia coli (41.6%), Coagulase negative staphlylococcus (35.1%), Klebsiella species (7.8%), Proteus mirabilis (5.2%), Group D streptococcus (5.2%), Enterobacter (2.6%), Pseudomonas aeruginosa (2.6%), Acinetobacter (2.6%), Baccilus (1.3%), Enterococuss species (1.3%), Stenotrophomonas Maltophilia and Staphylococcus Aureus.

Conclusion: The present study analyzed that in addition to gram positive and gram-negative bacterial infections, fungal infections were also coexisting in COVID-19 patients in Karachi Pakistan. Patients with increasing age were more prone to have co-infections.

Keywords: SARS-CoV-2; COVID-19; Antibiotic resistance; Bacterial infections; Respiratory diseases

Introduction

A respiratory disease with variant SARS-CoV-2, which was later names as corona virus was first detected in city of China, Wuhan in the end of the year 2019 that rapidly transmitted across the world.[1] The disease could turn into a serious conditions in some of the patients who requires hospital care with mechanical ventilation support in nearly 5-15%.[1,2] Approximately 10% of the infected patients required hospital admission due to thrombotic events, developing pneumonia or co-infections.[3]

Bacterial co-infection is a frequently occurring problem in viral respiratory tract infections leading to higher burden of morbidity and mortality.[4] Collectively, existence of co-infections further complicate the respiratory disease and are linked to severe outcomes such as respiratory failure, extended ICU stay, higher likelihood of shock and death.[5]

The point of focus for a physician is to take decision on starting right antibiotics after hospital admission. More than 90% of critical cases of COVID-19 receive antibiotic therapy in their ICU stay across the globe.[6] Further, distribution of infection varies from region to region so it of utmost important to develop understanding regarding the distribution of coexisting infection in COVID-19 locally for initiating proper treatment and ensure responsible use of antibiotics for decreased rates of antibiotic-resistant bacteria. Therefore, the present study was planned to show the pattern of bacterial co-infections in patients admitted with COVID-19 in a tertiary care hospital in Karachi, Pakistan.

Methodology

This prospective longitudinal study was carried in Ziauddin Univerity Hospital, North Campus Karachi, Pakistan, during April 2021 till June 2022. All COVID-19 patients admitted in ICU, HDU and COVID isolation ward, were included into the study. All of the patients were investigated after confirmation of COVID-19 through real-time polymerase chain reaction test.

Detailed history including comorbidity, smoking status and presenting symptoms was noted at the time of hospital admission. Patients admitting to intensive care unit were screened for bacterial co-infections within first 24 hours of their ICU admission. Blood and urine specimens were taken according to the hospital protocol. Sputum cultures were also taken from patients either they developed sputum after their admission or presented with sputum. Initially antibiotics were started according to management protocol which were later adjusted in accordance with the culture report sensitivity report. Data related to patients' demographic and clinical profile was documented in pre-designed study pro forma by the assigned data collectors.

The collected data was entered in SPSS version 21 for statistical analysis. Frequency and percentages were computed for categorical variables. Assumption of normality was first tested for numerical variables using Shapiro-Wilk test. Normally distributed variables were expressed as mean ± standard deviation. Non-normal variables were summarized as median with inter-quartile ranges (IQR). Chi-square or Fisher-exact test was applied to compare categorical variables whereas Mann-Whitney U test was applied for comparing non-normal distributed variables among patients with and without bacterial co-infection. Statistical significance was defined on the basis of two tailed p-value less than or equal to 0.05. Data was presented in tables and figure forms as appropriate.

Results

Total 99 patients were studied with mean age of 60.7 ± 15 years. Majority of the admitted patients were males (43.5%), non-smokers (85.9%) and had comorbidity (76.8%). The most prevalent comorbidity was hypertension (69.7%) followed by diabetes (67.7%), ischemic heart diseases (38.4%), cerebrovascular accident (18.2%), chronic obstructive pulmonary disease (15.2%) and renal failure (15.2%). Patients presented with symptoms of shortness of breath (90.9%), fever (81.8), cough (73.7%), fatigue (50%), diarrhea (22.2%), weakness (8.1%), chest congestion (7.1%), and vomiting (5.1%). At the time of admission median ferritin, d-dimer, CRP levels, LDH and PCT levels were 750 (IQR = 318 - 1842), 3337 (IQR = 1156 - 10940), 133.7 (IQR = 50.8 - 223.9), 462 (IQR = 337 - 655) and 0.5 (IQR = 0.1 - 3) respectively.

From (77.8%) of the patients, a total of 116 detected microorganisms could be isolated. Out of 99 patients investigated for blood and urine culture, 33 (33%) showed positive cultures from blood specimen whereas 59 (60%) patients came out to be positive from urine cultures. 20 patients developed sputum during their stay and 15 (75%) of them showed positive sputum cultures. Figure 1 shows the type of detected co-bacterial infections. Table 1 shows the frequency of detected microorganism from different specimens. Out of 77.8% patients having infections other than SARS-CoV-2, the most frequent infection was Candida albicans (44.2%), Ecoli (41.6%), Coagulase negative staphlylococcus (35.1%), Klebsiella species (7.8%), Proteus mirabilis (5.2%), Group D streptococcus (5.2%), Enterobacter (2.6%), Pseudomonas aeruginosa (2.6%), Acinetobacter (2.6%), Baccilus (1.3%), Enterococuss species (1.3%), Stenotrophomonas Maltophilia and Staphylococcus Aureus.

Table 2 displays the comparison of patients' socio-demographic and clinical profile among patients with and without co-bacterial infections. None of the factor was significantly different among the patients with and without

Table 1. Frequency of microorganisms detected from blood, urine and sputum

Microorganisms	Blood n (%)	Urine n (%)	Sputum n (%)
Coagulase negative Staphlylococci	27 (81.8)	0 (0)	0 (0)
Escherchia Coli	3 (9.1)	30 (50.8)	1 (6.7)
Klebsiella species	0 (0)	6 (10.2)	0 (0)
Proteus Mirabilia	0 (0)	4 (6.8)	0 (0)
Baccilus	1 (3)	0 (0)	0 (0)
Enterococuss species	1 (3)	0 (0)	0 (0)
Group D Streptococcus	1 (3)	3 (5.1)	0 (0)
Candida Albicans	0 (0)	24 (40.7)	12 (80)
Enterobacter	0 (0)	2 (3.4)	0 (0)
Pseudomonas Aeruginosa	0 (0)	1 (1.7)	1 (6.7)
Stenotrophomonas Maltophilia	0 (0)	0 (0)	1 (6.7)
Staphylococcus Aureus	0 (0)	0 (0)	1 (6.7)
Acinetobacter	0 (0)	0 (0)	1 (6.7)

co-existing infection except for age which was significantly higher in a group with co-infections.

Among 99 patients, majority of the patients developed complications (70.7%). Patients developed complications of acute kidney injury (52.5%), septic shock (34.3%), myocarditis (9.1%), encephalitis (15.2%), myocardial infarction (13.1%), pneumothorax (10.1%) and surgical emphysema (6.1%). 52.5% in-hospital moralities occured. Table 3 shows comparison of patients' complications and outcomes among patients with and without co-infection. Among all outcomes only encephalitis was significantly different among two groups of patients with higher frequency in patients with bacterial co-infections.

Discussion

In the present study 77.8% of the patients were identified form whom one or more organisms were isolated. Variable prevalence of coexisting infections in COVID-19 has been documented in literature. A lower prevalence of 7.7% was reported in a Chinese study[7] whereas another Chinese study reports a higher a co-infection prevalence of 49.8%.[8] A higher co-infection prevalence of 47.1% was outlined in an Indian study.[9] Another Indian study reported that total 290 samples were tested for microbial culture growth out of which 60 175 (60%) samples were found to have positive culture growth.[10] Another study demonstrated 28% co-infections in ICU admitted patients of COVID-19.[11] A higher frequency of co-infection in this study could be due to the fact due to different healthcare settings and environment of the community in developing country like Pakistan. The variability in results could also be occurred due to different detection method among studies.

In the present study total 116 microorganisms were detected with 59.5% gram positive, 27.6% were fungal infections and 12.9% were gram negative bacteria. Saeed NK et al conducted a similar study in Bahrain analyzing 1380 patients and detected total 472 organisms wit frequency 164(34.7%) gram positive and gram negative bacteria and 144(30.5%) were fungaemia including Candida galabrata, Candida tropicalis, Candida albicans, Aspergillusfumigatus, Candida parapsilosis, Aspergillusniger.[12] A study was conducted in Turkey aiming to describe profile of fungal infections in COVID-19 patients and opportunictic fungal infection was identified in 5.1% of the total cases.[13] Detection of invasive fungal infection was also reported from a UK based study.[14] Huges S et al

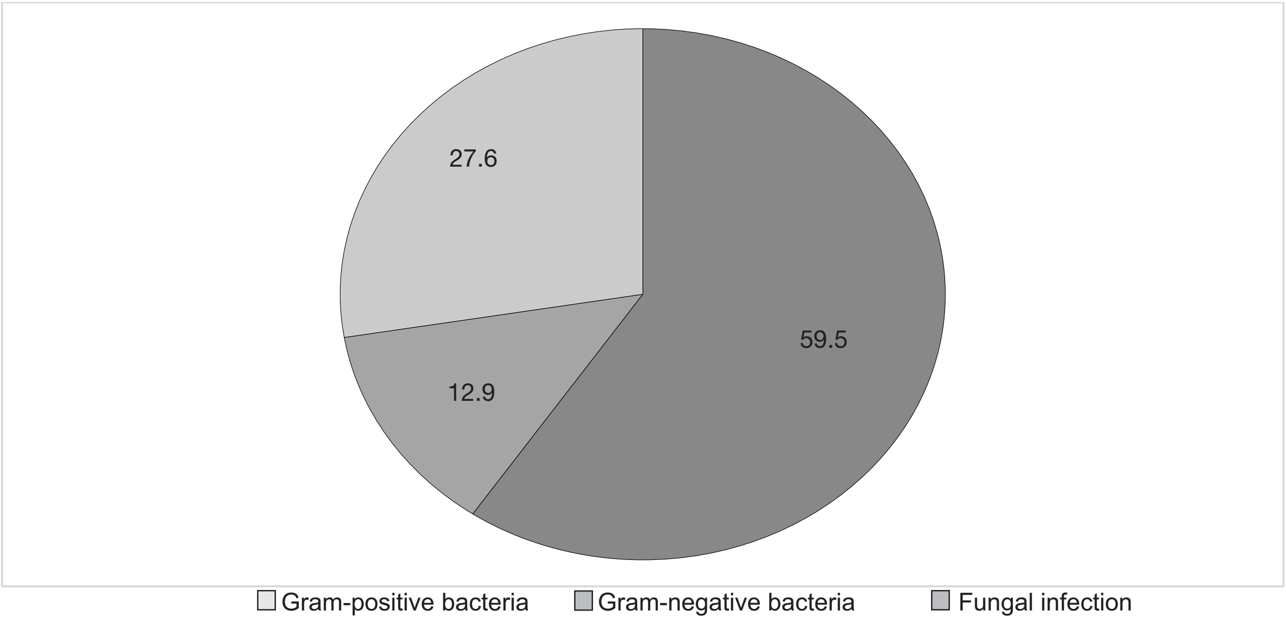

Figure 1. Frequency of type of infections

analyzed that 3.2% (n = 27) had early confirmed bacterial isolates in initial 5 days of hospital admission and there were (22.2%) (n = 6) cases of line-related bacteremia out of which 11.11% cases of fungal infection (Candida) (n = 3).[14] An Indian also reported the detection of fungal infections in COVID-19 patients. Sreenath et al tested total 191 COVID-19 patients for detection of cobacterial infection and detected fungal infections in 2.6% of these patients.[9] In contrast to our study, none of the fungal infection was reported in Saudi study.[15] Alqahtani et al demonstrated that among co-bacterial detected infection in COVID-19 patients, 55.6% were gram-negative bacteria while 44.4% were gram-positive bacteria.[15]

The most frequently detected organism in the present study was fungal infection Candida, mostly grown from Sputum culture. Second and third most common found microorganisms were Ecoli (41.6%) and Coagulase negative staphlylococcus (35.1%) respectively, grown in Urine culture mostly. In contrast to our findings, many of the studies reported lower frequency of fungal infection among COVID-19 patients.[12-14] The findings differs from Sreenath et al[9] and Hughes S et al[14] who did not identified Ecoli as co-bacterial infection in their studies. Coagulase-negative staphylococci was seen as most frequently detected infection in study of Hughes S et al.[14] However, it was not detected in a study of Sreenath et al[9] and Alqahtani.[15] In the present study Klebsiella species, Proteus mirabilies, streptococcus (5.2%), Enterobacter (2.6%), Pseudomonas aeruginosa (2.6%), Acinetobacter (2.6%), Baccilus (1.3%), Enterococuss species (1.3%), Stenotrophomonas Maltophilia and Staphylococcus Aureus were less detected organisms. In contrast to our study, many studies identified Staphylococcus Aureus and Klebsiella spp as highly frequently detected cobacterial infection in COVID-19 patients.[9,11,16] Acineto-bacterbaumannii,[9,15] Proteus mirabilis,[15,17] Enterococcus spp,[14,17] Enterobacter,[11,17] Stenotrophomonas Maltophilia,[12,17] Streptococcus spp,[14,17] Pseudomonas aeruginosa were also reported as less detected organisms in other studies.[14]

Several reports have shown dysregulation in different laboratory findings among patients diagnosed with and without other existing infection with COVID-19.[18,19] However, the current did not find significant difference among patients with and without coexisting infection in terms of comorbid and or any of the laboratory investigations. One of the possible reasons could be low sample size. Another plausible explanation was that laboratory investigations were performed at baseline whereas infection detection was done after 24 hours of the admission. However, another similar study also did not find significant differences for neutrophil lymphocyte ratio among patients having co-infections and patients without co-infections Furthermore, death rate was higher in our study in co-infections group but statistically it was not significant. Yet again, a lower sample could be the reason of non-significance of the result as many of the studies reported significantly higher mortality among this group of patients which is obvious self-explanatory fact.[15,17,20]

The present study was a single center experience with a limited sample size. The study did not identify the source of infection i.e. community or hospital acquired. Analysis of antimicrobial susceptibility pattern was also not the

Table 2. Patients' socio-demographic and clinical profile among patients with and without co-bacterial infections

Patients' characteristics	With co-infections n (%)	Without co-infections n (%)	p-value
Age (years)#	63 (54-73)	57 (49.7 - 65.5)	0.033
Male Gender	41 (77.4)	12 (22.6)	0.914
Smoker	11 (84.6)	2 (15.4)	ǂ0.726
Comorbidity	60 (78.9)	16 (21.1)	ǂ1.000
Hypertension	55 (79.7)	14 (20.3)	0.483
Diabetes	52 (77.6)	15 (22.4)	0.954
Ischemic heart diseases	29 (76.3)	9 (23.7)	0.782
Chronic obstructive pulmonary disease	12 (80)	3 (20)	ǂ1.000
cerebrovascular accident	12 (66.7)	6 (33.3)	ǂ0.222
Renal failure	11 (73.3)	4 (26.7)	ǂ0.737
Shortness of breath	70 (77.8)	20 (22.2)	ǂ1.000
Fever	63 (77.8)	18 (22.2)	ǂ1.000
Cough	54 (74)	19 (26)	0.127
Fatigue	36 (72)	14 (28)	0.162
Diarrhea	17 (77.3)	5 (22.7)	ǂ1.000
Weakness	7 (87.5)	1 (12.5)	ǂ0.680
Chest congestion	7 (100)	0 (0)	ǂ0.343
Vomiting	5 (100)	0 (0)	ǂ0.584
Ferritin#	750 (315 - 1792.5)	755 (415 - 5549.7)	0.671
d-dimer#	3575 (1131 - 11032)	3077 (1212.7 - 9603.5)	0.956
CRP levels#	134.8 (65.4 - 226.4)	72.5 (36.7 - 211.8)	0.239
LDH#	463 (357 - 633)	389 (304.7 - 946.7)	0.794
PCT#	0.5 (0.2 - 2.6)	0.5 (0.1 - 3.1)	0.827

CRP: C-reactive protein, LDH: lactate dehydrogenase, PCT: Procalcitonin, #: non-normally distributed variables are expressed as median (IQR), ǂ: Fisher-exact test is reported

focus of this study. However, it could be studied for initiating the antibiotics appropriately and avoiding its irrational usage. A future study is recommended to perform with a larger sample size by addressing all of the limitations of the present study to understand the pattern of bacterial co-infection in COVID-19 diseases and for the rationale use of antibiotics against the detected microorganisms.

Conclusion

The present study analyzed that in addition to gram positive and gram-negative bacterial infections, fungal infections were also coexisting in COVID-19 patients in Karachi Pakistan. Patients with increasing age were more prone to have co-infection.

Table 3. Comparison of outcomes among patients with and without co-infection

Complications	With co-infections n (%)	Without co-infections n (%)	p-value
Hospital stay	8 (5 - 14)	6 (3.7 - 13.7)	0.198
With complications	54 (77.1)	16 (22.9)	0.813
Acute kidney injury	40 (76.9)	12 (23.1)	0.830
Septic shock	24 (70.6)	10 (29.4)	0.213
Mayocarditis	7 (77.8)	2 (22.2)	ǂ1.000
Mayocardial infarction	9 (69.2)	4 (30.8)	ǂ0.477
Encephalitis	8 (53.3)	7 (46.7)	*0.037
Surgical Emphysema	4 (66.7)	2 (33.3)	ǂ0.612
Pneumothorax	8(80)	2(20)	ǂ1.000
Mortality	41(78.8%)	11(21.2%)	0.788

#: Hospital stay is expressed as median (IQR), ǂ: Fisher-exact test is reported, *Significant at p<0.05

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