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Secondary Microbial Infections among Covid-19 Patients and its Effect on Duration of Hospital Stay and Outcome

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Abstract

Novel corona virus or SARS-CoV-2 which lead to the pandemic still emerging with new variants worldwide. The disease may manifest with mild to severe acute respiratory syndrome especially in immunocompromised or in patients with comorbidities. The common symptoms of Covid-19 include fever, cough, sore throat, breathlessness, fatigue and malaise. Diagnosis of asymptomatic or mild Covid 19 disease is clinically challenging and necessitates laboratory assistance for confirmation. Real time reverse transcriptase polymerase chain reaction (RT-PCR) is the current gold standard for the molecular diagnosis of SARS-CoV-2 infection for the quantitative detection of viral nucleic acid. This retrospective cross-sectional study was conducted in the department of Microbiology, JSS Hospital, Mysuru, for a period of 3 months from July 2020 to September 2020. During the study period, 200 randomly selected RT-PCR confirmed COVID-19 patients admitted to our hospital were followed up for secondary infections, comorbidities and duration of hospital stay. Diabetes mellitus was the most common comorbidity associated with Covid-19. We also documented the COVID-19 with coinfection details of the patients. Among 200 patients, 28 patients' various samples were sent for culture and sensitivity. Among 28 patients who had secondary infections, Candida species was the most common isolate to cause secondary infection, followed by bacterial infections with gram positive and gram-negative bacteria. Coinfection with viruses, bacteria and fungi among the Covid-19 patients are serious problems in the COVID-19 pandemic. Bacterial co-infections have been a major cause of mortality and concerns for superinfection in COVID-19 patients. Infection with multi drug resistant bacteria such as *Acinetobacter baumannii, Staphylococcus aureus, Klebsiella pneumoniae* and *Candida* species especially in critical care units in COVID-19 patients may increase the mortality unless treated early in the course.

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Key Words

SARS-CoV-2, secondary infections, hospital stay

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INTRODUCTION

Since December 2019, SARS-CoV-2 which caused pandemic resulted in more than three million deaths. Emergence of the new Corona virus-SARS CoV-2 in the human population has a significant and historic economic impact, prompting public health agencies throughout the world to mobilize to combat the virus's rapid spread[1]. The SARS-CoV-2 contains nucleocapsid surrounded by an envelope. It measures 120 nm in size and has a helical symmetry, it has 4 structural proteins (N, S, M and E), 16 non-structural and several other accessory proteins[2].

Hospitalization of COVID-19 patients, particularly in intensive care units (ICUs), poses patients at risk for negative outcomes, the most serious of which are healthcare-associated infections (HAIs)/secondary infections[3]. The prevalence, etiology and patterns of bacterial infection in individuals infected with SARS coronavirus 2 (SARS CoV-2) are poorly characterized this has been recognized as a significant knowledge gap[4]. Antibiotics are administered in patients with suspected or proven COVID-19 for a number of reasons, despite the fact that they are of no use in treating COVID-19. This includes the challenge of excluding bacterial co-infection at the time of presentation, as well as the likelihood of bacterial secondary infection later in the disease. Several guidelines advise the use of empirical antibiotics for patients with severe bacterial superinfection, based on concerns about an increase in mortality in patients with bacterial superinfection during outbreaks COVID-19[5]. This study aimed to determine the bacterial or fungal secondary or coinfections among the Covid-19 patients simultaneously looking at outcome and duration of the hospital stay among the same group.

MATERIALS AND METHODS

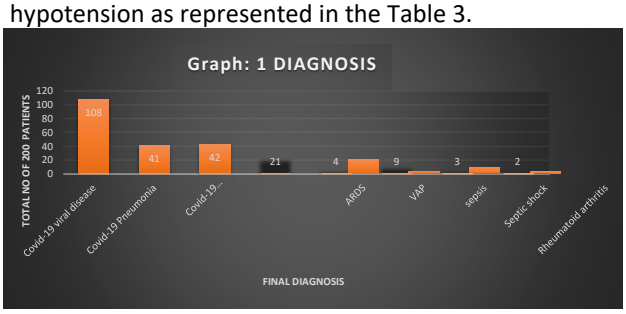
This retrospective cross-sectional study was conducted in the department of Microbiology, JSS Hospital, Mysuru, from July 2020-September 2020. A total of 200 SARS COV-2 RT-PCR confirmed positive patients admitted to various wards and ICUs were included in the study. Patients with rapid antigen test positive for SARS COV-2 and who were treated on outpatient basis were excluded from the study. The study was approved by institutional ethical committee. The patient demographic, microbiological and clinical details were collected retrospectively by reviewing the case records of the covid-19 patients. The presence of secondary bacterial or fungal infections was identified by bacterial and fungal culture of various samples from Covid-19 patients. The bacterial and yeast identification and antimicrobial susceptibility was performed with Vitek-2 system. Fungal culture: All respiratory samples that were sent for fungal culture were identified using Vitek-2 system and molds by conventional technique. All the data were entered in excel sheet and analysed.

RESULTS AND DISCUSSIONS

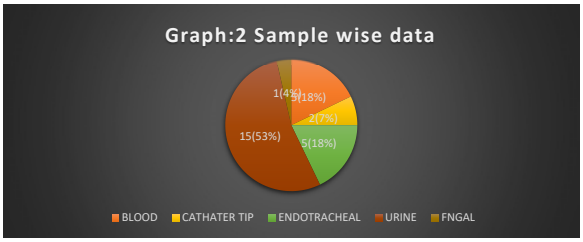
Among the 200 COVID 19 patients, 70% (140/200) of them were males and 60 (30%) were females. Distribution of patients according to age revealed that 51-60 years 23.5% (47/200) age group was predominantly affected followed by the age group of 61-70 years 22.5% (42/200) and 30 between the age group of 41-50 years, with the mean age of 18 years. Analysis of the data for duration of hospital showed 51/200 (25.5%) patients were admitted in hospital for less than 5 days. Maximum number of patients were admitted for the period of 6-10 days 78/200 (39%). 39 patients (19.5%) got admitted for 11-15 days. Considerable number of patients were admitted to hospital for more than 15 days-32/200 (16%) as displayed in the (Table 1).

The clinical profile of the SARS COV-2 patients exhibited fever in 112/200 (56%), severe cough in 96/200 (48%), next common symptom was difficulty in breathing 60/200 (30%) among COVID patients. The other symptoms among the admitted patients which were observed in few cases were fatigue, vomiting, abdomen pain, loose stools, headache as represented in the Table 2. Nine pregnant women were also admitted with Covid 19 among the 200.

Assessment of the 200 patients for associated diseases revealed diabetes mellitus as the most common comorbidity present in 100 (50%) patients, followed by hypertension 90(45%) and ischemic heart disease (IHD) 25 (12.5%) respectively. Other comorbidities observed in positive patients were chronic kidney disease in 16 (8%) hypothyroidism in 9 (4.5%), hyperthyroidism in 3 (2,5%) and 1 patient had hypotension as represented in the Table 3.



Graph.1 : Clinical diagnosis among the Covid 19 patients



Graph. 2: Sample wise data

Table:1 Hospital duration

Duration (days)	No of patients (n = 200)	Percentage
0-05	51	25.5
06-10	78	39
11-15	39	19.5
16-20	18	9
21+	14	7

Table 2: Clinical signs and symptoms among Covid-19 patients

Signs and Symptoms	Total no of patients	Percentage
Fever	112	56
Cough	96	48
Breathlessness	60	30
Fatigue	28	14
Vomiting	14	7
Weakness	8	4
Abdomen pain	10	5
Headache	8	4
Nausea	3	1.5
Loose stools	9	4.5
Loss of appetite	5	2.5
Myalgia	6	3
Chest pain	2	1
Pregnant women	9	4.5

Table 3 showing comorbidities observed in patients with COVID19.

Risk factors/Comorbidities	No of patients	Percentage
Hypertension	90	45
Hypotension	1	0.5
Hyperthyroidism	3	2.5
Hypothyroid	9	4.5
Diabetes mellitus	100	50
Ischemic heart disease (IHD)	25	12.5
Chronic kidney disease (CKD)	16	8
COPD	4	2
Acute kidney injury (AKI)	5	2.5
Asthma	5	2.5
Parkinson disease	2	1
Obesity	2	1

Of these 200 SARS CoV-2 positive patients, accurate clinical diagnosis of Covid-19 was made in total of 191/200 (95.5%) cases. The clinical diagnosis made were covid viral disease in 108 (54%) patients, covid-19 bronchopneumonia in 42(21%) patients, 41(20.5%) as covid-19 viral pneumonia, 21(10.5%) patients had ARDS, 4(2%) patients with VAP, 3(1.5%) patients with septic shock, 2(1%) patients with Rheumatoid arthritis it is showed in the (Graph: 01)

Among the 200 patients, 83 patient blood samples were sent for HIV testing, of which one patient turned out to be positive for HIV accounting for 1.2 % (1/83). 81 serum samples were subjected to hepatitis B infection, which revealed 2 (2.4%)patients to have HBsAg, 80 samples were sent for HCV testing, all of which turned out to be negative. Few of the patient samples were also subjected for Weil-Felix test (11), Widal test (7) and 8 for detection of malarial antigen, which showed all negative results. In the group of 200 patients, 20 patient samples were also sent for dengue ELISA, of which one patient (5%) was found to have IgM antibodies against dengue virus.

Out of 200 patients, 68 different samples were sent for culture and sensitivity for suspected secondary infections, of which growth was observed in 28 samples yielding 28 isolates. These samples include, 15urine, 5 blood, 5 endotracheal aspirates and 2 central venous catheter tip samples (graph 2). The culture isolates data was collected. Out of 28 isolates, culture isolates data was collected. Out of 28 isolates, 12 were Candida species, 4 were *Escherichia coli*, 4 were *Klebsiella pneumoniae*, 3 were *Acinetobacter baumanii* and 2 methicillin resistant *S. aureus* (MRSA), 2 were Enterococci and 1 Streptococcus species. Majority of the cases were from urban areas of Mysuru, which accounted for 118(59%) followed by Nanjangud taluk[19].

Analyzing the 200 Covid?19 patients admitted to various wards and ICUs, total of 70(35%) patients were admitted in ICU, of which 19 patients expired. Patients admitted to general wards were 130 (65%) wherein, 7 patients expired. 74(87%) patients recovered from the SARS COV-2 infection and 26(13%) patients succumbed to infection.

During the research period, 34.22 % tested positive for SARS COV-2. Another research by M.A. Andrews et al. found that during the outbreak's early stages, there were more than 70 thousand cases in countries other than China[6]. In another study, Priya Abraham et al. discovered that a total of 1,021,518 persons were tested for the coronavirus that caused severe acute respiratory syndrome (SARS), with 40,184 (3.9%) of the tests being positive[7]. The male prevalence (70%) among the 200 patients was found to be greater than the female (30%). Males were more susceptible to infection than females, which might be attributed to males' greater exposure to the outside environment or their lifestyle. Males were shown to be

more infected with covid-19 infection than females in several other investigations[8].

The 50-70-year-old age group, i.e. elderly aged were hit worse than the others. In a study published in 2020 by Jie Qian *et al,* individuals aged 50-69 were found to be commonly infected[9]. Other studies also revealed involvement of older individuals aged 60-69[10]. This might be due to decreasing immunity or an immunocompromised condition as a result of comorbidity. More than half of the patients in this study were hospitalised to the hospital for more than ten days. In a study published in 2020, Pham Quang Thai et al found that the median hospital stay was 21 days[11]. The length of time spent in the hospital varies depending on the comorbid conditions.

In this study, we identified that the most common symptoms patients had were fever which was present in 112 (56 %) patients, cough which was present in 96 (48%) patients and breathlessness (which was present in 60 patients), fatigue which was seen in 28 patients, loose stool in 9 patients, head ache seen in 8 patients, abdominal pain which was seen in 10 patients so on. In a study published in October 2020, Jun Yasuhara *et al.* found that fever, cough shortness of breath were the most common symptoms[12].

Diabetes mellitus (50%) and hypertension were found to be the most common comorbidities found in our study. Ischemic heart disease (IHD), was the next most common risk factor found among COVID-19 patients. These findings were in agreement with the studies conducted by Bolin Wang. et al April 2020[13], Adekunle Sanyaolu[14] showed that Diabetes mellitus, hypertension, ischemic heart disease (IHD), acute kidney infection (AKI), chronic obstructive pulmonary disease (COPD) chronic kidney disease (CKD) were the most common comorbidities found in their covid patients. Upon comparing our findings to them, it was found that some patients had more than one comorbidity these risk factors also explain for higher infection severity, longer hospital stays, most crucially, worse outcomes among the Covid-19 patients.

The early and specific clinical diagnosis was established in 200 covid-19 positive patients: 108 (54%) patients were solely diagnosed with covid viral illness, 42 (21%) patients with covid-19 bronchopneumonia 41 (20.5%) patients diagnosed with covid-19 viral pneumonia. Early and accurate diagnosis aids in the beginning of specific therapy leading to better outcome. The other diagnosis made at time of admission were ARDS in 21(10.5%) patients. Many other patients had Chronic kidney disease15(7.5%), sepsis, asthma and acute kidney injury. Few patients developed VAP (3, 1.5%). Various diagnosis methods, such as serological, molecular radiological, can assist health Centre's in detecting SARS-CoV-2, radiological methods such as High-resolution CT (HRCT) scan is useful in grading of the disease and to assess the severity of the disease. Use of multiple approaches in diagnosing the disease early is critical. With all the different modalities of diagnosis, it is possible to diagnose the infection quickly and accurately with fewer false-negatives. This is critical in decreasing the mortality associated with the disease and also curtail the spread of illness to others[15].

Early identification of concurrent or secondary infections aids in better patient care andthese infections can have an influence the management, necessitating extra care throughout treatment. As a result, testing for other coexisting infections may be recommended for the best management of Covid-19 and other coexisting infections[16]. The study's small sample size may have contributed to the low results. About 28 culture isolates were found in the current study of 200 covid-19 positive samples. There were 15 urine culture samples, 5 blood samples, 5 endotracheal aspirate samples, 2 catheter tip samples 1 fungal culture among the 28 culture samples. Surbhi Khurana *et al.* studied 1179 individuals and found that 175 samples were culture positive, indicating that the results were comparable[17].

Recognition of microbial co infection among the confirmed covid 19 patients, in the current study determined candida as the most common isolate to be isolated. The species of Candida isolated included *Candida albicans* (4), *Candida parapsilosis* (2) and *Candida tropicalis* (6). A study done by Surbhi Khurana et.al showed (9/18)50% of candida species were isolated from the fungal culture. (17). Five *Klebsiella pneumoniae* isolates among which one was multi drug resistant (MDR) *Klebsiella pneumoniae*. Total of 4 *Acinetobacter baumanii* were isolated in which 3 were multi drug resistant, followed by 3 *E. coli*, 2 *enterococci*, 2 *Pseudomonas aeruginosa*, 1 methicillin resistant Staphylococcus hominis and 1 methicillin resistant *Staphylococcus aureus*, 1 alpha hemolytic Streptococci ,1 Trichosporonasahii were isolated. A study done by S. Hughes. et al, Bradley J. Langford. et al, showed the low frequency of bacterial infection among the covid patients[18,4]. Study by Haocheng Zhang. *et al* study showed confirmed 52 pathogens to cause secondary infections[19], Study by Surbhi Khurana. *et al* had 151 patients with secondary infection and hadmulti drug resistant organisms also[17]. And both the studies[17,19] showed that there is a high risk of secondary infection. In our study, most of the organisms were candida species isolated from urine sample. It can be due to the use of catheter in these patients. And the MDR organisms were mainly from the patients diagnosed with the hospital/ventilator acquired infections.

CONCLUSION

Covid 19 is a new disease caused by a new version of the SARS COV-2 virus that has been spreading throughout the world since 2019. In the COVID-19 pandemic, coinfection with viruses, bacteria fungus among Covid-19 patients is a major concern. Other microbial co-infections may be the cause of death in COVID-19 positive patients with no underlying illnesses. In COVID-19 patients, bacterial co-infections have been a prominent source of death and worries about superinfection. Infection with multidrug-resistant bacteria including Acinetobacter baumannii, Staphylococcus aureus, Klebsiella pneumoniae Candida species, particularly in critical care units, may increase mortality and also hospital stay in COVID-19 patients.

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