Microbiology Section

Secondary Infections among COVID-19 Hospitalised Patients and their Antimicrobial Susceptibility Pattern: A Cross-sectional Study in a Tertiary Care Hospital

GOURI SANKAR SABAT[1], SUSMITA KUMARI SAHU[2], MONALISA PANIGRAHI[3], NIHAR RANJAN SAHOO[4], GANESWAR SETHI[5]

(CC) BY-NC-ND

ABSTRACT

Introduction: The novel coronavirus (2019-nCoV) is a contagious virus that causes respiratory infection and has shown evidence of human-to-human transmission. In this infection, the immunity of the patient is decreased; making them susceptible to various secondary infections. This leads to increased morbidity and mortality in these patients.

Aim: To estimate the profile of secondary infections in hospitalised Coronavirus Disease-2019 (COVID-19) patients and analyse their antimicrobial susceptibility pattern.

Materials and Methods: A cross-sectional study was conducted for a period of five months from June to October 2021, which included COVID-19 positive patients with secondary infection admitted in the dedicated COVID hospital, Maharaja Krishna Chandra Gajapati Medical College and Hospital (MKCG MCH), Berhampur, Odisha, India. Clinical samples like blood, urine, sputum, tissue biopsy and Bronchoalveolar Lavage (BAL) were collected aseptically from patients with COVID-19 and were processed in microbiology laboratory as per standard operating procedures. All the necessary information like demographic features (age, gender), associated co-morbidities and oxygen saturation levels of COVID-19 positive patients at the time of admission were collected and entered in a Microsoft Excel sheet for further analysis. Results of continuous variables were described by mean and range while categorical variables were described by frequency. All the generated data was analysed by Statistical Package for the Social Sciences (SPSS) 16.0.

Results: A total of 438 patients suspected of COVID-19 were admitted during the study period, out of which 138 patients were positive for COVID-19 by Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR). Out of 138 COVID-19 positive patients, 105 patients were willing to give samples and their samples were processed for bacterial and fungal culture and sensitivity. Total 18/105 (17.1%) samples were positive for bacterial and fungal growth. Blood Stream Infection (BSI) were seen in 14/18 (77.8%) and was predominantly associated with *Staphylococcus aureus* 5/14 (35.7%), followed by *Enterococcus* spp. 3/14 (21.4%). Out of total culture positive cases, 2/18 (11.1%) showed Urinary Tract Infection (UTI). Of the UTI cases, *Escherichia coli* was isolated from 1/2 (50%) of cases. Out of total culture positive cases, 2/18 (11.1%) were identified having mucormycosis. All gram positive bacteria had shown maximum resistant to ampicillin and gram negative bacteria were resistant to ampicillin-sulbactam, levofloxacin, cotrimoxazole.

Conclusion: In COVID-19 positive patients with secondary infection, early diagnosis and prompt treatment will lead to improved patient care and better outcome.

Keywords: Co-infection, Community acquired infection, Coronavirus disease 2019, Drug resistance, Hospital acquired infection, Superinfection

INTRODUCTION

Secondary infections are commonly identified in viral respiratory tract infections e.g. influenza and are important cause of mortality and morbidity which require prompt diagnosis and antimicrobial therapy [1-3]. These infections can have worse outcomes if not treated on time. Secondary infection in patients with severe influenza has been published as high as 20-30% [3,4]. It has been shown that most of the deaths reported in 1918-19 during influenza pandemic were due to secondary bacterial infections [5].

Coronaviruses have been known to the human kind as important pathogens causing respiratory tract infections in both children and adults. Severe pneumonia has been reported due to Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) and more recently the novel coronavirus (2019-nCoV) or SARS-CoV-2. Compared to the SARS and MERS the virulence of SARS-CoV-2 is relatively low, only few infected people developed severe manifestation [6]. It is a highly infectious virus that causes respiratory infection and human-to-human transmission. It spreads through inhalation or ingestion of viral droplets.

Its target receptor Angiotensin Converting Enzyme 2 (ACE2) is mainly expressed in the cells of cardiopulmonary system and the final outcome can be lung injury, myocarditis, inflamed and leaking vessels, rise or fall in blood pressure and organ damage [7-10]. India has reported 3.71 Cr cases of COVID-19 till 15th Jan 2022.

In COVID-19, secondary infection have been detected, including bacterial and fungal infections, especially in severe or critical cases [11-13]. The overall secondary infection rate in patients infected with COVID-19 is about 5-30% [14-20]. Early diagnosis, prompt identification and judicious use of antibiotics and antifungals will lead to improved patient care and better outcome. This would also justify the need for initial empiric antibiotic treatment and will decrease routine use and (overuse) of antibiotics and antimicrobial resistance. Present study aimed to estimate the profile of secondary infections in hospitalised COVID-19 patients and to determine the antimicrobial susceptibility pattern.

MATERIALS AND METHODS

A cross-sectional study was conducted for a period of five months in Department of Microbiology (June to October 2021) in

MKCG Medical College, Berhampur, a tertiary care 1190 bedded, teaching, and referral hospital in Odisha, India. With the onset of the COVID-19 pandemic, a dedicated COVID Hospital (DCH) with 150 beds capacity was established. The study was approved by the Institutional Ethical Committee (IEC), MKCG Medical College (IEC-870) and informed consent was taken from the participants. All the COVID-19 positive patients admitted in the DCH of MKCG Medical College during the above study period were included.

According to Centers for Disease Control and Prevention (CDC), infections that are identified after 48 hours of hospital admission should be referred as hospital-acquired infection and infections that are identified within 48 hours of admission as community-acquired infection [21,22]. According to CDC, co-infection is one occurring concurrently with the initial infection and super infection/secondary infection is an infection following a previous infection especially when caused by microorganisms that are resistant to the earlier used antibiotics, the difference being purely temporal [23,24].

Inclusion criteria: COVID-19 patients of all age group, with or without symptoms of Severe Acute Respiratory Infection (SARI), who were admitted for the above study period, within 48 hours of hospitalisation were included in the study.

Exclusion criteria: Unwilling patients were excluded from the study.

Study Procedure

Relevant clinical samples like blood, urine, sputum, tissue biopsy and BAL were collected aseptically [25] from the COVID-19 positive patients admitted in the DCH for the above study period were received in the microbiology laboratory and processed for the same as below [Table/Fig-1].
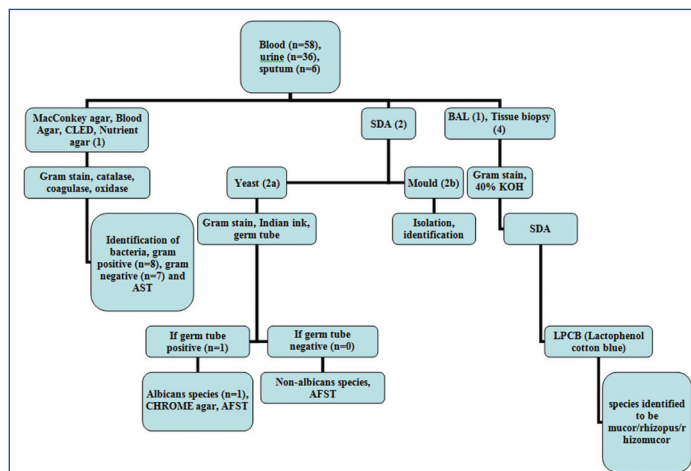

[Table/Fig-1]: Flow chart of sample processing.
CLED: Cystine lactose electrolyte deficient; BAL: Bronchoalveolar lavage; AST: Antimicrobial susceptibility testing; AFST: Antifungal susceptibility testing; SDA: Sabouraud's dextrose agar

Blood, sputum and BAL samples were inoculated on MacConkey agar, blood agar, nutrient agar and Sabouraud's Dextrose Agar (SDA). Urine was inoculated on Cystine Lactose Electrolyte Deficient agar (CLED) and processed as (1) in above flow chart and Antimicrobial Susceptibility Test (AST) was done according to the Clinical and Laboratory Standards Institute (CLSI) 2021 guidelines [26]. Growth on SDA (2) was identified as yeast or mould and processed under (2a) and (2b) respectively, as in the above flowchart. Antifungal Susceptibility Test (AFST) was done according to CLSI-2021 guidelines [26]. BAL fluid and tissue biopsy samples were subjected to gram stain and 40% Potassium Hydroxide (KOH) test to see for fungal elements and processed as (3) in the above flowchart. All the clinical samples were processed in the biosafety cabinet (BSL-2) [Table/Fig-2-6]. Personal protective equipments were used while processing the samples. All the clinical samples were disposed as per the biomedical waste management guidelines in India [27].
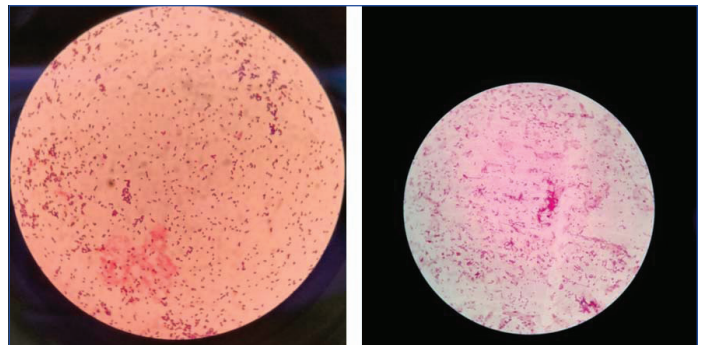
[Table/Fig-2]: Gram stain showing gram positive cocci in pairs 100X oil immersion.
[Table/Fig-3]: Gram stain showing gram negative bacilli 100X oil immersion. (Images from left to right)
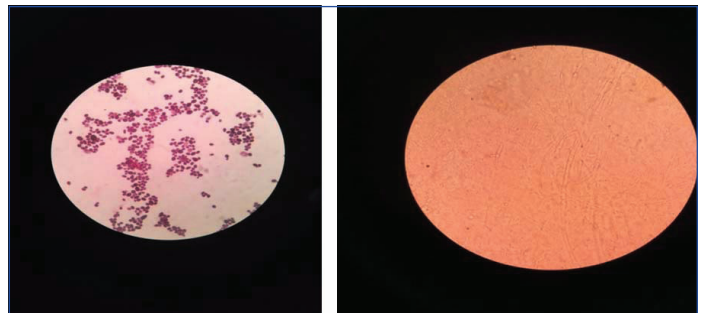
[Table/Fig-4]: Gram stain showing buddying yeast cells 100X oil immersion.
[Table/Fig-5]: KOH mount showing fungal elements 40X high power. (Images from left to right)
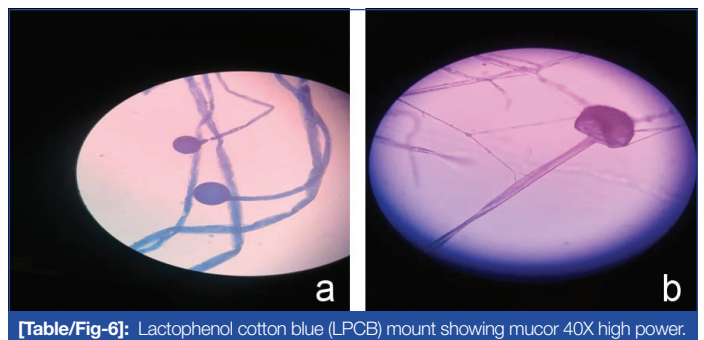
[Table/Fig-6]: Lactophenol cotton blue (LPCB) mount showing mucor 40X high power.

STATISTICAL ANALYSIS

All the necessary information like demographic features (age, gender), associated co-morbidities and oxygen saturation levels of COVID-19 positive patients at the time of admission were collected and entered in a Microsoft Excel sheet for further analysis. Results of continuous variables were described by mean and range while categorical variables were described by n (%). Here (n) is total number of COVID-19 positive patients, total samples collected for microbiological culture, microbiological culture positive for bacterial and fungal growth and organisms isolated from culture positive samples. All the generated data was analysed by Statistical Package for the Social Sciences (SPSS) version 16.0.

RESULTS

A total of 438 patients suspected of COVID-19 were admitted during the study period, out of which 138 (31.5%) patients were positive for COVID-19 by RT-PCR. Out of 138 COVID-19 positive patients, 71 (51.5%) were females and 19/138 (13.8%) had pregnancy. The mean age of the COVID-19 positive patients was 43 years with a range of 6 to 84 years. Mean saturation level of the COVID-19 positive patient's was 90%, with a range of 54%-94%. Out of 138 COVID-19 positive cases, 58/138 (42%) had co-morbidities. Diabetes with hypertension was seen in 23/138 (16.7%), hypertension alone in 8/138 (5.8%), asthma in 2/138 (1.4%).

Demographic features of COVID-19 positive patients and COVID-19 positive patients with secondary infection were compared in [Table/Fig-7]. Out of 138 COVID-19 positive patients, 105 patients were

willing to give samples and were processed for bacterial and fungal culture and sensitivity. Out of total samples tested, 58/105 (55.2%) were blood, 36/105 (34.3%) were urine, 6/105 (5.7%) were sputum, 1/105 (1.0%) was BAL fluid and 4/105 (3.8%) were tissue. Out of 105 samples collected for microbiological culture, 18/105 (17.1%) samples were positive for bacterial and fungal growth. Out of total culture positive cases, BSI was seen in 14/18 (77.8%) samples and was predominantly associated with *Staphylococcus aureus* 5/14 (35.7%). Out of 18 samples, 2/18 (11.1%) showed UTI in which *Escherichia coli* was isolated from 1/2 (50%) of cases, [Table/Fig-8]. Out of total culture positive cases, 2/18 (11.1%) were identified as having mucormycosis based on the growth on SDA.

The antibiotic susceptibility pattern of the isolated organisms is tabulated in [Table/Fig-9] and [Table/Fig-10]. All gram positive bacteria had shown maximum resistant to ampicillin and gram negative bacteria were resistant to ampicillin-sulbactam, levofloxacin, cotrimoxazole. *Staphylococcus aureus* was isolated in five cases, of which 3/5 (60%) were methicillin resistant *Staphylococcus aureus* (MRSA). Of the pathogens isolated gram negative bacteria isolated were seven, of which 7/7 (100%) were Extended Spectrum Beta-Lactamases (ESBL) producers and carbapenem resistance was seen in 2/7 (28.6%). Among gram positive isolates 8/8 (100%) were sensitive to linezolid. Among the gram negative pathogens 4/7 (57.1%) were sensitive to Piperacillin/Tazobactam, and 5/7 (72%) were sensitive to meropenem.

Demographics	COVID-19 patients n=138, n (%)	COVID-19 patients with secondary infection, n=18, n (%)
Mean age in year	43 (Range-6 to 84)	49 (Range-20 to 65)
Age distribution (years)		
01-20	15 (10.9)	01 (5.5)
21-40	52 (37.7)	05 (27.8)
41-60	41 (29.7)	09 (50)
61-80	28 (20.3)	03 (16.7)
81-100	02 (1.4)	0
Gender M/F (M:F)	67/71 (1:1.05)	09/09 (1:1)
Mean saturation level (%)	90 (Range-54%-94%)	91 (Range-65%-93%)
Co-morbidities		
Diabetes mellitus with hypertension	23 (16.7)	07 (38.9)
Hypertension	08 (5.8)	01 (5.5)
Pregnancy	19 (13.8)	00
Asthma	02 (1.4)	00
Tuberculosis	01 (0.7)	00
Ischaemic heart disease	01 (0.7)	00
Death	28 (20.3)	02 (11.1)
Discharged	110 (79.7)	16 (88.9)

[Table/Fig-7]: Demographic and clinical characteristics of COVID-19 positive patients.

Samples collected	Total sample collected (n=105)	Culture positive (n=18)
Blood	58	14 (77.8)
Urine	36	2 (11.1)
Sputum	06	0
Broncoalveolar lavage (BAL) fluid+tissue	05	2 (11.1)
Total	105	18
Bacterial profile of secondary infections (two samples excluded as two patients were dead)		
Blood	n=14	
Staphylococcus aureus	05 (35.7)	
Enterococcus spp.	03 (21.4)	
Klebsiella spp.	02 (14.3)	
Acinetobacter spp.	02 (14.3)	
Escherichia coli	01 (7.1)	
Pseudomonas aeruginosa	01 (7.1)	
Urine	n=02	
Escherichia coli	1 (50)	
Candida tropicalis	1 (50)	

[Table/Fig-8]: Results of microbiological culture.

Antibiotic	*Staphylococcus aureus* (n=5)		*Enterococcus* spp. (n=3)	
	Sensitive (%)	Resistant (%)	Sensitive (%)	Resistant (%)
Clindamycin	2 (40)	3 (60)	-	-
Linezolid	5 (100)	0	3 (100)	0
Ampicillin	0	5 (100)	0	3 (100)
Levofloxacin	4 (80)	1 (20)	0	3 (100)
Cefoxitin	2 (40)	3 (60)	-	-
Gentamicin	4 (80)	1 (20)	-	-
Cotrimoxazole	3 (60)	2 (40)	-	-
Vancomycin	-	-	3 (100)	0

[Table/Fig-9]: Antibiotic susceptibility pattern of gram positive isolates.

Antibiotic	Escherichia coli (n=2)		Klebsiella spp. (n=2)		Acinetobacter spp. (n=2)		Pseudomonas aeruginosa (n=1)	
	Sensitive (%)	Resistant (%)	Sensitive (%)	Resistant (%)	Sensitive (%)	Resistant (%)	Sensitive (%)	Resistant (%)
Amikacin	2 (100)	0	0	2 (100)	1 (50)	1 (50)	1 (100)	0
Meropenem	2 (100)	0	1 (50)	1 (50)	1 (50)	1 (50)	1 (100)	0
Piperacillin/Tazobactam	2 (100)	0	0	2 (100)	1 (50)	1 (50)	1 (100)	0
Cotrimoxazole	0	2 (100)	0	2 (100)	0	2 (100)	-	-
Cefotaxime	0	2 (100)	0	2 (100)	0	2 (100)	-	-
Ampicilin/Sulbactam	0	2 (100)	0	2 (100)	0	2 (100)	-	-
Levofloxacin	0	2 (100)	0	2 (100)	0	2 (100)	1 (100)	0
Cefepime	-	-	-	-	-	-	0	1 (100)
Ceftazidime	-	-	-	-	-	-	0	1 (100)
Aztreonam	-	-	-	-	-	-	0	1 (100)

[Table/Fig-10]: Antibiotic susceptibility pattern of gram negative isolates.

Antifungal susceptibility pattern of *Candida albicans* tabulated in [Table/Fig-11]. Out of 138 patients, 28/138 (20.3%) patients succumbed to death and rest were discharged.

Antifungal	Candida albicans (n=1)	
	Sensitive	Resistant
Fluconazole	1 (100)	0
Voriconazole	1 (100)	0
Nystatin	1 (100)	0
Amphotericin B	1 (100)	0

[Table/Fig-11]: Antifungal susceptibility pattern of fungal isolates.

DISCUSSION

The present study identified the profile and incidence of secondary infections in COVID-19 infected hospitalised patients over a period of five months. Among 138 COVID-19 positive patients, 105 patients were willing to give samples and 105 samples were sent to the microbiology department for the processing. Out of these, culture positive were seen in 18 (17.1%) samples. This results were similar with reports from other studies where the secondary infection rate ranged from 5-30% [14-20,28,29]. Majority of patients were females and constituted around 51.5%. In contrast to this, other studies showed male predominance [7,28,30]. The mean age of the COVID-19 positive patients was 43 year with a range of 6-84 years. Other study showed almost similar results with age range of 1 to 97 years with a mean of 53.3 year [29]. When co-morbidity was compared, diabetes with hypertension was seen in 16.7% patients, hypertension in 5.8%, and 13.8% positive cases were seen in pregnant women. Report from other study showed associated co-morbidities were diabetes mellitus 18%, hypertension 46.8%, asthma 6.5%, heart disease 24% [28]. BSI constitute majority of secondary infections with 14/18 culture positive samples. *Staphylococcus aureus* was the most common bacteria isolated followed by *Enterococcus* spp. which were gram positive organisms. Few previously documented studies were in line with this result, showed BSI was predominantly due to gram positive pathogens [28,31]. In contrast to this other previously reported studies showed BSI was predominantly due to gram negative pathogens [29,32,33]. Present study showed gram negative septicaemia was predominantly associated with *Klebsiella* spp. and *Acinetobacter* spp. This result was similar to the previously reported studies which showed among gram negative organisms *Klebsiella* spp. was the commonest organism followed by *Acinetobacter* spp. or vice versa [29,32].

After BSI, UTI constitute 2/18 (11.1%) culture positive samples. Previous study showed total urine culture positive cases in the first wave of COVID-19 pandemic were 9.3% and 18.8% in the second wave [33]. UTI was mainly due to *Escherichia coli* and *Candida tropicalis*. These results were in line with the previously reported studies, which showed among COVID-19 positives predominant urinary pathogens were *Escherichia coli*, *Klebsiella* spp., *Candida* spp. [29,34].

All gram positive bacteria have shown maximum resistant to ampicillin and gram negative bacteria were resistant to ampicillin-sulbactam, levofloxacin, cotrimoxazole. This was in contrast with previously documented studies, which showed gram negative pathogens pathogens isolated from blood and urine of COVID-19 positive patients showed highly resistant to ampicillin, levofloxacin, piperacillin/tazobactam [29,34]. MRSA strain was seen in 60% of the *Staphylococcus* isolates. In contrast to this result, previously reported study showed methicillin resistance was observed in 100% of *Staphylococcus aureus* isolates [32]. Among the gram negative isolates in the study, 100% were ESBL strains and 28.6% were carbapenem resistance strains. Most of the previously documented studies showed high level of meropenem resistance (carbapenem resistance) among *Klebsiella* spp. and *Acinetobacter* spp., which was about 60-90% [29,34,35] in contrast to the present study. Present study showed the incidence of secondary infection in COVID-19 positive patients was maximum due to gram positive organisms followed by multiple drug resistance gram negative bacilli. BSI was predominant among COVID-19 positive patients followed by UTI and mucormycosis. As most of secondary infections in the present study were community origin, as they occurred within 48 hours of admission.

Limitation(s)

Present study was done as a single centre study done in a tertiary care hospital so the results cannot be generalised. Our hospital is a referral centre from PHCs (Primary Health Centres) and CHCs (Community Health Centres), they might acquire these pathogens at the previous hospital where they admitted.

CONCLUSION(S)

Secondary infections are more commonly seen in COVID-19 patients with co-morbidities and BSI are more commonly reported due to gram positive bacteria and multi-drug resistant gram negative bacteria. It may be difficult to differentiate which patient have co-infection/hospital acquired infection and which do not; however, proper history taking and examination should be made to determine if a bacterial co-infection is present on admission of a patient with COVID-19. Strict hospital infection control programs should be followed at all healthcare set-ups without non compliance. Antimicrobial stewardship programmes should be administered to treat patients and to decrease multiple drug resistant infections. Although secondary infections appear to be prevalent among COVID-19 patients, it is still an understudied phenomenon.

REFERENCES

[1] Esper FP, Spahlinger T, Zhou L. Rate and influence of respiratory virus coinfection on pandemic (H1N1) influenza disease. J Infect. 2011;63(4):260-66.

[2] Klein EY, Monteforte B, Gupta A, Jiang W, May L, Hsieh YH, et al. The frequency of influenza and bacterial co-infection: A systematic review and meta analysis. Influenza Other Respiratory Viruses. 2016;10:394e403.

[3] Rice TW, Rubinson L, Uyeki TM, Vaughn FL, John BB, Miller RR, et al. Critical illness from 2009 pandemic influenza A virus and bacterial co-infection in the United States. Crit Care Med. 2012;40:1487e98.

[4] Shah NS, Greenberg JA, McNulty MC, Gregg KS, Riddell J, Mangino JE, et al. Bacterial and viral co-infections complicating severe influenza: Incidence and impact among 507 US patients, 2013e14. J Clin Virol. 2016;80:12e9.

[5] Feldman C, Anderson R. The role of co-infections and secondary infections in patients with COVID-19. Pneumonia. 2021;13(1):01-05.

[6] Abdelrahman Z, Li M, Wang X. Comparative review of SARS-CoV-2, SARS-CoV, MERS-CoV, and influenza a respiratory viruses. Front Immunol. 2020;11:552909.

[7] Vijay S, Bansal N, Rao BK, Veeraraghavan B, Rodrigues C, Wattal C, et al. Secondary infections in hospitalized COVID-19 patients: Indian experience. Infection and Drug Resistance. 2021;14:1893.

[8] Boopathi S, Poma AB, Kolandaivel P. Novel 2019 coronavirus structure, mechanism of action, antiviral drug promises and rule out against its treatment. Journal of Biomolecular Structure and Dynamics. 2021;39(9):3409-18.

[9] Zhang X, Tan Y, Ling Y, Lu G, Liu F, Yi Z, et al. Viral and host factors related to the clinical outcome of COVID-19. Nature. 2020;583(7816):437-40. Doi: 10.1038/s41586-020-2355-50.

[10] Long QX, Liu BZ, Deng HJ, Wu GC, Deng K, Chen YK, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med. 2020;26(6):845-48. Doi: 10.1038/s41591-020-0897-91.

[11] Zhang H, Zhang Y, Wu J, Li Y, Zhou X, Li X, et al. Risks and features of secondary infections in severe and critical ill COVID-19 patients. Emerg Microbes Infect. 2020;9(1):1958-64. Doi: 10.1080/22221751.2020.1812437.

[12] Mirzaei R, Goodarzi P, Asadi M, Soltani A, Aljanabi HAA, Jeda AS, et al. Bacterial co-infections with SARS-CoV-2. IUBMB Life. 2020;72(10):2097-11. Doi: 10.1002/iub.2356.

[13] Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: A systematic review and meta-analysis. J Infect. 2020;81(2):266-75. Doi: 10.1016/j.jinf.2020.05.046.

[14] Yu Y, Xu D, Fu S, Zhang J, Yang X, Xu L, et al. Patients with COVID-19 in 19 ICUs in Wuhan, China: A cross-sectional study. Crit Care. 2020;24:219.

[15] Dudoignon E, Caméléna F, Deniau B, Habay A, Coutrot M, Ressaire Q, et al. Bacterial pneumonia in COVID-19 critically ill patients: A case series. Clin Infect Dis. 2021;72(5):905-06. https://doi.org/10.1093/cid/ciaa762.

[16] Hughes S, Troise O, Donaldson H, Mughal N, Moore LS. Bacterial and fungal coinfection among hospitalised patients with COVID-19: A retrospective cohort study in a UK secondary care setting. Clin Microbiol Infect. 2020;26:1395e9.

[17] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult in patients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet. 2020;395:1054e62.

[18] Cao J, Tu WJ, Cheng W, Yu L, Liu YK, Hu X, et al. Clinical features and short-term outcomes of 102 patients with coronavirus disease 2019 in Wuhan, China. Clin Infect Dis. 2020;71(15):748-55.

[19] Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical characteristics of COVID-19 in New York city. N Eng J Med. 2020;382(24):2372-74.

[20] Clancy CJ, Nguyen MH. COVID-19, superinfections and antimicrobial development: What can we expect? Clin Infect Dis. 2020;71(10):2736-43.

[21] Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for infections, 1988. Am J Infect Control. 1988;16:128-40.

[22] Henderson KL, Müller-Pebody B, Johnson AP, Wade A, Sharland M, Gilbert R. Community-acquired, healthcare-associated and hospital-acquired bloodstream infection definitions in children: A systematic review demonstrating inconsistent criteria. J Hospital Infect. 2013;85(2):94-105.

[23] Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2019. US Department of Health and Human Services, Centres for Disease Control and Prevention. 2019.

[24] Kwon WJ, Li G, Zheng M, Kaur H, Magbual N, Dalai S. Superinfections and coinfections in COVID-19–separating the signal from the noise. Medpage Today. 2020;28.

[25] Collee JG, Mackie TJ, McCartney JE. Mackie & McCartney practical medical microbiology. Harcourt Health Sciences. 1996.

[26] CLSI 31st edition M100. Available at: https://www.treata.academy/wp-content/uploads/2021/03/CLSI-31-2021.pdf.

[27] Guidelines for Handling, Treatment, and Disposal of Waste Generated during Treatment/Diagnosis/Quarantine of COVID-19 Patients– Rev. 4; CPCB Guidelines on COVID-19 related Waste Management 17th July, 2020.

[28] Ripa M, Galli L, Poli A, Oltolini C, Spagnuolo V, Mastrangelo A; COVID-BioB study group. Secondary infections in patients hospitalized with COVID-19: Incidence and predictive factors. Clin Microbiol Infect. 2021;27(3):451-57.

[29] Langford BJ, So M, Raybardhan S, Leung V, Westwood D, MacFadden DR, et al. Bacterial co-infection and secondary infection in patients with COVID-19: A living rapid review and meta-analysis. Clin Microbiol Infect. 2020;26(12):1622-29.

[30] Guo M, Gao M, Gao J, Zhang T, Jin X, Fan J, et al. Identifying risk factor for secondary infection post-SARS-CoV-2 infection in patients with severe and critical COVID-19. Front Immunol. 2021;12:715023.

[31] Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, et al. Bacterial and fungal coinfection in individuals with Coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis. 2020;71(9):2459-68.

[32] Sharma B, Sreenivasan P, Biswal M, Mahajan V, Suri V, Sehgal I, et al. Bacterial coinfections and secondary infections in COVID-19 patients from a tertiary care hospital of north India. Qatar Med J. 2021;2021(3):62.

[33] Behera B, Tripathy S, Venkateshan M, Mahapatra A, Mohanty S, Gupta K, et al. Spectrum of bacterial pathogens in critical COVID-19 patients admitted in intensive care units of a tertiary care hospital during the first and second wave of the pandemic. J Assoc Physicians India. 2022;70(2):11-12.

[34] Khurana S, Singh P, Sharad N, Kiro V, Rastogi N, Lathwal A, et al. Profile of co-infections & secondary infections in COVID-19 patients at a dedicated COVID-19 facility of a tertiary care Indian hospital: Implication on antimicrobial resistance. Indian J Med Microbiol. 2021;39(2):147-53.

[35] Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, et al. Gender differences in patients with COVID-19 focus on severity and mortality. Front Public Health. 2020;8:152.

PARTICULARS OF CONTRIBUTORS:
1. Junior Resident, Department of Microbiology, MKCG Medical College, Berhampur, Odisha, India.
2. Associate Professor, Department of Microbiology, MKCG Medical College, Berhampur, Odisha, India.
3. Assistant Professor, Department of Microbiology, SJMCH, Puri, Odisha, India.
4. Assistant Professor, Department of Medicine, MKCG Medical College, Berhampur, Odisha, India.
5. Associate Professor, Department of Medicine, MKCG Medical College, Berhampur, Odisha, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Gouri Sankar Sabat,
Lanjipo, Llychaka, Khala Street, Berhampur, Odisha, India.
E-mail: gourisankarsabat19292@gmail.com

AUTHOR DECLARATION:
• Financial or Other Competing Interests: None
• Was Ethics Committee Approval obtained for this study?   Yes
• Was informed consent obtained from the subjects involved in the study?   Yes
• For any images presented appropriate consent has been obtained from the subjects.   NA