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Clinical Profile and Outcome of Covid-19 Intensive Care Patients with Nosocomial Infections: A Single-Centred Experience from India

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ABSTRACT

Background: Incidences of nosocomial infections in COVID-19 patients admitted to the intensive care unit (ICU) have become a common occurrence. Hospital-acquired infections (HAI) present increased mortality, cost-of-care, especially relevant in multidrug resistant (MDR) infections. Our study aimed to assess the clinical implications associated with HAI-infected COVID-19 patients.

Patients and Methods: We conducted retrospective single-centred study on ICU-admitted adult COVID-19 patients for a year i.e., 2021-22 at a tertiary Indian institute and collated data of HAI epidemiological, clinical and microbiological reports.

Results: Rate of HIA at our centre was estimated to be 10.29% and the mortality rate was 40.4%. 10 different organisms(Bacteria: 8, Fungi: 2) were detected in HAI, of which the incidence of Gram-negative infections (GNI) was highest i.e., 60% and that of Gram-positive infections (GPI)/Fungi (Fungi infected) were 20% each. Mortality was highest among GPI (36.67%), FI (13.46%), followed by and GPI (7.69%). Tocilizumab treatment decreased the risk of survivability with no significant difference in the treatment outcomes.

Conclusion: This study provides a comprehensive picture of nosocomial infections characteristics among COVID-19patients and provides insights regarding the impact of treatment on the outcome of these patients with suggestions for strategies. We found that critically ill patients with COVID-19 are at a high risk of developing HAI, especially MDR mediated CLABSI and CAUTI. Clinicians must therefore be cautious and mindful during implementing protocols for management of infectious complications with COVID-19 patients.

KEYWORDS: Hospital-acquired infection, COVID-19, multi-drug resistant, retrospective study, Tocilizumab

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HIGHLIGHTS

HAI, majorly contributed by MDR bacterial/fungal strains, add to the existing infection burden and treatment challenges in Covid inflicted individuals. Careful speculation and scrutinization should be exercised in treatment measure design in such sophisticated infection challenges to target and achieve reliable healthcare outcomes in already compromised individuals.

INTRODUCTION

Since its initial outbreak in Wuhan, China, in December 2019, the COVID-19 outbreak, caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread globally and was declared a pandemic by WHO on 11th March 2020.1 The clinical presentation of this disease varies from asymptomatic to severe, fatal hypoxic pneumonia, thus leading to a rapid increase in the demand for intensive care and mechanical ventilation.2,3 In the past, several pandemics caused due to viral respiratory infections have resulted in nosocomial infections in acutely infected patients kept on mechanical ventilation support. Despite stringent infection control measures, nosocomial infections have been reported, and therefore, reducing the incidence of these infections remains a challenge.4 Moreover, these nosocomial infections account for a notable increase in intensive care unit (ICU) length of stay and increased risk of

in-hospital mortality.5 As COVID-19 is a recent event, the analysis or the study on prevalence of nosocomial/hospital-acquired infections (HAI) among COVID- 19 patients admitted to the ICU has been performed at several facilities6,7; however, limited and inconspicuous knowledge of the concerned subject is available in the literature.

Antibiotics are usually preferred for disease management; however, the risk of co-infection in COVID-19 patients on ventilation support has resulted in the uncharted use of antibiotics eventually contributing in antimicrobial resistance spurt, thus urging the judicious use of antibiotics. Recent studies have demonstrated low rates of bacterial and fungal co-infections and superinfections in COVID-19 patients, ranging from 3 percent to 14 percent.8-10 Alternatively, several other studies have reported the incidences of secondary infection in 13.5 percent to 44 percent of COVID-19 patients admitted to the ICU.11,12 Some studies have reported fewer bacterial co-infections than secondary bacterial infections.13, 14. Carbapenem-resistant Acinetobacter baumannii is a type of pathogen that typically causes infections in healthcare facilities and has been considered as a potential public health concern during the times of COVID-19.15,16Such instances of nosocimal fungal/ bacterial infections in Covid patients have been reported in Indian context as well, albeit not well-rounded. Therefore, clarity on the subject, that is, the characterization and prevalence of theseinfections is required, for scrutinized use of antibiotics and avoid their over utilization, risk of antimicrobial resistance and the occurrence of potential side effects, toxicity, and adverse events, which precipitates into greater mortality rates and inflating healthcare. Furthermore, Sogaard et al. have reported that hospital-acquired bacterial and fungal infections were higher among ICU patients (36.6 percent) than other patients (1.7 percent).17 Thus, in this retrospective study, we primarily aimed to assess the clinical features andoutcomes associated with nosocomial infections in COVID-19 patients admitted to the ICU at a tertiary care hospital in India. This is a novel study wherein nuances about the outcomes among the Indian population have been presented.

MATERIALS & METHODS

This retrospective study was conducted at a tertiary healthcare facility in Mumbai, India, after the approval from the Institutional Ethics Committee (IEC) (IEC Protocol No:-HNH/ IEC /2021/OCS/CCM /3).

Study design

The current study is a single-centered, retrospective, observational analytical study without any control group for COVID-19-positive cases. Additionally, IEC waived the requirement for written informed consent since the study only involved retrospective data analysis. Our study group included all adult patients (aged 18 years and above) confirmed with SARS-Cov-2 infection using reverse transcriptase quantitative polymerase chain reaction (RT-qPCR) test conducted on nasal and pharyngeal swab specimens confirmed as per the WHO interim guidelines6 and admitted to the hospital for more than 24 hours within the study period for a years duration between March 2020-21. However, patients transferred from other facilities were excluded from the study. Data including epidemiological history, demographics, comorbidities, radiological assessments, laboratory findings upon admission, treatments, and clinical outcome concerning device-related and non-devices-related nosocomial infections were analyzed.

Study parameters

Data were retrieved from the medical health record system with regards to baseline demographic data, PaO2/FiO2 ratio at admission and time of intubation, comorbidities profile, previous hospitalization, oxygen therapy, High- frequency Nasal cannula, ventilation therapies in the form of invasive or non-invasive ventilation prone ventilation of COVID-19 patients were recorded (Table 1). Clinical characteristics such as time from the onset of symptoms to hospitalization, APACHE II score, and radiological investigation using high-resolution computed tomography (HRCT) with CT severity index (CTSI) score were recorded. Microbiological investigations of HAI in COVID-19 patients admitted to the ICU were analyzed in accordance to hospital infection control committee protocol. Other clinical parameters, such as septic shock and gastrointestinal bleeding, were recorded in each patient. Treatment therapies were initiated as per the government task force COVID-19 treatment protocol. Antibiotics were provided per the hospital's antibiotics policy and stewardship recommendation, even during the follow-up.

Outcomes

The primary outcome measures were positive blood, urine, or tracheal aspirate cultures, body fluid cultures (others), and the classification of healthcare-associated infections per the hospital infection control policy. Secondary outcomes included patients with HAI with in-hospital mortality, ICU admission, use of non- invasive or invasive mechanical ventilation, total hospital length of stay, and ICU length of stay, all were considered while performing the analysis.

Statistical analysis

Categorical data were expressed as numbers and percentages. Chi- Square test was used for comparison of categorial variables. Fisher's exact test was employed instead of the $\chi 2$ test when >20% of cells had expected frequencies <5. Continuous parameters were presented as mean ± SD or median quartiles (25th/75th) wherein significance among groups was analyzed using Student's t-test or Mann Whitney U test, respectively. A two- tailed P-value of <0.05 was considered statistically significant for all analyses. All statistical analyses were performed using IBM SPSS 21 (IBM

SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp. IBM Corp. Released 2013).

RESULTS

Out of 505 COVID-19 patients admitted to the ICU of the hospital within the study period, 60 events of HAI occurred in 52 (10.29 percent), of which 8 were early HAI (within seven days of ICU admission). Out of these 52 patients, 60 percent survived the infection, and the rest, 40 percent, succumbed to the infection, hereon referred to as non-survivors.

Demographic & comorbidity characteristics

The median age of patients amongst the survivors was 70 years, and that amongst non-survivors was 73 years. There was no significant difference between the median age of survivors and non-survivors (p = 0.526). Further, the study population consisted of 38 males and 14 females. Among 38 males, 55 % of patients survived the HAI, and the rest 45 percent of patients succumbed to the HAI. Similarly, out of 14 female populations, 72 percent of patients were survivors, and 28 percent were non-survivors. Furthermore, no significant difference in comorbidities such as hypertension (p = 0.613), diabetes mellitus (p = 0.870), ischemic heart disease (p = 0.700), chronic kidney disease (p = 0.281), and obesity (p = 0.449) was observed between the two groups (Table 1).

Severity Index:

No significant difference was seen between the groups concerning the period from the onset of symptoms to hospitalization (p = 0.618). Additionally, there was no significant difference found in the PaO2/FiO2 ratio of patients recorded at the time of admission between the two groups (survivors and non-survivors) (p = 0.957). However, the PaO2/FiO2 ratio between the two groups of patients recorded at the time of intubation (p = 0.041) was statistically significant. Upon considering the severity scores, we found that non-survivors had high 136 APACHE II score [7.75 (10/12.25), p = 0.173] and CT severity index [20 (15.75/22), p = 0.089] as compared to their counterparts.

Treatment Variables:

The duration of oxygenation therapy via high-flow nasal cannula (p = 0.197), non-invasive ventilation (p = 0.458), non-rebreathing mask (p = 0.574), and prone positioning (p = 0.465) was noted between survivors and non-survivors and analysis showed lack of statistical significance. Further, 36 patients (69.23 percent) had to be intubated, of which 18 (i.e.,50 %) succumbed to the infection.

Outcome variables:

Out of 505 patients in the ICU study duration, 31 patients survived (60 %), whereas 21 patients (40%). The median (IQR) ICU length of stay (LOS) among survivors was 26 (22) days, whereas that among non-survivors was found to be 21 (19.5) days, suggesting that LOS in the ICU among non-survivors was shorter by 19.2 percent than among survivors. No significant difference in ICU LOS between the two groups was found (p = 0.226); however, a significant difference in total hospital LOS between the two groups was noted (p = 0.007), wherein non-survivors had shorter hospital LOS (36.7 %) than among survivors. Septic shock was observed among non- survivors (85.7 %) as compared to survivors (58 %) (p = 0.064). It was observed that 76.2 percent of deaths among non-survivors were on the account of septic shock. Lastly, gastrointestinal bleeding was observed in 14 patients (26.9 %), of which ten survived and four did not (Table 2).

1. Characterization of nosocomial infections

Predominantly, eight bacteria and two groups of fungi were identified as causative agents for the 60 events of HAI in 52 patients in our study population. We found that 64 percent of the patients who survived the infection were infected with a gram-negative bacteria (60 %), Pseudomonas aeruginosa (15 %), Acinetobacter baumannii & Kliebselia pneumoniae (11 %), and E. faecium [Vancomycin-resistant enterococci (VRE), gram- positive bacteria] (11 %) followed by Candida Auris (10 %). On the other hand, 27 patients who succumbedto the infection were predominantly infected with gram-negative organisms such as Acinetobacter baumannii (7.6 %), Klebselia pneumoniae (7.6 percent), and fungi such as non-Candida Auris (7.6 percent). Upon further categorizing isolates into multi-drug resistant (MDR) or non-MDR strains, we found that MDR strains were identified in 51 samples; in contrast, only 11 samples were of non-MDR type. However, no significant difference in the distribution of MDR strains between survivors and non-survivors was observed (p = 1.000) (Table 3). Furthermore, 22 percent were identified with no devices-related HAI, while 78 percent were catheter/device- related. Among device-related infections, the incidence of ventilator-associated pneumonia (VAP) was estimated to be 6.24/1000 ventilator days. In contrast, the incidence of catheter-associated urinary tract infections (CAUTI) was 3.61/1000 catheter days, and central line-associated bloodstream infections (CLABSI) was 10.41/1000 line days.

2. Drug therapies used in infected COVID-19 patients

A high number of patients receiving Tocilizumab were non-survivors 57 percent compared to the survivors 43 percent; however, no significant difference in the treatment outcomes of the two groups was observed (p = 0.135). Interestingly, patients treated with Itolizumab had more survivors, 56 percent, than non-survivors, 44 percent. However, similar to the Tocilizumab treatment outcome, no significant difference in the Itolizumab treatment outcomes of the two groups was observed (p = 1.000). There was no significant difference in the distribution of patients receiving steroid treatment (p = 0.269). Moreover, patients receiving steroid treatments were

mainly provided with dexamethasone, which may have proven effective, as 60.7 percent of patients survived and 40 percent failed to survive because of the infection. This trend was not picked up in patients receiving methylprednisolone and hydrocortisone. However, the efficiency of dexamethasone may also be attributed to the fact that it was administered for 15.5 days (median) to survivors as against five days (median) to non-survivors. Lastly, no significant difference in the treatment outcomes of antibiotics (BLBI, Carbapenem, and non- Carbapenem) and antifungals (fluconazole, Anidulafungin, Micafungin, Caspofungin, Posaconazole, amphotericin B, and Voriconazole) between survivors and non-survivors was observed (Table 4).

3. Strategies to reduce HAI (figure1 & 2)

Figure 1 shows the monthly incidence of HAI in our study population. A total of 60 HAI events were recorded among 52 patients. Of 60, 37 were MDR bacteria, followed by 11 non-MDR bacteria. The highest HAI incidences were reported in September (14) and October (11). 5 PRONG strategy was implemented to control the incidence of HAI post-October. The monthly HAI incidence rate declined; just 14 HAI cases were reported in the next five months. Figure 2 shows the HAI rates pre and post-5 PRONG strategy. Pre-5 PRONG strategy, the VAP infection rate was 6.19, slightly increasing to 6.39 in the post-5 PRONG. However, the CAUTI infection rate reduced from 4.03 to 2.57 post-5 PRONG implementation. A 36.22 percent decrease in CAUTI infection was observed. 197 Also, the CLABSI infection rate reduced from 11.79 in the pre-5 PRONG strategy to 7.70 in the post-5 PRONG. A 34.69 percent reduction was seen in the CLABSI infection rate post-5 PRONG implementation.

DISCUSSION

In this study, we investigated epidemiological features and risk factors associated with HAI and their outcomes in ICU patients affected with COVID-19 during the study period of one year at a tertiary care hospital. We found that almost 52 patients (10.29 %) acquired HAI, and the mortality rate was reported to be 40.4 percent. Khurana et al. have reported a slightly higher incidence of secondary infection (13 percent) with an in-hospital mortality rate of 33 percent.18 In a comparative analysis by He et al., notably higher mortality (15.4 percent) was reported among COVID-19 patients with HAI than those amongst COVID-19 patients without HAI (7.3 percent).19 Further, upon performing microbiological analysis, ten different organisms were detected in HAI; among these, 56 percent were Gram Negative bacteria. This finding is in accordance with the findings of Vincent et al., that reported the presence of Gram-negative microorganisms in majority than that of Gram- positive microorganisms in specimens collected from patients with HAI.5 Amongst Gram-negative bacteria, Pseudomonas aeruginosa 15 percent, Acinetobacter baumannii 13 percent and Klebselia pneumonia 12 percent were found to be the most common cause of HAI. On the other hand, amongst Gram-positive bacteria, Enterococcus faecium (VRE) 12 percent was found to be the most common cause of HAI. Similar studieshave demonstrated the presence of Gram-negative bacteria (Enterobacterales, A. baumannii, P. aeruginosa), with few other findings reporting the most common causative agents of HAI to be Mycoplasma pneumoniae, P. aeruginosa, H. influenza, and Klebselia sp., which is similar with the finding of our study.9-10,20 Another valuable finding with a potentially crucial clinical relevance is that MDR bacteria were identified in 85 percent of HAI. Out of 52 HAI-infected patients, 31 were infected with MDR strains, and the rest 21 patients were non- MDR with no considerable impact on the two groups. This outcome is probably due to prolonged use of broad- spectrum antibiotics, steroids, and COVID-19 inflammatory process leading to increased mucus production, impaired mucociliary clearance, and epithelial cell breakdown in addition to the lack of adherence to infection control measures because of understaffing and unexpected increased workload in the ICU during the pandemic. Furthermore, among device-related infections, we found that the incidence of ventilator- associated pneumonia (VAP) was 6.24 /1000 ventilator days, which is comparatively low as compared to the high incidence of VAP (28/1000 and 18/1000 ventilator days) found among critically ill COVID-19 patientsin a similar study conducted by Maes et al. and Giacobbe et al.22,23 Similarly, in a study conducted by Meynaar et al., 24 the incidence of CLABSI was estimated to be 6.25/1000 line days among COVID-19 patients, whichis only slightly lower than the incidence of CLABSI (10.41 /1000 line days) estimated in the COVID-19 patients of our study group. Thus, we can say that the incidence of device-related infections in our study group was comparatively less than those documented in other literatures. Lastly, in our study, Tocilizumab waswidely used as an immune-modulatory therapy and was found to be associated with an increase in mortalityrisk amongst HAI-infected COVID-19 patients. However, the difference between the survivability and non- survivability of patients was insignificant. Similarly, Guaraldi et al. 25 reported increased co-infections among COVID-19 patients when treated with Tocilizumab, suggesting that Tocilizumab may not be the best treatment strategy for COVID-19-infected patients. Additionally, Chowdhary et al. have reported Candida Auris as the predominant causative agent of HAI among COVID-19 patients with a fatality rate of 60 percent, suggesting adverse outcomes for these patients.[21]

Strategies implemented to reduce HAI **(Figures 1 & 2)**

In order to curtail this increasing incidence of HAI among COVID-19 patients, stringent infection control measures were adopted. Besides the repetitive education sessions on the

importance of hand hygiene, we also implement the following strategies: restricting the use of Carbapenem as part of antibiotic stewardship to prevent the rising resistance of Gram-negative bacteria22. We also introduced blue-colored glovessurveillance, where healthcare personnel in the ICU were only allowed to use blue-colored gloves for bedside care and nowhere else in the unit; this was an attempt to prevent cross-contamination. Patients with MDR infections were cohorted separately to prevent the spread of MDR infections, and specialized, focused care was given to such groups of patients. In addition, environmental hygiene, especially for disinfection of high- touch surfaces carried out every 4 hours (Monitor knob, bed rails, door handle, etc.,) was done using higher concentration formaldehyde in rooms with patients harboring MDR bugs. Fungal infection and MDR bacteria tend to grow more rampantly with a high humidity factor in the ICU; we targeted a relative humidity of <60 percent was controlled with de- humidifier machines installed in the ICU.

LIMITATIONS

There were some limitations to our investigation. First, as it is a retrospective analysis of data collected primarily for clinical reasons in one of the COVID-19 hotspots, not all data were available for all patients. The current study was conducted in a single center in western India. It may be inappropriate to generalize and extrapolate the study findings to the entire population.

CONCLUSION

The current study provides a comprehensive look at not only the characteristics of nosocomial infections among COVID-19 patients but also provides insights regarding the impact of treatment on the outcome of HAI-infected COVID-19 patients and suggests strategies to control HAI infections. We found that critically ill patients with COVID-19 are at a high risk of developing HAI, especially CLABSI and CAUTI, frequently caused by MDR bacteria. Therefore, clinicians must undertake every effort to implement protocols for surveillance and prevention of infectious complications while treating COVID-19 patients. Thus to conclude,at our center, Gram-negative organisms such as Pseudomonas, Acinetobacter baumannii Klebselia pneumoniae, and fungi such as Candida Auris were equally responsible for mortality due to HAIand MDR contribution to this mortality was significant.

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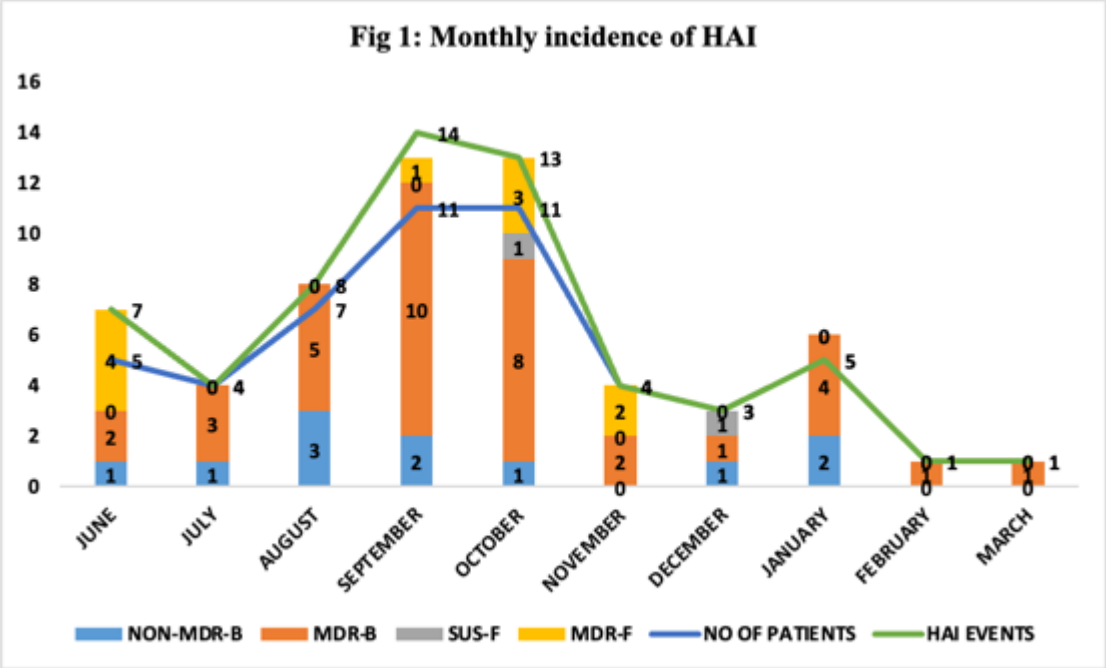

Figure 1: Monthly HAI incidence

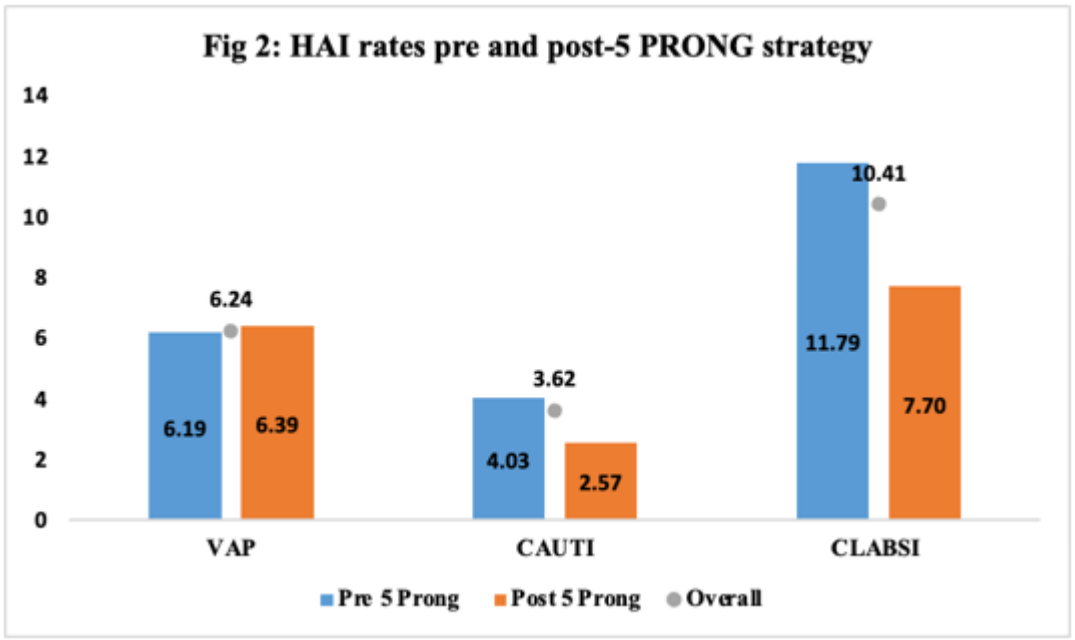

Figure 2: HAI rates pre and post-5 PRONG strategy

Table1. Demographic and clinical data of HAI patients Table 2. Characteristics and severity of patients with HAI in COVID-19

	Survivors	Non-survivors	*p*-value
APACHE II[2]	8 (6.00/12)	7.75 (10/12.25)	0.173
CTSI[2]	14.5 (11.5/20)	20 (15.75/22)	0.089
Intubation[1]			
No	13 (41.94%)	03 (14.29%)	0.064
Yes	18 (58.06%)	18 (85.71%)	
HFNC (Days) [2]	0(0/1)	0 (0/0.0)	0.197

Covariates	Survivors	Non-survivors	*p*-value
NUMBER	**31(59.6%)**	**21(40.3%)**	
Gender[1]			
Male	21 (67.74)	17 (80.95)	0.353
Female	10 (32.26)	04 (19.05)	
Age (Years)[2]	70 (59.00/78.00)	73 (62.50/80.00)	0.526
Time of symptoms onset to hospitalization[2]	4 (3.00/7.00)	5 (3.00/ 7.00)	0.618
Obesity[1]			
No	25 (80.65)	19 (90.48)	0.449
Yes	06 (19.35)	2 (9.52)	
Hypertension[1]			
No	14 (45.16)	8 (38.10)	0.613
Yes	17 (54.84)	13 (61.90)	
Diabetes Mellitus[1]			
No	14 (45.16)	9 (42.86)	0.870
Yes	17 (54.84)	12 (57.14)	
Ischemic Heart Disease[1]			
No	27 (87.10)	17 (80.95)	0.700
Yes	04 (12.90)	04 (19.05)	
Chronic Kidney Disease[1]			
No	26 (83.87)	15 (71.43)	0.281
Yes	05 (16.13)	6 (28.57)	
Note: 1= Numbers and Percentages, 2 = Median and IQR			

Table 2. Characteristics and severity of patients with HAI in COVID-19

NIV (Days) [2]	2 (0/9)	3 (1/9)	0.458
O2 Therapy NRBM (Days) [2]	1 (0/5)	1 (0/4)	0.574
Prone (Days) [2]	2 (0/9)	0 (0/8.5)	0.465
P/F at admission[1]			
≤100-1	15 (48.39)	10 (47.62)	0.957
>100-2	16 (51.61)	11 (52.38)	
P/F at Intubation[1]			
Not intubated	13 (41.94)	3 (14.29)	0.041
≤100-1	14 (45.16)	17 (80.95)	
>100-2	04 (12.90)	1 (4.76)	
Admitted Elsewhere[1]			
No	14 (45.16)	9 (42.86)	0.870
Yes	17 (54.84)	12 (57.14)	
LOS (ICU) (Days) [2]	26 (18/40)	21 (14.5/34)	0.226
LOS in Hospital (Days) [2]	34 (26/42)	21.5 (14.25/38.75)	0.007
Septic Shock[1]			
No	13 (41.94)	03 (14.29)	0.064

Yes	18 (58.06)	18 (85.71)	
GI Bleeding [1]			
No	21 (67.74)	17 (80.95)	0.353
Yes	10 (32.26)	04 (19.05)	
Cause of Death - Septic Shock[1]			
No	NA	05 (23.81)	
Yes	NA	18 (76.19)	
Multi-Drug Resistant[1]			
No	6 (19.35)	5(23.80)	1.000
Yes	25 (80.64)	16 (76.19)	
Note: 1= Numbers and Percentages, 2= Median and IQR			

Table 3. Distribution of microorganisms between survivors and non-survivors of HAI patients.

Sr.no	TYPE OF ORGANISM	CLABSI			CAUTI			VAP			BACTEREMIA			SUTI			Total	% incidences	Survived	% survival	Not-Survived	% non survival
	Gram-negative Organism	MDR	Non-MDR	Total	MDR	Non- MDR	Total	MDR	Non- MDR	Total	MDR	Non-MDR	Total	MDR	Non- MDR	Total						
1	Enterobacter Cloacae	1	1	2	0	0	0	1	0	1	0	0	0	0	0	0	3	5.00%	1	1.923076923	2	3.85%
2	Ac. baumannii	4	0	4	1	0	1	2	0	2	1	0	1	0	0	0	8	13.33%	4	7.692307692	4	7.69%
3	Pseudo aerugi	2	1	3	1	0	1	1	1	2	1	0	1	1	1	2	9	15.00%	8	15.38461538	1	1.92%
4	Escherichia coli	0	0	0	3	0	3	0	0	0	0	0	0	1	0	1	4	6.67%	3	5.769230769	1	1.92%
5	Klebselia Pneumoniae	2	0	2	0	0	0	3	0	3	1	0	1	1	0	1	7	11.67%	3	5.769230769	4	7.69%
6	Others	2	0	2	1	0	1	3	0	3	0	0	0	0	0	0	5	8.33%	1	1.923076923	4	7.69%
	Total Gram negative	11	2	13	6	0	6	10	1	11	3	0	3	3	1	4	36	60.00%	20	38.46153846	16	30.77%
	Gram Positive Organism																					
1	Enterococcus Faecium	0	1	1	0	2	2	0	0	0	0	0	0	0	1	1	4	6.67%	3	5.769230769	1	1.92%
1	E. Faecium (VRE)	1	0	1	2	0	2	0	0	0	2	0	2	2	0	2	7	11.67%	5	9.615384615	2	3.85%
2	E. fecalis	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1.67%	0		1	1.92%
	Total gram positive	1	2	3	2	2	4	0	0	0	2	0	2	2	1	3	12	20.00%	8	15.38461538	4	7.69%
	Fungal organisms																					
1	Candida auris	3	0	3	2	0	2	0	0	0	1	0	1	0	0	0	6	10.00%	3	5.769230769	3	5.77%
2	Non candida auris	2	1	3	0	0	0	2	0	2	0	1	1	0	0	0	6	10.00%	2	3.846153846	4	7.69%
	Total fungal	5	1	6	2	0	2	2	0	2	1	1	2	1	0	1	12	20.00%	5	9.615384615	7	13.46%
	Total Hai Events	17	5	22	10	2	12	12	1	13	6	1	7	6	2	8	60		33	63.46153846	27	51.92%

(CLABSI= Central line associated blood stream infection; CAUTI=Catheter associated urinary tract infection; VAP= Ventilator associated pneumonia; SUTI= ; VRE= Vancomycin resistant enterococcus)

Table 4. Pharmacological therapies used in HAI-infected COVID-19 patients

	Survivors	**Non-survivors**	***p*-value**
Tociluzumab[1]			
No	25 (80.65)	13 (61.90)	0.135
Yes	06 (19.35)	08 (35.00)	
Itolizimab[1]			
No	26 (83.87)	17(80.95)	1.00
Yes	5 (16.13)	4 (19.05)	
Predominant steroid[1]			
No	0 (0.00)	2 (10.00)	0.269
Dexamethasone	17 (60.71)	08 (40.00)	
Methylprednisolone	9 (28.57)	09 (35.00)	
Hydrocortisone	5 (10.71)	02 (15.00)	
Antibiotics			
Initial antibiotic[1]			
No	13 (35.71)	4 (15.00)	0.188
Yes	18 (64.29)	17 (85.00)	
BLBI antibiotics[1]			
No	5 (17.86)	1 (5.00)	0.379
Yes	11 (82.14)	20 (95.00)	
Carbapenems[1]			
No	21 (75.00)	12 (60.00)	0.349
Yes	10 (25.00)	9 (40.00)	
Non-carbapenam[1]			
No	9 (21.43)	3 (5.00)	0.214

Yes	22 (78.57)	18 (95.00)	
Antifungals			
Flucanazole[1]			
No	19 (64.29)	16 (70.00)	0.763
Yes	12(35.71)	5(30.00)	
Anidulafungin [1]			
No	24 (75.00)	17 (75.00)	1.000
Yes	7 (25.00)	4 (25.00)	
Micafungin[1]			
No	27 (85.71)	16 (80.00)	0.703
Yes	9 (14.29)	5(20.00)	
Caspofungin[1]			
No	24 (82.14)	15 (80.00)	1.00
Yes	7 (17.86)	6(20.00)	
Posaconazole[1]			
No	30 (96.43)	17 (85.00)	0.294
Yes	1 (3.57)	4 (15.00)	
Amphotericin b[1]			
No	29 (92.86)	18 (85.00)	0.636
Yes	2 (7.14)	3 (15.00)	
Voriconazole[1]			
No	29 (92.86)	21 (100.00)	0.504
Yes	2 (7.14)	0 (0.00)	
Note: 1= Numbers and Percentages, 2= Median and IQR			