ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 08 | August - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY OF BLOOD CULTURE ISOLATES IN COVID-19 PATIENTS IN TERTIARY CARE TEACHING HOSPITAL

Microbiology

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ABSTRACT

Background: Coronavirus is known to cause respiratory tract infection with illness ranging from mild to severe disease depending upon morbidity. This retrospective observational study was done to determine the prevalence of bloodstream infections in COVID-19 patients admitted in a tertiary care centre in civil hospital, Ahmedabad. **Methods:** The study objectives were as follows: (a)To determine the prevalence of blood stream infection in COVID-19 positive patients. (b)Antimicrobial susceptibility testing of these isolates as per standard guidelines. All blood cultures received from COVID-19 positive patients with signs and symptoms of BSI admitted into various wards and ICUs of COVID-19 hospital were included in the study. Blood samples were received in automated blood culture bottles and monitored on automated blood culture system. ID and susceptibility of all the isolates were performed on automated system (VITEK 2). **Results:** A total of 9936 patients which were further reported rRT-PCR positive for SARS nCoV2 during the period of August 2020 to July 2022. 700 patients developed sepsis like syndrome and were subjected to blood culture. The Blood culture positivity was 140/700 (20%). 85 (61%) patients needed intensive care in ICU. Significant correlation of blood culture positivity was found with parameters like ICU admission, presence of an indwelling device, underlying comorbidity, and adverse clinical outcome. **Conclusion:** The incidence rate and the risk of developing BSI increased with ICU stay. Staphylococcus aureus and Enterococcus was the commonest amongst Gram positive bacteria. Gram negative secondary bacterial infections such as Acinetobacter baumannii and Klebsiella pneumoniae were more common with patients on ventilator. The susceptibility pattern would help in decision making of empirical antibiotic therapy.

KEYWORDS

BSI, Coronavirus, COVID-19, SARS-CoV-2, Sepsis

INTRODUCTION:

Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in December 2019 in Wuhan, China.[1] Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a newly emerging, highly transmissible, and pathogenic coronavirus in humans.

The outbreak of SARS CoV-2 was declared as 'Public Health Emergency of International Concern (PHEIC)' on 30th January 2020. It causes global public health emergencies and economic crises. Till July ,2022 there are reported cases of COVID-19 more than 4 crores and more than 5 lakh deaths occurred in India. In India waves of explosion in cases of COVID-19 was seen in September 2020, second wave in April 2021 and third wave in January 2022.

Blood Stream Infections (BSI) are the major cause of morbidity & mortality among COVID-19 positive patients admitted in Intensive Care Unit (ICU) & surveillance of etiological agents in these infections are important for their prevention & treatment.[2] Bacterial coinfection is a common complication of many viral respiratory tract infections and leads to significantly increased morbidity and mortality[2]. Bacterial coinfections were associated with increased risk of shock and respiratory failure, prolonged ICU length of stay, and mortality.[3,4]

Information regarding secondary bacterial infections is limited. Thus, this retrospective study was done to determine the prevalence and spectrum of bloodstream infections in COVID-19 patients, and also find out the common causative agents of blood stream infections in Covid 19 patients admitted to ICU and wards in a tertiary care center in Civil hospital Ahmedabad. The study also determine antimicrobial sensitivity pattern of these isolates and clinical outcome of patients.

MATERIALS AND METHOD:

This Retrospective laboratory based observational study was carried out at tertiary care center of Civil hospital Ahmedabad from August 2020 to July 2022. After institutional Ethical Committee approval, this study was conducted at Microbiology Department, Tertiary Care Teaching Hospital. Informed consent was obtained from the patients before their enrolment in the study. The diagnosis of COVID-19 was confirmed by positive result of real-time reverse-transcription polymerase chain reaction (rRT-PCR) for respiratory specimens (throat and nasopharyngeal swabs). The blood culture were received from patients admitted into various wards and ICUs of COVID-19 Hospital. During this period a total of 9936 confirmed cases were reported based on rRTPCR test for Covid19. According to sequential Organ Failure Assessment (SOFA) score, 700 patients developed sepsis like syndrome and were subjected to blood culture.

Blood samples were received in automated blood culture bottles. Specimens are received in the Bacteriology Laboratory and were processed for the isolation and identification and antimicrobial susceptibility testing of isolated organisms using standard microbiological methods which includes conventional and automated VITEK 2 Compact system, Screen agar test and Broth Microdilution (BMD) Test.

The objectives of studies are as following: 1. To know the Prevalence of secondary blood stream infection in Covid 19 patients. 2. To study the common etiological agents involved in blood stream infection in Covid 19 patients. 3. To study the pattern of antimicrobial susceptibility to predict empirical treatment.

Inclusion criteria: COVID-19 rRT-PCR positive cases with sign & symptoms of blood stream infections such as: Fever with or without chills, diaphoresis, tachypnea, tachycardia, leukocytosis and leucopenia. Exclusion criteria: COVID-19 rRT-PCR negative cases.

Identification of BSI and its sensitivity pattern:8-10 ml of blood for adult patient and 1-3 ml blood for pediatric patient was dispensed in a properly labelled Bact Alert bottle. The bottles were then transported to the Bacteriology laboratory where they were loaded into the BacT Alert 3D 120 Automated Microbial Growth Detection System. The bottles were incubated for minimum 5 days. Upon flagging positive, the bottles were taken out of the instrument and the time to detection (TTD) was noted. All those bottles which did not flag positive within 5 days were considered as no growth. The positively flagged bottles were subjected to Gram's stain and culture into Blood agar, Chocolate agar and MacConkey agar. After 16-18 h of incubation at 37°C the cultures were read for the Growth of colonies morphology, Gram's stain and various biochemical reaction. Organism also confirmed by VITEK2 Compact Automated System. Antibiotic susceptibility testing was performed by Kirby Bauer's disk diffusion method. The zone of inhibition for different antibiotics is compared to the criteria

set by the Clinical and Laboratory Standards Institute (CLSI). [6]

RESULTS:

During the study period of two years (August 2020 to July 2022), a total of 59,974 samples received. Out of them 9936 patients were tested positive with real-time RT-PCR confirmed COVID-19 were admitted to various wards/ICUs.

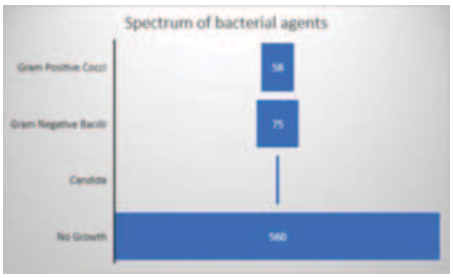

Chart 1: Organism Wise Distribution Of Blood Culture Positive Isolates In Covid-19 Rtpcr Positive Cases

A total of 700 Blood Cultures were received from COVID-19 RTPCR positive cases during this time. Out of these 140 (20%) showed positive blood cultures and 560 (80%) showed negative. There were 58 (8%) gram Positive cocci (GPC), 75(10%) gram Negative bacilli and 7 candida are also isolated from Blood culture. 80% samples were seen with no growth. The majority of patients 66% (92/140) were males.

Table 1: Ward Wise Distribution Of Bsi In Covid-19 Rtpcr Positive Cases

LOCATION	BLOOD CULTURE POSITIVE	BLOOD CULTURE NEGATIVE
ICU	85 (61%)	192
OTHER WARDS	55(39%)	368
TOTAL	140(100%)	560

Highest number of blood culture positivity seen in sample received from ICU patients (61%).

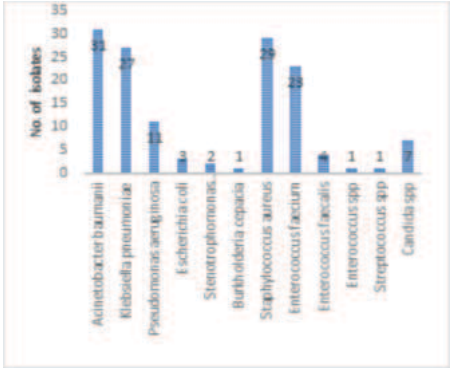

Chart 2: Distribution Of Microbial Profile Of Covid 19 Patients With Sepsis

Total culture positive organism 140. Gram positive organism were 58(41%). In gram positive most common isolated organism *Staphylococcus aureus* 29 (20%) followed by Enterococcus faecium 23 (16%). Gram negative organism were 75(54%). Most commonly isolated Gram negative organisms were Acinetobacter baumanii 31(23%) followed by Klebsiella pneumoniae 27(19%). Candida species isolated from 7 patients.

Chart 3: Antimicrobial susceptibility of Staphylococcus Aureus

Total 29 Staphylococcus aureus were isolated. Out of them 7(25%) were MRSA and most of the isolates were sensitive Linezolid, Vancomycin and Tigecycline (100%), also Amikacin, Tetracycline and Doxycycline (80%).

Antimicrobial susceptibility pattern seen in Enterococcus spp. Out of 29 ,1 were shown resistance to Linezolid (7%) LZR, 2 were shown resistance to Vancomycin (14%) VRE and 11 were shown to high level gentamycin (78%) HLAR. 1 Enterococcus faecium isolates were having resistance to Vancomycin and High level Gentamicin confirmed by VITEK 2 Compact automated system.1isolates were resistant to all the 3drugs: Vancomycin, Linezolid and High level Gentamicin.

Total 31 *Acinetobacter baumannii* were isolated. Out of them 100% sensitive to Colistin and 71% sensitive to tigecycline. 26 (83%) isolates were Extended spectrum β lactamase producing (ESBL). 18 isolates were carbapenemase producing.

Total 27 *Klebsiella pneumoniae* were isolated. Out of these 70% were Carbapenemase resistant. Other than that, more no of *Klebsiella pneumoniae* were Resistant to Cephalosporins, Ciprofloxacin. 24 isolates were Extended spectrum β Lactamase producing *Klebsiella pneumoniae*. 19 isolates were Carbapenemase producing.

DISCUSSION:

Bacteremia has been described as a complication of COVID-19 infection.[7-10] Blood culture constitutes an important investigation for bringing more clarity into clinical judgment.

Patients with severe COVID-19 are likely to develop sepsis like syndrome with cytokine storm. The secondary blood stream infection in such patients may result in longer hospital stay and poor prognosis. The risk factors for acquisition of secondary blood stream infection can vary amongst the patients depending on the individual co morbid conditions as well as ongoing drug treatment. As many patients are subjected to steroids for immune suppression to prevent cytokine storm the chances of secondary infections rise. The incidence of secondary bacterial infections reported from different countries varies. [12]

Early identification of bloodstream pathogens and their antibiotic resistance profile is necessary to improve clinical outcome.[11]

This study was conducted to identify the prevalence, characteristics, etiological agents involved, antimicrobial sensitivity pattern, and clinical outcomes in COVID-19 patients with bloodstream infections admitted in our tertiary care hospital.

This study found a 20% incidence of BSIs in a population from tertiary care teaching hospital Ahmedabad which is slightly higher than previously reported rates in patients from New York,[15,16]Sweden,[19] London,[17]and Italy,[18] but lower than those from New Jersey.[20]

Majority of patients who developed bacteremia in our study were critically ill and admitted in ICU. About a third of our population was admitted to the ICU, and patients with positive blood cultures were more likely to be admitted to the ICU, have more severe disease. Association of blood culture positivity and need for intensive care in ICU was found to be significant.

In our Study overall incidence of Blood culture positivity rate higher that is 20%. In study conducted by Rachana patel[12]at Gujarat, India in year2020, Incidence was found to be 22.28%. Similar study was conducted by Ekadashi Rajni [13] at Jaipur, India in year 2020 in which incidence was 9.4%.

In our Study, out of total positive patients, 66% were male while 34% were female. So, the incidence was more in males than females, which is comparable to Rachana patel (76%), Ekadashi Rajni(67%), Naveenraj Palanisamy(66%), In which incidence was more in males. In Our Study, out of total 61% Positivity rate in ICU patients, which is comparable to 67% in Ekadashi Rajni study.

In the our study, most common Gram-Negative organisms were *Acinetobacter baumannii* (23%) which is agreement with the study of

Naveenraj palanismay that reported. Among Gram Positive organisms, most common *Staphylococcus aureus* (21%) and Enterococcus spp (20%). which is agreement with the study conducted by Naveenraj Palanisamy(17.2%) and Rachana patel which is(35%). In our study Candida (6%) isolated, which is comparable to study of Rachna Patel in which candida isolated(8.1%).

In our study among Gram positive cocci most of them were sensitive to Linezolid, Tigecycline and Trimethoprim -sulfamethoxazole is comparable to the study done by Rachana patel.

The study done by Rachana patel also indicates higher incidence of Gram positive bacterial sepsis in Covid 19 patients. In the same study they have reported higher prevalence of secondary blood stream infections due of Enterococcus species because of their intrinsic resistance against routine prophylactic third generation cephalosporins. Enterococci spp were isolated in 58/140 Gram positive cocci isolates. Of the 28 Enterococcus spp, Enterococcus faecium (23), Enterococci faecalis (4), Enterococcus spp (1) in our study.

Gram negative secondary blood stream infection rates in our study was 54%. The incidence of gram negative sepsis was found to be more amongst patients on Ventillator. Among Gram negative bacilli *Acinetobacter baumannii*(31/75),Klebsiella pneumonia (27/75),Pseudomonas aeruginosa (11/75)followed by Escherichia coli(3/75) and Stenotrophomonas maltophila (2/75),The uncommon organisms were Burkholderia cepacia (1/75). The Klebsiella and Acinetobactor spp. Isolates were multidrug resistant.

Few studies have reported fungal coinfections in COVID-19 patients.[21,22]Candida tropicalis (2/140) was isolated in two patients and was susceptible to all available antifungal agents. Candida albicans (1/140) was isolated in one patient and was resistant to fluconazole. Candida spp (4/140) was isolated. out of them 2 were resistant to clotrimazole and 1 was resistant to fluconazole. And rest 1 is sensitive to all antifungal agents.

All COVID-19 positive symptomatic patients in our hospital were given antibiotic azithromycin empirically. exposure to antimicrobials increases the risk of drug resistance. According to a recent study, the use of combination antimicrobials was found to be associated with secondary infections[23]. Patients in whom secondary bacterial infection was suspected, further antibiotics were added on a case-to-case basis after blood culture sample collection. Later, therapy was tailored according to antibiotic susceptibility reports provided by the laboratory.

CONCLUSION:

Incidence of bloodstream infections appears to be low for COVID-19 patients. Covid 19 has complex disease pathogenesis. Patients on immunosuppressive therapy are at risk of developing secondary blood stream infections. Initially most of the secondary BSI were endogenus as *Enterococcus spp* was most prevent organisms. Patients admitted to the ICUs are also at risk of developing nosocomial infections.

The patients on mechanical ventilator are at risk of ventilator associated infections. Gram negative organisms were more common in VAP.

The study will guide in selection of antibiotic during secondary blood stream infections depending the stage of the disease.

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