Clinical Profile of Severe Covid-19 Patients with Sepsis associated Multiorgan Dysfunction Syndrome

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ABSTRACT

Background: The uninhibited spread of a novel coronavirus termed as severe acute respiratory disease coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV), has led to the emergence of the coronavirus disease 2019 pandemic worldwide, more popularly known as the COVID19 pandemic. There have been over 86 million global confirmed cases till date, and the disease is known to have a 2.2% case fatality rate, having claimed over 1.87 million lives. Initially having being regarded as a purely respiratory disease with symptoms of viral pneumonia such as fever, fatigue, dry cough, and lymphopenia, Covid19 is now also known to wreak havoc on organs such as the kidney, heart, liver and on organ systems such as the blood and the immune system and lead to development of sepsis induced multiorgan dysfunction syndrome. Many older patients with existing comorbidities such as cardiovascular disease, liver disease, kidney disease or malignant tumors, have been recorded to have a more severe infection and have reportedly been at a higher mortality risk. Hence there is a need to be more attentive of the potential multi-organ injuries and to determine the factors that contribute to their progression in order to prevent the worsening prognosis that has come to be associated with COVID-19.

Objectives: To determine epidemiological profile of the patients with severe covid 19 infections associated with multi-organ dysfunction syndrome.

To correlate clinical, biochemical and radiological profile of Covid patients with sepsis.

To assess the outcome (Discharge, death and duration of ICU stay) in Covid 19 patients with sepsis.

Methodology: The data would be collected from the medical profiles of the patients severely infected with Covid 19, being treated according to the guidelines issued by WHO. The group of cases progressing further to septicemia will be compared with the control group of the severe covid cases not landing into sepsis. The outcomes of the cases will then be analyzed based on the clinical parameters. The study will be conducted in the states of Maharashtra, Uttar Pradesh and Delhi as these are amongst the worst hit states in the second wave of Covid 19.

Results: The study would play a key role in in assessing the epidemiological as well as the clinical parameters leading to the MODS in severe Covid 19 infections associated with sepsis

Conclusion: The results concluded from this study could possibly put a curb on the worsening prognosis by identifying a particular set of factors beforehand.

Key words: Covid 19, Septic shock, Cytokine storm, Multi-organ dysfunction syndrome, Extra-pulmonary pathologies

INTRODUCTION

The World Health Organization (WHO) has coined the gripping coronavirus as SARS-CoV-2, which was previously known as 2019-nCov. This virus has now turned out to be a rapidly expanding pandemic [1], the

virus shows confirmed transmission through respiratory droplets, and proximity to mucosal facets with fomites [2,3]. The spread of infection is also determined from the stools of already infected patients [4].

The coronavirus infection has been known to show a wide range of signs and symptoms from asymptomatic and severe patterns [5]. In general, a high rate of patients has been found to be asymptomatic and the ones with mild infection exhibit the common cold manifestations, fever, dry cough, and myalgia [5], and show a favorable prognosis. The healthcare professionals are working tirelessly, and are honoring their services towards the general population, despite the threat of getting infected. Worsening prognosis has been seen in the patients who present with certain co-morbities [6] who, therefore, had poorer prognosis and comparatively narrow chances to recover successfully [7]. Coronavirus infection often presents with the complications of dyspnea and orthodoxia syndromes. In addition to lungs, the virus has been known to cause detriment to other organs such as the kidneys, liver, and heart, along with body systems such as nervous and hematological and induce multiorgan failure [8].

The complete blood count parameters including the D-dimer levels, lactose dehydrogenase levels and interleukins along with tumor necrosis factors, platelet-derived growth factor (PDGF), are seen deranged [9-13]. Another high mortality risk factor in COVID infected patients was reported to be a high neutrophil-to-lymphocyte ratio (NLR) [14] In addition to this, activation of the complement system leading to cytokine storm that results in inflammatory cells infiltration, amplified and poorly regulated immune responses and impaired coagulation in SARS-CoV2 infection has been known to induce the multi-organ failure in the patients. Counteracting effects such as these hinder the complete obliteration of the virus and pave the way for opportunistic pathogens to cause secondary infections, thus resulting in a sepsis-like state, which was recorded in 17% of patients, 65% of whom have worsened and succumbed to the illness. Greater increases in serum concentration of several pro-inflammatory mediators, brought on by the cytokine storm, have been recorded in the patients admitted to the Intensive care units (ICU), which indicates a direct correlation with severity of the disease [10-13].

Hence, it is seen that, there is a need to determine the epidemiological and clinical factors for the infected patients progressing towards the multiorgan dysfunction syndrome, and further information about the precise mechanisms of pathogenesis of sepsis caused by the novel coronavirus needs to be computed to increase the clinician's knowledge facilitating their determination of the clinical characteristics of viral sepsis and the identification of the risk factors more accurately, so that the mortality and morbidity rate decreases and the outcomes become more favorable.

Aim

This study aims to accurately determine the clinical parameters and the epidemiological profile of the patients infected with corona virus disease 19, which are further progressing to septicemia and Multi organ dysfunction syndrome.

Objectives

To determine the epidemiological profile of the patients with severe covid 19 infections associated with multi-organ dysfunction syndrome.

This study will help to correlate the clinical parameters, biochemical investigations and the radiological profile of Covid 19 patients presenting with sepsis.

This survey will assist in assessing the outcome [Discharge percentage, fatality rates and duration of the stay in Intensive care unit] in Covid 19 infected patients with sepsis.

MATERIALS AND METHODS

Study design

This survey will be conducting as a retrospective cohort study.

Study population

Corona virus disease cases, that were diagnosed using the RT-PCR testing kit, who also showed associated symptoms of septicemia and are undergoing the World Health Organization (WHO) specified guidelines for treatment; classified on the basis of the sequential organ failure assessment (sofa) score. The sample population from the states of Maharashtra, Uttar Pradesh and Delhi shall be considered.

Study period

This survey will be conducted for the duration of 3 months, between April 2021–July 2021.

Study setting

The demographic as well as the clinical data would be collected from the medical records of the patients. The questionnaire will be sent via an online link through the social media platforms. In the second wave of this pandemic, the states of Maharashtra, Uttar Pradesh and Delhi are much more affected comparatively. For the same reasons this study will be carried out amongst the sample population residing in these states. The patients diagnosed positive through RT-PCR test and undergoing the treatment guidelines given by the world health organization (WHO) will be included.

The inclusion criteria for this particular study define the sample population as follows:

Corona virus disease 19 infected patients, admitted in the Intensive care unit, with the below mentioned parameters.

Patients who have oxygen saturation should be (less than) <90%.

Covid cases with the presentation of respiratory rate indicating (more than) >30 cycles per minute.

Cases requiring supplemental oxygen therapy due to the reduced oxygen saturation levels.

Elevated serum levels of cytokines and interleukins (IL 8, IL 6, IL 2) indicating presence of sepsis.

Severely infected Covid 19 Cases indicating high values of the sequential organ failure assessment (SOFA) score.

The patients fulfilling the above criteria would be grouped under the category including the progression of sepsis associated with severe covid disease [14]. From the data which will be acquired from the medical records of the patients and the clinical parameters assessed after certain investigations performed, the cases shall further be classified into two divisions. The cases landing in septicemia and the ones not. This classification will be done on the basis the sequential organ failure assessment (SOFA) scoring system [15]. The patients classified in the experimental group will further be assessed for multiorgan failure based on the stated definition (Table 1) [16].

The survey will be done after the approval of the institutional ethical committee. Based on the guidelines and the questionaries, which is previously consulted in the studies of China and France [17,18]. The improvised version of this questionnaire will contain the questions defining the demographic data of the patients. The questions would also assess the parameters symbolizing the multi-systemic functions of the body computed tomography (CT) score, complete blood count (CBC), erythrocyte sedimentation rate (ESR), enzyme lactose dehydrogenase levels (LDH), along with that interleukin 8 (IL 8) and cytokine levels to determine the spread of septicemia. To assess the liver function, enzyme levels of alanine transaminase, aspartate transaminase and alkaline phosphatase (ALP) would be taken into consideration. Glomerular filtration rate (GFR), average urine output, presence of hematuria and albuminuria would be investigated]. The fluctuations between these clinical parameters will then be assessed to determine the group that is particularly landing into multi organ dysfunction syndrome (MODS).

Implications

The results concluded from this survey will help in accurately determining the clinical, epidemiological and radiological factors which are associated with the septic progression and multi-organ dysfunction syndrome in cases having the prognosis of severe Covid 19 infection.

Methodology in PICOT format

P (Population)

The sample size that will be included in this study will be, Covid 19 cases diagnosed using the RT-PCR test and undergoing treatment as per the WHO guidelines in the states of Maharashtra, Uttar Pradesh and Delhi.

I (Intervention)

This study will help in determining the factors associated

with Multi organ dysfunction syndrome in sepsis associated corona virus disease19 cases.

C (Comparison)

The sample experimental population will be compared with the control group of covid 19 infected patients, not progressing towards sepsis associated organ failure.

0 (Outcome)

This study aims to measure the outcomes of the duration of intensive care units (ICU) stay along with the discharge rates of the treated patients and estimating the fatalities of the cases succumbing to aggravating sepsis despite undergoing the treatment.

T (Time)

This study will be conducted over a period of 3 months, during which patients will be assessed to collect the data, (April 2021 – July 2021)

Measurements

To conclude the results of this survey, a questionnaire based statistical evaluation of the collected data with analytical tests will be performed on the basis of the sequential organ failure assessment (SOFA) score and multi organ dysfunction score (MODS), along with this, a comparative analysis will be executed with the control group, which was defined earlier.

Quantitative variables

No comparative variables will be used in the statistical analysis of this particular survey.

Statistical methods

The data collected through the process of assessing responses to the online questionnaire will then be analyzed, using various statistical tests and shall be depicted in a suitable graphical manner.

Expected results

This particular study would definitely play a key role in assessing the epidemiological factors as well as the clinical parameters, resulting in the progression to multi organ dysfunction syndrome (MODS), in cases with severe Corona virus disease19 infection, associated with septicemia. As it has been already proven that the association of multi organ dysfunction syndrome in the Corona virus disease 19 infection has given rise to a rather rampant rise in the resulting fatalities. The results concluded from this study could be used to possibly put a curb on the worsening prognosis by identifying a particular set of demographic and medical factors beforehand.

Table 1: RT-PCR.

Severe Covid-19 cases–real time polymerase chain reaction [RT-PCR diagnosed]	
Experimental group	Control group
Cases progressing towards septicemia	Cases not progressing towards septicemia

DISCUSSION AND CONCLUSION

The vigorous spread of Covid 19 pandemic has affected almost each and every sector in the community as well as the medical fraternity. While on the one hand, many countries have been facing the consequences of this insisted state of lockdown and medical burdens due to the pandemic on the other hand India is suffering under the wrath of the widespread of this Covid 19 virus. The said covid 19 pandemics has recently taken an aggressive widespread course which has resulted into an increased number of cases, majority of who are succumbing to the pathogenesis of this severe disease. The rapidly elevating graph of the fatalities is observed due to the extra-pulmonary advancing ability of the coronavirus infection. In the cases with the clinical presentation of with Corona virus infection 19 infection, almost 5% of patients are seen progressing to the clinical pathology known as multi–Organ Dysfunction Syndrome [MODS] [16].

According to the survey conducted in March 2020 by Mehta, et al., it was seen that significant number of patients presented with the symptoms of sepsis and deranged serum coagulation factors corresponding to the clotting features. That further contributed to development of multi organ dysfunction syndrome (MODS) [19-21]. The cases are landing into septic shocks associated with the multi-systemic pathologies. The prognosis of such cases is substandard, taking into consideration the mysterious virulent characteristics of the recently discovered mutant strains of Sars-coV-2.

Collange, et al. recently conducted a research study in France [17] in which they reported the cases showing extra-pulmonary pathologies that were associated with Covid 19 infection. On examination these patients revealed multi systemic findings such as Mesenteric vascular ischemia resulting in bowel resection, thrombotic microangiopathy and Anti-phospholipid syndrome.

From the study done by the researchers of China and Iran it was concluded that, in addition to the impact on the respiratory system, the coronavirus involves multi-systemic manifestations with derangement in blood chemistry profiles [17]. Mao, et al. [22,23], concluded that, cases with coronavirus infection presents with central and peripheral nervous symptoms. Other studies related to Covid-19 were reviewed [24-28].

Although the eventual progress towards multi-organ failure in severe Corona virus disease 19 cases is established, the factors that contribute towards this menacing prognosis, still are rather an enigma. The clinical elements which serve as an important milestone in the course of this deteriorating prognosis, till date remains a mystery. The conclusions derived from this study would surely help in enlightening the lesser-known facts about the strong virulence of the said virus and in determining an accurate clinical profile of patients landing in multi-organ dysfunction syndrome, thereafter helping to put a curb on this pathological condition.

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