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Original Research Article

A Retrospective Analysis of COVID-19 Severity and Mortality Data with Special Reference to Biochemical Parameters.

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Abstract:

Background: The coronavirus disease 2019 (COVID-19) pandemic has presented the menace of century. Severity and mortality of COVID 19 infection is due to upregulated inflammatory response in a short span of time. Patients with altered biochemical parameters are more susceptible to COVID –19. Therefore, we tried to explore blood biochemical parameters with severity and mortality of COVID –19 patients. Timely detection of these parameters may help in appropriate course of treatment and reduction in mortality.

Aims and Objectives: Aim of this study was to evaluate and compare the biomarkers of inflammation in severe and deceased cases of SARS CoV 2.

Materials and Methods: It is retrospective observational study carried out in tertiary care DCH (Dedicated Covid Health) facility of Pune center. Inflammatory parameters of total 294 diagnosed Covid-19 patients were studied and compared in two groups, survivor and non-survivor. The parameters included CRP, Ferritin, Lactate dehydrogenase, D dimer, Interleukin 6 and Procalcitonin.

Results: The mean difference between survivor group and non-survivorgroup was extremely statistically significant for parameters like serum CRP, ferritin, Lactate dehydrogenase, D dimer and Interleukin 6. (p value less than 0.001) The difference between levels of procalcitonin in survivor and non-survivor group was statistically significant. (p value less than 0.05)

Conclusion: The classical inflammatory markers are highly raised in covid patients especially in non-survivor group. They indicate high chances of mortality in severe and critical patients. Their values should be estimated early and their closer monitoring may indicate future mortality and hence timely intervention may be possible.

Keywords: COVID 19, biomarkers, inflammation, mortality.

Introduction

The 2019 novel coronavirus disease (COVID-19) that had emerged in December 2019 is the greatest public health problem till date. As per WHO (World Health Organisation) Coronavirus Update Report of December17, 2023, there have been 772, 838, 745 confirmed cases of COVID-19 and 6, 988, 679 deaths worldwide [1].

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of coronavirus disease 2019 (Covid-19), emerged in Wuhan city, China from a zoonotic source [2].The clinical presentation of COVID-19 patients varies from asymptomatic condition, fever, dry cough, diarrhea and mild upper respiratory symptoms to severe pneumonia with respiratory failure, multisystem disease and even death [3,4]. Critical condition of patients is contributed by cytokine storm and hypercoaguable state. One of the predominant cytokines, IL-6 may be the leading

cause of inflammatory response in COVID-19 [5]. Along with IL6, there is rise in other inflammatory markers like CRP, ferritin, LDH, procalcitonin. Hypercoaguable state is marked by significant rise in D dimer levels [6].

Aim and Objectives: The primary aim of this study was to evaluate and compare the biomarkers of inflammation in severe and deceased cases of SARS CoV 2.

Materials and Methods:

Study Design: Retrospective observational study

Study Population: This study was conducted in Dedicated COVID Hospital (DCH) of Pune region (between 1 April 2020 and 30 July 2020). Institutional ethical clearance was taken (BJGMC/IEC/Pharmac/ND-1023329-329). The study population was RT PCR confirmed positive admitted cases of Covid-19 of 18 to 70 years of age.

A. Inclusion Criteria

The classification of patients was done according to NIH guidelines which categorised the patients into asymptomatic, mild, moderate, severe and critical illness as per NAAT or antigen testing, clinical features, chest imaging, oxygen saturation, respiratory rate, lung infiltrates, respiratory failure, shock and/or multiple organ failure. We included RTPCR positive patients of age 18 to 70 years with severe and critical category. Severe category included individuals who have SpO2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%. Critical illness included individuals who had respiratory failure, septic shock, and/or multiple organ dysfunctions. The outcome included hypoxia, ARDS, ICU admission or mechanical ventilation and death. Thus, two groups of patients i.e. survivor and non-survivor were studied.

B. Exclusion criteria

Covid-19 suspects, RT PCR negative cases on laboratory confirmation and referred cases from other institutions were excluded.

Study Procedure:

The age, gender, co morbidities, hospital stay of the patients were recorded. The co morbidities included were hypertension, diabetes mellitus, ischaemic heart disease and pulmonary disease. The values of laboratory parameters of the cases including levels of CRP, Ferritin, Lactate dehydrogenase, D dimer, Interleukin 6 and Procalcitonin were entered in excel format. Only those values were considered which were estimated within 24 hours of categorisation or admission of patients. We used SPSS software for statistical analysis and used chi square test and Student's t test to compare the data between survivor and non-survivor group of patients. p value less than 0.05 was considered to be statistically significant.

Results

Table 1: Demographic details of patients admitted, DM- diabetes mellitus, HT – Hypertension, IHD- Ischemic heart disease, SD- standard deviation

*p value < 0.001, extremely statistically significant and ** p value< 0.05, statistically significant

Variable	Total n	Survivor	Non survivor	P value
n (%)	294	166 (56.46)	128 (43.54)	---
Age in years (mean± SD)	52 ± 12	49 ± 11	61 ± 15	0.0001*
Male n (%)	186 (63.26)	92(49.46)	94(50.53)	---
Female n (%)	108 (36.74)	60 (55.55)	48 (44.44)	---
Co morbidities (DM, HT, Pulmonary disease, IHD) n (%)	102 (34.69)	31(30.39)	71(69.60)	0.001**
Hospital stay (in days) (mean± SD)	8.1±6.1	9.2± 6.2	7.7±5.5	0.0316**

Table 2: CRP- C reactive protein, LDH- Lactate dehydrogenase, IL 6- Interleukin 6 PCT- Procalcitonin

Parameter	Survivor (mean± SD)	Non-survivor (Mean± SD)	P value
CRP (mg/L)	49.5± 43.6	165.2± 9.9	0.0001*
Ferritin (ng/ml)	910.3 ± 1103.8	2100.5± 3123.6	0.0001*
LDH(IU/L)	410.1 ± 119.3	919.6 ± 1221.5	0.0001*
D dimer mcg/ml)	2.23± 6.56	16.5± 18.47	0.0001*
IL 6(pg/ml)	17.23± 15.39	39.5 ±42.33	0.0001*
PCT (ng/ml)	1.33± 5.62	3.95± 11.63	0.0115**

*p value <0.0001, extremely statistically significant and** p value <0.05, statistically significant

As shown in table 1, a total of 294 patients included in the study had mean age of 52 ± 12 years. Number of survivor and non-survivor cases was 166 and 128 respectively. The mean age of survivor and non-survivor patients was 49 ± 11 years and 61 ± 15 years respectively. This difference was statistically significant (p value less than 0.001). Majority of patients were males having 63.26 percentage and females were 36.74 %. The most common co morbidities found in Covid patients were diabetes mellitus, hypertension, ischemic heart disease and pulmonary disease. A total of 102 patients (34.69%) had either one or more of these co morbidities. Out of all 102 co morbid patients, 31 (30.39%) patients survived and 71 (69.60%) died. This difference was statistically significant. (p value less than 0.05). The mean stay of Covid patients in hospital in days was 8.1±6.1 days. The patients who survived had mean stay in hospital in days was 9.2± 6.2 whereas non-survivorgroup had mean stay of 7.7±5.5 and difference was statistically significant.

Table 2 shows the inflammatory parameters estimated in two groups of Covid patients. The values are represented in mean± SD. The mean difference between survivor group and non-survivor group was extremely statistically significant for parameters like serum CRP, ferritin, Lactate dehydrogenase, D dimer and Interleukin 6. (p value less than 0.001) The difference between levels of Procalcitonin in survivor and non-survivorgroup was statistically significant. (p value less than 0.05)

Discussion:

The pathophysiology of SARS CoV 2 in its severe form mainly involves cytokine storm and hypercoagulable state in human body [7]. Cytokine storm further leads to release of interleukins while coagulative cascade disrupts the healthy vascular endothelium leading to thrombosis and inflammation [8]

Cytokine storm is a life-threatening systemic inflammatory response to infections, therapies, cancers, autoimmune conditions. It leads to excessive activation of immune cells and the generation of pro-inflammatory cytokines [9]. Many studies showed that severely ill COVID-19 patients tended to have a higher concentration of pro-inflammatory cytokines, especially interleukin 6 [10]. IL6 further induces C-reactive protein (CRP) synthesis by the liver resulting in marked increase in this acute phase reactant protein [11].

Furthermore, raised LDH level is a frequent biochemical anomaly seen in severely ill patients, which is considered as a lung tissue damage marker.Yuan et al. [12] revealed that in the first six days of hospitalization, patients in severe covid 19 clinical conditions showed significantly higher levels of IL-6 and LDH in serum than those of the moderate group.

Ferritin, intracellular iron binding protein is an acute phase protein. It is released due to proinflammatory effect of cytokines. Chen N et al. [13] found that hyperferritinemia has a direct link with cytokine storm and serious outcome in COVID-19.

Procalcitonin is also often raised due to the inflammatory cascade caused by a cytokine storm in COVID-19 patients. Emerging evidence suggests that mildly elevated PCT can also help identify COVID-19 patients at higher risk for clinical deterioration [14]. Jian box u et al found that in group of critical Covid patients, CRP level is highest and it along with procalcitonin is independent predictor of survival. [15]

Cytokine storm in COVID-19 is also associated with activation of coagulation cascades, resulting in thrombotic complications and coagulopathies including DIC which is indicated by rise in D dimer [16]. In a study by Zangrillo et al, authors conclude that high CRP and D dimer are associated with deaths in ventilated patients [17].

These two responses, cytokine storm and hypercoaguable condition, are responsible for tissue damage and multiple organ involvement. Most commonly, the systems involved are respiratory, renal, hematological, skin, neurological, cardiovascular and endocrine. [18] Respiratory failure, acute coronary syndrome, acute kidney injury and stroke were the among common complications [19].

The consequent effect of infection is rise in inflammatory markers and coagulation markers. These are CRP, ferritin, Lactate dehydrogenase, Interleukin 6 and D dimer. [20] . Some initial studies showed that these can be used to diagnose Covid 19 in early stages [21,22]. Early detection of rise of these markers may help to monitor and treat the patients better and shift to intensive care units. Various studies show that these markers are highly raised in Covid infection [23,24,25,26].

Ferda Bilgir et al supports our study and conclude that Ferritin, LDH, D dimer and CRP are most effective parameters to predict ICU admissions and mortality [27].Our study shows that these markers are highly raised in severe covid infection. Also, in deceased group of patients, increase is statistically highly significant.

Conclusion:

CRP, ferritin, Lactate dehydrogenase, Interleukin 6, procalcitonin and D dimer are the important markers which should be estimated for early risk stratification and further management. High increase in these markers indicate poor outcome for Covid-19 patients.

Limitations: Serial monitoring of these markers is necessary in Covid patients. Also, their estimation in

mild and moderate cases should be done to compare with severe and critical cases.

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