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REVIEW ARTICLE

POST COVID-19 PATIENTS VERSUS ORGAN FUNCTION DISORDERS OF BIOCHEMICAL PROFILE

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ABSTRACT

The pandemic out break of novel corona virus disease (covid19) was initially noticed in a seafood market in wuhan city in china in mid December, 2019, has spreader to 215 countries world wide. 2020 january 7th and was temporally named 2019 n- co.v Corona virus belongs to a large family of virus that causes illness ranging from the common cold to more severe disease, A novel corona virus is a new strain that has not been previously identified in humans on January 30th 2020 declared the novel corona virus out break of public health emergency of international concern (PHEIC). At that time there was 98 cases and no death in 18 countries out side china. The official name covid-19 and SARS –COV2 was issued by the WHO on 11th February 2020 Viruses are named based on their genetic structure to facilitate the development of diagnostic test, Vaccine and medium. Virologist and the wider scientific committee do this work, so virus is are named by the international committee on taxonomy of viruses. A recent review of the survival of human corona virus on surface found large variability ranging from 2 hours to 9 days. The survival time depends on number of factors, including the type of surface, temperature, relative humidity and specific strain of viruses. March 11th 2020, the rapid increase in the number of cases out side china. 118000 cases had been reported in 114 countries and 4291 deaths had been reported. Middle of the march 2020 corona out break could be characterized by “Pandemic” reporting over 40108 globally confirmed cases. As of 28th April 2020, 63% of global mortality from the virus. The impact of the dieses on the world has been staggering both from public health and economic perspective. we evaluated whether prior or active corona virus infection influenced hematological, Biochemical and Clinical parameters of the such patients. But active corona fever resulted in higher hospitalization rate. Our data support the nation that SARS-COV-2 and co morbidity weather affects an important percentage of covid 19 pateints and leads to worse parameters, requiring greater attention from health authorities.

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INTRODUCTION

The severe acute respiratory syndrome corona virus-2 (SARS-CO-V-2) quickly spread to several countries, infecting millions of people world wide. Thereafter, the number of infected individuals from all countries continued to grow daily reaching day by day expressive figures. Most (SARS-CO-V-2) infective individuals are asymptomatic on present non-specific, flu-like symptoms, such as fever, headache, fatigue and dry cough. However, clinically conditions can rapidly progress to sever pneumonia an ultimately death, mainly in patients who present comorbidity such as obesity, type II DM, CVS, neurological disorders. Although research is happing at over whelming speed to biochemical, hematology data and day to day investigations for effective treatment.

The impact of this disease on the world has been staggering, both from the public health and economic perspectives. A worse scenario has been witnessed in south America. Specially in Brazil, Ecuador, Argentina, and Peru. Recently highest number of cases of covid 19 in the region. It has been hypothesized that such countries possible experienced an aggravated covid 19 pandemic due to socioeconomic and health factors. Co- morbidity infection being mostly reported in endemic and various non- endemic countries. Corona fever is an endemic disease, by continuous vector transmission in several tropical areas around the world. The covid-19 pandemic brought additional uncertainty to countries that already needed to deal with Co-morbidity of obesity, MI, CVS, Type II DM. The circulation of both viruses represents a major challenge for hospitals that will have to face difficulties in determining to biochemical parameters to diagnosis due to

overlapping symptoms between Co-morbidity and covid-19. The consequences of covid-19 and Co-morbidity disease misdiagnosis are relevant and may include ineffective patient management. The clinical consequences of SARS-CO-V-2 and Co-morbidity disease infection are still unknown. Justifying investigations in the theme and dose vigilance by health authorities. Data regarding patients hematological and biochemical parameters, as well as clinical outcomes, were collected and analyzed. We detected that a significant percentage of Covid 19 patients presented by virus infection did not significantly influence clinical and laboratorial parameters, active SARS-CO-V-2 was associated with more frequent detectable lung alterations and hospitalization, our data may provide important information to health authorities to improve the identification and the management of these patients.

Aims and objective

We are planned to 500 patients ages of 18+ who were admitted and treatment taken for Coved 19 Patient recurrent complaints rule out and analysis for treatment Medical History and record with data regarding age, History of Compliance, duration of the complaints after post Covid 19. Patient's clinical follow up data has investigate and outcome assignment on medical record have final determine&discuss for conclusion.

Analytical parameters

- Complete urine analysis.
- Complete Blood Hematological analysis.
- Complete Blood Biochemical analysis.
- Rpt Throat Swab - Naso pharngial, saliva RT-PCR.
- CRP, Ferritin, D-dimmer, IL-Vitamins, Minerals, electrolytes, gas analysis
- Electrophoresis – Hemoglobin
 - Protein
 - Lipoprotein
 - CSF
- USG – abdomen
- ECG, ECHO, Color Doppler, HRCT-Thorax, CT-Brain, MRI-Brain.

MATERIALS AND METHODS

The Study was performed with a convenience sample of patient assessed in JNU Hospital and study have to be approve & grant by Ethics committee of JNUIMSRC. Covid-19 diagnosis have confirmed by Reverse transcription-polymerase chain reaction (RT-PCR) assay of nasopharyngeal swab sample. Viral RNA was extracted using the high pure viral nucleic acid version by the step are plus reactive PCR systems methods. Hematology blood sample were used to analyze by flow cytometry. Biochemical samples were used to analyzed by fully auto analyzer diagnostic equipment. Serology test were carried out the methods based on indirect ELISA technique, immune plates are coated with a mixture of purified viral antigen and probe using the patient serum. And all Radiological investigations by highly modular technique of the Radiological Equipments

Inclusion Criteria: Patients with a history of fever more than one week with cough, dyspnea, fatigue, sore throat, chest pain, diarrhea, vomiting, anosmic, agusia and inappetite.

Patient clinical follow-up as assessed after covid19 treatment duration of 4to 6 wks Blood samples have used to analyze hematological parameters by flow cytometry. Serum samples were characterized according to the liver profile, renal profile, lipid profile, diabetic profile, coagulation profile, cardiac markers, CRP, D- dimer, ferritin, ABG parameters, electrolyte analysis and urine complete analysis by equipment of Randox Imola Autoanalyzer and used high resolution computed tomography (HRCT) was used to asses patient lung condition and reapt RT-PCR to identify corona virus infection and rapid antibody test for the scoring to corona virus infection.

All statistical analysis have performed quantitative data were submitted to analysis of frequently using procedure with subsequent chi-square analysis at 95 % confidence interval to assess whether clinical parameters would significantly varies between Covid-19 co morbidity infection and Covid-19 past fever positive.

Quantitative data were normality test using and then submitted to detect difference between post Covid-19 Patience organ function disorders parameters morbidity infection and post Covid-19 past fever group patients. All subjects were evaluated and selected by detailed medical history and physical examination , each subject gave informed consent and the study have approval from institutional ethical and research committee.

PROFORMA STATUS: JNU University Institute of Medical Science and Research Center (Jaipur, Rajasthan)

DEPARTMENT OF BIOCHEMISTRY

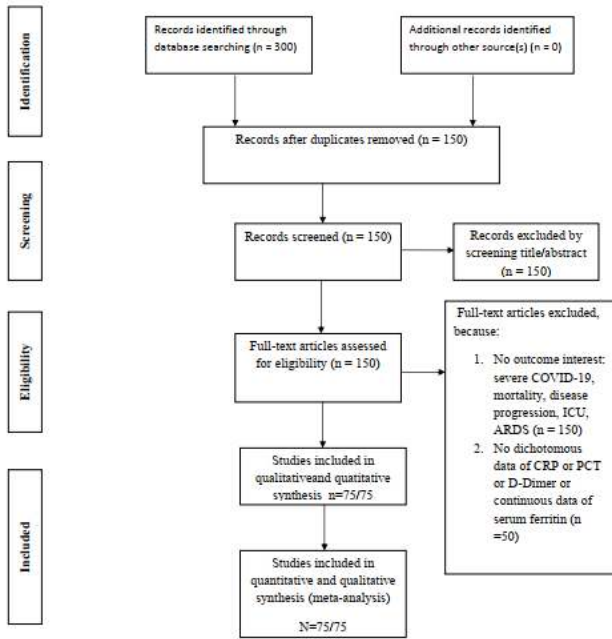
Research topic: Post Covid 19 Versus Organ Functions Disorder Profile

Investigator name: . , Dr. Shivasubramaniam M.D Avdesh, Vaisali

- Patient name/detail: Total 500 Patients
- Age: 25-70 yrs old Sex: Male-140 Patients Female-360 Patients
- Patient Id: Hospital Registration OP/IPD NUMBER
- Weight: 32 kg – up to 90 kg various
- Height: 132 cm. to 180 cm. various
- BMI: 20 to up to 45 various
- Religion: Hindu /Muslim/Sikh/Christion/Others
- Area: Urban 300 Patients. Rural: 200 Patients
- Tribal 50 Patients Non tribal: 450 Patients
- Deit: Vegetarian 150 Patients Non Vegetarian: 350 Patients
- Smokers 80% Patients Non Smokers: 40% Pateints
- Chewing habit: 80% Patients
- Alcoholism: 40 %Patients Non Alcoholism: 35% Patients
- Medical History: Fever, Cough, Cold, Tiredness, Breathlessness, with Hypertension, Diabetics, Renal Failure, Alcoholic cirrhosis, Acid peptic disorders 60 Patients in Covid-19. Covid-19 only 40 Patients
- Patient Medical Co-Morbidity Disease History. 75 Patients
- Post Covid -19 Patient History:

ARDS, acute respiratory distress syndrome; COVID-19, corona virus disease – CRP, C-reactive protein; ICU, intensive care unit; PCT, procalcitonin.

Study flow diagram

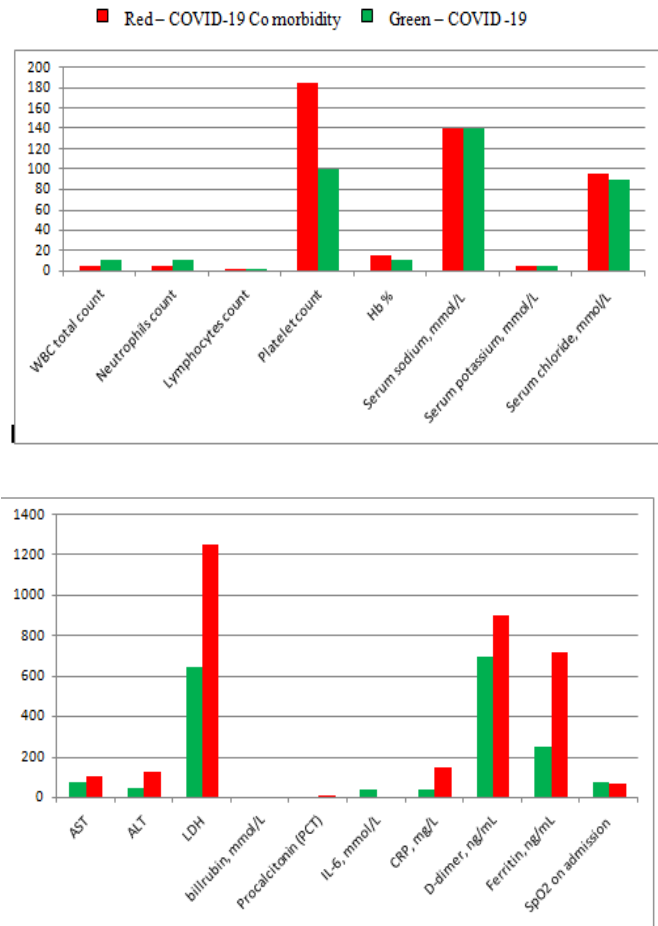


DISCUSSION

This disease has a peculiar natural course. This starts off with mild symptoms and then suddenly the signs and symptoms blows out of proportion and eventually is very hard to treat. So identification of the stage is very important so that the treating doctor gets a chance to effectively treat the patient.⁸ Some of the reports have already marked the importance of the hematological and biochemical markers to identify the prognosis of the disease^{4,9} No such study has been done in the present population and this is one such sincere effort, some study has also reported the importance of inflammatory markers in the patients, C-reactive protein (CRP) is one such, others like erythrocyte sedimentation rate (ESR), and interleukin-6 are also extensively studied.³ Likewise, another work reported lymphocytopenia, high blood sugar, gamma-glutamyl transaminase (GGT), high lactate dehydrogenase (LDH) in more COVID-19 patients.¹⁰ Further, laboratory findings of 77 COVID-19 deaths and 150 COVID-19 patients also demonstrated an increase in urea, cardiac troponin, creatine kinase, D-dimer, C-reactive protein (CRP), lactate dehydrogenase (LDH), IL-6, and lower level of lactic acid levels and lymphocytes.^{11,12} Analysis of 100 cases of COVID-19 revealed a higher level of C-reactive protein, D-dimer, lactate dehydrogenase, serum amyloid, and lower level of albumin are directly associated with developing a critical illness.⁹ The hematological and biochemical markers have been studied and this study successfully proves the difference. This can be used as a prognostic tool. Majority of the study has been done in the east and none of them in this region. The pandemic is still not over and this study is one novel effort to find the difference so as to help the practicing physician to diagnose the severity earlier and be helpful in the treatment of the disease. This meta-analysis showed that elevated serum CRP, PCT, D-dimer, and serum ferritin levels were associated with an increased composite poor outcome that comprise mortality, severe COVID-19 WARDs, and the need for ICU care in patients with COVID-19. The effect estimate was not significant modified by gender, age, cardiovascular disease, diabetes, and COPD. In the systemic hyperinflammation phase of COVID-19 proposed there significant elevation of inflammatory cytokines and biomarkers, such as interleukin (IL)-2, IL-6, granulocyte-colony stimulating factor, macrophage inflammatory protein 1- α , tumor necrosis factor (TNF- α), CRP, ferritin, PCT, and D-dimer. This stage consists of the most severe manifestation cytokine storm, in which excessive hyperinflammation may lead to cardiopulmonary collapse or multi-organ failure.^{35,36} CRP is an acute phase inflammatory protein produced by the liver that may be elevated in several conditions, such as inflammation, cardiovascular disease, and infection.³⁷ In our meta-analysis studies, an elevated CRP was associated with severe COVID-19, the need for ICU care, but not mortality. Although there is no general agreement on a cutoff point to determine the severity of COVID-19, the majority of the studies used a > 10 mg/L cutoff. Our SROC analysis showed the diagnostic value of serum CRP > 10 mg/L for a composite poor outcome in COVID-19 (51% sensitivity, 88% specificity, an LR + of 4.1 and an LR - of 0.5). Previous studies that attempted to predict mortality in sepsis by the presence of an elevated serum CRP were inconclusive. A study showed that an elevated serum CRP level was associated with a 30-day mortality rate,³⁸ while other studies showed otherwise.³⁹⁻⁴¹

RESULTS

Table to describe the hematological and biochemical profile in COVID-19 and Co morbidity COVID-19:



Graph 1 & 2. To describe the biochemical markers in COVID-19 and Co morbidity COVID-19

Markers	COVID -19	Co Morbidity COVID -19	Sig
WBC total count (10 ⁹ /L)	4.8 ± 3.7	8.9 ± 6.0	Not Sig
Neutrophils count (10 ⁹ /L)	5.9 ± 1.5	8.4 ± 2.1	<0.001 Sig
Lymphocytes count (10 ⁹ /L)	2.4 ± 1.4	1.3 ± 0.5	Not Sig
Platelet count. (10 ⁹ /L)	184.07 ± 38.15	101.58 ± 70.27	<0.001 Sig
Hb %	12.81 ± 1.72	10.27 ± 1.29	Not Sig
Serum Sodium, mmol/L	138.21 ± 2.38	140.35 ± 7.39	Not Sig
Serum Potassium, mmol/L	4.12 ± 0.13	4.41 ± 0.92	Not Sig
Serum Chloride, mmol/L	96.71 ± 6.18	94.49 ± 7.8	Not Sig
AST U/L	68.38 ± 34.29	90.8 ± 114.98	Not Sig
ALT U/L	49.82 ± 38.92	121.38 ± 187.48	Not Sig
LDH U/L	620.28 ± 318.09	1216.16 ± 1129.29	<0.001 Sig
Direct billrubin, mmol/L	0.61 ± 1.23	0.79 ± 1.12	Not Sig
Indirect billrubin, mmol/L	0.41 ± 1.17	0.75 ± 1.39	Not Sig
TBIC, mmol/L	1.11 ± 1.22	1.45 ± 1.92	Not Sig
CRP, mg/L	39.29 ± 57.12	116.26 ± 91.9	<0.001 Sig
D-dimer, ng/mL	682.00 ± 114.19	892.13 ± 412.38	<0.001 Sig
Ferritin ng/mL	249.91 ± 38.15	1006.16 ± 112.39	<0.001 Sig
Procalcitonin	3.92 ± 6.99	2.90 ± 10.22	<0.01 Sig.
IL-6	42 ± 70	68 ± 1.10	<0.01 Sig.
SpO2 on admission	93.82 ± 6.39	86.28 ± 6.0	Not Sig

These inconsistencies might be caused by the different cutoff value used. In the study by Koozi *et al.*, the cutoff value for an elevated serum CRP was > 1000mg/L, while in the study by Ryoo *et al.*, the cutoff point of >140mg/L was used.⁴¹ Liu *et al.* proposed cutoff value of > 41.8 mg/L to predict severe COVID-19.⁴² In our analysis, the cutoff values of serum CRP varied widely, with the lowest and highest values being >3 mg/L and > 100 mg/L, respective these findings reflected the paramount need for pursuing the optional serum CRP cut off value for COVID-19 Prognostication. The time period for serum CRP measurement was critical in light of timely manner of serum CRP increment, which culminates 72 h after the initial insults.^{37,41} Desj value in predicting a poor outcome in COVID-19, it should we noted that various factors could a serum CRP levels, including age, gender, smoking status, weight, lipid levels, blood pressure, are injury.³⁷ These factors should be taken into account while interpreting the serum CRP level. In addition, recent evidence has shown that serum CRP level could also be used in monitoring the progression and improvement of patients with COVID-19.⁴³

A peptide precursor of the hormone calcitonin, PCT, has been widely investigated as a promising biomarker for the initial investigation of a bacterial infection.⁴⁴ An elevated serum PCT is often in patients with sepsis and septic shock.³⁹ While it is still controversial whether PCT can accurate distinguish bacterial or viral pneumonia,⁴⁵ it was found that PCT-guided therapy in acute respire infections reduces the antibiotic exposure and side effects, and improves the survival rate.⁴⁶ Bac infections trigger extrathyroidal synthesis of PCT, which is actively maintained by elevated valu IL-6, IL-1 β , and TNF- α , while viral infections hinder PCT production due to interferon- γ .⁴⁷ This explains why serum PCT concentrations remain normal in uncomplicated cases of COVID-19 at inflated values may indicate bacterial co-infection in severe cases.⁴⁸ In this meta-analysis, we fo that an elevated serum PCT was associated with mortality and severe COVID-19. Our SROC an showed the diagnostic value of serum PCT >0.5 mg/L for a composite poor outcome in COVID. (88% sensitivity, 68% specificity, LR+2.7 and LR-0.2). In our study, we also found that an elevated D-dimer was associated with an increased composit outcome, especially mortality and severe COVID-19. This finding supports the hypothesis that s acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection could induce the dysfunction hemostatic system, leading to a

hyper coagulable state, a condition which we commonly encount sepsis.^{49,50} Recent evidence of lung pathology dissection has shown occlusion and micro-throm formation in pulmonary small vessels of patients critically ill with COVID-19.⁵¹ However, the e of elevated serum D-dimer level is multifactorial and the optimal cutoff value of elevated D-dim patients with COVID-19 remains to be established. It is clear that COVID-19-associated coagul warrants distinct emphasis and special treatment. According to the International Society of Thro and Hemostasis (ISTH) guideline, a markedly elevated serum D-dimer level (which is still poorl defined as a three-to four-fold increase) implies an increased thrombin production. Patients with COVID-19 with markedly elevated D-dimer levels may require hospitalization, despite the sever clinical presentation.⁵² In the absence of contraindications, a prophylactic dose of an anticoaguli recommended for all hospitalized patients with COVID-19. Along with other biomarkers included in this study, we also found that a higher serum ferritin le independently associated with ARDS, mortality, and severe COVID-19. This may lead to the no the presence of secondary hemophagocytic lymphohistiocytosis (sHLH) in COVID-19.⁷ sHLH i condition of hyperinflammation characterized by a cytokine storm causing fatal multi-organ fail This condition is most commonly triggered by viral infections,⁵⁴ which might lead to a hypothe SARS-CoV-2 inducing this hyperinflammatory syndrome. Despite the fact that some authors suj using HScore to identify subgroups of patients that may benefit from immunosuppressive therapy still controversial whether or not this specific condition in severe COVID-19 needs to be treated sHLH. A recent systematic review by Veronese *et al.* including 542 patients reported conflicting evidence in 4 studies.⁵⁵ The authors concluded that the current evidence did not support the rout of corticosteroids in COVID-19, but some findings suggested corticosteroids may reduce the me rate in COVID-19 cases aggravated with ARDS.

CONCLUSION

- Virus is inside the body detects a virus has never seen and will throw everything against it. The body eliminate the virus but can cause sometimes deadly collateral damage through the body. The study include only people who were unvaccinated and had at least and one risk factor for

developing a severe case of Covid-19. The people who are older than 60, obese, Type II DM, CVS, RS, CNS, Abdominal Organ underlying disease, an immunocompromized from another condition like prophylactic vaccine is enough to be hospitalization.

- Corona virus SARS –COV2 significantly reduces the risk of hospitalization and death in people who take it early in the course of their post Covid-19. There was also less likely to die, reported within a month of treatment and now in those who received the medicine. All of the antiviral medicines available today, including remdesivir and the monoclonal antibodies are much more affected against Covid and cut risk of hospitalization and death by up to 85 % but this treatment cost almost higher than normal
- The research, Study has to be conduct in numerous place sites around Rajasthan in Jaipur, JNUIMSRC became the results have promising to against corona virus and clinical parameters investigations is improve the identification and the management of the post Covid 19 patients. (SARS-COV-2)

The hematological and biochemical markers may be used as prognostic markers in COVID-19 and Analysis show that status of serum CRP, PCT, D-dimer IL6, and serum ferritin associate with a composite with outcome in patients with COVID-19. Post Covid 19 the above parameters have analyze appropriately. The virus that causes disease disturbs not just smell and taste. but all the ways humans perceive the world for some the loss may be permanent in all organs. After becoming severely ill with covid 19 and post covid-19 co morbidity very long treatment in ICU with support of ventilation. Recoverd patients parameters are to be analyse. This people something many co morbidity suffered from covid19 discovered when they unexpectedly lost their sense of smell and taste and other system organs involved Through it have become apparent that post covid 19 infection can also affect sight, hearing and touch and brain, cerebellum, lungs, heart, and abdominal organ disease In the short term and the long term, this virus can affect all the ways are perceive and analyze biochemical parameters and interacted with world. The virus that causes disease disturbs not just smell and taste. but all the ways humans perceive the world for something loss may be permanent .

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