

Clinical and Outcome Study Of COVID-19 At Semi Urban Medical College Hospital in Telangana.

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Abstract

Corona virus infection rapidly spreading and producing morbidity and mortality in all over the world over the past one and half year. The virus triggered immune system dysfunction leading to life threatening cytokine storm indicating severe forms of lung injury .Need to understand the clinical profile and risk factors leading to mortality is much needed .

Aim: To determine the clinical profile of patients having COVID 19 using the inflammatory markers at a semi urban center

Methods and materials: A retrospective study conducted on cases that were admitted in CAIMS during the period of 3 months, with CT chest grading CORADS > 3, COVID RT-PCR or rapid antigen test positive , pulse oximetre saturation less than 90%

Conclusion : 515 cases were taken into study ,clinical presentation was observed .Most cases were likely to have CT chest CORADS grading > 3 , inflammatory markers like LDH, Sr Ferritin, CRP have been elevated. Cases have shown high IL-6 , which was estimated selectively in cases with oxygen support suggesting cytokine storm.16.4 % cases showed mortality. This is attributed among cases with severe form of Covid 19.

Introduction

In January 2020, coronavirus SARS-CoV-2 was identified as the cause of an outbreak of severe pneumonia ,now known to be a complication of the coronavirus disease¹.Corona virus infection rapidly spreading and producing morbidity and mortality in all over the world in extensive pandemic pattern for the last one and half years. The origin is Wuhan but its presentation from which source is not clear. It is a complicated mutant variety of corona group of viruses. The mode of spread thought to be mainly airborne but other modes of transmission like contamination and Oro-fecal route is also described². Total world economy is shattered. Millions of deaths occurred all over the world. Investigations for the diagnosis

like RT-PCR, Antigen and Antibody test were available to the general population a bit late. Air travel is the major route of spread among continents. In India major cosmopolitan cities like Delhi, Mumbai, Chennai, Bangalore and Hyderabad were worst affected. This may be attributed to overcrowding at working places and entertainment centers. SARS-COVID-2 viruses are generally genetically simple to highly diverse. Corona virus are crown like particles with spikes protruding from their surface. They are enveloped viruses with single stranded positive sense RNA genomes of approximately 26-32 kb which is currently the largest known genome size for RNA virus genome. The major proteins include spike (S), membrane (M), nucleocapsid (N) and envelope (E). It has many accessory proteins. The virus injures target cells directly and subsequently triggers immune system dysfunction leading to life threatening cytokine storm or injury causing varying degrees of acute lung injury. 10% cases may land in severe Acute respiratory distress syndrome. That is the major cause of death in COVID infection. In recovered patients also we noted sequelae like hypercoagulable states, myocarditis³, ischemic and hemorrhagic strokes, altered mental status, Guillain Barré syndrome, acute hemorrhagic necrotizing encephalopathy and neurological retardation like low mentation^{4,5,6,7}. Children frequently have milder disease than adults, with few or no symptoms at all⁸. More mortality is noted in elderly patients with comorbid conditions like diabetes, hypertension, IHD, CRF. During peak pandemic infection of COVID in Telangana area between August 2020 to October 2020 in Chalmeda Anand Rao Institute of Medical Sciences had screened patients with RT-PCR, CT chest and admitted with facilities of quarantine and medical treatment with ventilator facilities in separate ICU. Hereby we present this paper to focus mode of infection and outcome results at this semi urban center.

Materials and methods

A retrospective study conducted on cases that were admitted in semi urban hospital Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar during a period of 3 months, from August 2020 to October 2020.

Inclusion criteria:

- 1) All the cases with CT CHEST CORADS grading 3 or above.
- 2) All the cases with COVID 19 RT-PCR and Rapid Antigen test positive.
- 3) Pulse oximeter showing saturation <90%.

Exclusion criteria:

- 1) Cases with COVID 19 RT-PCR negative.

Study procedure: Cases admitted at CAIMS under proper observation till the period of discharge. Informed consent and ethics approval has been taken for the study. During the peak epidemic period of COVID-19 in Telangana CAIMS center has admitted 515 cases from August 2020 to end of October 2020. The criteria for admission is RT-PCR positive with high grade fever with myalgia, severe cough with dyspnea, pulse oximeter showing saturation less than 90%, on CT-Chest showing CORAD > 3 and elderly patients above age of 60 with comorbid conditions like diabetes and hypertension. Cases with positive RT-PCR isolation recommended by government authorities were also admitted.

Results

Clinical features: Moderate to high grade fever is the commonest presentation among the patients (58.33%). Myalgia and dry cough are present in almost all the cases. After 4-5 days onset of fever, grade 3 dyspnea is the most common presentation for the admission. CT-Chest shows CORAD 4-5 in all the dyspneic cases. CT scoring was not done. RT-PCR positiveness on number of revolutions was also not recorded. Distribution of comorbid conditions is as

follows: Above 60 years (39%), Diabetes mellitus (44.6%), Hypertension (49.2%). No case was admitted below age of 18 years. Male patients are predominantly admitted (83%). Past history of COPD in these cases were not recorded.

Investigations:

Hematological examination showed lymphopenia with neutrophilia. Thrombocytopenia < 1 lakh count is seen in 12%. 8% of patients showed significant thrombocytopenia < 50,000, but there were no significant bleeding manifestations. Almost all the case showed mild rise of serum creatinine between 1-2 mg/dl may be attributed to hypotension (SBP < 90 mm Hg). Few people required inotrope support.

Table 1:

Investigation	Normal range	Alteration in study population	Percentage of alteration in study population
D-dimer	<0.5mg/L	310/515	60.2%
Sr LDH	<280 IU/L	406/515	79%
Sr ferritin	20-250ng/ml	268/515	52%
CRP	0.0-0.6mg/dl	32/515	6.2%
IL-6	<1.5pg/ml	490/515	95%

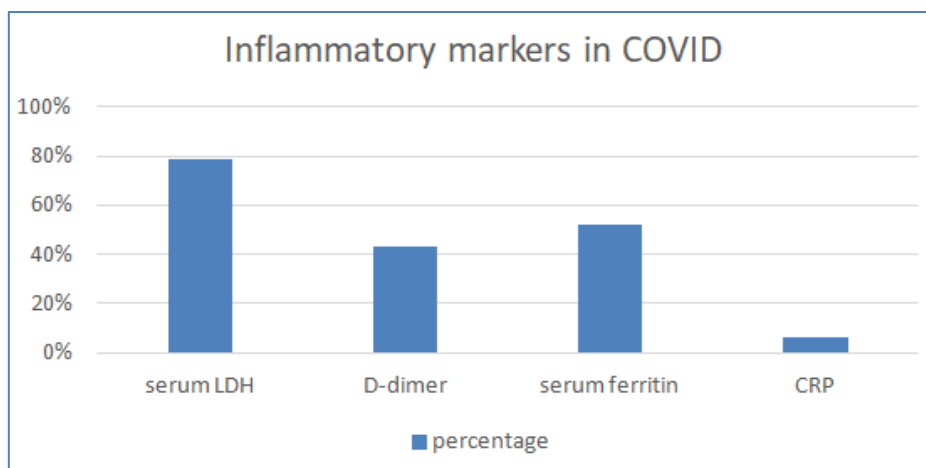
Rise of inflammatory markers in the study group

Elevated ferritin levels may be predictive of an imminent inflammatory reaction in Covid 19 or may be associated with viral spread in the human body and affect iron metabolism^{9,10}

LDH is an intracellular enzyme found in cells in almost all organ systems, which catalyses the inter conversion of pyruvate and lactate with concomitant inter conversion of NADH and NAD⁺¹¹

CRP is well established as a marker of systemic inflammation and severe infection. As an acute phase reactant, CRP binds to phosphocholine in pathogens and membranes of host cells, and acts as an opsonin to enhance phagocytosis and facilitate clearance. Ligand-bound CRP also efficiently activates the classical pathway of the complement system, an important component of innate host defence¹². Some studies suggest that ferritin helps in protecting the host body system against active infection by restricting the availability of iron to pathogen^{13,14}.

43.2% of cases reported to have mild raised D-dimer levels > 0.4. 17% of the cases showed high D-dimer levels > 10 (normal value <0.5mg/L) indicating high inflammatory state. 79% of the cases showed raised serum LDH levels 550-600 U/L (normal value <280 U/L). serum ferritin levels were increased in majority of cases 52% having >330 mcg/l. 6.2% of cases showed raised CRP levels between 1-2.5. Inflammatory responses triggered by rapid viral replication and cellular destruction can recruit macrophages and monocytes and induce release of cytokines and chemokines¹⁵. These cytokines and chemokines then attract immune cells and activate immune responses leading to cytokine storm in majority of the patients¹⁶.



Rise of inflammatory markers in relation to mortality:

Inflammatory marker	Mean rise in inflammatory marker in mortality
Serum LDH	607
Serum ferritin	882
D-dimer	17.1
CRP	10.7

Those patients who are kept on CPAP and High flow nasal oxygen were investigated selectively for IL-6. 95% of the patients showed high levels of IL-6 with range between 40-50 Pg/ml (normal range <1.5 Pg/ml) All these above parameters like D-dimer, Serum LDH, Serum ferritin, CRP, IL-6 are raised showing the magnitude of cytokine storm.

Management:

Those who were not requiring oxygen support were started on Favipiravir, Doxycycline, Ivermectin and Dexamethasone 4mg / bd given and IV fluids. 10-15% people required high flow nasal oxygenation, CPAP and invasive ventilation. Those people who were requiring oxygen support were started on Inj. REMDESIVIR 200mg/stat followed by 100mg/dl OD for next 4 days. Few patients developed MI as post COVID complication and required high doses of heparin and other management. Average hospital stay for patients is 7-10 days.

16.4% of cases died during hospital stay because of severe respiratory distress syndrome. This mortality rate is related to hospital admitted cases not related to all COVID cases in general population.

Discussion

Total number of 515 cases were admitted in CAIMS hospital on priority basis. The criteria for admission includes high grade fever with myalgia, SpO₂ on pulse oximeter showing < 90%. Dyspnea on mild exertion and cases referred by Govt. officials for isolation. Majority of cases showing moderate leukocytosis with severe lymphopenia, the interesting finding noticed is lymphocyte to neutrophil ratio grossly reduced (average lymphocytes = 14.7%, average neutrophils =77%). All the case were subjected for CT- chest they were showing CORAD 4-5, but CT severity scoring was not done. All the cases were grouped into 3 tertiles. Group 1 consists of mild fever, myalgia, no dyspnea, spo₂> 90% and based on CRP < 3. 2nd group consists of high grade fever, myalgia, mild dyspnea, spo₂< 85-90% requiring oxygen inhalation and CRP > 3-6. There hospital stay ranged from 7-10 days. Group 3 consists of severe complications of COVID presenting with grade 4 dyspnea, CRP > 6, SpO₂ <85%,and requiring high flow nasal oxygen therapy. In addition to CRP, majority of the

cases were subjected for investigation for LDH, Sr ferritin levels and D- dimer. IL-6 estimation was carried out for only 50 patients for those who can afford.

Group 1 was kept on Ivermectin, Doxycycline, mild doses of dexamethasone and in selective patients flavipiravir is given.

Group 2 in addition to above drugs instead of dexamethasone, methyl prednisolone was given, some cases were shifted to remdesivir therapy

Group 3 consists of severe degree of complications showing high levels of CRP, serum ferritin and LDH, D-dimer was not showing direct correlation. All these people were kept on high flow oxygen therapy.

CRP, LDH and serum ferritin were showing direct correlation with severity of the disease.

Unfortunately we lost 80 cases. This figure is showing high death rate 16% because it is the index noted in high risk patients who were admitted not the total cases of the COVID in the community. Mortality depends upon the duration of the disease to the hospital admission, majority of the deaths occurred to late arrival to the hospital. Those patients with remdesivir therapy showed less hospital stay. In 3rd group majority of the patients are above 60 years and mortality rate was high. (16%).

Conclusion

515 total cases were admitted during 3months period in this COVID center. Fever, cough, myalgia, dyspnea are the main clinical features. Almost all cases showed on CT-Chest >3 CORADS. Leucocytosis and lymphopenia is the common haematology feature. Inflammatory markers like LDH, D-dimer, CRP, Serum ferritin levels were estimated in all the cases,40% of the cases showed marked elevation of these markers. Selective cases who can afford were subjected for investigation of IL-6 .All these patients showed increased level of IL-6 suggestive of severe cytokine storm.Out of all these inflammatory markers IL-16 shows prognostic importance . 16.4% of cases showed mortality. This is attributed among cases admitted with severe form of COVID 19 with above the age of 60 years.

Limitations of the study

1. Majority of the cases came very late, we cannot assess the prognosis
2. Role of plasma therapy was not studied
3. Aggressive management by ECMO was not available in this institution

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