Association of Inflammatory markers with COVID-19 Outcomes and Severity: A Retrospective Cohort study

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Background

The 2019 coronavirus disease (COVID-19) originating in Wuhan China was found to be the cause of unexplained viral pneumonia[1]. The virus originates from Novel coronavirus Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) associated with severe respiratory compromise which spread to become a worldwide pandemic [2-4]. COVID-19 symptoms range from pyrexia, a new continuous cough, anosmia and ageusia to gastrointestinal, haematological or dermatological symptoms [5]. However, the disease can progress to dyspnoea, severe viral pneumonia requiring ventilator support and Intensive Care Unit (ICU) admission [4]. The three phases of the disease progression have been extensively researched and increasing evidence suggests that inflammatory responses play a critical role in COVID-19 [6].

COVID-19 Phases

There are three identified phases of COVID-19 see (Figure 1):

Stage 1-Early infectious phase

- Symptoms– Pyrexia, cough, diarrhoea, and headache,
- Diagnostic signs – confirm using COVID-19 Polymerase Chain Reaction (PCR) swab test, lymphopenia, increased D-dimer, elevated Lactate Dehydrogenase (LDH) and increased prothrombin time.

Stage 2- Pulmonary phase

- Symptoms - Hypoxia and shortness of breath,
- Diagnostic signs - normal to high Procalcitonin (PCT), abnormal chest imaging

Stage 3-Hyperinflammatory phase

- Symptoms – acute respiratory distress syndrome (ARDS), Systemic Inflammation Response System (SIRS) and cardiac failure,
- Diagnostic signs - raised inflammatory markers (C-Reactive Protein (CRP), LDH, D-Dimer, Ferritin (Fer), raised Pro Beta type Natriuretic Peptide (ProBNP) and elevated Troponin T (TnT) [6].

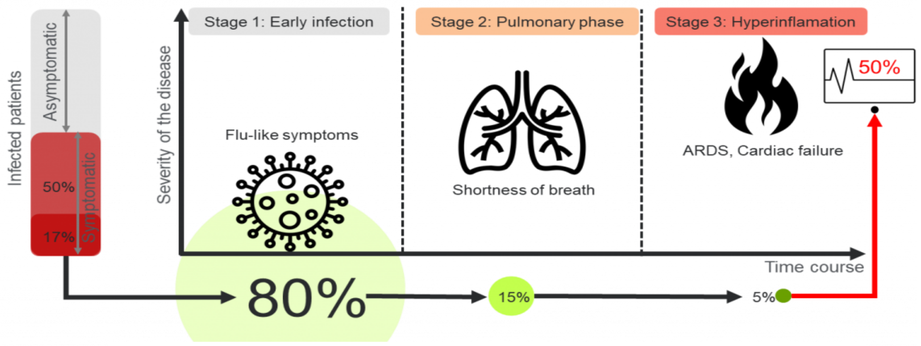

Figure 1: classification of COVID-19 disease states [7]

Aim

This study sought to determine if there was significant evidence that laboratory assays such as:

- CRP
- PCT,
- White Blood Cell Count (WBC)
- Neutrophils
- Lymphocytes
- Neutrophil Lymphocyte Ratio (NLR)

could effectively predict prognosis of COVID-19 patients and morbidity.

Method

A 200-patient cohort were divided into a control and test group depending on their CRP concentration within 24 hours of their positive COVID-19 diagnosis by RT-PCR using the Cepheid Gene Xpert RT-PCR method. Control group patient CRP <20mg/L; Test group patients CRP >20mg/L. Inflammatory marker results were recorded for all patients if available. Both groups were followed post admission or attendance for 28 days post covid positive swab result until the endpoint of discharge or mortality.

The following data was recorded:

- Patient age, gender, history, and diagnosis
- Length of stay
- Discharge date
- ITU admission
- Treatment type given including respiratory support.
- Cause of death and date deceased.

Results

Results showed COVID-19 patients in the control group (CRP <20 mg/L) demonstrated significant reduction in ITU admission (Figure 2); 4.3% of the control group compared with 24.7% of the test group were admitted to ITU.

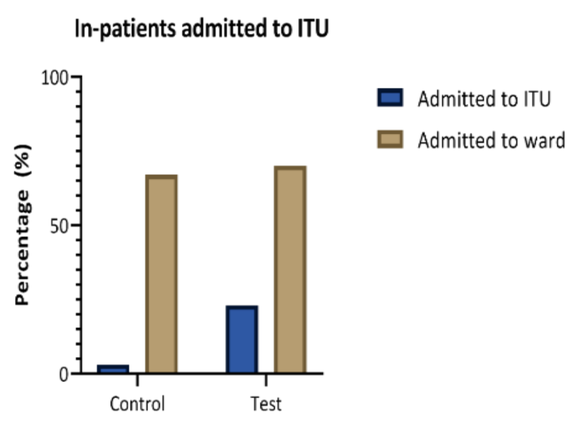

Figure 2

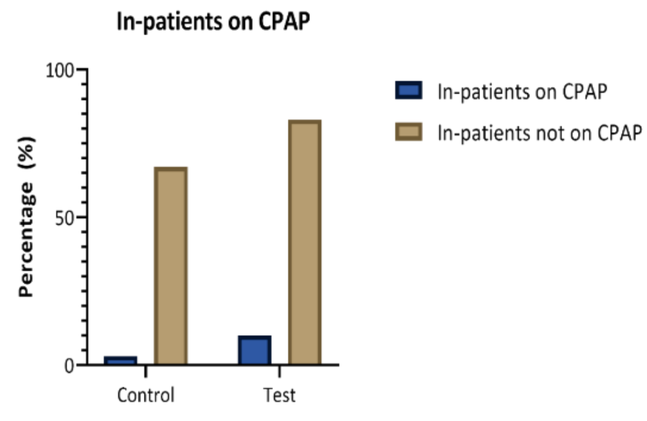

Figure 3

The number of COVID-19 patients treated with Continuous Positive Air Pressure (CPAP) was significantly higher in the test group (CRP >20 mg/L) (Figure 3); 10.8% of the test group were treated with CPAP vs 4.3% of the control group. The control group demonstrated improved survival rates within 28 days that were maintained to 360 days (Figure 4 and 5).

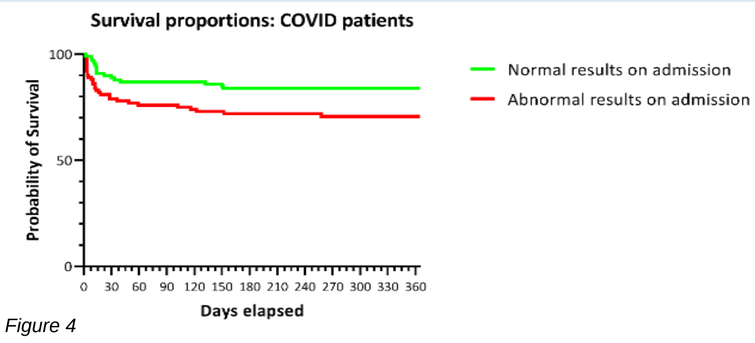

Figure 4

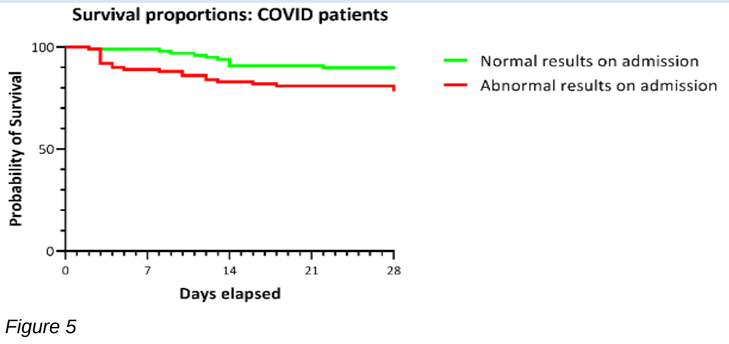

Figure 5

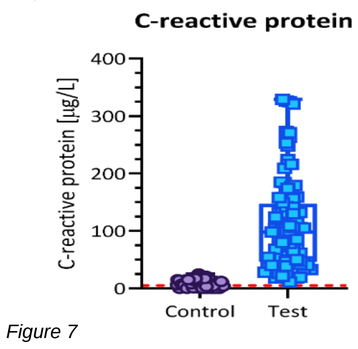

Figure 7

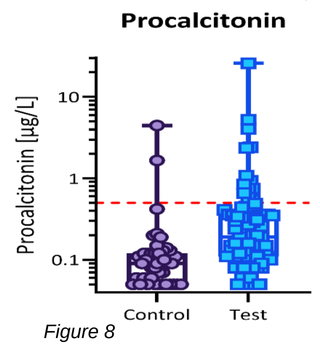

Figure 8

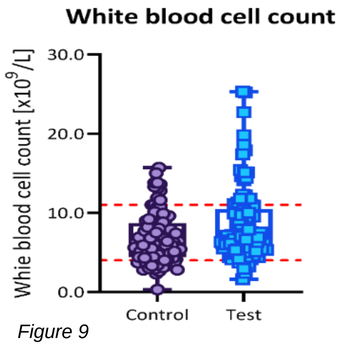

Figure 9

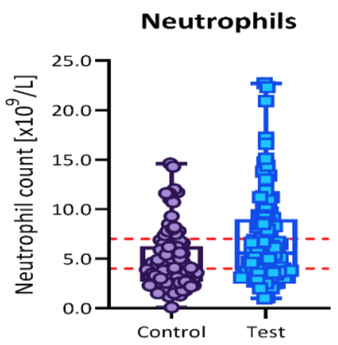

Figure 10

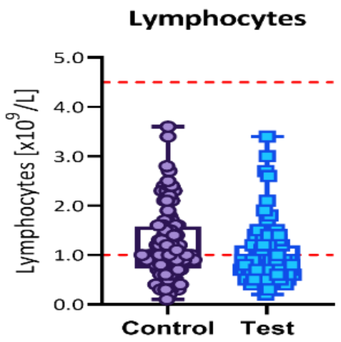

Figure 11

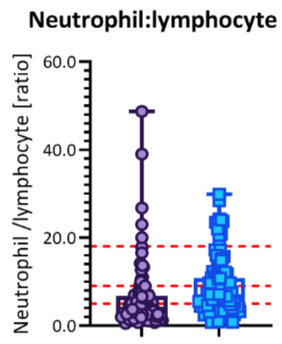

Figure 12

Significant differences (*P=<0.05*) were observed between test and control group patients for initial results for CRP, Procalcitonin, White blood cell count, Neutrophil count, Lymphocyte count, and NLR inflammatory markers (Figures 7 – 12).

Conclusion

This study demonstrated that inflammatory markers measured at COVID-19 diagnosis are associated with COVID-19 outcomes and progression. CRP, PCT, WBC, Neutrophil count, Lymphocyte count and NLR have been shown to be effective markers or COVID-19 disease severity, and patient morbidity. When these analytes are used in conjunction with treatment methods which have been researched, developed, and repurposed to treat COVID-19, severely ill patients have an improved chance of survival

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