Severity Markers in Critical Care Patients with COVID-19 Infection

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Introduction

Following the emergence of the novel Coronavirus 2019 (Covid-19), there has been an influx of critically unwell patients globally.

Despite huge quantities of research and data on the subject, there still remains significant challenges in the interpretation of laboratory results and their ability to recognize patients at higher risk of serious illness or mortality (1).

A meta-analysis of sixteen heterogeneous studies from China reported that patients with severe Covid-19 infection had higher C-reactive protein (CRP), procalcitonin (PCT), Interleukin-6, erythrocyte sedimentation rate and ferritin levels (2). High d dimer levels have been associated with higher risk of mortality (3), with high rates of clinically significant clots in critically unwell patients (4). Furthermore, normal d dimer levels on admission to hospital have a positive predictive value of 93% for survival and a negative predictive value of 30% (5).

This study aimed to describe the routinely available biochemical markers in a cohort patients with severe COVID-19 infection in a single Intensive Care Unit in Scotland.

Methods

In this project, we report routinely available biochemical markers, along with outcome measures taken from patients with confirmed Covid-19 infection who required admission to Intensive Care. The patients were treated in a district general hospital in Scotland, with a usual ICU capacity of 7 beds between March and May 2020.

Data was collected from case notes of all twenty one patients admitted to the ICU with PCR confirmed Covid-19 infection over the period. Admission and peak values for the markers were recorded, as was outcome. P values were calculated using Mann-Whitney U testing.

Permission was gained from our local audit lead and all data was anonymised.

Results

Data was collected for 21 patients. Overall survival was 38% (8/21), and survival in those invasively ventilated was 33% (6/18). Median length of ICU stay was 28 days in survivors and 16 days in non-survivors.
The table below shows the median peak level according to patient outcome

	Survivors- Median, (Range)	Non-survivors Median, (Range)	P value
Ferritin (µg/L)	1945 (1226-3094)	1703 (337-6978)	0.26
CRP (mg/L)	254 (75-407)	373 (295-684)	0.02
Procalcitonin (PCT) (ng/ml)	0.36 (0.17-3.62)	2.88 (0.22-5.31)	0.28
D dimer (ng/ml)	1966 (342-10000)	10000 (915- 36470)	0.07
Troponin (µg/L)	0 (0-0.16)	0.04 (0-1.95)	0.20

Table 1: Median peak levels according to outcome

D dimer
Measurements were taken in 20 patients. In patients who died, 53% (7/13) had a d dimer over 10,000, compared to just one patient who survived with a d dimer above 10,000. In our hospital a d dimer <500 is classed as negative. Twelve patients had serial measurements taken, with an median increase from admission to peak levels of 2,342 in survivors (n=4) and 12,197 in non-survivors (n=8).

Ferritin
Ferritin was measured in all patients, with 15 patients having serial measurements. Median peak levels were 1945 and 1703 in survivors and non-survivors respectively. Change from baseline to peak was 254 in non-survivors (n=9) and 267 in survivors (n=6).

Troponin
In our hospital assay a troponin <0.03 is negative. Accordingly 62% (n=8) of non survivors and 25% (n=2) of survivors had positive troponin measurements.

CRP
All patients had serial CRP measured. In patients who survived, median peak CRP was 254 and median change in CRP from admission was 82. In patients who didn't survive median peak CRP was 373 with a change from admission of 200. The four patients with the highest peak CRP didn't have PCT measured.

PCT
Fourteen patients had PCT measured. One survivor had a PCT of 3.62, the remaining patients who survived had a PCT<1. Median PCT was 2.9 in non-survivors and 0.4 in survivors.

Table 2 shows patients ordered by ascending peak CRP, alongside peak PCT, total ICU days, number of days of antibiotics and outcome

Peak CRP	Peak PCT	Total antibiotic days	Total ICU Days	Outcome
75	3.62	5	40	Survived
177	NK	4	4	Survived
206	0.32	4	15	Survived
247	0.3	29	41	Survived
260	0.17	4	9	Survived
295	NK	12	18	Died
311	0.22	6	6	Died
313	0.36	18	53	Survived
345	0.48	6	10	Died
349	3.38	23	30	Died
357	2.88	8	16	Died
362	5.31	20	20	Died
373	4.25	24	24	Died
374	NK	14	16	Died
385	0.3	1	13	Died
386	0.38	39	46	Survived
407	0.78	10	4	Survived
426	NK	12	16	Died
517	NK	8	4	Died
559	NK	2	2	Died
684	NK	5	8	Died

Table 1: Peak CRP, PCT and other clinical information ordered according to ascending CRP
NK= Not known, test not performed

Take Home Message

CRP is significantly higher in non survivors of Covid-19 infection

Although not statistically significant, non survivors with Covid-19 tend to have high and rising d dimers

Limitations

This is a descriptive analysis of a cohort of patients treated in a single center during the initial emergence of the novel coronavirus. As such, the results are of interest in guiding future data collection and research.

One of the main limitations of the data collected was the heterogeneity. Patients had a variety of biochemical markers taken on admission and during their illness according to their clinical course, current guidelines and changing laboratory availability. In addition, utility of the dataset was limited by its small sample size, especially in the group of survivors.

Discussion

As the global impact of Covid-19 continues, there is a huge volume of data and publications globally. All of the biomarkers described in this project have been associated with mortality (2, 3), however it is difficult translate this into the clinical environment.

The high reported mortality in Covid-19 still remains unexplained, with a variety of speculative causes from systemic micro-thrombosis and dysregulation of hypoxic pulmonary vascoconstiction, to systemic hyperinflammation or primary severe lung injury (6,7)

As more data emerges, and the results of awaited clinical trials into therapeutic options are reported, it will remain important to have a robust and standardised system in place to try and identify and intervene in patients at risk of poor outcomes. The collection of routinely available biochemical markers to assess disease severity and possible therapeutic interventions is likely to remain an important component in this process.

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