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LABORATORY BIOMARKERS OF COVID-19 DISEASE, SEVERITY AND OUTCOME

A.shaik Sulaimann Meeran Professor, Department of General Medicine, Government Royapettah Hospital, Kilpauk Medical College, Chennai-10.

P. Syed f. Munnaver Assistant Professor, Department of General Medicine, Government Royapettah Hospital, Kilpauk Medical College, Chennai-10.

C. Krishna Kumar* Post Graduate, Department of General Medicine, Government Royapettah Hospital, Kilpauk Medical College, Chennai-10. *Corresponding Author

ABSTRACT

Aim: To study the laboratory biomarkers that predict disease severity and outcome among COVID-19 patients admitted to the Government Kilpauk Medical College.

Methods: A prospective study was conducted among 430 RT-PCR confirmed COVID- 19 patients who were on admitted and treated from November 2020 to January 2021 and with complete clinical and laboratory data.

Results: Among the 430 patients studied, of which 248 (57.6%) had Non-severe disease (15.6% mild and 42.0% moderate) and 182 (42.4%) had Severe disease at admission. Regarding the disease outcome, 45 (10.5%) died and 385 (89.5%) were discharged alive. Following factors- Age group, Serum glutamic oxaloacetic transaminase (SGOT) Neutrophil to Lymphocyte ratio (NLR), Sodium and Potassium were found to be significant predictors of COVID-19 disease severity.

Conclusions: The laboratory markers such as raised SGOT, NLR and deranged sodium and potassium levels (both hypo- and hyper-states) were found to be significant predictors associated with severe COVID-19 disease. In addition, deranged values of white blood cell count and sodium levels were significantly associated with worse outcome of the disease. Therefore, it becomes pivotal to assess and monitor these laboratory markers at the earliest stage of the disease could have a considerable impact in halting disease progression and death.

INTRODUCTION

The growing threat due to the COVID-19 pandemic has caused numerous losses to the entire world. This study aims to identify important clinical and laboratory biomarkers that can predict disease severity and outcome. So far different clinical, laboratory and radiologic markers that can predict disease severity have been identified with varying results in the face of changing behavior of the disease and geographical disparity. Therefore, understanding predictors of disease severity and outcome are crucial to provide early preventive measures for a better outcome especially in developing country setup where intensive care setup might not match the increasing demand in the service.

Different laboratory markers are implicated as an indicator of disease severity, progression and outcome. Deranged cell counts, like anemia, polycythemia, leukopenia and leukocytosis with neutrophil predominance and decreased platelet count are found to be associated with severe disease and worse outcome in hospitalized patients. Similarly raised liver enzymes and total bilirubin levels were identified in severe and critical patients.

Raised inflammatory response of the body as manifested by raised laboratory values of various interleukins and C-reactive proteins are also reported. In addition, raised coagulation markers like fibrinogen and prothrombin time are identified in severe and critical patients.

Electrolyte imbalance, hypo- and hyper- levels were reported for sodium, potassium and calcium levels among patients with severe disease and worse outcome, hypothesized to result from the effect of the disease on the body system or the medication side effects.

METHODS AND MATERIALS

Study setting, design and population

An institution based cross sectional study was conducted at Government Kilpauk COVID-19 Care Center from November, 2020 to January 2021. The source population was all cases of COVID-19 admitted at KMC with a confirmed diagnosis of COVID-19 using RT-PCR. With these criteria, a total of 430 COVID-19 patients were included in the final analysis.

Data Collection Procedures and Quality Assurance

Data was extracted from patients' admission, follow up and discharge charts. Data consistency and completeness was checked before an attempt was made to enter the code and analyze the data.

RESULT

COVID-19 Severity and Disease Outcome

Among the 430 patients studied, 182 (42.4%) had severe disease and the rest 248 (57.6%) had non-severe disease (15.6% mild and 42.0% moderate) at admission. Regarding disease outcome, 45 (10.5%) died and 385 (89.5%) were discharged alive.

Socio-demographic, comorbid illness and presenting symptoms

More than half of the participants were younger than 50 years (61.8%) and males (65.1%). 188 patients (43.8%) had a history of one or more preexisting co-morbid illness. The majority had hypertension (25.2%), Type II diabetes mellitus (19.8%), Asthma (6.1%) and cardiac disease (5.6%). Other co-morbid illness including chronic diseases of the lung, kidney, liver and neurology constituted less than 1% of the total cases.

More than three fourth (76.0%) of the patients were symptomatic at presentation. The commonest symptoms were cough (69.2%), followed by fatigue (29.1%) and fever (26.1%). (**Table 1**)

Table 1: Socio–demographic, co-morbid illness and presenting symptom related variables among COVID-19 patients (n=430)

Variable	Total (%)	Variable	Total (%)
Age category (in years)		**Runny nose**	

< 50	261 (61.8)	No	401 (93.9)
≥ 50	169 (38.2)	Yes	29 (6.1)
Sex		**Chest pain**	
Female	154 (34.9)	No	344 (80.8)
Male	276 (65.1)	Yes	86 (19.2)
Preexisting Co-morbid Illness		**Myalgia**	
No	242 (56.8)	No	378 (88.8)
Yes	188 (43.2)	Yes	52 (11.2)
Cardiac disease		**Arthralgia**	
No	406 (94.8)	No	369 (85.8)
Yes	24 (5.2)	Yes	61 (14.2)
Hypertension		**Fatigue**	
No	322 (73.8)	No	305 (70.2)
Yes	108 (26.2)	Yes	125 (29.8)
Type II Diabetes Mellitus		**Shortness of breath**	
No	344 (80.9)	No	282 (65.9)
Yes	86 (19.1)	Yes	148 (34.1)
Asthma		**Headache**	
No	403 (93.3)	No	337 (78.3)
Yes	27 (6.7)	Yes	91 (21.7)
Presence of symptom		**Abdominal pain**	
Asymptomatic	91 (21.5)	No	418 (97.8)
Symptomatic	339 (78.5)	Yes	12 (2.2)
Fever		**Nausea/ vomiting**	
No	317 (73.1)	No	406 (94.1)
Yes	113 (26.9)	Yes	24 (5.9)
Cough		**Diarrhea**	
No	132 (30.1)	No	411 (95.2)
Yes	298 (69.9)	Yes	19 (4.8)
Sore throat			
No	352 (81.7)		
Yes	78 (18.3)		

Baseline Laboratory biomarkers

Table 2: Baseline Laboratory biomarkers related variables among COVID-19 patients (n=430)

Variables	Total (%)	Variables	Total (%)
Hematocrit (%)		**Urea** (mg/dl)	
<36	21(5.1)	< 20	86 (18.1)
36-45	257 (58.7)	≥20	344 (81.9)
>45	152 (36.2)		
White Blood Cell (cells/ul)		**Creatinine** (mg/dl)	
<4.5	66 (14.23)	<0.6	48 (11.2)
4.5-11	299 (69.7)	0.6-1.1	316 (74.1)
>11	65 (16.0)	>1.1	66 (14.7)
Neutrophil %		**SGPT** (IU/L)	
<40	22 (4.3)	< 41	248 (56.9)
40-70	128 (28.7)	≥ 41	182 (43.1)
>70	280 (67.1)	**SGOT** (IU/L)	
Lymphocyte %		< 40	325 (75.8)
<20	306 (71.3)	≥ 40	105 (24.2)
20-50	119 (26.8)	**ALP** (IU/L)	
>50	5 (1.9)	< 100	351 (81.3)
NLR		≥ 100	79 (18.7)
≤ 3	110 (25.2)	**Na** (mequ/l)	
>3	320 (74.8)	<135	66 (14.9)
Platelet count (cells/ul)		135-145	348 (81.1)
<150	37 (8.1)	>145	17 (4.0)
15-450	361 (85.0)	**K** (mequ/l)	
>450	32 (6.9)	<3.5	16 (4.1)
		3.5-4.5	285 (66.2)
		>4.5	129 (29.9)

DISCUSSION

In this study, we assessed the effect of clinical and laboratory markers on COVID-19 disease severity and outcome among 430 COVID-19 patients who were admitted to COVID-19 Care Center from November, 2020 to January, 2021. In this study, we identified the markers of disease severity and outcome. Timely identification of biomarkers of COVID-19 disease severity and death would help to provide targeted intervention and patient management. Among the 430 patients studied, 248 (57.8%) had Non-severe disease (15.6% mild and 42.0% moderate) and the rest 182 (42.2%) had Severe disease at admission. Regarding disease outcome, 45 (10.4%) died and 385 (89.6%) were discharged alive. Age group, NLR, SGOT, Sodium and Potassium were found to be significant predictors of COVID-19 disease severity and outcome.

Accordingly, after adjusting for other covariates, being 50 years and older was found to be associated with a 2.83 times increased risk of developing severe disease. Age is implicated to be associated with severe disease and outcome in different studies conducted globally. The reasons behind could be the increased possibility of weaker immune defense mechanism and co-morbid illnesses making older individuals prone to different illnesses with severe progression and worst outcome.

Symptoms of fever and fatigue were found to be significant predictors of disease severity showing a 1.26 and 1.48 times increased risk of having severe disease as compared to patients with no such symptoms, respectively. Having symptomatic disease, other than symptoms used in disease classification, in general is reported to delay disease recovery and also found to be associated with more severe disease category.

NLR of greater than three is associated with a 4.86 times increased risk of developing severe disease as compared with those with a value of three and less. NLR, an inflammatory biomarker above three indicates the body's stress. With more stress, as in severe and critical patient states, the level increases to even higher level. Therefore, this biomarker is an indirect indication of the body's stress level due to the severity of the disease. This is also similar with findings from other studies where NLR was found to an important predictor of disease severity and outcome.

Having a raised SGOT of 41 and above was associated with a 1.48 times increased risk of having severe disease as compared with those with value of a normal range. Different mechanisms are pointed to the possible effect of the SARS-CoV-2 Virus on liver; the virus could directly affect the hepatocytes or the liver could get injured indirectly through enhanced inflammatory response due to the raised immune markers and drug toxicity that are meant to treat or halt the progression of the disease resulting in liver damage and thereby an increase in liver enzymes. Raised in liver enzymes associated with more severe disease category is also reported in other studies.

The risk of developing severe disease among patients with deranged values of Na and K level (both hypo- and hyper-levels) was 1.42 and 1.34 times than patients with a normal values of Na and K, respectively. Electrolyte imbalances in any disease condition can result from fluid losses from the body through different routes, renal damage and effect of medication that is administered to treat the disease and/or concomitant illnesses. It is also implicated to be due to the decreased activity of ACE- 2 which is claimed to be a receptor for the SARS- coronavirus 2. This is also demonstrated in other studies, where both increased and decreased levels of Na and K are found to be associated with severe disease states.

After being adjusted for other factors, having deranged laboratory markers (both lower and raised values) of white

blood cell count was associated with a 4.38 times higher odds of dying compared to those with normal values. Both leukopenia and leukocytosis are found to be associated with severe COVID-19. Having decreased white cell count increases the potential to develop serious infection and expansion of an already existing pathogen thereby leading to the development of critical disease stage in any infection. Similarly, although a raised white cell count is an indication of a strong immune system responding to external threat; it also implies that the body is under a lot of stress from the pathogenic organism.

CONCLUSION

In this study we have assessed laboratory markers that can predict disease severity and outcome. Accordingly, NLR greater than three, raised SGOT and deranged Na and K levels (both hypo- and hyper-states) were found to be significantly associated with severe COVID-19 disease. In addition, deranged values of WBC and Na levels were significantly associated with worse outcome of the disease.

Therefore, assessing and monitoring these laboratory markers at the earliest stage of the disease could have a considerable input in halting disease progression and death.

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