



ISSN: 0975-833X

Available online at <http://www.ijournalcra.com>

INTERNATIONAL JOURNAL  
OF CURRENT RESEARCH

International Journal of Current Research  
Vol. 13, Issue, 12, pp.19861-19864, December, 2021

DOI: <https://doi.org/10.24941/ijcr.42675.12.2021>

## RESEARCH ARTICLE

# VALIDATION OF PARAMETERS AT THE TIME OF ADMISSION IN COVID-19 PATIENTS: A RETROSPECTIVE STUDY

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### ARTICLE INFO

#### Article History:

Received 15<sup>th</sup> September, 2021  
Received in revised form  
18<sup>th</sup> October, 2021  
Accepted 20<sup>th</sup> November, 2021  
Published online 29<sup>th</sup> December, 2021

#### Keywords:

C-Reactive Protein,  
Neutrophil-Lymphocyte Ratio,  
D-dimer

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### ABSTRACT

**Background:** The morbidity and mortality in COVID-19 positive cases has been associated with changes or fluctuations in inflammatory markers. However, the predictive power of each of these indicators in disease classification and prognosis remains largely unclear. **Objectives:** To validate the laboratory parameters at the time of admission in prognosis of the disease and also assess its relevance in short term mortality. **Methods:** We retrospectively collected information on the below parameters in 182 patients with COVID-19 classified them into survivors and non-survivors. Parameters such as Neutrophil/Lymphocyte ratio (NLR), C-reactive protein (CRP), Lactate dehydrogenase (LDH), Ferritin, D-Dimer, Liver function tests, COVID-19 RT-PCR Cycle Threshold (CT) score and Computed Tomography (CT) scan lung involvement were studied among both the group at the time of admission and its influence in mortality was studied. **Results:** NLR, CRP, D-Dimer and CT score were significantly raised in survivors compared to non-survivors. NLR was the most significant indicator and can be considered as an early warning signal to differentiate critically ill from moderate or mild illness. **Conclusions:** NLR at the time of admission can be used as a predictor for the assessment of severity of infection in remote areas.

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Citation: Dr. Santhya S.T., MBBS, MD, Dr. Ramya B, MBBS, MD and Dr. Bhaskaran K, MBBS, MD. "Validation of Parameters at the time of admission in COVID-19 Patients: A Retrospective Study", 2021. International Journal of Current Research, 13, (12), 19861-19864.

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an acute respiratory infective disease caused by the Severe Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus (Forni, 2017). An increasing number of studies suggested that people of all ages are susceptible to COVID-19 infection, which can result in severe and fatal respiratory diseases (Wang, 2020). Studies have shown CRP (C-reactive protein), Pro-calcitonin (PCT), Interleukin-6 (IL-6), Lymphocytes, and RT-PCR CT value could predict the prognosis and guide classification of COVID-19 patients (Tan, 2020). However the predictive power of these indicators in the prognosis of disease remains largely unclear. Acute shortage of medical care facilities during the pandemic caused a havoc and increase in mortality. So if prognostic parameters at the time of admission if assessed with course of the disease, guidelines can be made for in-hospital care and better utilization of health care facilities can be achieved, thereby mortality can be reduced.

Aim of the study is to validate the laboratory parameters at the time of admission in prognosis of the disease and also assess its relevance in short term mortality.

## MATERIALS AND METHODS

This is a single center, retrospective, cohort study including SARS-CoV2 infected patients admitted in Arunai Medical College & Hospital, Tiruvannamalai. All consecutive patients diagnosed with COVID-19 admitted in the month of May 2021 were enrolled in the study. A confirmed case was defined as a positive real-time RT-PCR for the presence of SARS-CoV 2 in naso-pharyngeal swab specimens. The assay was performed using Neo-Dx Covid detect kit, according to manufacturer's protocol.

**Data Collection:** The epidemiological data, medical history, underlying co-morbidities, symptoms and signs at admission, laboratory findings, Computed tomographic (CT) scan chest, real-time RT-PCR results and survival data was obtained from

electronic medical records and case sheets. The collected data was reviewed by two physicians. Symptoms and signs were noted at the time of admission and patients were followed up till discharge. We retrospectively collected information on the above parameters in 182 patients with COVID-19 classified them into survivors (n=153) and non-survivors (n=29). Parameters such as Neutrophil/Lymphocyte ratio (NLR), C-reactive protein (CRP), Lactate dehydrogenase (LDH), Ferritin, D-Dimer, Liver function tests, COVID-19 RT-PCR CT score and CT scan lung involvement were studied among both the groups. All these parameters were studied at the time of admission and prognosis of the patient was assessed based on these parameters in short-term mortality of patients. Statistical analysis were reported as percentage and compared using the  $\chi^2$  test. A value of  $P < 0.05$  was considered statistically significant.

## RESULTS

**Baseline characteristics:** A total of 182 COVID-19 patients confirmed with RT-PCT detection were included in the study. The mean age was 53.8 years (Table 1). Among these patients, 73 (40.1 %) were men and 109 (59.9 %) were women. Of 182, 76 (41.8%) patients had at least one co-morbid illness such as diabetes (21.4%), hypertension (32.1 %), cardiovascular disease (10.2 %) and respiratory disease (4.8 %) (Fig 1).

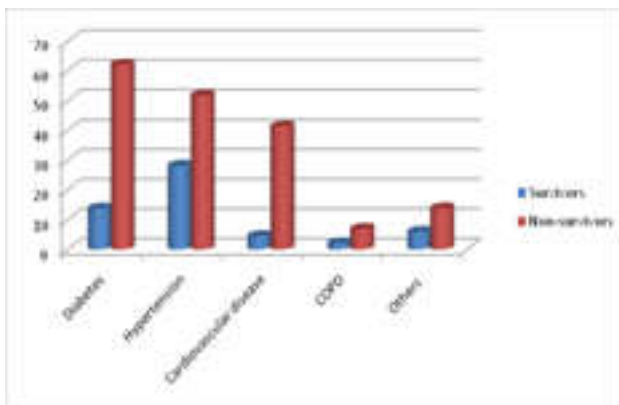


Figure 1. Comorbidities association with COVID-19 positive study subjects

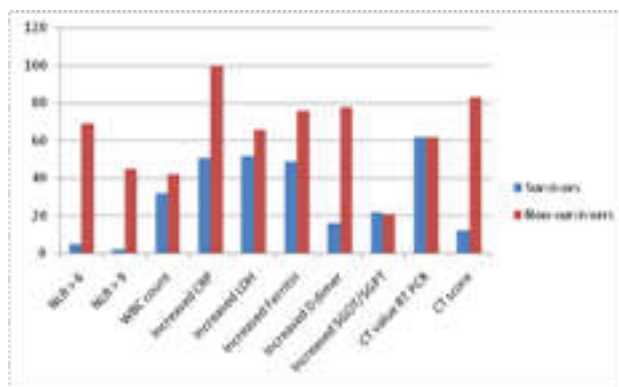


Figure 2. Validation of Indicators for the prognosis of COVID-19 patients

**Mortality and associated risk factors:** The laboratory and imaging parameters were assessed at the time of admission and its association with mortality was studied in 182 COVID-19 positive patients.

**Neutrophil Lymphocyte Ratio:** NLR more than 6 at the time of admission was observed in 15 % (n= 28) of total subjects, of which 8 (5% of survivors) were from survivors and 20 (69 % of non-survivors) were from non-survivors group. NLR more than 9 was seen in 2 % (n=2) of survivors and 45 % (n=13) of non-survivors. Hence, there was a significant difference of NLR detected at the time of admission in prognosis of the disease. Significant number of patients in non-survivors 45% group had elevated leukocyte count compared to survivors group 32%. (Table 2)

**Inflammatory parameters:** CRP was elevated in 107 (59%) out of 182 subjects at the time of admission. Out of 107, 29 (100%) of non-survivors and 78 (51%) of survivors demonstrated elevated CRP. LDH and ferritin was raised in 99 (54%) and 97 (53%) of subjects (Fig 2). There was no significant difference observed LDH & ferritin between survivors and non-survivors at the first visit. D-dimer was significantly elevated in 78% (n=23) among survivors and 16% among non-survivors when evaluated retrospectively at the time of admission. In Liver function tests such as SGOT/SGPT, there was no significant difference between both the study groups (Table 2). COVID-19 RT-PCR CT score didn't have much influence on survival status of the patients irrespective of its value. 83% of survivors compared to 12 % of non-survivors showed significant CT chest findings.

## DISCUSSION

Given the world-wide prevalence of COVID-19 and inadequate in-hospital services available, prognostic indicators are of great significance in guiding treatment, conserving medical resources and to reduce mortality. If early indicators are available better care can be given to the critically ill patients. In this study, few reported prognostic factors of COVID-19 were validated retrospectively in disease outcome. NLR can be used as an early warning signal for deteriorating severe COVID-19 infection and can provide an objective basis for early identification and management of severe COVID-19 pneumonia.<sup>4,5</sup> In our study, NLR positively correlated in non-survivors group so it can be used as an early warning signal for prognosis of COVID-19. Systemic inflammation, as measured by CRP and D-dimer, is strongly associated with mortality in COVID-19.<sup>6</sup> Also these parameters can be used as early warning signal in disease prognosis among COVID-19 patients as evidenced in other studies also (Dujardin, 2020; Pepys, 2021; Petrilli, 2020). In another retrospective cohort study originating in NYC, older age, admission levels of D-dimer of more than 1000 ng/mL, CRP of more than 200 mg/L and lymphopenia were associated with mortality in individuals hospitalized for COVID-19 (Chilimuri, 2020).

Our study suggests that, Chest CT scoring system can aid in predicting COVID-19 disease outcome early and significantly correlates with lab tests which significantly correlated with previous studies (Jafari, 2020). No correlation was observed between RT-PCR CT value and disease outcome in our study. Recently the ability of Ct values to reflect the true viral load has been questioned. Experts state that the Ct values for a specimen vary between different kits and techniques (including target genes, primers and threshold fluorescence values) and Ct values may vary between different runs of the same kit. The Ct value also depends on the method of collection of the sample and hence there may be variation in Ct values between two

**Table 1. Baseline Characteristics of the COVID-19 subjects in the study group**

Parameters	Total (n=182)	Survivors (n=153)	Non-survivors (n=29)	P value
Age mean (range)	53.8 (34- 82)	51.2 (34 – 71)	60.2 (43 – 82)	
< 60	69 (37.9)	57 (37.3)	12 (41.4)	0.176
≥ 60	113 (62.1)	96 (62.7)	17 (58.6)	
Male	73 (40.1)	54 (35.2)	19 (65.5)	0.003
Female	109 (59.9)	99 (64.8)	10 (34.5)	
<b>Co-morbidities</b>				
Diabetes	39 (21.4)	21 (13.7)	18 (62.1)	<0.001
Hypertension	58 (32.1)	43 (28.1)	15 (51.7)	0.020
Cardiovascular disease	19 (10.2)	7 (4.5)	12 (41.3)	0.002
COPD	8 (4.8)	3 (2)	5 (6.9)	0.003
Others	13 (7.4)	9 (5.9)	4 (13.8)	<0.001

**Table 2. Validation of Laboratory results and image findings in COVID-19 subjects**

Parameters	Total (n=182 ) n (%)	Survivors (n=153) n (%)	Non-survivors (n=29) n (%)	P value
NLR > 6	28 (15)	8 (5)	20 (69)	0.0001
NLR > 9	16 (8)	3 (2)	13 (45)	0.0002
<b>WBC count</b>				
Increased	62 (34)	50 (32)	12 (42)	0.0001
Increased CRP	107 (59)	78 (51)	29 (100)	0.0002
Increased LDH	99 (54)	80 (52)	19 (66)	0.06
Increased Ferritin	97 (53)	75 (49)	22 (76)	0.08
Increased D dimer	48 (26)	25 (16)	23 (78)	0.005
Increased SGOT/SGPT	40 (22)	34 (22)	6 (21)	0.1
CT value RT PCR	114 (62)	96 (62)	18 (62)	0.5
CT score	42 (23)	18 (12)	24 (83)	0.002

different samples obtained from the same person on the same day and run on the same kit (Shah, 2021). However, CRP levels in patients with COVID-19 who may progress from non-severe to severe cases need to be further studied in large-scale multicenter studies. Duration of symptoms before admission was not considered in the study which can be major factor in influencing the inflammatory parameters. Further study is required to combat these limiting factors for a better understanding. In conclusion, we recommend using these risk factors on admission to triage patients to the critical care units to maximize the utilization of medical services. NLR was the most significant indicator and can be considered as an early warning signal to differentiate critically ill from moderate or mild illness. Inflammatory parameters based approaches to risk stratification and treatment should be tested further.

**Conflicts of interest:** The authors declare no conflict of interest.

**Author contributions:** All the authors have made substantial contributions to this work and have approved the final manuscript.

**Acknowledgement:** We thank all the patients involved in the study. I also thank the institution for the support.

#### Glossary of Abbreviations

COPD – Chronic obstructive pulmonary disease  
 CRP – c-reactive protein  
 CT scan- Computed tomography  
 CT value – Cycle threshold  
 IL-6 – Interleukin-6  
 LDH- Lactate dehydrogenase  
 NLR- Neutrophil lymphocyteratio  
 PCT – Procalcitonin  
 RT-PCR - Real time Polymerase chain reaction  
 SGOT -Serum glutamic oxaloacetic transaminase  
 SGPT -Serum glutamic pyruvic transaminase

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