

ORIGINAL RESEARCH

A Study on Role of LDH/ Lymphocyte Ratio (LLR) in Severity of Covid 19 Disease**C Jyothi Jeevana¹, Srujana Raparathi², Ravi Kumar³**¹Assistant Professor, Department of Biochemistry, TIMS,Hyderabad, Telangana, India.²Assistant Professor, Department of Pathology, TIMS,Hyderabad, Telangana, India.³Professor and HOD, department of Biochemistry, TIMS,Hyderabad, Telangana, India.**ABSTRACT**

Background:COVID-19 disease caused by novel beta (β) coronavirus eventually has variable clinical presentation requiring intensive care unit (ICU) admission and mechanical ventilation. Identification and stratification of predictors of COVID-19 disease severity in an effort to guide medical management is a challenging issue.

Materials and Methods: The data from 200 patients diagnosed as COVID-19 and admitted in tertiary care hospital between August 2020 and January 2020 were retrospectively analyzed. They were divided into two groups according to ICMR guidelines severity of COVID-19 as non-severe (n = 100) and severe (n = 100). Demographic data, comorbidities, COVID test results, laboratory values, Lactate Dehydrogenase (LDH)/Lymphocyte ratio at the time of admission, were recorded. The comparison of laboratory test results in both groups were done using Z test. The diagnostic power of LLR in differentiating severity of COVID-19 and Cut off values of all the parameters for severe and non-severe group were analyzed statistically using ROC.

Results: Severe COVID-19 patients had higher mean age, higher levels of LDH and lower levels of Lymphocyte count (P < 0.0001). Compared with non-severe patients (mean, 0.32 ± 0.2), patients with severe COVID-19 had higher LLR (mean, 0.82 ± 0.4 ; P < 0.001). ROC curve analysis assigned 0.45 as the cut-off value for LLR for differentiation of severe COVID-19 (AUC = 0.87, 83% (CI, 0.8227 to 0.9215) sensitivity, 80% specificity, P < 0.001)

Conclusion: Initial assessment of LDH, ALC, and LLR values at hospital admission may be important predictors of severity in COVID-19 patients.

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INTRODUCTION

COVID-19 disease caused by novel beta (β) coronavirus eventually named SARS-CoV-2 has variable clinical presentation from asymptomatic and milder symptoms to more severe and emergent manifestation including chest pain, hypoxemia, pneumonia and other complications requiring mechanical ventilation. SARS-CoV-2 binds ACE 2 receptors causing inflammation and activation of signalling pathways, resulting in cytokine storm and thus contributing to tissue injury. Lactate dehydrogenase (LDH), a key enzyme in the glycolytic pathway and a cytoplasmic enzyme found in most organs, has been linked to inflammation response and cell damage. Lymphocytes express the receptor ACE2 and may be a direct target of viruses, resulting in lymphopenia which is hallmark of covid 19 disease. The present study conducted

with the hypothesis that the combination of these laboratory values(LDH and Lymphopenia) would yield a more sensitive result in identification of disease severity.

Aim of the study:

- To assess significance of LLR(LDH/Lymphocyte ratio) in severity of covid disease.

Objectives of the study:

- To estimate the levels of serum LDH, Absolute Lymphocyte Count(ALC) and LDH/Lymphocyte ratio(LLR) in Severe and non- severe Covid -19 patients.
- To compare LDH/lymphocyte ratio in patients in severe and non severe type of Covid -19 patients.

MATERIALS & METHODS

A Retrospective cross sectional study was done and data from the patients diagnosed as Covid 19 pneumonia and admitted in Telangana Institute of medical sciences And Research Institute, Gachibowli, from period August 01 2020 to January 31 2021 were recorded. The diagnosis of Covid 19 was confirmed by positive results of SARS- CoV-2 nucleic acid detection tests from nasal or pharyngeal swab specimens of the patients.

Total 363 patients were divided into two groups based on ICMR guidelines as 1) Mild and Moderate group/ non severe group(n = 251). 2) Severe group(n = 112).

GROUP I: Severe disease: shortness of breath(SOB), respiratory rate > 30/min, SpO₂<90% on room air.

GROUP 2: Non Severe: Mild disease : Upper respiratory tract symptoms with or without fever and without SOB. Moderate disease: SOB, respiratory rate > 24/min and SpO₂ 90% to 93% on room air. Patients with incomplete data were excluded from the study.

The protocols for the study and proforma were approved by the ethics committee of TIMS Hospital. General information of patients demographic data, age, gender, comorbidities, clinical features, were recorded. Serum LDH and ALC were obtained from hospital data. Normal serum LDH is <248U/L. Normal Absolute Lymphocyte Count is 1.00-4.80 x 10⁹/L.

Statistical analysis:

Statistical analysis was performed using the software GraphPad Prism version 9.1.2. Continuous variables were expressed as mean and standard deviation and compared using Z-test. For all tests, P < 0.05 was considered statistically significant.

RESULTS

The baseline characteristics of the patients with critical COVID-19 are summarized in [Table1].

Table 1: Baseline demographic characteristics in group 1 and group 2

Category	Severe (n=112)	Non severe(n=251)
AGE in years(median)	62	46
Males	74%(n=83)	70%(n=179)
Co morbidities	43%(n=48)	17%(n=43)

Table 2: Laboratory parameters in two groups

Parameter	Group 1		Group 2	
	Mean	±S.D	Mean	±S.D
Serum LDH(U/L)	570	246	324	132

ALC(*10 ⁶ /L)	747	454	1443	832
LLR	0.89	0.4	0.35	0.2

Table 3: comparison of study parameters in two groups using z test

Parameter	Z-value	P-value
LDH	10.4	<0.0001
ALC	5.01	<0.0005
LLR	11.6	<0.0001

The LDH level in non-severe patients amounted to 324 ± 132 U/L, the higher LDH levels were found in the severe group with a level of 570 ± 246 U/L ($P < 0.0001$). ALC in non-severe patients is $1443 \pm 832 * 10^6$ /L, lower ALC were found in the severe group with a value of $747 \pm 454 * 10^6$ /L ($P < 0.0005$). Mean of LLR in severe patients is 0.89 ± 0.4 which is higher than non-severe group with mean of 0.35 ± 0.2 ($P < 0.0001$).

DISCUSSION

Our results showed that increased LDH, lower ALC and raised LLR seen in severe group when compared with the non severe group. Our findings indicated that elevated serum LDH could be used as a severity indicator in patients with COVID-19 pneumonia. A pooled analysis conducted by Brandon Michael Henry et al demonstrated an association between elevated LDH values and worse outcomes in patients with COVID-19.^[1] Possible sources of elevated serum LDH levels during infection may be immunologic changes after SARS-COV-2 infection of respiratory tract which result in an early acute respiratory inflammatory response with consequent release of pro-inflammatory cytokines, which is a mediator of lung inflammation and fibrosis.

Present study showed that ALC is much lower in severe group compared to the non severe group indicating lymphopenia could be the indicator of severity in covid disease. Previous studies showed that lymphopenia is an effective and reliable indicator of the severity and hospitalization in COVID-19 patients.^[2] This can be due to direct attack of virus on lymphocytes expressing ACE-2 receptors leading to lymphocyte death or inflammatory cytokines inducing lymphocyte apoptosis.

Our study also showed that LLR is increased in severe patients than in non severe group. In a study conducted by Serin et al, concluded that LLR can be used as a diagnostic and mortality parameter.^[3]

CONCLUSION

Thus, LLR can be used as predictor of severity in patients with covid 19.

REFERENCES

- Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, Plebani M, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. *The American Journal of Emergency Medicine*. 2020;38(9):1722–6.
- Tan, L., Wang, Q., Zhang, D. et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Sig Transduct Target Ther* 5, 33 (2020).
- Serin I, Sari ND, Dogu MH, Acikel SD, Babur G, Ulusoy A, et al. A new parameter in COVID-19 pandemic: initial lactate dehydrogenase (LDH)/Lymphocyte ratio for diagnosis and mortality. *Journal of Infection and Public Health*. 2020;13(11):1664–70.