International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 02 Issue 05 May 2022

Page No: 322-330

DOI: https://doi.org/10.47191/ijmscrs/v2-i5-06, Impact Factor: 5.365

Correlation between Lactate Dehydrogenase Levels and Severity by Pulmonary Tomography in Patients with Sars-Cov-2

Hugo Eduardo Guerrero-Topete[1], Ma. Natalia Gómez-González[2], Carlos Jiménez-Correa[3], Martha Alicia Hernández-González[4], Juan Pablo Fernández-Hernández[5], Pedro Luis González-Carrillo[6]

[1]Critical Care Medicine and Emergency Medicine Physician. Instituto Mexicano del Seguro Social, Unidad Médica de Alta Especialidad, Hospital de Especialidades No. 1, Centro Médico Nacional del Bajío (IMSS, UMAE HE No. 1 CMN), León, Guanajuato, Mexico. Intensive Care Unit.

[2]Master's degree in clinical research, Critical Care Medicine and Anesthesiologists Physician. IMSS, UMAE HE No. 1 CMN, León, Guanajuato. Mexico. Intensive Care Unit

[3]Critical Care Medicine and Emergency Medicine Physician. IMSS, UMAE HE No. 1 CMN, León, Guanajuato, Mexico. Intensive Care Unit.

[4]Master's degree in clinical research and cardiology physician. IMSS, UMAE HE No. 1 CMN, León, Guanajuato. Intensive Care Unit, México

[5]Internist Physician. IMSS, UMAE HE No. 1 CMN, León, Guanajuato. Intensive Care Unit, Mexico.

[6]Critical Care Medicine and Internist Physician. IMSS, UMAE HE No. 1 CMN, León, Guanajuato. Intensive Care Unit, Mexico.

ABSTRACT

Serum lactate dehydrogenase (LHD) concentration has been described as a biomarker to predict severe lung injury and severe hypoxemia in patients with ARDS. The aim of the study was to correlate lactate dehydrogenase concentrations with the tomographic severity index in SARS-CoV-2 pneumonia cases, considering lung CT as the gold standard for severity diagnosis in this population based on the presence of ground glass pattern and the score given in the segmental assessment. A total of 110 patients were included in the study, in the period from April to September 2020. From the results, a moderate correlation was obtained between serum LHD levels and severity score by pulmonary tomography, with an r=0.474 and *p* <0.0001; with a severity-associated serum LHD cut-off point of 396 mg /dl (*p* < 0.001, sensitivity 86.02%, specificity 75%, AUC 0.806). Serum DHL levels may be useful for predicting severity in patients with COVID pneumonia 19t.

KEYWORDS: SARS-CoV-2; lactate dehydrogenase; Severity; Pneumonia; Mexico

ARTICLE DETAILS

Published On:
06 May 2022

Available on:
https://ijmscr.org/

HIGHT LIGHTS

The new COVID 19 pandemic has given way to a large number of investigations in the context of deciphering the behavior of the disease, however, despite this, there are still variables to be clarified, from accurately determining the evolution, defining severe cases and having a one hundred percent effective treatment.

The accurate diagnostic tests for assessing the severity of SARS-CoV-2 are few; to date, pulmonary tomography remains the gold standard for more accurately assessing lung damage and defining severity, and although many studies mention other promising biomarkers for this purpose, unfortunately they are not available in all hospital centers.

Lactate dehydrogenase (LHD) has historically been of interest as a biomarker associated with lung damage, with a greater boom during the influenza A H1N1 pandemic, with favorable results in terms of sensitivity and specificity of diagnosis and severity.

In view of the current pandemic, there is renewed interest in DHL as a diagnostic test that could easily and affordably predict severe cases of SARS-CoV-2. The main objective of the present study was to correlate LHD concentrations with the tomographic

severity index in SARS-CoV-2 pneumonia cases, considering lung CT as the gold standard for severity diagnosis in this population, based on the presence of ground glass and the score given in the segmental evaluation. A total of 110 patients were included in the study, in the period from April 1, 2020 to September 30, 2020. From the results, a moderate correlation was obtained between serum LHD levels and severity score by pulmonary tomography, presenting great statistical weight according to the p value; a severity-associated serum LHD cut-off point of 396 U/l is proposed, with a promising accuracy ($p < 0.001$, sensitivity of 86.02%, sensitivity of 86.02%). 001, sensitivity 86.02%, specificity 75%, AUC 0.806), therefore it is concluded that DHL can be an accessible, simple and fast biomarker that helps to define severe cases of SARS-CoV-2.

I. INTRODUCTION

Since the WHO declared COVID 19 as a public health emergency with international impact, its spread has been increasing. The first confirmed case in Mexico was recorded on February 27, 2020; as of August 2021, it has claimed the lives of more than 244,000 people[1,2].

SARS-CoV-2 has respiratory transmission, with rapid evolution of the disease and significant pulmonary involvement with development of acute respiratory distress syndrome (ARDS) and development of multiple organ failure. Although it has been possible to determine the incubation time and timing of complications, most research has been aimed at determining the evolution of the disease and the timely detection of severe SARS-CoV-2 cases, so far the chest CT scan is considered the gold standard for diagnosis and prognosis of the disease, however other laboratory findings have been proposed to be associated with severe cases, including increased white blood cell count with lymphopenia, prolonged prothrombin time, elevated levels of liver enzymes, lactate dehydrogenase (LHD), d-dimer (DD), interleukin-6, C-reactive protein (CRP) and procalcitonin[3–5].

Serum measurement of LHD levels is presented as a simple biomarker that can predict severe cases of SARS-CoV-2 pneumonia as in other scenarios such as H1N1 influenza and other causes of pneumonia, it has been described in critically ill patients with significant increases in lactate, pyruvate dehydrogenase enzyme dysfunction and increased LHD concentrations[6–9].

An incubation period of up to 14 days has been determined, without being able to determine the time of onset of severe symptoms[10,11]. There is a discrepancy in the definition of severe cases in patients with COVID pneumonia 19, with the description of phenotypes as proposed by Gattinoni even with more specific and expensive laboratory tests such as the measurement of interleukins its operationalization remains confusing[11–15].

In terms of severity, most of the literature describes a rapid evolution of the cases, with severe disease states and the need for intensive care in up to 5% of cases [5]. The median duration between the onset of symptoms and admission to the ICU has been reported to be 9 to 10 days. Several risk factors for death have been identified in hospitalized adults, particularly advanced age, DD levels greater than 2,000 ng/mL, severity score by tomographic assessment greater than 15 points, PaO_2/FiO_2 less than 200 mm Hg, and an elevated SOFA score since admission[4, 5, 16, 17].

Within the imaging studies, tomographic assessment by CORADS classification constitutes a discriminatory power to diagnose COVID 19 with high certainty; according to international consensus, the severity of the lung lesion is classified according to scores and severity stratification [17–19]. Since the 1960s, the study of serum DHL concentrations has been used to determine the degree of infection by influenza virus and other viremias. It has traditionally been considered that the lactate-pyruvate index is a more specific indicator than isolated lactate for reflecting metabolic alterations induced by tissue hypoxia, since it allows some hypermetabolic processes in which lactate levels rise significantly to be ruled out as anaerobic metabolism[20–23].

Serum LHD determination (taking into account its 5 isoforms, LHD 1: heart and red blood cells; LHD 2: white blood cells; LHD 3: lungs; LHD 4: kidneys, placenta and pancreas; LHD 5: liver and skeletal muscles), is used to assess tissue damage in multiple causes, including liver function tests, pancreatitis, acute coronary syndrome[8, 24–26].

In respiratory infections with the development of ARDS, LHD concentrations have been proposed as a reliable biomarker to predict severe lung injury and severe hipoxemia. (21,26,27). On the other hand, it has also been used in cases of sepsis, associated with other inflammatory mediators and 28 day mortality, suggesting that elevated serum LHD levels are probably associated with unfavorable outcomes in septic patients (28). In SARS-CoV-2, despite being mentioned in previous studies only as a finding with a cut-off point of 250 U/dl, and included in the severity scale in COVID 19 (Call Score), it is not widely validated, in addition to being evaluated in small populations[29]. In Mexico there are no studies on serum LHD levels related to severe cases of SARS-CoV-2, so it is proposed to correlate with the severity predictors described in the literature (severity index by chest CT, PAO_2/FiO_2 ratio and serum levels of DD) and to have a cut-off point that is applicable to these patients.

II. MATERIAL AND METHODS

A prospective, analytical study was conducted in the Intensive Care Unit of the Instituto Mexicano del Seguro Social, Unidad Médica de Alta Especialidad, Centro Médico Nacional del Bajío, León, Guanajuato, México. From April 1, 2020 to September 30, 2020. The population included patients with a diagnosis of severe acute respiratory syndrome due to SARS-CoV-2 infection who were admitted to the ICU. The sample was non probabilistic. Inclusion criteria were: older than 18 years, previous diagnosis of COVID 19 with positive laboratory test (RT-qPCR), Admission to Intensive Care Unit and presenting ARDS with PaO_2/FiO_2 less than 200. Patients with the following characteristics were excluded: known liver disease, active cancer.

The objective was to correlate serum lactate dehydrogenase concentrations with the tomographic severity index in cases of pneumonia due to SARS-CoV-2. Secondary objectives were to correlate LHD, DD, PaO_2/FiO_2 levels at ICU admission with the initial chest CT severity score and to present a cut off point for serum LHD level as a predictor of severity in SARS-CoV-2.

Blood sampling was performed with the appropriate Personal Protective Equipment (PPE) and according to the current standards issued by the WHO and adapted by the IMSS; the serum measurement of LHD and DD, venous blood sample was used, in red tube (vacutest kima) and blue one (BD Vacutainer Buff Na Citrate 0.109 M, 3.2%), serum LHD levels were determined by an automatic analyzer, with quality control by Standatrol S-E 2 levels of Wiener lab. The DD sample using the Alere Triage® D-Dimer test as a single-use fluoroimmunoassay device used to determine the concentration. To obtain the PaO_2/FiO_2 ratio, an arterial blood sample is taken by radial arterial puncture and the sample is processed in a gasometer, taking into account the FiO_2 supply to the patient at the time of sample collection. The imaging study was performed by computed tomography, interpreted by an expertise radiologist. The extent of the lung lesions was evaluated as follows Mild: <5%, 1 to 5 points; Moderate >5-25% involvement, 6 to 15 points; Severe >25-50% involvement; >15 points.

This work was performed with the approval of the institutional research and ethics committees with registration number: R-202-1001-076. The present study is considered without research risk in accordance with the regulations of the general health law on health research. For all statistical analyses, *p* values of less than 0.05 were considered significant

III. RESULTS

From April 1, 2020 to September 30, 2020, 145 patients were registered in the census of the intensive care unit, Unidad Medica de Alta Especialidad, Centro Médico Nacional del Bajío, León, Guanajuato, after applying the inclusion criteria a sample of 110 patients was obtained (Figure 1).

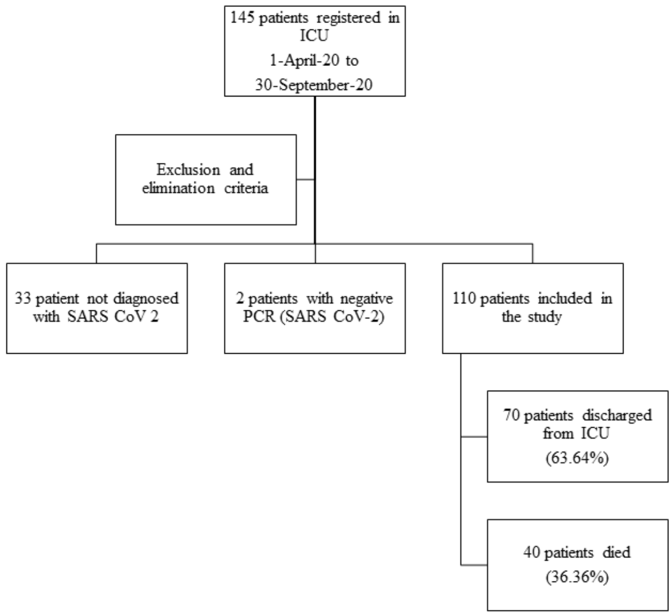

Figure 1. Flow chart of patients included in the study

The 110 patients were distributed according to sex (I Table) with 62.73% male (n=69) and 37.27% female (n=41); of the total sample included, age was distributed with a mean of 51.9 years, a minimum of 18 years, a maximum of 76 years and standard deviation of 13.52 years. When ICU stay was evaluated, a mean of 9 days, a maximum of 30 days and a minimum of 1, with a standard deviation of 5.67 was observed. According to the number of days of mechanical ventilation, a maximum of 23 days and a minimum of 0 was recorded, with a mean of 8.64 and a standard deviation of 5.85. When analyzing the risk factors present, there was a higher percentage of overweight and obesity with 55.45% (n=61), 38.18% were hypertensive, 34.54% had diabetes mellitus and 32.72% were smokers (I Table).

TABLE I. Demographic characteristics of the population, length of stay, days of mechanical ventilation.

	n=110
SEX	
Male	69 (62.73%)
Female	41 (37.27%)
RISK FACTORS	
Diabetes Mellitus	38 (34.54%)
HAS	42 (38.18%)
Immunocompromise	7 (6.36%)
Smoking	36 (32.72%)
ASMA	4 (3.63%)
COPD	13 (11.81%)
Obesity	61 (55.45%)
REGISTERED AGE (YEARS)	
Media	51.90 (13.52)
OBESITY CLASSIFICATION	
Low weight	--
Normal	14 (2.72%)
Overweight	35 (31.81%)
Obesity-I	38 (34.54%)
Obesity-II	14 (12.72%)
Obesity-III	9 (8.18%)
LENGTH OF STAY IN UCI (DAYS)	
Media	9.93 (5.67)
MECHANICAL VENTILATION (DAYS)	
Media	8.64 (5.86)

Values not expressed as proportions refer to means and medians.

A one-factor analysis of variance (ANOVA) was performed, comparing the serum levels of LHD on admission to the ICU and the severity score by simple chest tomography (classified as mild, moderate and severe), reporting a significant difference between groups with a $p < 0.001$ (F=0.337); in the analysis of each group, greater statistical significance was observed in the severe ones. Subsequently, a post hoc analysis was performed, using Tukey's test, with a statistically significant report p 0.012, finding a significant difference with the mild group.

A slightly correlation with immunocompromise was observed between LHD levels at admission and risk factors with a p 0.03 (II Table).

TABLE II. Spearman's correlation between LHD levels and risk factors

Correlations							
		DM[1]	HAS[2]	Inm.[3]	Smo[4]	Asthma	COPD[5]
LHD	Correlation coefficient	0.168	0.052	0.203	0.023	0.145	0.055
	Sig. (bilateral)	0.080	0.586	0.033*	0.810	0.130	0.565
	n	110	110	110	110	110	110

1 Diabetes Mellitus. 2 Systemic Arterial Hypertension. 3Immunocompromised. 4Smoking. 5Chronic Obstructive Pulmonary Disease
**extadistically significant*

Stratification was performed according to the WHO Obesity classification and a contingency table was made between the strata and the levels of LHD at admission and severity assessed by pulmonary CT; by Chi-square we obtained an $X^2 = 20.004$ with a $p < 0.001$, constituting a risk factor associated with high levels of LHD and tomographic severity.

Correlation and scatter plots were performed between serum LHD values at admission with the CT severity score, PaO_2/FiO_2 ratio and DD values. A moderate correlation was obtained between high levels of LHD (according to the cut-off point obtained DHL >396 mg/dL), and CT severity score, with a p <0.0001 (r=0.474); there is correlation between PaO_2/FiO_2 ratio at admission and DHL at admission with a p 0.003 (r= 0.380); between LDH value and DD no significant correlation was observed, however, a p 0.017 (r=0.228). (III Table, Figure 2, Figure 3).

TABLE III. **Correlation between serum LHD levels with CT Severity Score, PaO2/FiO2, Dimero D, (at ICU admission).**

		PaO_2/FiO_2	D-dimer	TAC Severit Index
LHD (>396	Correlation coefficient	-0.380	0.228	0.474
severity)	Sig. (bilateral)	0.003*	0.017*	0.000*
	n	110	110	110

**significant p value*

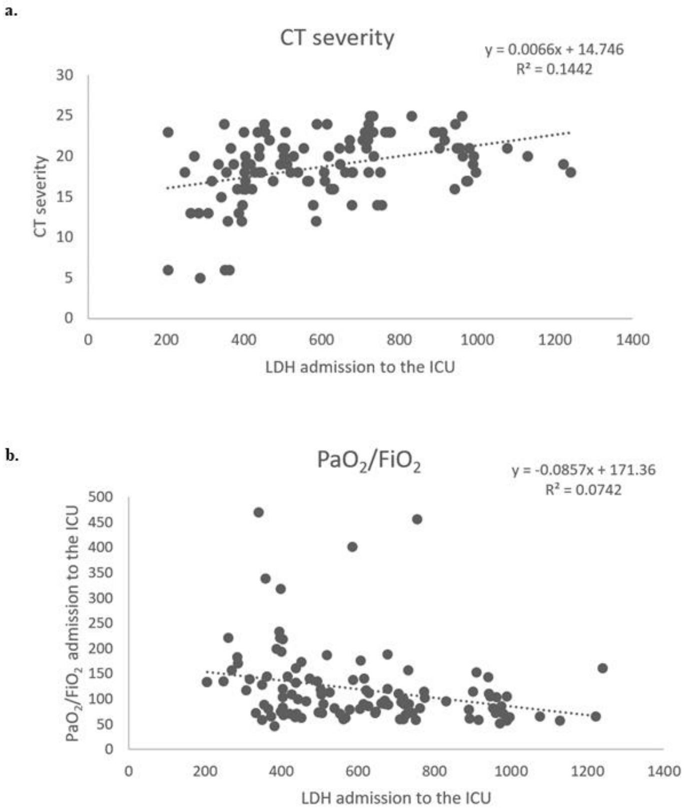

Figure 2. Dispersion curves, Correlation between serum LHD levels with chest CT severity index (a) and PaO2/FiO2 ratio (b); at ICU admission

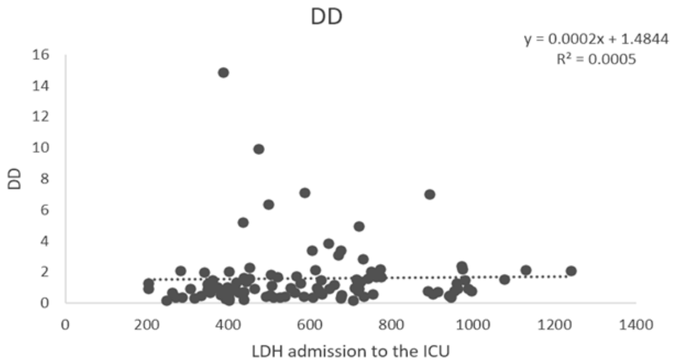

Figure 3. Dispersion curves, Correlation between serum LHD with serum Dimero D (DD) level.

The different scales used as a prognostic of mortality and organ dysfunction, indirectly describe severity in critical patients; the SOFA and APACHE scales were calculated at ICU admission, from the statistical analysis correlation tests were used, obtaining a slightly correlation between the SOFA and APACHE score with a *p* 0.004 (*r*=0.271) and *p* 0.018 (*r*=0.225), respectively (Figure 4).

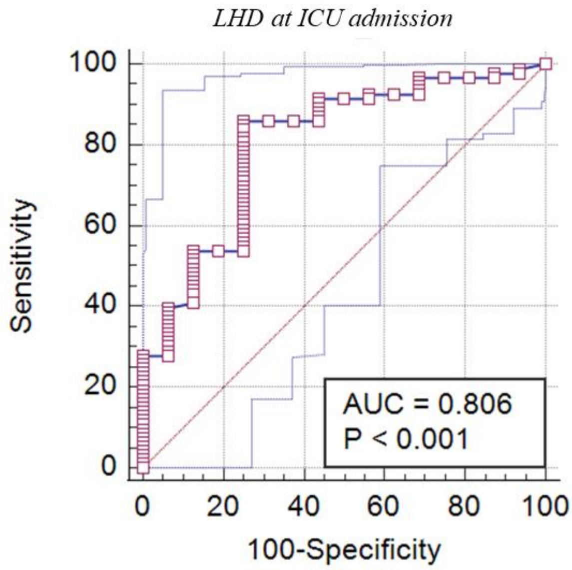

Figure 4. ROC curve, determination of the LHD cutoff point, comparison between LHD at ICU admission and CT severity

To determine the cut-off point of serum LHD levels as a predictor of severity, a comparison was made with the results of chest CT as a severity index, using ROC curves, a cut-off point of LHD of 396 mg/dl was obtained, with a p <0.001, sensitivity of 86.02% and specificity of 75%, positive predictive value of 95.2 and negative predictive value between 89.5 - 97.9%. The ROC curve shows an area under the curve of 0.806, with a p <0.001 (Figure 4).

IV. DISCUSSION

SARS-CoV-2 disease resulted in a large number of investigations, all aimed at determining the behavior of the infection, from the incubation period, associated risk factors and to predict the evolution of the disease, taking into consideration the criteria for hospitalization or severity. However, despite the existence of multiple data regarding the behavior of the virus, all the results remain unclear or contradictory.

A data base review using PubMEd, Scielo and Medscape, obtained 24,000 articles with the words "severity in SARS-CoV-2 " and the keywords "LHD levels, correlation with SARS-CoV-2 severity". None of them consider the levels of lactate dehydrogenase as a predictor of severity in patients with COVID 19.

Sociodemographic variables and risk factors

Most studies highlight some predisposing risk factors for SARS-CoV-2 infection, many of these factors will be associated with severe presentations of the disease, in our study there was no correlation between risk factors and disease severity, of the variables included as a risk factor, immunocompromise has a slightly correlation as well as overweight and obesity patients as the most frequent risk factor in the study population. In contrast with other authors such as Muthiah Vaduganathan [et al], where systemic arterial hypertension stands out as the main risk factor for disease severity, this in relation to angiotensin converting enzyme, angiotensin II and virus receptors. Angiotensin II activity may be partly responsable for organ dysfunction in COVID 19, after integration with the SARS-CoV-2 peak protein[30].

Gandhi [et al] points out a list of risk factors associated with greater complications from COVID 19 including advanced age (> 65 years), cardiovascular disease, chronic obstructive pulmonary disease, systemic arterial hypertension, diabetes and obesity. In addition, other conditions include renal disease, immunocompromise, cancer and human immunodeficiency virus (HIV) infection, with a higher risk of complications(3). In comparison with this study, the presence of immunocompromise highlights as a risk factor correlated with severity.

Considering the age, we differ the mean age reported in the literature is >60 years, in contrast to the mean age of 50 years obtained in this study. However, Verity [et al] founds an age ≥ 60 years associated with unfavorable outcomes, as well as the presence of hypertension, diabetes, cardiovascular disease, chronic respiratory disease, and cancer[5].

Lactate dehydrogenase as a predictor of severity

The study of LHD has been of interest since the last century. In 1960, Kelly [et al] demonstrated a strong correlation between LHD concentrations and the level of tissue damage involving the rupture of cell membranes associated with multiple causes, including virus infections(20). [19] Serum LHD determination has been used to assess tissue damage in liver function tests, pancreatitis cases and acute coronary syndrome studies[22, 23].

Fernández Carvajal [et al] determined serum LHD concentrations in patients with community-acquired pneumonia and described a cut-off value for LHD of 230 IU/L (representing a value below the curve of 0.93) with a sensitivity of 80.3%, specificity of 81.2%, positive predictive value of 82.0% and negative predictive value of 79.5%, concluding that patients with community-acquired pneumonia have elevated lactate dehydrogenase concentrations[31].

In the influenza pandemic, the measurement of LHD levels was the interest of some researchers[32]. Caprotta [et al], in Argentina, included pediatric patients with a diagnosis of ARDS due to influenza A H1N1 pneumonia, all with severe pulmonary lesions and severe hypoxemia, and used LHD levels for their assessment[27].

García Arroyo [et. al] discusses LHD concentrations as a prognostic biomarker in patients with influenza A H1N1 pneumonia, concluding that LHD concentrations > 350 IU/L can be considered a biomarker of severity and negative impact on survival in patients with pneumonia[21].

Lu J [et al] in the publication "Lactate dehydrogenase is associated with 28-day mortality in patients with sepsis: a retrospective observational study" associated LHD levels and 28-day mortality. Among the results they mention that serum LHD levels was an independent risk factor for death in patients with sepsis (95% CI 1.002-1.007, *p* 0.001), with significant correlations between LHD, interleukin-1b (r=0.514, p<0.0001), thus concluding that elevated serum LHD levels are likely to be associated with 28-day mortality in patients with sepsis(28).

Yi Han [et al] ("Lactate dehydrogenase, a Risk Factor of Severe COVID 19 Patients: A Retrospective and Observational Study"), included 17 patients, demonstrating that LHD levels could identify lung injury and severe cases in patients with COVID 19, thus elevated LHD levels are considered as an early recognition biomarker, concluding its correlation with disease severity[33].

Ma C [et al] postulate that increased LHD, CRP, DD, and decreased blood platelet and lymphocyte counts were highly associated with COVID-19 categorized as severe (all for p<0.001). In the analysis was included a cutoff point of LHD levels of 378.47 as a predictor of severity; 34 being a lower cutoff than that obtained in our study[34].

Our study proposes a cut-off point as a predictor of severity in patients with SARS CoV-2 (LHD 396 mg/dl), with a sensitivity of 86.02% and specificity of 75%, positive predictive value (PPV) of 95.2 and negative predictive value (NPV) between 89.5 - 97.9%. Compared to other literature using other laboratory tests as a predictor of severity in SARS-CoV-2, in this study were obtained superior results in terms of sensitivity, specificity and statistical value.

Other biomarkers and diagnostic tests in SARS-CoV-2 vs LDH

Other laboratory tests have been considered as biomarkers in the assessment of severity in SARS-CoV-2; Ma [et al] in the meta-analysis founds that elevated CRP, LHD and DD, along with reduced lymphocyte count and platelet count were the prominent features of severe cases (all for p <0.001)[34].

Ferrando [et al] in the study "Characteristics, clinical evolution and factors associated with ICU mortality in critically ill patients infected with SARS-CoV-2 in Spain: a prospective, cohort, multicenter study"; a total of 663 patients were included, important inflammatory markers were significantly higher in non survivors at ICU admission: DD [1.599 (697-3,810) vs. 940 (interquartile range RIC: 576-2, 030); p 0.002], and LHD [487 (RIC: 393-643) vs. 404 (RIC: 339-514); p < 0.001]. They conclude in the study population that peak procalcitonin level and platelet count were predictive of mortality on multivariate analysis, with an overall ICU mortality of 31%, which is similar to reports of non COVID 19 ARDS[35].

Li Tan [et al] determined that the severity and outcome of COVID19 cases has been associated with the percentage of circulating lymphocytes (LYM%), CRP levels, interleukin-6 (IL-6), procalcitonin (PCT), lactic acid (LA) and viral load; however, the predictive power of each of these indicators in disease classification and prognosis remains unclear. Despite this, the study concludes that the most sensitive and reliable factors to distinguish between severe and non severe cases, as well as mortality, only lymphocyte levels were significantly different between severe and moderate types, being one of the most sensitive and reliable indicators to discriminate between critically ill, severe and moderate patients[36].

Coagulopathy is a common feature of SARS-CoV-2 infection, and an increased DD is the most common finding. One of the largest initial studies found abnormally elevated DD levels in 260 of 560 cases (46.4%) with a prevalence of 43% in non-critically ill patients compared with 60% in critically ill ICU patients; DD levels of more than 2.0 mg/L could predict mortality with a sensitivity of 92.3% and a specificity of 83.3%[37].

Peng [et al] performed lung ultrasound on 20 patients with COVID 19 using a 12-zone method. Characteristic findings included the following: pleural line thickening with pleural line irregularity; B lines in a variety of patterns including focal, multifocal, and confluent; consolidations in a variety of patterns; appearance of A lines during the recovery phase; pleural effusions are infrequent. The patterns observed occurred along a continuum from a mild alveolar interstitial pattern to a severe bilateral interstitial pattern and/or pulmonary consolidation. The findings of lung ultrasound features of SARS-CoV-2 pneumonia/ ARDS are related to the stage of disease, severity of lung injury, and comorbidities. However, one of the limitations of using sonography is that cannot detect deep lung injury, as the aerated lung blocks ultrasound transmission, ultimately requiring chest CT to assess severity and structural damage[38].

CT evaluation, is considered the gold standard for the diagnosis and assessment of the evolution of COVID 19 infected patients. Ground glass opacities predominated in the early phase ($\leq$ 7 days from symptom onset), while consolidation and "paving" pattern as well as fibrosis characterized by late stage disease (> 7 days). The CT score was significantly higher in critical and severe cases than in mild stage (p <0.0001), and among late-stage than early stage patients (p <0.0001). The TAC score correlated significantly with CRP (p <0.0001, r=0.6204) and DD (p <0.0001, r=0.6625) levels. A CT score of $\geq$ 18 was associated with an increased risk of mortality. Multivariate analysis demonstrated that CT parenchymal assessment may more accurately reflect short term outcome, providing direct visualization of anatomic injury compared to non specific inflammatory biomarkers[39].

It is important to have more tools that provide an assessment of severity, taking into consideration health care costs, and therefore to provide appropriate care in order to reduce mortality. The timely detection of excess mortality from all causes can be particularly useful for estimating and monitoring the evolution of the epidemic in Mexico, regardless of what is recorded in the epidemiological surveillance system, which depends on the interaction between individuals and the health system, as well as on the sensitivity and specificity of the diagnostic tests applied. Five states accounted for 54.0% of the excess of deaths from all causes: the State of Mexico, Mexico City, Veracruz, Puebla and Guanajuato, with SARS-CoV-2 infection being the leading cause of mortality[40]. The mortality observed during the study period was 36%, coinciding with some of the authors cited.

Our results were aimed at determining whether LHD levels on admission to the ICU would correlate with other markers cited in the literature as a determinant of severity, taking into account the characteristics and supplies of our hospital unit. When correlated with DD levels there was no significant correlation, however, with the evolution of PaO_2/FiO_2 levels we obtained a statistically significant negative correlation, as well as a correlation with the tomographic severity score, these two variables being statistically significant (p <0.001). During the study we presented some limitations due to the size of the sample obtained, in addition to the fact that serum LHD levels and tomographic assessment could not be followed up during their stay in the ICU, due to the availability of supplies.

V. CONCLUSIONS

According to the definition of a severe case of SARS-CoV-2 pneumonia, our hypothesis was aimed to determine whether the levels of LHD on admission to the ICU would correlate with other markers cited in the literature as a determinant of severity, taking into account the characteristics and supplies of our hospital unit. A moderate correlation was obtained with some of the tests that define severity in patients with COVID 19 infection (severity index by thorax tomography, PaO_2/FiO_2 ratio, p=0.001), therefore, LHD concentrations are proposed as a predictor of severity in patients with SARS-CoV-2.

Sponsorship:

The authors declare not having received support from any sponsor or resources outside those granted by the medical institution

.

Conflicts of interest:

The authors declare that they have no conflicts of interest.

REFERENCES

I. COVID-19: chronology of WHO action [online] WHO; 27 April 2020 www.who.int.

II. COVID-19 in Mexico: cases by entity and chronology of the coronavirus [online] Mexico City. La Razón; 2020.

III. Gandhi R, Lynch J, Del Rio C. Mild or Moderate Covid-19. N Engl J Med 29;383(18):1757–66.

IV. Lauer S, Grantz K, Bi Q, et al. The incubation period of coronavirus disease 2019 (CoVID-19) from publicly reported confirmed cases: Estimation and application. Ann Intern Med 5;172(9):577–82.

V. Verity R, Okell L, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. Lancet Infect Dis 2020; 20: 669–77

VI. Merino M, Sahuaquillo J, Borrull A, et al. ¿Es el lactato un buen indicador de hipoxia tisular? Resultados de un estudio piloto en 21 pacientes con un traumatismo craneoencefálico. Neurocirugía 2010; 21: 289-301.

VII. Adeva M, López M, Funcasta R, et al. Comprehensive review on lactate metabolism in human health. Mitochondrion 17 (2014) 76–100.

VIII. Sánchez M, Olive C, Caballero M, et al. Isoenzimas de lactato deshidrogenasa en el suero y aspirado bronquial de recién nacidos con dificultad respiratoria de etiología diversa. An Esp Pediatr 1996;45:62-66.

IX. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? Critical Care (2020) 24:154.

X. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 20;382(8):727–33.

XI. Giwa A, Desai A. Novel Coronavirus COVID-19: an Overview for emergency clinicians. Emerg Med Pract 2020 Feb 27;22(2 Suppl 2):1-21

XII. Sánchez M, Carrillo R. Coronavirus-2019. Consideraciones Generales. Rev Mex Anestesiol, 2020; 43 (2): 83-91.

XIII. Baig A, Khaleeq A, Ali U, et al. Evidence of the COVID-19 Virus Targeting the CNS: tissue distribution, host-virus interaction and proposed neurotropic mechanisms. ACS Chem. Neurosci. XXXX, XXX, XXX−XXX.

XIV. Gattinoni L, Chiumello D, Caironi P, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? Intensive Care Med. 2020; 46(6): 1099–1102.

XV. Mendoza A, Valencia G, Quintana A, et al. Clasificación clínica y tratamiento temprano de la COVID-19: reporte de casos del Hospital de Emergencias Villa El Salvador, Lima Perú. Acta Med Peru. 2020;37(2)

XVI. Elizalde J, Fortuna J, Luviano J, et al. Guía COVID-19 para la atención del paciente crítico con infección por SARS-coV-2 Colegio Mexicano de Medicina Crítica. Med Crit 2020;34(1):7-42

XVII. Truog R, Mitchell C, Daley G. The toughest triage - allocating ventilators in a pandemic. N Engl J Med 2020; 382:1973-1975.

XVIII. Prokop M, Van Everdingen W, Van Rees V, et al. CO-RADS: A categorical CT assessment scheme for patients suspected of having COVID 19 definition and evaluation. Radiology 2020; 296:E97–E104.

XIX. Wang Y, Dong C, Hu Y, et al. Temporal changes of CT findings in 90 patients with COVID-19 pneumonia: a longitudinal study. Radiology 2020; 296:E55–E64.

XX. Kelly R, Greiff D. The level of lactic dehydrogenase activity as an indicator of the grwoth of influenza virus in the embryonate egg. J Exp Med. 1961 Jan 1;113(1):125-9.

XXI. García A, Rosas M, SantoyoA, et al. Deshidrogenasa láctica como factor pronóstico en neumonías. Med Int Méx. 2017 September;33(5):563-571.

XXII. Aranda E. Interpretación de la deshidrogenasa láctica. Rev Soc Bol Ped 2010; 49 (2): 132 - 4

XXIII. Goulabchand R, Guilpain P. Anomalías biológicas frecuentes: lactato deshidrogenasa elevada. EMC - Tratado de Medicina, 20(4), 1–5.

XXIV. Fernández J, Hinestroza L, Villasmil E, et al. Deshidrogenasa láctica sérica en pacientes con neumonía adquirida en la comunidad. Pulmón. 6. 19.

XXV. Fink M. Cytopathic hypoxia. Mitochondrial dysfunction as mechanism contributing to organ dysfunction in sepsis. Crit Care Clin. 2001 Jan;17(1):219-37.

XXVI. Garrido C, Cano C, Salcedo M, et al. Influenza A H1N1 (swine flu) en niños estudiados en el Instituto Nacional de Enfermedades Respiratorias. Acta Pediatr Mex 2010;31(4):162-167.

XXVII. Caprotta G, González P, Primucci Y, et al. Infección respiratoria por influenza A H1N1 en cuidados intensivos de la República Argentina. An Pediatr(Barc).2010;72(1):62–66.

XXVIII. Lu J, Wei Z, Jiang H, et al. Lactate dehydrogenase is associated with 28 day mortality in patients with sepsis: a retrospective observational study. J Surg Res. 2018 Aug;228:314-321.

XXIX. Ji D, Zhang D, Xu J, et al. Prediction for progression risk in patients with COVID-19 pneumonia: The CALL score. Clin Infect Dis. 2020 Sep 12;71(6):1393-1399.

XXX. Vaduganathan M, Vardeny O, Michel T, et al. Renin-Angiotensin-Aldosterone System inhibitors in patients with Covid-19. N Engl J Med. 2020 Apr 23;382(17):1653-1659.

XXXI. Fernández J, Hinestroza L, Villasmil E, [et al]. Deshidrogenasa láctica sérica en pacientes con neumonía adquirida en la comunidad" Pulmón 6. Enero 2015

XXXII. Neri S, Barranco G, León M, et al. Factores predictores de defunción en pacientes con neumonía por influenza A H1N1. Med Int Mex. 2011;27(5):421-428.

XXXIII. Han Y, Zhang H, Mu S, et al. Lactate dehydrogenase, an independent risk factor of severe COVID-19 patients: a retrospective and observational study. Aging (Albany NY). 2020;12(12):11245-11258.

XXXIV. Ma C, Gu J, Hou P, et al. Incidence, clinical characteristics and prognostic factor of patients with COVID-19: a systematic review and meta analysis. medRxiv 2020.03.17.20037572.

XXXV. Ferrando C, Mellado R, Gea A, et al. Características, evolución clínica y factores asociados a la mortalidad en UCI de los pacientes críticos infectados por SARS-CoV-2 en España: estudio prospectivo, de cohorte y multicéntrico. Rev Esp Anestesiol Reanim. 2020;67(8):425---437.

XXXVI. Tan L, Kang X, Ji X, et al. Validation of Predictors of Disease Severity and Outcomes in COVID-19 Patients: A Descriptive and Retrospective Study. Med (N Y). 2020;1(1):128-138.e3.

XXXVII. Iba T, Levy J, Levi M, et al. Coagulopathy of Coronavirus Disease 2019. Crit Care Med. 2020;48(9):1358-1364.

XXXVIII. Peng Q, Wang X, Zhang L, et al. Findings of lung ultrasonography of novel coronavirus pneumonia during the 2019–2020 epidemic. Intensive Care Med.

XXXIX. Francone M, Iafrate F, Masci GM, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. Eur Radiol. 2020;30(12):6808-6817.

XL. Gobierno de México. Boletín estadístico sobre exceso de mortalidad por todas las causas durante la emergencia por COVID-19 2020.