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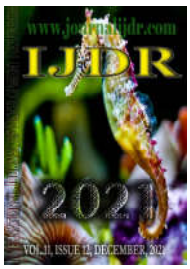

RESEARCH ARTICLE OPEN ACCESS

CORRELATION OF LDH AND PRESENCE OF LUNG INJURIES IN PATIENTS WITH COVID-19

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ABSTRACT

Given the importance of knowing more about the SARS-Cov-2 infection, a study was carried out using the medical records of 104 individuals during up to 14 days of COVID-19, treated at an outpatient clinic, between January and April 2021, in the Amazon region, northern Brazil. The objective was to correlate the levels of lactic dehydrogenase (LDH), a biomarker of tissue damage, with the presence and extension of lung lesions through lung CT scans. All patients were over 18 years old, of both genders, with mild or moderate clinical symptomatic form, and had the following demographics: male (42.1%), female (57.9%), with the age groups (years) of 18-25 (2.6%), 26-35 (7.0%), 36-45 (17.5%), 46-60 (40.4%) and over 60 (32.5%). CT scans showed mainly bilateral involvement (92.3%), with a typical pattern (92.3%), affecting 10-25% (42.5%) of the lung fields, with a predominance of three types of lesions: interlobular septal thickening (30.8%), nodules (16.3%) and ground-glass (11.5%), sometimes concomitant. LDH was the biomarker with more normal results (97.3%). There was no correlation between high levels of LDH and lung parenchyma changes, possibly because normality prevailed in both parameters and it is a cohort under extra-hospital care. There is a need for prospective and multicenter studies of patients with clinical forms with no severity, in order to bring contributions to outpatient care, the most prevalent in the world, through algorithms that can ensure intervention measures to reduce the possibility of unfavorable evolution and sequelae after COVID-19.

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INTRODUCTION

COVID-19 disease was declared a pandemic in March 2020 by the World Health Organization (WHO) which released a technical note indicating that the SARS-CoV-2 infection represented a public health emergency of international concern (WHO, 2020). This virus belongs to the Coronaviridae family characterized by having the presence of enveloped RNA, being the seventh identified in the Betacoronavirus group. Possibly, it has bats as the primary reservoir of the pathogen (ZHOU *et al*., 2020). Coronaviruses are responsible for infections in vertebrate animals, with respiratory impairment of varying severity, ranging from the common cold to severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), such as those caused by SARS-CoV and MERS-CoV4, respectively (COUSINS, 2018).

There is a need for further clarification on the factors that determine the evolution and prognosis of each patient (FEHR; PERLMAN, 2015). Studies show that after respiratory cells are infected by the virus, there is a stimulus for the acute inflammatory response with increased blood flow, plasma and leukocyte extravasation and increased local temperature and pain, accompanied by activation of pro-inflammatory cytokines or chemokines, which recruit more cells to the injury site, with consequent tissue damage (YUKI *et al*., 2020; ZHOU *et al*., 2020; CARSANA *et al*., 2020). This modulation, which is shown with different intensity in individuals, will be clinically evidenced, in most cases, in an asymptomatic or mild manner, similar to a flu condition, or moderate when, in addition to fever, there is dry cough, shortness of breath, chest pain or pressure, headache, myalgia, fatigue, anosmia, ageusia, sore throat, rhinorrhea, chills, nausea, vomiting, diarrhea, eye pain, accompanied by dyspnea, which begins a few days after the onset of the symptoms. In a minority of times it

can present itself in a severe way with systemic involvement, possibly leading to death, which is more common among the elderly and those of other age groups with comorbidities (BRASIL, 2020; CHEN *et al*., 2020; FU *et al*., 2020). Elevated D-Dimer, lactate dehydrogenase (LDH), C-Reactive Protein (CRP), fibrinogen, interleukin 6 (IL6), ferritin, creatine phosphokinase (CPK), troponin I, prothrombin time and thrombocytopenia have been reported in patients with SARS - CoV-2 and correlated with disease severity. However, these biomarkers, mainly inflammatory tests, are altered in several other clinical situations (ZHOU *et al*., 2020; GHANDI *et al*., 2020; FU *et al*., 2020). The enzyme lactate dehydrogenase (LDH or DHL) is found in the various tissues of the body, especially the heart, lung, kidney and muscles. It is released into the bloodstream when cells are damaged or destroyed and, therefore, can be used as a marker of cellular injury, which justifies its elevation resulting from tissue aggression in COVID-19, especially when there is significant pulmonary involvement (Mcclelland, *et al*., 2003; SUDO, 2002). According to Henry *et al*. (2020) advanced age and high level of LDH are independent risk factors in patients with mild clinical conditions. Chest tomography has been used in patients with COVID-19, but it is not indicated for screening or as a first-line test for diagnosing SARS-CoV-2 infection. No radiological findings can definitively exclude the possibility of this infection, as patients may present a chest CT scan without significant findings within the first two days of symptoms. Images with ground-glass opacification are usually seen between the first and fourth day of onset of disease symptoms, most often between 6 and 10 days and reach the apex between 6-13 days (WANG *et al*., 2020; PAN *et al*., 2020). The aim of this study is to retrospectively assess the correlation between increased LDH and lung lesions in non-hospitalized patients with mild or moderate forms of COVID-19, residing in Brazil, observed between January and April 2021.

MATERIALS AND METHODS

We retrospectively evaluated 104 electronic medical records from a cohort of symptomatic individuals diagnosed with up to 14 days as mild or moderate acute COVID-19, treated at the Amaral Costa Laboratorial and Diagnostic service. All patients were 18 years old or older, of both genders, coming from Belem, Para, who underwent lung CT scan and LDH blood test, in addition to other tests. All patients were under outpatient care. There was no personal contact or commitment to clinical follow-up, and all ethical parameters for research on human beings established in Brazil were complied with. Inflammatory tests were performed in accordance with the manufacturers' guidelines and the parameters for evaluation of pulmonary tomography followed the protocols of the Brazilian College of Radiology (PROKOP *et al*., 2020).

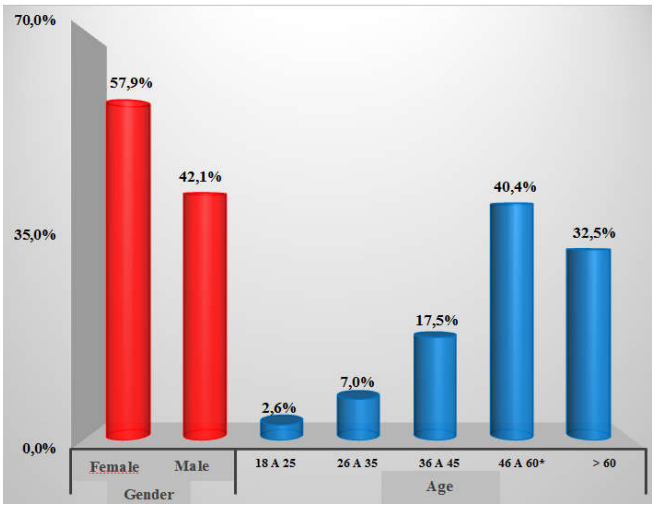
RESULTS

The cohort consisted of 104 individuals, among whom the exams performed were chest CT scan and LDH blood test, and they had the following demographics: 42 (42.1%) males, 62 females (57.9%), with age groups (years) of: 18-25 (2.6%), 26-35 (7.0%), 36-45 (17.5%), 46-60 (40.4%) and over 60 (32.5 %) (Table 1, Figure 1).

Table 1. Distribution of patients with COVID-19 by sex and age group, Amazon cohort, Northern Brazil, 2021

Variables	Frequency	% (N = 104)	p-value
Sex			0,0624
Female	62	57,9%	
Male	42	42,1%	
Age (years)			< 0.0001*
18 a 25	3	2,6%	
26 a 35	5	7,0%	
36 a 45	17	17,5%	
46 a 60*	42	40,4%	
> 60	37	32,5%	

*G-adherence test
Source: authors.



Source: authors.

Figure 1. Distribution of patients with COVID-19 by sex and age group, Amazon cohort, northern Brazil, 2021

Table 2. Distribution of patients with COVID-19 according to the pattern, extent and laterality of pulmonary involvement observed on CT scan, Amazon cohort, northern Brazil, 2021

Variables	Frequency	% (N = 104)	p-value
Pattern of involvement			< 0.0001*
Typical*	96	92,3%	
Undetermined	4	3,8%	
Not informed	4	3,8%	
Impairment			< 0.0001*
< 10%	26	25,0%	
10 a 25%*	47	45,2%	
25 a 50%	17	16,3%	
50 a 70%	10	9,6%	
Not informed	4	3,8%	
Laterality			< 0.0001*
Bilateral*	96	92,3%	
Unilateral Left	6	5,8%	
Unilateral Right	2	1,9%	

*G-adherence test.
Source: authors.

Table 3. Distribution of patients with COVID-19 according to the types of lesions observed on pulmonary CT scans, Amazon cohort, northern Brazil, 2021

Types of injuries	Frequency	% (N = 104)
Interlobular septa thickening	32	30,8%
Nodules	17	16,3%
Ground-glass	12	11,5%
Atheromatous calcifications in the aorta and coronary arteries	7	6,7%
Bronchiectasis	4	3,8%
Lymph node enlargement	3	2,9%
Atelectasis	2	1,9%
Hepatic steatosis	2	1,9%
Dorsal spondylosis	2	1,9%
Others	13	12,5%

Source: authors.

CT scans showed bilateral involvement (92.3%), with a typical pattern (92.3%), affecting 10-25% (42.5%) of the lung fields (Table 2, Figure 2), showing a predominance of three types of lesions: interlobular septal thickening (30.8%), nodules (16.3% and ground-glass (11.5%), sometimes concomitantly (Table 3).

DHL was the inflammatory test where there was a greater predominance of normal results (97.3%) (Table 4, Figure 3). There was no relationship between LDH abnormality and pulmonary CT scans with greater impairment.

Table 4. Distribution of patients with COVID-19 according to LDH results and other laboratory tests, Amazon cohort, northern Brazil, 2021

Laboratory exams	Within normal values		Outside of normal values		No record / Not collected	
LDH	97	93,3%	7	6,7%	0	0,0%
Leukocytes	87	83,7%	3	2,9%	14	13,5%
Segmented	85	81,7%	5	4,8%	14	13,5%
Lymphocytes	82	78,8%	8	7,7%	14	13,5%
C-reactive protein	80	76,9%	22	21,2%	2	1,9%
D-dimer	80	76,9%	9	8,7%	15	14,4%
Ferritin	69	66,3%	30	28,8%	5	4,8%
ESR	64	61,5%	9	8,7%	31	29,8%

*G-adherence test; ESR: erythrocyte segmentation rate.

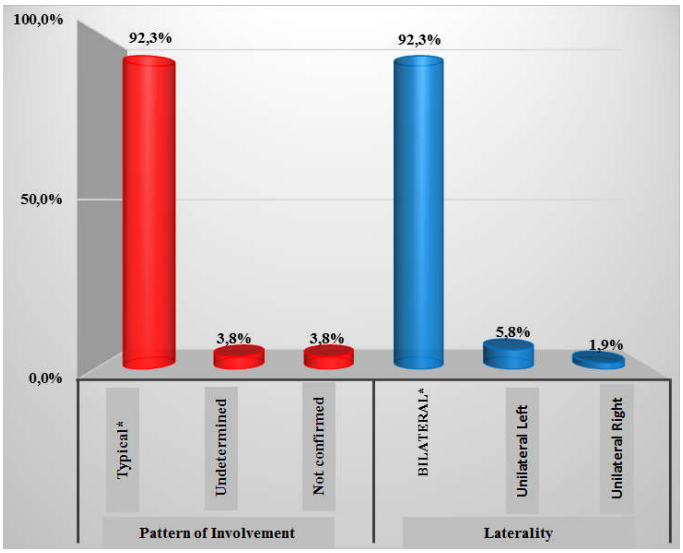
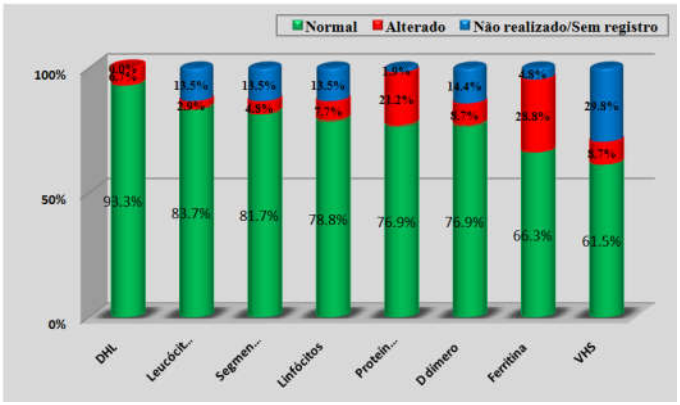


Figure 2. Distribution of patients with COVID-19 according to the pattern, extent and laterality of pulmonary involvement observed on CT scan, Amazon cohort, northern Brazil, 2021



Source: authors.

Figure 3. Distribution of patients with COVID-19 according to LDH results and other laboratory tests, Amazon cohort, northern Brazil, 2021

DISCUSSION

The clinical experiences obtained after nearly two years of the COVID-19 pandemic are being shared by different services around the world, in the growing search to reduce morbidity and mortality (XAVIER *et al*., 2020). Several algorithms were established with clinical and laboratory parameters for the prognosis of disease progression based on age, comorbidities and inflammatory tests, aiming to establish early decision-making and monitoring (AYANIAN *et al*., 2020). Our results are consistent with studies carried out around the world, when patients with COVID-19 treated outside the hospital present mild or moderate clinical conditions, with few alterations in the complementary exams. Only 6.7% had abnormal LDH and 45.2% had pulmonary involvement between 10-25%, and in only 10 patients this involvement was above 50%, with no correlation between both parameters. The three main lesions observed in the lung parenchyma were thickening of the interlobular septa (30.8%), nodules (16.3%) and ground-glass (11.5%). In most published studies, cohorts of hospitalized patients with severe and sometimes fatal conditions predominate. Among 72,314 cases of COVID-19 investigated in China, about 81% were considered mild (some with pneumonia), 14% severe, and 5% were critical. The overall fatality rate was 2.3%. Among critically ill patients, it was 49% (FU *et al*., 2020; HUANG *et al*., 2020; ZHOU *et al*., 2020). Another study also carried out in China, identified in 500 hospitalized patients that changes in the levels of LDH, C-reactive protein and

lymphocytes predict the risk of death with 90% accuracy, noting that it is of great value to identify the relationship between the biomarkers and the mortality rate (HOPE *et al*., 2020). These results are related to the pathogenesis of COVID-19: LDH is a marker of tissue destruction and, in severe forms, there is an increase in its serum levels proportional to the degree of lung injury; CRP, as an inflammatory marker, signals the degree of persistent inflammation and is a poor prognostic marker in acute respiratory distress syndrome (ARDS); and lymphopenia is a common laboratory feature of this disease, probably representing the immune dysfunction that results in the more severe forms. The joint analysis of these three tests resulted in an accuracy of 90%, indicating that the analysis can really be used for tests at any stage of disease evolution (even at the onset of symptoms). In Washington, USA, evaluating blood samples from 299 patients, it was observed that 200 had high rates of LDH, C-reactive protein, ferritin, IL-6, D-Dimer, and that they were more likely to be admitted to the ICU, to be intubated and more likely to die (AYANIAN *et al*., 2020). Imaging exams help in the screening, diagnosis and follow-up of patients with suspected or confirmed infection by SARS-CoV-2, however, although the radiological findings are suggestive of the disease, RT-PCR is still required for diagnostic confirmation, because the imaging exams cannot accurately distinguish the findings of COVID-19 from those of pneumonias caused by other viruses (AI *et al*., 2020). A retrospective study of 2,732 chest CT scans showed that the main findings in patients with COVID-19 were: ground-glass-like opacification (83.31%), ground-glass opacity with mixed consolidation (58.42%), and adjacent thickening of the pleura (52.46%), interlobular septal thickening (48.46%) and air bronchograms (46.46%). Imaging findings mainly involved the peripheral region of the lungs. However, the infection can affect all lobes, especially the lower bilateral ones (BAO *et al*., 2020; WANG *et al*., 2020). It is important to mention that such observations were analyzed most of the time in hospitalized patients.

CONCLUSION

Even with large gaps in knowledge about the pathophysiology, evolution and prognosis of COVID-19, the advances achieved to this point allow for better management of cases in the absence of specific therapy to date. There was no relationship between LDH parameters and chest CT scans, possibly because it is a cohort of non-severe patients. There is a need for prospective and multicentric studies of patients with clinical forms of mild and moderate severity, to bring contributions to the most prevalent cases in the world with algorithms with several and new biomarkers. These, when evaluated together, can establish intervention measures to reduce the probability of manifestations post COVID-19, or even the new clinical form recognized as prolonged-COVID.

REFERENCES

Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, Tao Q, Sun Z, Xia L. (2020). Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology. 296, pp. 32-40.

Ayanian, S, Reyes, J, Lynn, L, Teufel, K. (2020). The association between biomarkers and clinical outcomes in novel coronavirus pneumonia in US cohort.Biomark Med. 14, pp. 1091-1097.

Bao C, Liu X, Zhan H, Li Y, Liu J. (2020). Coronavirus Disease 2019 (COVID-19) CT Findings: A Systematic Review and Meta-analysis. Journal of the American College of Radiology. 17, pp. 701-709.

BRASIL, Ministério da Saúde. Coronavírus COVID-2019: diretrizes para diagnóstico e tratamento da COVID-19. 3. ed. Brasília: Ministério da Saúde; 2020.

CARSANALuca, Sonzogni A, Nasr A, Rossi R S. (2020). Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study.Lancet Infectious Diseases.20, pp.1135-40.

Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, Wang T, Zhang X, Chen H, Yu H, Zhang X, Zhang M. (2020). Clinical and immunological features of severe and moderate coronavirus disease 2019. Journal of Clinical Investigation. 30, pp. 2620-2622.

Cousins S. (2018). WHO hedges its bets: the next global pandemic could be disease, 361:k2015.

Fehr AR, Perlman S. (2015). Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol. 1282, pp.1-23.

Fu L. (2020). Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis. The Journal of Infection. 80, pp. 656-665.

GANDHI RT, LYNCH JB, DEL RC. (2020). Mild or Moderate Covid-19.New England Journal of Medicine.383, pp.1757-1766.

Hope MD, Raptis CA, Shah A, Hammer MM, Henry TS. (2020). A role for CT in COVID-19? What data really tell us so far.Lancet. 395, pp. 1189–1190.

Huang Yihui. (2020). Clinical characteristics of laboratory confirmed positive cases of SARS-CoV-2 infection in Wuhan, China: a retrospective single center analysis. Travel Medicine and Infectious Disease. 36, pp. 101606.

Mcclelland GB. (2003).Peroxisomal membrane monocarboxylate transporters: evidence for a redox shuttle system?. Biochemical and biophysical research communications, 304, pp. 130-135.

Pan F, *et al*. (2020).Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19).Radiology.295, pp.715-721.

Prokop, M., Everdingen, W., Vellinga, T. R., Ufford, H. Q., Stöger, L., Beenen, L., Geurts, B., Gietema, H., Krdzalic, J., Schaefer-Prokop, C., Ginneken, B., Brink, M. (2020). CO-RADS: A Categorical CT Assessment Scheme for Patients Suspected of Having COVID-19 – efinition and Evaluation. Radiology. 296, pp. 97-104.

Sudo K. (2002). Lactate dehydrogenase M subunit deficiency. Rinshobyori.The Japanese journal of clinical pathology. 50, pp. 571-575.

Wang C, Xie J, Zhao L, Fei X, Zhang H, Tan Y, Nie X, Zhou L. (2020). Alveolar macrophage dysfunction and cytokine storm in the pathogenesis of two severe COVID-19 patients. EBioMedicine. 57, pp 20.

Xavier A R, Silva JS, Almeida JPCI, Conceição JFF, Lacerda GS, Kannan S. (2020). COVID-19: manifestações clínicas e laboratoriais na infecção pelo novo coronavírus. J. Bras.Patol. Med. Lab. 56, pp. 1-9.

Yan L, Zhang Hai-tao, Goncalves J, Xiao Y, Wang M, Guo Y, Sun C, Tang X, Jing L, Zhang M. (2020). An interpretable mortality prediction model for COVID-19 patients.Nature Machine Intelligence. 2, pp. 283-288.

YUKI K, FUJIOGI M, KOUTSOGIANNAKI S. COVID-19 pathophysiology: A review. Clinical Immunology. 215, pp. 108427.

Zhou F. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet.395, pp.1054-1062.

Zhou p. (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature, 579, pp.270-273.

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