THE RELATIONSHIP BETWEEN DE RITIS RATE AND FATTY LIVER IN COVID-19 PATIENTS

Received: 29/05/2023 **Published:** 30/06/2023

Mehmet Ozdin

Sakarya University Education and Research Hospital, Medical Biochemistry Laboratory, Sakarya, Turkey, drmozdin33@gmail.com

ABSTRACT

Objective

This study aimed to comparatively examine the relationship between the rate of De Ritis and fatty liver in COVID-19 patients.

Method

A total of 182 COVID-19 patients, 133 men and 49 women, were included in the study. The study was carried out on patients with a definitive diagnosis of COVID-19 between May 1, 2020 and March 29, 2021. This study is retrospective and the data were obtained from the hospital information management system. The diagnosis of COVID-19 in the included patients was made by a real-time polymerase chain reaction and computed tomography lung scanning. In COVID-19 patients, fatty liver was graded ultrasonographically, and the relationship between the De Ritis rate and the correlation was compared.

Results

De Ritis rate was found to be significant between patients with and without COVID-19 infection. De Riti's rate of patients with COVID-19 infection was found to be significantly lower. De Ritis rate was found to be considerably lower in men with COVID-19 infection than in women with COVID-19 infection. When the GRADEs of COVID-19 patients with NAFLD and non-patient groups were compared, no statistical difference was detected.

Conclusion

The De Ritis rate was significant between patients with and without COVID-19 infection, and the significantly low De Ritis rate in patients with COVID-19 infection revealed that COVID-19 disease reduced the rate of De Ritis. When the GRADEs of COVID-19 patients with NAFLD were compared with non-patient groups, the lack of statistical difference revealed that COVID-19 infection did not affect the fatty liver.

KEYWORDS

COVID-19, nonalcoholic fatty liver disease, De Ritis

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is contagious zoonotic infection. COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Çelik et al.). Although the majority of COVID-19 patients develop the disease 4-5 days after contact with the patients, it is stated that this incubation period can be extended up to 14 days (Ak, 2020). In symptomatic COVID-19 patients, the initial clinical findings of the disease are similar to other viral infections, and it is impossible to distinguish them from others. COVID-19 affects the respiratory tract and can lead to inflammation and internal organ failure, leading to high fever, cough, acute respiratory infection and death. While fever in more than 80% of the patients, cough is seen in more than 60%. Fatigue, myalgia, and shortness of breath are reported to occur in approximately 20 to 50% of patients. Less frequently, headache and sore throat, anorexia, hemoptysis, nausea, diarrhoea, impaired sense of smell and taste, and conjunctivitis have also been reported (Fu et al., Yazar et al., 2021).

Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) are intracellular enzymes. Both enzymes are released from these cells into the circulation as a result of damage to hepatocytes and are called transaminases. Both enzymes are among the most commonly used tests in all laboratories. Transaminases, which have been known among liver function tests for a very long time. Transaminases are among the important biomarkers of the COVID-19 pandemic. Increased blood levels of these enzymes indicate liver damage but not liver function (Prati et al., 2002, Yazar et al., 2020). The level of transaminases above average values means inflammation in the liver. In addition, it has been determined that the increase in transaminases is caused by many factors that cause liver damage (Kwo et al., 2017). AST; It is also found the liver, heart muscle, skeletal muscle, kidney, and brain. If ALT; is found primarily in the liver. Therefore, ALT a more specific marker of hepatocellular injury. (Nannipieri et al., 2005). Diagnostic approaches using parameters such as elevation, rate and elevation of transaminases in liver diseases have also been defined. The “De Ritis ratio” is obtained by dividing the serum AST level by the ALT level (Botros et al., 2013).

Fatty liver is defined as more than 5% fat by weight. Fatty liver disease, despite not drinking alcohol, is called nonalcoholic fatty liver disease (NAFLD). (Çolak et al., 2010).

Since the COVID-19 pandemic is still new, new studies on the characteristics and treatment of the virus and the disease are being added to the literature. However, even though many scientific studies take place in the literature daily, there needs to be more precise information about COVID-19 infection and its treatment. Considering the pathogenesis of the disease, the clinical picture and test results in the patients, It is known that there is an increase in transaminases in this infection. There are few publications in the literature investigating transaminases in patients with COVID-19 infection. This study, it was aimed to comparatively examine the relationship between the rate of De Ritis and fatty liver in COVID-19 patients.

MATERIAL AND METHOD

This retrospective study was approved by the Ethics Committee of the Faculty of Medicine (Ethics No: E-71522473-050.01.04-25250). A total of 182 COVID-19 patients, 133 men and 49 women, were included in the study. The study was carried out on patients with a definitive diagnosis of COVID-19 between May 1, 2020 and March 29, 2021. This study is a retrospective study and the data were obtained from the hospital information management system. The diagnosis of COVID-19 of the included patients was made by real-time polymerase chain reaction and computed tomography lung scanning. In COVID-19 patients, fatty liver was graded ultrasonographically and the relationship between De Ritis rate and the correlation was compared. Both enzymes were studied in Beckman Coulter AU5800 biochemistry autoanalyzer.

Share This Paper:

Statistical analysis

Independent T-test was used for comparing the two parameters in groups. Anova test was used multiple comparison of groups. Data that had a normal distriburtion were presented as mean ± SEM. The significance level was set at $P < 0.05$.

RESULTS

De Ritis rate was found to be significant between patients with and without COVID-19 infection. De Ritis rate of patients COVID-19 was found to be significantly lower.. De Ritis rate was found to be considerably lower in men with COVID-19 infection than in women with COVID-19 infection (Table 1). Distribution of COVID-19 Patients by Gender (Graph 1) is shown in the NAFLD Rating for COVID-19 Patients (Graph 2).

No correlation was found between age and De Ritis rate in patients with COVID-19 infection (Table 2). There was no significant difference in De Ritis rate between men and women without COVID-19 infection. No correlation was found between age and De Ritis rate in those without COVID-19 infection. Men with COVID-19 disease had a significantly lower rate of De Ritis than all groups. However, no significant difference was found in the female groups regarding De Ritis rate (Table 3). No statistical difference was found between the GRADEs of COVID-19 patients with NAFLD. NAFLD Grading in Patients Without COVID-19 (Graph 3).

Table 1. De Ritis rates according to gender in patients with and without COVID-19

Gender	Gender	Mean Difference	SEM	P.	95% Confidence Interval	
					Lower Bound	Upper Bound
CM	Covid female	-,13879*	,04393	,010	-,2525	-,0251
	No covid male	-,20402*	,06050	,005	-,3606	-,0475
	No covid female	-,20791*	,05112	,000	-,3402	-,0756
CF	Covid male	,13879*	,04393	,010	,0251	,2525
	No covid male	-,06522	,06746	,768	-,2398	,1093
	NO covid female	-,06911	,05919	,648	-,2223	,0841
NCM	Covid male	,20402*	,06050	,005	,0475	,3606
	Covid female	,06522	,06746	,768	-,1093	,2398
	No covid female	-,00389	,07235	1,000	-,1911	,1833
NCF	Covid male	,20791*	,05112	,000	,0756	,3402
	Covid female	,06911	,05919	,648	-,0841	,2223
	No covid male	,00389	,07235	1,000	-,1833	,1911

*. The mean difference is significant at the 0.05 level. CM: Covidmale, CF: Covidfemale; NCM: NOcovidmale, NCF: NOcovidfemale . Men with COVID-19 infection had a significantly lower rate of De Ritis than all groups.

Table 2. The Relationship Between Age and De Ritis in COVID-19 Patients

GROUP			AGE	DE-RITIS
COVID-19	AGE	Pearson Correlation	1	-,139
		Sig. (2-tailed)		,062
		N	182	182
	DE-RITIS	Pearson Correlation	-,139	1
		Sig. (2-tailed)	,062	
		N	182	182

No correlation was found between age and De Ritis rate (p>0.05).

Share This Paper:

Fig 1. Distribution of COVID-19 Patients by Gender

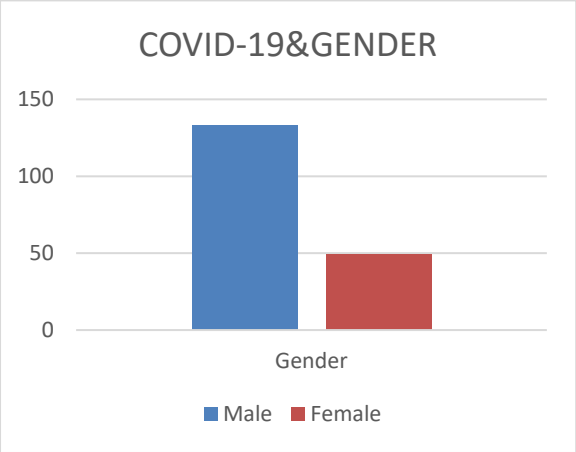

Fig 2. NAFLD Grading in Patients with COVID-19

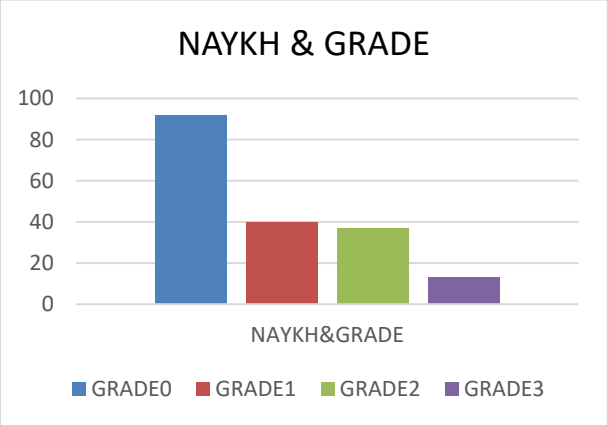

Fig 3. NAFLD Grading in Patients Without COVID-19

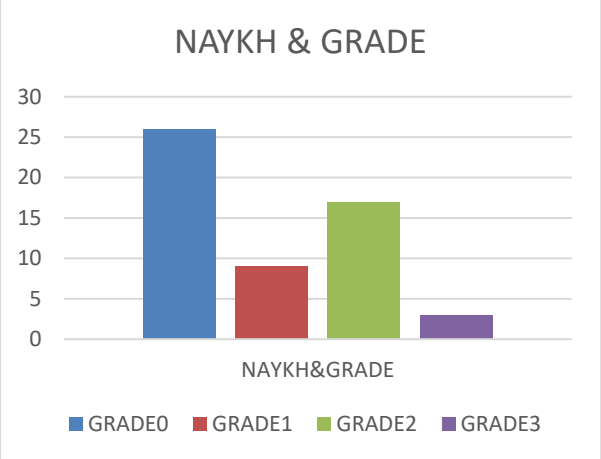

Table 3. De Ritis and GENDER in Patients Without COVID-19

	Group	Gender	N	Mean	SD	SEM
De Ritis	NO COVID	male	22	,0870	,14959	,03189
		female	33	,0909	,20587	,03584

SD: Std. Deviation SEM: Std. Error Mean. No significant difference was found between gender and De Ritis (p>0.05).

DISCUSSION

Considering the pathogenesis of COVID-19 disease, it is seen to affect the respiratory tract and cardiovascular system (CVS) and causes abnormalities in some blood parameters. It has been reported that extrapulmonary organ involvement. Liver function damage may occur frequently during the course of SARS-CoV infection. COVID-19 hastalarının almost half of the patients have different degrees of liver function damage. (Fan et al., 2020). In this study, the correlation of De Ritis in patients with COVID-19 infection was examined by considering fatty liver.

In a study conducted in COVID 19 patients, they found mild lobular and portal activity with moderate microvascular steatosis as pathological findings in liver biopsy samples (Xu et al., 2020). In other studies on the rate of dermatitis, it has been revealed that this rate has a prognostic value not only in liver damage but also in other diseases (Gorgel, 2017, Ikeda, 2020). A study of COVID-19 patients in China reported higher rates of liver damage and liver dysfunction in severe COVID-19 patients. AST/ALT was found to be increased by 18.2% / 19.8% in mild and severe COVID-19 patients, and 39.4% / 28.1% in those with severe COVID-19 disease, respectively. (Shi et al, 2020). Similar results were found in another study conducted in China. High AST values were found in 62% of the patients in the intensive care unit (ICU). AST values were found to be high in only 25% of those who did not need intensive care (Huang et al., 2020).

Studies in patients with COVID-19 show that AST rises more frequently than ALT. Regarding this situation, in a study conducted with 31 COVID-19 patients, it was revealed that the mitochondrial proteins of the SARS-CoV-2 virus were directly affected by the virus. The reason for AST elevation is

that it directly causes liver damage as a result of mitochonril interaction (Gordon et al., 2020). If liver involvement occurs during COVID-19 infection, it adversely affects the prognosis. It also prolongs the hospital stay of patients (Portincasa et al., 2020). A mortality study was conducted in 2780 people with COVID-19 disease (including 250 patients with chronic liver disease). In this study, it was determined that mortality was higher in patients with chronic liver disease than in patients without liver disease (Singh et al., 2020). In a cohort study of 152 patients with COVID-19 and chronic liver disease the mortality rate was 40% (Moon et al., 2020). In a meta-analysis of 3772 patients obtained from 326 studies examining COVID-19 and liver damage, it was concluded that there was a relationship between liver dysfunction and mortality. In particular, it was stated that the drugs used and the severity of COVID-19 were effective in this table (Zeng-hong et al., 2020). In studies, it was determined that 6.4% of COVID-19 patients had severe liver damage. However, while the liver damage seen was mild in 45%, it was reported to be moderate in 21%. The resulting liver damage is more associated with drugs and inflammation (Phipps et al., 2020). In our study, it was determined that there was no difference in GRADE between patients with NAFLD and those with COVID-19 infection. We decided that the rate of De Ritis in patients with COVID-19 infection was significantly lower than in the control group, and it was lower in men than in women. In addition, our study reveals that the rate of De Ritis is unrelated to age.

CONCLUSION

According to the results of our study, without ignoring liver fat, The rate of De Ritis is significantly lower in patients with COVID-19 infection. Namely, The rate of De Ritis in men with COVID-19 infection is considerably lower than in women with COVID-19 infection, but the difference between age and the rate of De Ritis should be taken into account.

Share This Paper:

REFERENCES

Ak G. (2020). COVID-19'un Klinik ve Radyolojik Özellikleri. ESTÜDAM Halk Sağlığı Dergisi, 5(COVID-19 Özel Sayısı):61-69.

Botros M, Sikaris KA. (2013). The de ritis ratio: The test of time. Clin Biochem Rev, 34:117-30.

Çelik D, Köse Ş. (2020). Erişkinlerde COVID-19: Klinik bulgular. Tepecik Eğit. ve Araşt. Hast. Dergisi, 30(Ek sayı):43-48.

Çolak Y, Tuncer İ. (2010). Nonalkolik Karaciğer Yağlanması Ve Steatohepatit. İst Tıp Fak Derg, ;73:3:85-91.

Fan Z, Chen L, Li J, Cheng X, Yang J, Tian C. (2020). Clinical Features of COVID-19-Related Liver Functional Abnormality. Clin Gastroenterol Hepatol, 18(7):1561-1566. doi: 10.1016/j.cgh.2020.04.002.

Fu L, Wang B, Yuan T. (2020). Clinical characteristics of coronavirus disease 2019 (COVID 19) In China: A systematic review and meta-analysis. J Infect, 80(6):656-665. doi:10.1016/j.jinf.2020.03.041

Gordon DE, Jang GM, Bouhaddou M, Xu J, Oberner K, White KM. (2020). A SARS-CoV-2 protein interaction map reveals targets for drug repurposing. Nature, 583;459–468. doi.org/10.1038/s41586-020-2286-9

Gorgel SN. (2017). The prognostic significance of preoperatively assessed AST/ALT (De Ritis) ratio on survival in patients underwent radical cystectomy. International Urology and Nephrology, 49(9):1577–1583.

Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Yl. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet, 395;497-506. doi:10.1016/S0140- 6736(20)30183-5

Ikeda T. 2020. The De Ritis (aspartate transaminase/alanine transaminase) ratio as a prognosticator in patients with end-stage renal disease-associated renal cell carcinoma. Clinical Genitourinary Cancer, 18(3):236–240.

Kwo PY, Cohen SM, Lim JK. (2017). ACG Clinical Guideline: Evaluation of abnormalliver chemistries. Am J Gastroenterol, 112:18-35.

Moon AM, Webb GJ, Aloman C, Armstrong MJ, Cargill T, Dhanasekaran R. (2020). High mortality rates for SARS-CoV-2 infection in patients with pre-existing chronic liver disease and cirrhosis: Preliminary results from an international registry. J Hepatol, 73(3):705-708. doi:10.1016/j.jhep.2020.05.013

Nannipieri M, Gonzales C, Baldi S. (2005). Liver enzymes, the metabolic syndrome, and incident diabetes: the Mexico City diabetes study. Diabetes Care, 28:1757-62.

Phipps MM, Barraza LH, LaSota ED, Sobieszczyk ME, Pereira MR, Zheng EX, et al. (2020). Acute Liver Injury in COVID-19: Prevalence and Association with Clinical Outcomes in a Large U.S. Cohort. Hepatology, 72(3):807-817. doi: 10.1002/hep.31404.

Prati D, Taioli E, Zanella A. (2002). Updated definitions of healthy ranges for serum alanine aminotransferase levels. Ann Intern Med, 137:1- 10.

Portincasa P, Krawczyk M, Machill A, Lammert F, Di Claula A. (2020). Hepatic consequences of COVID-19 infection. Lapping or biting? Eur J Intern Med, 77:18-24. doi: 10.1016/j. ejim.2020.05.035.

Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J. (2020). Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis, 20(4):425-434. doi: 10.1016/S1473-3099(20)30086-4.

Singh S, Khan A. (2020). Clinical Characteristics and Outcomes of Coronavirus Disease 2019 Among Patients With Preexisting Liver Disease in the United States: A Multicenter Research Network Study. Gastroenterology, 159(2):768-771

Xu Z, Shi L, Wang Y. (2020). Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med, 8:420–422.

Yazar H, Kayacan Y, Özdin M. (2021). Investigation of C-reactive Protein and D-dimer Findings in Patients with COVID-19. Bezmialem Science, 9(Supplement 1):4-8.

Yazar H, Kayacan Y, Ozdin M. (2020): De Ritis ratio and biochemical parameters in COVID-19 patients. Archives of Physiology and Biochemistry, 128(6):1676-1680. DOI: 10.1080/13813455.2020.1788604.

Zeng-hong W. Dong-liang Y. (2020). A meta-analysis of the impact of COVID-19 on liver dysfunction European Journal of Medical Research, 25(1):54-57.