IJPSR (2022), Volume 13, Issue 6 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 26 February 2022; received in revised form, 09 April 2022; accepted, 25 April 2022; published 01 June 2022

DE RITIS RATIO OF COVID-19 PATIENTS ADMITTED DURING FIRST, SECOND AND THIRD WAVE

Saurabh Kumar Deo [1], Nitin Tangri [2], Neeru Bhaskar [1] and Vijay Chaudhary [*3]

Department of Biochemistry [1], Department of Tuberculosis & Respiratory Diseases [2], Adesh Medical College and Hospital, Mohri, Shahbad (M) - 136135, Haryana, India.
Department of Biochemistry [3], M. M. Medical College and Hospital, Laddo, Sultanpur Road, Kumarhatti, Solan - 173229, Himachal Pradesh, India.

Keywords:

Covid-19, SARS-CoV-2, De Ritis ratio, AST, ALT, Acute respiratory distress syndrome

Correspondence to Author:
Dr. Vijay Chaudhary

Assistant Professor,
Department of Biochemistry,
M. M. Medical College and Hospital,
Laddo, Sultanpur Road, Kumarhatti, Solan - 173229, Himachal Pradesh, India.

E-mail: bchmystry@hotmail.com

ABSTRACT: Background: To date, the 2019 novel coronavirus pneumonia (COVID-19) is the greatest public medical issue in the world. World Health Organization (WHO) declared this outbreak a "public health emergency of international concern" on January 31, 2020. Therefore, it bodes well to look for a potential biomarker that could quickly and effectively distinguish serious cases early. Of the total confirmed Covid-19 patients, the severe cases often suffer from underlying diseases such as cardiovascular disease and diabetes that can accelerate the movement of 2019 novel coronavirus (SARS-CoV-2) infection. Moreover, acute respiratory distress syndrome could lead to death in some severe Covid-19 patients, and various disorders often accompany this. Biochemical findings showed representative features of acute respiratory distress syndrome and association of multiple organs. **Aim:** To estimate routine biochemical parameters of patients admitted to the Covid-19 ward. **Method:** Clinical samples from cases of Covid-19 admitted to Adesh Medical College and Hospital, Mohri, Shahbad (M), Haryana, India, during 1st, 2nd, and 3rd waves were collected and analyzed. **Result:** In this study, we investigated routine biochemical investigations (RBS, LFT, RFT & Serum Electrolyte) of Covid-19 patients and calculated De Ritis ratio. It was found that biochemical parameters and De Ritis ratio were worse affected than the first and second waves. **Conclusion:** De Ritis ratio may be a good marker for liver abnormalities and prognosis and a hospital stay of the Covid-19 patients.

INTRODUCTION: At present, the world is overwhelmed by a pandemic disease caused by a novel coronavirus which emerged in Wuhan, Hubei, China at the end of December 2019, named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV- 2) [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(6).2534-38

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(6).2534-38

The 2019 novel coronavirus pneumonia (Covid-19) is the greatest public health issue on the planet. The disease is sustained by a coronavirus named Covid-19 by the World Health Organization due to more than 79% homology with SARS-CoV, SARS-CoV-2 was responsible for coronavirus disease 2019 (Covid-19) [2].

The number of cases is exponential; however, related data concerning the clinical highlights and hematological changes of infected patients is restricted [3-6]. The serious cases regularly experience the ill effects of hidden sicknesses like cardiovascular illness and diabetes that can quicken

the movement of 2019 novel coronavirus (SARS-CoV-2) contamination [7, 8]. Furthermore, acute respiratory distress syndrome could prompt demise in some extreme Covid-19 patients, and this is often accompanied by heart failure, liver failure, and kidney failure [9]. In this manner, an early, basic, and effective diagnosis of severe Covid-19 pneumonia and prognosis would greatly decrease mortality and shorten the hospitalization period. In this study, we investigated routine biochemical parameters (RBS, LFT, and RFT) of Covid-19 patients during the first, second and third waves in India, calculated De Ritisratio and compared the data for further application in diagnosis and prognosis of covid related complications.

Aim: To estimate routine biochemical parameters of patients admitted to Covid-19 ward of Adesh Medical College and Hospital, Mohri, Shahbad (M).

MATERIALS AND METHODS: The study was carried out in the Department of Biochemistry in collaboration with Respiratory Medicine of Adesh Medical College and Hospital, Mohri, Shahbad (M). Confirmed cases[by real-time (RT)-PCR] of Covid-19, admitted to Covid-19 ward of the hospital [special hospital for isolating and treating SARS-CoV-2 infection]during the first, second, and the third wave, were taken.

Inclusion Criteria:

A. Covid-19 Positive cases.

B. Age matched

Exclusion Criteria:

i. Negative cases

Total 60, age-matched, Covid-19 positive cases (20 cases from each pandemic wave) were taken for the study. The cases were selected randomly independent of sex. After approval from the Institutional Ethical Committee (IEC) of Adesh Medical College and Hospital, Mohri, Shahbad (M), Haryana, the study was undertaken.

Data Abstraction: The routine investigations of RBS (Radom Blood Sugar), LFT, RFT, and Serum Electrolytes were identified, enlisted, and analyzed in blood samples using Chem-7^{TM} Semi-Automated Clinical Chemistry Analyzer (Transasia Bio-medicals Limited, Mumbai, India). The data obtained was further processed to find biochemical relationships among the parameters.

RESULTS AND DISCUSSION: Total 60 Covid-19 positive cases were taken. 20 patients during each wave were selected independent of sex. The patients selected were of the same age group during 3 waves. The mean age was found to be 33.18±17.19 years (range 09 - 68 years). Various studies have demonstrated that males are more likely affected by the SARS-CoV-2 infection across all age groups [10, 11, 12].

On studying liver functions test (LFT) among Covid-19 patients, it was found that mean serum bilirubin (Total) was within the normal range with a slight increase during the second wave **Table 1**. Mean total serum protein (TSP) was within the normal range. The mean serum albumin level during the second wave was reported to be below the normal range. Serum AST and ALT levels were reported to be highest during the second wave. The most rearranged LFT values are observed during the second wave compared to the two other waves. But during the first and second waves, the LFT parameters like bilirubin (T), AST, and ALT are also on the upper borderline and serum albumin on the lower borderline. Table 1 indicates that the viral infection might have affected the liver.

TABLE 1: DE RITIS RATIO AND OTHER PARAMETERS UNDER LFT

Year	AST	ALT	TP	Albumin	Bil. (T)	De Ritis Ratio
2020	37.6	35	6.9	4.1	0.54	1.15
2021	209	137	6.3	2.9	0.75	1.4
2022	40.2	30.5	6.6	3.1	0.6	1.3

Zhao *et al* (2020), conducted a comparative study on the clinical features of Covid-19 pneumonia to other pneumonia" and reported that liver function damage is more frequent in Covid-19 [13]. Cai *et al.* (2020) also found that 76.3% out of 417 Covid-19 patients had abnormal liver test results having AST, ALT and total bilirubin levels raised to more than 3× the upper limit.

The abnormal liver tests turned out to be more pronounced during hospitalization within about fourteen days. They also suggested that patients with abnormal liver tests were at higher risk of progressing to severe illness [14]. In their study, Fan et al. (2020) also showed that more than 33% of patients admitted to the hospital with SARS-CoV-2 disease have abnormal liver function, which is related to longer hospital stay [15]. Because SARS-CoV-2 can specifically target the liver, specifically cholangiocytes, through ACE2 and along these lines, the hepatobiliary injury seems conceivable [16].

Increased concentrations of serum AST and ALT are reported in Covid-19 patients. However, their capacity to predict mortality, particularly the AST/ALT ratio, commonly referred to as the De Ritis ratio, is unknown. De Rities ratio was highest during the second wave compared to two other waves **Table 1**. This may be evident with the deadly effect of the virus during the second wave. The low De Ritis ratio during the first and third waves may indicate the low effect during the waves. The raised De Ritis ratio has been linked to a longer hospital stay and even mortality of the patients. Various studies have been carried out to seek the relation of De Ritis ratio with factors of the Covid-19 patients across the gender and age groups. Drácz *et al.* (2022) found raised De Ritis ratio among 322 Covid-19 patients. They also found that patients with De Ritis ratio ≥ 1.218 were significantly associated with mortality, severity, and higher AST. Patients with De Ritis ratio ≥1.218 are significantly susceptible to liver damage and cytokine released storm[17]. Yazar *et al.* (2020) found De Ritis ratio of Covid-19 patients was higher than in healthy individuals and this ratio was significantly higher in females than in male patients. They also suggested that De Ritis ratio could be considered as a parameter possible to be a prognostic biomarker for females with Covid-19 [18].

Paliogiannis *et al.* (2020), in their preliminary report, stated that a higher De Ritis value of 1.50±0.66 among Covid-19 Pneumonia against 1.11±0.46 among Non-Covid Pneumonia. They also found that De Ritis ratio was higher among non-survivor due to Covid-19 than those survived (2.00 ± 0.79 against 1.27 ± 0.44respectively) [19].

Zinellu *et al.* (2020) from Italy also reported that the De Ritis ratio was significantly lower in survivors than non-survivors (1.25 against 1.67 respectively) [20]. A meta-analysis done by Pranata *et al.* (2021) associated raised De Ritis ratio with poor prognosis among the patients with Covid-19 disease [21]. No data from India have been reported to support or counter our findings.

TABLE 2: OTHER BIOCHEMICAL PARAMETERS

Year	Blood glucose	Urea	Creatinine	Uric Acid	Na^+	K^+	Cl^-
2020	96.8	22.7	0.9	4.4	137.5	4.0	102
2021	289	60.4	1.4	5.2	138.7	4.7	105.8
2022	147	42.1	1.13	5	137.2	3.7	100.2

Glycemic control is significant in Covid-19 patients. Diabetes is related to the increased frequency and seriousness of Covid-19. There is experimental evidence of the impact of diabetes on viral passage into cells and fiery reaction to the infection [22]. On studying blood glucose levels among Covid-19 patients during 3 waves, the mean blood glucose concentration was observed at 96.8 mg/dl, 298 mg/dl and 147 mg/dl Table 2 during the first, second and third waves, respectively.

Emerging information proposes that people with diabetes are at increased risk for complexities, including passing. Guo *et al.* (2020) conducted a study on "Diabetes is a risk factor for the progression and prognosis of Covid-19" His data support the idea that diabetes ought to be considered a risk factor for a fast movement and terrible prognosis of Covid-19 [23]. A study by Zhang *et al.* (2020), in 140 patients with Covid-19 in Wuhan, China, suggested that diabetes was not a risk factor for serious infection course [24]. Diabetes and different comorbidities are noteworthy indicators of morbidity and mortality in patients with Covid-19and the probable cause may be:

Chronic inflammation, increased coagulation activity, immune response impairment, and potential direct pancreatic damage by SARS-CoV-2 might be among the underlying mechanisms of the association between diabetes and Covid-19 [25]. It was also found that the mean serum urea, creatinine

and uric acid levels were not alarming Table 2 during the three waves, suggesting that SARS-CoV-2 infection might not affect the kidney, which is consistent with part of the latest findings. ButLi *et al.* (2019) reported that SARS-CoV-2 disease could harm the kidney in severe patients [26]. Wang *et al.* (2020), showed acute kidney injury was uncommon in Covid-19 with a gentle increment of blood urea nitrogen or creatinine [27]. Ronco *et al.* (2020) also suggested the low prevalence of acute kidney infection among patients with Covid-19 [28]. A similar result in **Table 2** has been observed during the second wave in our study. The mean serum electrolytes level was also found to be within the normal range, and a slight increase was seen during the second wave **Table 2.**

A study conducted on 334 Covid-19 patients by Shi *et al.* (2020), found only 5.1% of the patients have electrolyte disturbances [29]. Shi *et al.* (2020) also conducted a study on 161 patients with severe and critical Covid-19 and reported that 29.81% of the patients had electrolyte disorders [30]. The renal function may be determined by the severity of the disease, age of the patients, presence of comorbidities, and use of drugs. Therefore, more studies should be carried out. Two limitations are inherent in our study. To start with, the study zone is moderately restricted. Also, the moderately modest number of members in the study may not completely mirror the general circumstance. Along these lines, further studies are important to execute many data surveys in multiple regions by multicenter participation.

CONCLUSION: Covid-19 is the greatest public health issue on the planet. The number of cases is exponential; however, related data concerning the clinical highlights and hematological changes of infected patients is restricted. Therefore, a small effort was made to gather biochemical data to help the treatment. The study found that De Ritis ratio might play an essential role in managing Covid-19 cases because the raised De Ritis ratio and death rate during the second wave is evidence of the virus's effect.

ACKNOWLEDGEMENTS: The authors wish to thank all the enrolled patients in this study.

Funding: None

Ethical Statement: This study was approved by the Ethics Commissions of the Adesh Medical College & Hospital, Mohri, Shahbad (M), Kurukshetra (AMCH/BIO/202/07/03).

CONFLICTS OF INTEREST: The authors declare that they have no competing interests, and all authors have confirmed the accuracy of this statement.

REFERENCES:

1. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol. 2020; 5:536-44.
2. WHO. Clinical management of severe acute respiratory infection when Novel coronavirus (nCoV) infection is suspected: interim guidance. Mar 13, 2020. https://www.who.int/publications-detail/ clinical-management-of-severe-acute-respiratory-infection-whennovel-coronavirus-(ncov)-infection-is-suspected
3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ and He JX: (2020) Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. https://doi.org/10.1056/NEJMoa2002032. [Online ahead of print].
4. Huang CL, Wang YM, Li XW, Ren LL and Zhao JP: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497-506.
5. Chen NS, Zhou M, Dong X, Qu JM and Gong FY: Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395: 507-13.
6. Wang DW, Hu B, Hu C, Zhu FF and Liu X: Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 2020; 323: 1061–9.
7. WHO Coronavirus Disease (COVID-19) Dashboard.https://covid19.who.int/?gclid=EAIaIQobChMIz_6mf3k6QIVkB0rCh1jwA5eEAAYASAAEgKCDPD_BwE (Data last updated: 2020/6/2, 2:42pm CEST).
8. Paules CI, Marston HD and Fauci AS: Coronavirus Infections-more than just the common cold. JAMA 2020; 323: 707-8.
9. Liang J, Jin G, Liu T, Wen J, Li G, Chen L, Wang W and Wang Y: Clinical characteristics and risk factors for mortality in cancer patients with COVID-19. Front Med 2021; 15: 264-74.
10. Li Y, Jerkic M, Slutsky AS and Zhang H: Molecular mechanisms of sex bias differences in COVID-19 mortality. Critical Care 2020; 24: 405.
11. Giamarellos-Bourboulis EJ, Netea MG, Rovina N, Akinosoglou K and Antoniadou A: Complex immune dysregulation in COVID-19 patients with severe respiratory failure. Cell Host Microbe 2020; 27: 992-1000.
12. Dudley JP and Lee NT: Disparities in age-specific morbidity and mortality from SARS-CoV-2 in China and the Republic of Korea. Clin Infect Dis 2020. https://doi.org/10.1093/cid/ciaa354.
13. Zhao D, Yao F, Wang L, Zheng L and Gao Y: A comparative study on the clinical features of COVID-19

pneumonia to other pneumonias. Clin Infect Dis 2020; 71: 756-61.
14. Cai Q, Huang D, Yu H, Zhu Z and Xia Z: COVID-19: Abnormal liver function tests. J Hepatol 2020; S0168-8278(20): 30218-X.
15. Fan Z, Chen L, Li J, Cheng X and Yang J: Clinical Features of COVID-19-Related Liver Functional Abnormality. Clin Gastroenterol Hepatol 2020; 18(7): 1561-1566.
16. Alqahtani SA and Schattenberg JM: Liver injury in COVID-19: The current evidence. United European Gastroenterol J 2020; 8: 509-19.
17. Drácz B, Czompa C, Müllner K, Hagymási K, Miheller P and Székely H: The elevated De Ritis ratio on admission is independently associated with mortality in COVID-19 patients. 2022, PREPRINT. [https://doi.org/10.21203/rs.3.rs-1333042/v1].
18. Yazar H, Kayacan Y and Ozdin M: De Ritisratio and biochemical parameters in COVID-19 patients. Arch Physiol Biochem 2020; 1-5.
19. Paliogiannis P, Zinellu A, Scano V, Mulas G, De Riu G, Pascale RM, Arru LB, Carru C, Pirina P, Mangoni AA and Fois AG: Laboratory test alterations in patients with COVID-19 and non-COVID-19 interstitial pneumonia: a preliminary report. J Infect Dev Ctries 2020; 14(7): 685-90.
20. Zinellu A, Arru F, De Vito A, Sassu A, Valdes G and Scano V: The De Ritis ratio as prognostic biomarker of in-hospital mortality in COVID-19 patients. Eur J Clin Invest 2021; 51: 13427.
21. Pranata R, Huang I, Lim MA, Yonas E and Vania R: Elevated De Ritis ratio is associated with poor prognosis in Covid-19: A systematic review and meta-analysis. Front Med (Lausanne) 2021; 8: 676581.
22. Singh AK, Gupta R, Ghosh A and Misra A: Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes Metab Syndr 2020; 14: 303-10.
23. Guo W, Li M and Dong Y: Diabetes is a risk factor for the progression and prognosis of COVID-19 [published online ahead of print, 2020 Mar 31]. Diabetes Metab Res Rev 2020; 3319.
24. Zhang JJ, Dong X, Cao YY, Yuan YD and Yang YB: Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China, Allergy 2020 doi: 10.1111/all.14238.
25. Hussain A, Bhowmik B and do Vale Moreira NC: COVID-19 and diabetes: Knowledge in progress. Diabetes Res Clin Pract 2020; 162: 108142.
26. Z Li, M Wu, J Guo, J Yao and X Liao: Caution on Kidney Dysfunctions of 2019-nCoV Patients. med Rxiv. doi: https://doi.org/10.1101/2020.02.08.20021212.
27. Wang L, Li X, Chen H, Yan S and Li D: Coronavirus Disease 19 Infection Does Not Result in Acute Kidney Injury: An Analysis of 116 Hospitalized Patients from Wuhan, China. American Journal of Nephrology 2020; 51: 343-8.
28. Ronco C and Reis T: Kidney involvement in COVID-19 and rationale for extracorporeal therapies. Nat Rev Nephrol 2020; 16: 308-10.
29. Shi S, Qin M, Shen B, Cai Y and Liu T: Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020; 5(7): 802-810.
30. Shi M, Chen L, Yang Y, Zhang J and Xu J: Analysis of clinical features and outcomes of 161 patients with severe and critical COVID-19: A multicenter descriptive study. J Clin Lab Anal 2020; 23415.

How to cite this article:
Deo SK, Tangri N, Bhaskar D and Chaudhary V: De ritis ratio of Covid-19 patients admitted during first, second and third wave. Int J Pharm Sci & Res 2022; 13(6): 2534-38. doi: 10.13040/IJPSR.0975-8232.13(6).2534-38.