



SERUM LIPASE IN COVID-19 PATIENTS ADMITTED IN JNIMS, A CROSS SECTIONAL STUDY

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ABSTRACT Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is the causal agent of corona virus disease 2019 (COVID-19). Angiotensin-converting enzyme 2 (ACE2) receptor acts as the mediator of entry for the virus. Besides the respiratory epithelium, several other tissues including the gastrointestinal tract, liver and pancreas also express high levels of ACE2. With the present scenario of increasing gastrointestinal manifestations, we aim to study the level of serum lipase and find its characteristics in patients with COVID-19. A cross sectional study was done in the Department of Biochemistry, JNIMS for a period of 5 months from July to November 2021. Serum lipase levels of 50 COVID-19 positive ICU patients were measured in Semi-auto Chemistry Analyser. Statistical analysis was performed using SPSS Software version 21 where the values were expressed as mean±SD and significance value of $p < 0.05$. Serum lipase level was elevated in 13 out of 50 patients. The average increase in serum lipase level was 77.78 ± 34.42 which was statistically significant. Among the gastrointestinal symptoms, pain abdomen showed statistically significant p value with elevated lipase. T2DM patients were found to have a significant increase in serum lipase level. There was one patient whose serum lipase level was elevated more than 2 times the upper normal value and he ultimately succumbed to death. From the study, it may be concluded that even though it may not be feasible to advise HRCT Scan in all admitted COVID-19 patients having gastrointestinal symptoms, simple and cheap investigation like serum lipase estimation could be helpful in detecting serious complication like acute pancreatitis in cases deteriorating in spite of good SPO₂ and help in improving COVID-19 morbidity and mortality.

KEYWORDS : COVID-19, ACE2, Serum lipase

I. INTRODUCTION

As the pandemic of COVID-19 progressed, various data about its clinical manifestations started accumulating. Typical presentations consist of simple pulmonary symptoms to severe respiratory failure^[1]. However, cases with a variety of extra-pulmonary manifestations have also appeared over the past few months^[2]. Therefore, COVID-19 may cause inflammation of multiple organs^[3], leading to a plethora of clinical symptoms and laboratory abnormalities with severe disease process^[1].

It has been demonstrated that SARS-CoV-2 does not target only lung type 2 alveolar cells but also any other tissue cell expressing angiotensin converting enzyme 2 (ACE2) receptor and transmembrane protease serine 2 (TMPRSS2). ACE2 is used as cell entry receptor by the virus and TMPRSS2 is a protein needed for successful virus entrance. Both are co-expressed in organs like ileum, colon in the gut, and pancreas besides lungs^[4].

Pancreatic injury may be indicated by increase in serum lipase level which has been described in up to 18% of patients admitted with severe COVID-19 in China^[5]. However, the data on the significance of elevated lipase in COVID-19 is limited^[5,6]. Pancreatic involvement in COVID-19 infection is of particular interest because the ACE2 receptor levels is higher in pancreas than in the respiratory epithelium^[5]. It is therefore possible that pancreatic injury is likely in COVID-19.

II. AIM: To estimate the level of serum lipase and find its characteristics in COVID-19 patient.

III. MATERIALS AND METHOD

This was a cross sectional study done in the Department of Biochemistry, Jawaharlal Nehru Institute of Health and Medical Sciences, Imphal, Manipur. The course of the study lasted for a period of five months starting from July, 2021 to November, 2021. A total of 50 patients participated in the study.

The study population consisted of 50 COVID-19 positive ICU patients

(confirmed by RT-PCR technique) who were above 18 years of age. The exclusion criteria were patients with h/o alcohol abuse, gallstones, chronic biliary or pancreatic diseases and pregnant woman.

Informed consent was taken from the patients who participated in the study. Ethical clearance was also obtained from the Institutional Ethics Committee of JNIMS prior to the study.

Fasting blood samples were collected from ante-cubital vein of COVID-19 positive patients at around 8 a.m. in the morning from the COVID ICU. The collected samples were centrifuged after 2 hrs and serum was separated for analysis under strict precautionary measures. Serum lipase level of 50 COVID-19 positive ICU patients were analysed in the Semi-auto chemistry analyser CataliaSA-Click, China using IRIS Healthcare Kit (Spectrophotometric method). Normal range of serum lipase level is 0-60U/L. Elevated serum lipase level is >60 U/L.

IV. STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS software version 21. Mean and Standard deviation was generated for continuous variables. Frequency and proportions were reported for categorical variables. The χ^2 - test and Independent t-test was performed to assess the association between increased serum lipase and presenting symptoms or outcome. Significance level was taken at p -value < 0.05 at 95% confidence interval.

V. RESULTS

Table 1: Demographic parameters, presenting symptoms and hospitalisation course of patients

	All COVID-19 (N=50)	Increased Lipase (n=13)	Normal Lipase (n=27)	P Value
Age, Yr±SD	56.04±10.38	56.69±8.75	55.81±10.9	0.343
Female, n(%)	17 (34)	6 (46.15)	11 (29.73)	0.282
Male, n (%)	33 (66)	7 (53.85)	26 (70.24)	
Fever	26 (52)	5 (53.85)	21 (56.8)	0.256
SOB	27 (54.0)	10 (76.9)	17 (45.9)	0.054

Cough	19 (38.0)	4 (30.8)	15 (40.5)	0.532
Weakness	8 (16.0)	2 (15.4)	6 (16.2)	0.944
Co morbidities, n (%)				
HTN	17 (34)	5 (38.46)	12 (32.43)	0.693
DM	22 (44)	12 (92.31)	10 (27.03)	0.000*
Death	2 (4)	1 (7.69)	1 (2.70)	0.430
Serum lipase, U/L±SD	56.30±22.2	77.78±34.42	48.76±7.13	0.021*

P value < 0.05, Significant *

Table 2: Gastrointestinal symptoms in COVID-19 patients

	All COVID-19 (N=50)	Increased Lipase (n=13)	Normal Lipase (n=27)	P Value
Gastrointestinal symptoms, n (%)				
Nausea/Vomiting	5 (10)	3 (23.1)	2 (5.4)	0.068
Anorexia	6 (12)	3 (23.1)	3 (8.1)	0.153
Pain Abdomen	8 (16)	5 (38.46)	3 (8.11)	0.010*
Diarrhoea	7 (14)	1 (7.7)	6 (16.2)	0.466

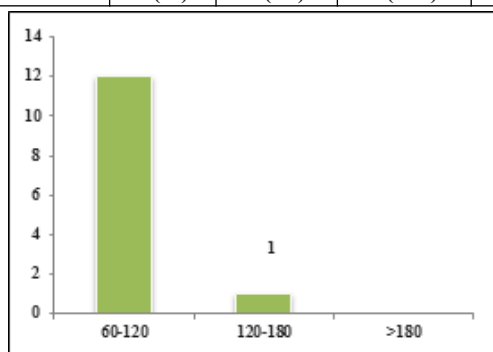


Figure 1: Distribution of COVID-19 cases having high serum lipase

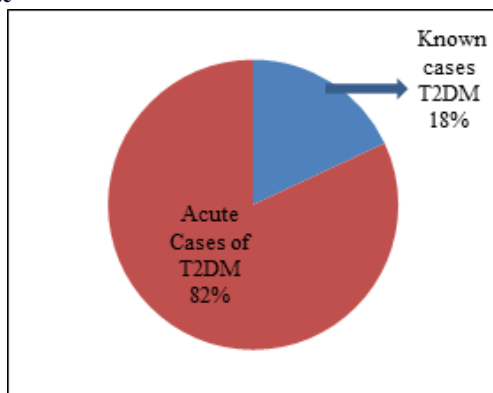


Figure 2: Diabetes Mellitus in COVID-19 patients of the study

Mean age of the COVID-19 patients in the study was 56.04±10.38. There were 33 males and 17 females who took part in the study. Serum lipase level was elevated in 13 patients out of 50 patients where 6(46.15%) were females and 7(53.85%) were males. Male: female ratio that showed increased serum lipase level was 1.2:1.

Mean of the COVID-19 patients with increase in serum lipase level was 77.78±34.42 which showed a statistically significant p value of 0.021(p value<0.05).

Fever, cough, shortness of breath (SOB), weakness and gastrointestinal symptoms (nausea/vomiting, anorexia, pain abdomen, diarrhoea) were the common clinical manifestations of the disease. Fever and SOB constituted one of the most common symptoms in our study population. Among the gastrointestinal symptoms, pain abdomen (38.46%) showed statistically significant p value of 0.010 with increase in serum lipase level (p value<0.05).

Among T₂DM, 82% of them were acute cases and 18% were known or diagnosed cases. All case of T₂DM also showed statistically

significant p value of 0.000 with increase in serum lipase level (p value<0.05). One of the patients whose serum lipase level was increased by >2 times the upper limit ultimately succumbed to death.

VI. DISCUSSION

In our study, out of 50 patients, 33 were males and 17 were females. 13 patients showed increase in serum lipase level. Out of 13 patients with increased serum lipase level, 7 were males and 6 were females giving a male: female ratio of 1.2:1. This shows slight preponderance of increase serum lipase level in males of the study group. The average age of the patient in the study was 56 years for both categories i.e., COVID-19 patients and COVID-19 patients with increase serum lipase level.

Our study showed an increase in serum lipase level seen in 13 COVID-19 ICU patients. The mean of the increase serum lipase level was 77.78±34.42 which is statistically significant with p value of 0.021. A study done by Usman Barlass et al^[7] showed elevated lipase in fourteen (of 83;16.8%) patients. With the requirement of ACE2 receptors by SARS-CoV-2 for cell entry^[8], and expression of this receptor in pancreas^[9,5], the elevation of lipase in COVID-19 may be present. In addition, a study done in China has shown pancreatic injury with increase in serum lipase level^[5,6]. So far, the mechanisms underlying COVID-19 induced-pancreatic damage have not been completely understood. It has been hypothesized that SARS-CoV-2 may cause injury of pancreas by direct cytopathic effect or by several indirect events including cytokine storm, immune response, and endothelial damage leading to the multiple organ failure (MOF)^[10].

Although a meta-analysis of various studies has proven the prevalence of gastrointestinal symptoms like nausea, vomiting and pain abdomen in COVID-19^[11], the knowledge about pancreatic involvement in the disease process is minimal. Some studies have reported that gastrointestinal symptoms may occur in up to 35% of COVID-19 cases^[12]. Among other gastrointestinal manifestations, several papers described increase serum lipase in COVID-19 patients in a percentage ranging from 11 to 43%^[6,7,13-19]. The wide range of frequencies reported may depend upon several aspects, from the population enrolled in terms of either selection criteria or number of patients^[20]. Our study also showed the emergence of gastrointestinal symptoms as one of the main symptoms besides the common symptoms like fever and cough. Pain abdomen constituted one of the main presenting complaints in patients with increase serum lipase level (38.46%) and showed a statistically significant p value of 0.010 with increase serum lipase level.

In the present study, among T₂DM, 82% of them were cases of acute diabetes. This finding suggest pancreatic injury leading to acute diabetes. Diabetes and obesity are considered as major risk factors for severe forms of COVID-19^[11]. Amerta Ghosh et al^[21] conducted a case study in T₂DM patient who was diagnosed with acute pancreatitis with confirmed biochemical (elevated lipase) and radiological findings. A study reported damage of islet cells of pancreas by SARS-CoV-2 leading to acute diabetes^[22]. A statistically significant p value of 0.000 with increase in serum lipase level among the diabetic patients with COVID-19 was also highlighted although diagnosis of acute pancreatitis could not be made as per the Atlanta Classification. This is due to the fact that CT imaging could not be done due to logistic issues and resource limitation during pandemic.

The revised Atlanta classification for acute pancreatitis requires any two of the following:

- Acute onset of severe epigastric pain, often radiating to the back;
- Serum lipase or amylase levels greater than three times the upper limit normal; and
- Characteristic findings of acute pancreatitis on abdominal imaging (contrast enhanced CT, ultrasound, magnetic resonance imaging)^[6].

In our study, there was one patient among those with increase serum lipase level who had an elevated serum lipase level more than two times the upper normal value. In the course of the study, this patient ultimately succumbed to death. This was supported by a study conducted by Priya Bansal et al^[23] although no association could be observed between serum lipase level and mortality of the patient.

The limitation of our study was small sample size with convenient sampling technique. Lack of proper abdominal imaging of the

pancreas to appropriately assess for pancreatic injury as a source of increase serum lipase level, led to the non-exclusion of non-pancreatic sources of lipase elevation. Therefore, the mechanism of lipase elevation may be related to other gastroenterology manifestations of the virus including gastritis, enteritis or colitis, rather than a marker of pancreatic injury. In summary, although elevated lipase was observed in a minority of patients with COVID-19, acute pancreatitis is uncommon^[13]. Further studies are needed to better understand the implications of increase serum lipase level in patients with COVID-19.

VII. CONCLUSION

With the finding of an increase in serum lipase level and frequency of GI symptoms encountered in COVID-19 patients, it is of paramount importance to give an insight into the possible pancreatic injury in COVID-19 patients. Although the increase in serum lipase level alone could not be attributed to pancreatitis, COVID-19 patients with GI signs and symptoms should be further evaluated to rule out acute pancreatitis which is life threatening in few cases.

VIII. REFERENCES

- Guan, W.J., Ni, Z.Y., Hu, Y., Liang, W., Ou, C., He, J., Liu, L., Shan, H., Lei, C., ... Zhong, N. (2020). Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*, 382:1708–20.
- Jin, X., Lian, J. S., Hu, J. H., Gao, J., Zheng, L., Zhang, Y. M., Hao, S. R., Jia, H. Y., Cai, H., Zhang, X. L., Yu, G. D., Xu, K. J., Wang, X. Y., Gu, J. Q., Zhang, S. Y., Ye, C. Y., Jin, C. L., Lu, Y. F., Yu, X., Yu, X. P., ... Yang, Y. (2020). Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. *Gut*, 69(6), 1002–1009.
- Tian, Y., Rong, L., Nian, W., & He, Y. (2020). Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. *Alimentary pharmacology & therapeutics*, 51(9), 843–851.
- Gupta, A., Madhavan, M. V., Sehgal, K., Nair, N., Mahajan, S., Sehrawat, T. S., Bikdeli, B., Ahluwalia, N., Ausiello, J. C., Wan, E. Y., Freedberg, D. E., Kirtane, A. J., Parikh, S. A., Maurer, M. S., Nordvig, A. S., Accili, D., Bathon, J. M., Mohan, S., Bauer, K. A., Leon, M. B., ... Landry, D. W. (2020). Extrapulmonary manifestations of COVID-19. *Nature medicine*, 26(7), 1017–1032.
- Liu, F., Long, X., Zhang, B., Zhang, W., Chen, X., & Zhang, Z. (2020). ACE2 Expression in Pancreas May Cause Pancreatic Damage After SARS-CoV-2 Infection. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*, 18(9), 2128–2130.e2.
- Wang, F., Wang, H., Fan, J., Zhang, Y., Wang, H., & Zhao, Q. (2020). Pancreatic Injury Patterns in Patients With Coronavirus Disease 19 Pneumonia. *Gastroenterology*, 159(1), 367–370.
- Barlass, U., Williams, B., Dhana, K., Adnan, D., Khan, S. R., Mahdavinia, M., & Bishehsari, F. (2020). Marked Elevation of Lipase in COVID-19 Disease: A Cohort Study. *Clinical and translational gastroenterology*, 11(7), e00215.
- Dalan, R., Bornstein, S. R., El-Armouche, A., Rodionov, R. N., Markov, A., Wielockx, B., Beuschlein, F., & Boehm, B. O. (2020). The ACE-2 in COVID-19: Foe or Friend? *Hormone and metabolic research=Hormon-und Stoffwechselforschung=Hormones et metabolisme*, 52(5), 257–263.
- Xu, H., Zhong, L., Deng, J., Peng, J., Dan, H., Zeng, X., Li, T., Chen, Q. (2020). High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci* 12, 8.
- Li, H., Liu, L., Zhang, D., Xu, J., Dai, H., Tang, N., Su, X., & Cao, B. (2020). SARS-CoV-2 and viral sepsis: observations and hypotheses. *Lancet (London, England)*, 395(10235), 1517–1520. [https://doi.org/10.1016/S0140-6736\(20\)30920-X](https://doi.org/10.1016/S0140-6736(20)30920-X)
- Cheung, K. S., Hung, I., Chan, P., Lung, K. C., Tso, E., Liu, R., Ng, Y. Y., Chu, M. Y., Chung, T., Tam, A. R., Yip, C., Leung, K. H., Fung, A. Y., Zhang, R. R., Lin, Y., Cheng, H. M., Zhang, A., To, K., Chan, K. H., Yuen, K. Y., ... Leung, W. K. (2020). Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples From a Hong Kong Cohort: Systematic Review and Meta-analysis. *Gastroenterology*, 159(1), 81–95.
- Nobel, Y. R., Phipps, M., Zucker, J., Lebwohl, B., Wang, T. C., Sobieszczyk, M. E., & Freedberg, D. E. (2020). Gastrointestinal Symptoms and Coronavirus Disease 2019: A Case-Control Study From the United States. *Gastroenterology*, 159(1), 373–375.e2.
- McNabb-Baltar, J., Jin, D. X., Grover, A. S., Redd, W. D., Zhou, J. C., Hathorn, K. E., McCarty, T. R., Bazarbashi, A. N., Shen, L., & Chan, W. W. (2020). Lipase Elevation in Patients With COVID-19. *The American journal of gastroenterology*, 115(8), 1286–1288.
- Liu, F., Long, X., Zhang, B., Zhang, W., Chen, X., & Zhang, Z. (2020). ACE2 Expression in Pancreas May Cause Pancreatic Damage After SARS-CoV-2 Infection. *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association*, 18(9), 2128–2130.e2.
- Aghemo, A., Piovani, D., Parigi, T. L., Brunetta, E., Pugliese, N., Vespa, E., Omodei, P. D., Pretoni, P., Lleo, A., Repici, A., Voza, A., Cecconi, M., Malesci, A., Bonovas, S., Danese, S., & Humanitas COVID-19 Task Force (2020). COVID-19 Digestive System Involvement and Clinical Outcomes in a Large Academic Hospital in Milan, Italy. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*, 18(10), 2366–2368.e3.
- Bruno, G., Fabrizio, C., Santoro, C. R., & Buccoliero, G. B. (2021). Pancreatic injury in the course of coronavirus disease 2019: A not-so-rare occurrence. *Journal of medical virology*, 93(1), 74–75.
- Rasch, S., Hermer, A., Schmid, R. M., Huber, W., & Lahmer, T. (2021). High lipasemia is frequent in Covid-19 associated acute respiratory distress syndrome. *Pancreatology: official journal of the International Association of Pancreatology (IAP)*, 21(1), 306–311.
- Ahmed, A., Fisher, J. C., Pochapin, M. B., Freedman, S. D., Kothari, D. J., Shah, P. C., & Sheth, S. G. (2021). Hyperlipasemia in absence of acute pancreatitis is associated with elevated D-dimer and adverse outcomes in COVID 19 disease. *Pancreatology: official journal of the International Association of Pancreatology (IAP)*, 21(4), 698–703.
- Pezzilli, R., Centanni, S., Mondoni, M., Rinaldo, R. F., Davi, M., Stefanelli, R., Melzi d'Eril, G., & Barassi, A. (2021). Patients With Coronavirus Disease 2019 Interstitial Pneumonia Exhibit Pancreatic Hyperenzymemia and Not Acute Pancreatitis. *Pancreas*, 50(5), 732–735.
- Rathi, S., Sharma, A., Patnaik, I., & Gupta, R. (2020). Hyperlipasemia in COVID-19: Statistical Significance vs Clinical Relevance. *Clinical and translational gastroenterology*, 11(12), e00261.
- Ghosh, A., Gupta, V., & Misra, A. (2020). COVID19 induced acute pancreatitis and pancreatic necrosis in a patient with type 2 diabetes. *Diabetes & metabolic syndrome*, 14(6), 2097–2098.
- Yang, J. K., Lin, S. S., Ji, X. J., & Guo, L. M. (2010). Binding of SARS coronavirus to its

receptor damages islets and causes acute diabetes. *Acta diabetologica*, 47(3), 193–199. <https://doi.org/10.1007/s00592-009-0109-4>

- Bansal, P., Margekar, S. L., Suman, V., Sud, R., Meena, S., Sharma, A. K., Islam, S. Y., Gurtoo, A., Agrawal, A., Pangtey, G. S., & Prakash, A. (2020). Pancreatic Injury in COVID-19 Patients. *The Journal of the Association of Physicians of India*, 68(12), 58–60.