



Comparison of serum amylase and lipase levels in diagnosed Covid-19 survivors at a North Indian Hospital in Lucknow, India

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ABSTRACT

Background: Coronavirus disease 2019 (Covid-19) is caused by SARS-CoV-2 that causes severe acute respiratory syndrome (SARS). The upregulation of angiotensin-converting enzyme II (ACE-II) cell receptors or inflammatory cytokines play a major role in predisposing respiratory and pancreatic injury in SARS-CoV-2 patients. The aim of the present study was to critically evaluate the serum lipase and amylase levels in Covid-19 survivors in order to provide an insight into the possibility of pancreatic injury.

Methods: In this case control study, two groups of subjects (35 Covid-19 survivors and 35 controls) aged between 35 to 70 years were selected which recovered from mild to moderate Covid-19 (diagnosed using reverse transcription-polymerase chain reaction/rapid antigen test) and a control group of healthy individuals without any history of Covid-19. The serum amylase and lipase were determined by the direct substrate method and turbidimetric UV method, respectively using a semi-autoanalyzer.

Results: The study showed that the pancreatic biomarkers such as serum amylase ($p=0.023$) and lipase ($p=0.002$) were significantly elevated in Covid-19 survivors compared to control subjects. These findings suggest that the Covid-19 patients had a substantially higher mean level of serum amylase and lipase than the control subjects.

Conclusions: The Covid-19 patients are prone to severe respiratory illness including pancreatic injury.

Keywords: Coronavirus disease 2019; SARS-CoV-2, serum lipase, serum amylase; Covid-19

Introduction

Coronavirus disease 2019 (Covid-19), the extraordinarily contagious viral disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), emerged as an international medical crisis that resulted in millions of deaths worldwide [1]. Covid-19 causes liver and gastrointestinal disorders, but also has an effect on the pancreatic functions [2]. A recent study found an elevated pancreatic lipase in 17% of active Covid-19 patients [3]. Lipase is primarily secreted by the pancreas in adults is an important enzyme in the digestion of triglycerides [4] and is excreted by

the kidneys. Amylase, which is required for the digestion of starch, is primarily secreted by the salivary glands and pancreas [4, 5], including the lungs which is also a potential source of amylase and are removed by the reticuloendothelial system (RES) and kidneys. The extrapulmonary organ compromise has also been reported in Covid-19 involving the gastrointestinal (GI), pancreatic and hepatobiliary systems [6]. The pancreatic injury may lead to asymptomatic amylase and lipase enzyme elevation and severe acute pancreatitis [7].

It has been hypothesised that SARS-CoV-2 enters the cells by binding to the angiotensin-

converting enzyme II (ACE-II) receptor and initiates viral replication. The ACE-II is mostly expressed on vascular endothelial cells (ECs) and renal tubular epithelium (RTE), but has also been found in the lungs and GI tract. By using the ACE-II receptor, the SARS-CoV-2 can spread to other digestive organs, such as the liver [8, 9]. Studies have shown that there is upregulation of G protein-coupled receptors (GPCR) in Covid-19 patients, leading to an increase in inflammatory cytokines [10], known as “cytokine storm”. Some of these cytokines, such as interleukin-6 (IL-6), have been found to be involved in GI health and pathology. The increase in cytokines was interpreted as a protective mechanism against Covid-19 but may cause damage to the GI system [11]. Therefore, we investigate the risk factors associated with Covid-19 infection in order and identify the effects of acute pancreatitis on the diagnosis and prognosis of Covid-19 infected and recovered patients.

Methods

A case controlled study was conducted in which a total of 70 adult subjects (35 Covid-19 and 35 controls) having age 35 to 60 years were selected [12]. The Covid-19 survivor patients were enrolled from those attending the out-patient department (OPD), Integral Hospital, Lucknow. The demographic details and clinical history of subjects were obtained and recorded through the sample collection proforma. The Covid-19 patients were diagnosed with reverse transcription-polymerase reaction (RT-PCR)/rapid antigen test (RAT) with mild to moderate Covid-19 illness without oxygen support or hospitalization at Integral Hospital, Lucknow. The patients also did not have any comorbidity and were not on hormonal steroids, diuretics or any other therapy. The control subjects were apparently healthy individuals, enrolled from the general population, aged between 35-60 years without history of Covid-19. The study was approved by the Institutional Ethical Committee (IEC/ IIMS&R/2022/13), Integral Institute of Medical Sciences and Research Lucknow.

Estimation of serum amylase

Serum amylase was determined by the direct substrate method through a semi autoanalyzer. The substrate for the determination of pancreatic amylase (PAMY) activity is 2-chloro-4-nitrophenol- β -1-4-galactopyranosyl maltotrioxide (CNP-G) which does not require the presence of ancillary enzymes. The rate of formation of 2-chloro-4-nitrophenol (2-CNP) is monitored at 400-420 nm and is proportional to the α -amylase activity. The normal reference range for serum amylase is 90 U/L.

Estimation of serum lipase

Serum lipase was determined by the turbidimetric UV method through a semi-autoanalyser. The pancreatic lipase (PL) catalyzes the hydrolysis of triolein in the presence of colipase to form monoglycerides and fatty acids. The rate of decrease in turbidity is measured at 340 nm which is proportional to the lipase activity. The activities of other lipases in the serum are inhibited by cholic acid salts in the reagent. The normal reference range of serum lipase is 190 U/L.

Statistical analysis

The results are expressed as the mean \pm SD. The amylase and lipase levels were compared by using the unpaired t test between controls and subjects. The Pearson's correlation coefficient was calculated among the study parameters. The p-value <0.05 was considered significant. The analysis was carried out by using the SPSS version 23 software.

Results

In this study, a total of 70 subjects were taken including 35 apparently healthy controls and 35 Covid-19 recovered patients having age between 35-60 years were selected. The mean age of the controls determined was 41.06 ± 3.99 and the Covid-19 survivors was 41.74 ± 4.33 (Table 1), showing no significant difference between in mean ages of the groups ($p=0.494$). All the subjects were tested for serum amylase and

Table 1. Age of Covid-19 patients selected for the study

Group	N	Age in years		Unpaired t test		
		Mean	SD	t-value	p-value	Significance
Control	35	41.06	3.99	0.69	0.494	Not significant
Patients	35	41.74	4.33			

Table 2. Correlation analysis showing relationship between amylase and lipase in Covid-19 patients (n=35)

		Amylase	Lipase
Amylase	Pearson Correlation	1	.210
	Sig. (2-tailed)	-	.226
Lipase	Pearson Correlation	.210	1
	Sig. (2-tailed)	.226	-

lipase activity. A significant increase in amylase level was found among Covid-19 patients as compared to control subjects ($p=0.023$) (Fig. 1). A significant increase in serum lipase level was also found in Covid-19 patients as compared to control subjects ($p=0.002$) (Fig. 2). The result of our study suggests that Covid-19 can affect the digestive system even after the recovery especially the pancreas. A positive correlation between the amylase and lipase levels in Covid-19 patients is shown in Table 2.

After a negative RT-PCR test for SARS-CoV-2, the mean amylase level of control subjects was 66.60 ± 17.12 U/L and Covid-19 survivors was 75.77 ± 15.81 U/L (Fig. 1), indicating significant increase in amylase level among patients as compared to control subjects ($p=0.023$). After a negative RT-PCR test for SARS-CoV-2, the mean lipase levels of control subjects was 119.34 ± 21.53 U/L and Covid-19 survivors was 144.03 ± 39.09 U/L (Fig. 2) indicating a significant increase in serum lipase level among patients as compared to control subjects ($p=0.002$).

Discussion

The primary organ system affected by the SARS-CoV-2 is the respiratory tract including the upper and the lower respiratory respiratory tract. There is increasing evidence that it has an

impact on extrapulmonary systems, including the gastrointestinal tract. A number of studies have shown pancreatic involvement, including acute pancreatitis in Covid-19 patients. Given the increasing number of cases of GI symptoms in Covid-19 patients, studies have focused on determining the extent of GI diseases, particularly pancreatic injury [7]. In our case-control study, we enrolled Covid-19 survivors along with apparently healthy controls to reduce the effect of confounding factors. A strong relationship between pancreatic disease and Covid-19 has been reported. Several studies have shown that age and abnormalities of various clinical biomarkers may be essential to understanding the disease. In our present study, the clinical variables like serum amylase and lipase were significantly elevated in Covid-19 patients as compared to control subjects. The serum amylase (75.77 ± 15.81 U/L) was found to be remarkably raised in patients as compared to control subjects (66.60 ± 17.12 U/L) ($p=0.023$). The serum lipase (144.03 ± 39.09 U/L) was also found to be remarkably raised in patients as compared to controls subjects (119.34 ± 21.53 U/L) ($p=0.002$). Also, the correlation analysis between the serum amylase and lipase shows a positive correlation relationship.

These results were similar to other studies which show that increased concentration of serum amylase and lipase may be associated with

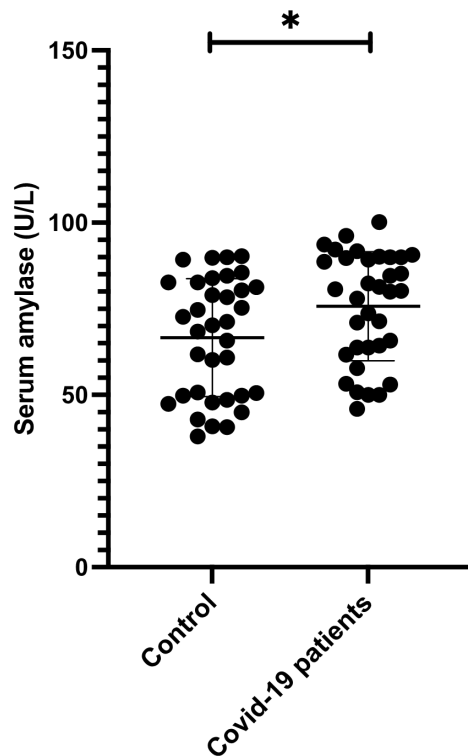


Figure 1. Amylase level in Covid-19 patients and controls (n=35)

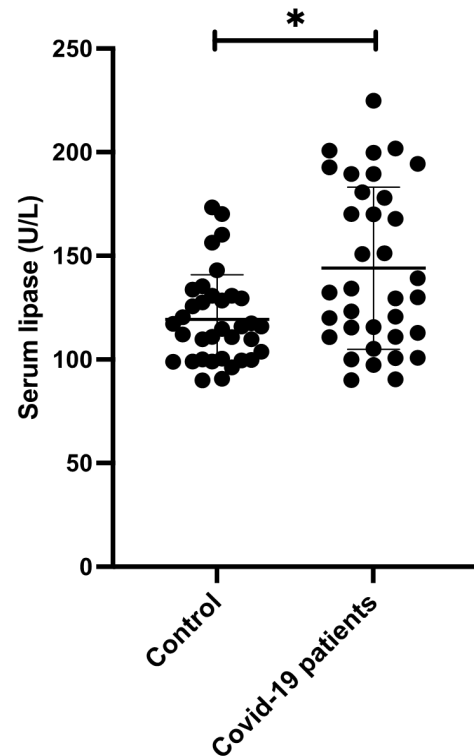


Figure 2. Lipase level in Covid-19 patients and controls (n=35)

Covid-19. Our findings are consistent with those of Gameil *et al* [12] which suggests that Covid-19 patients have elevated serum amylase and/or lipase levels. The SARS-CoV-2-induced pancreatic injury was also reported by Liu *et al* [13]. They investigated the expression of ACE-2 receptors in normal human pancreas using RNA sequencing data from the Genotype Tissue Expression (GTEx) database. These receptors have been identified as the entry points for SARS-CoV-2 into human cells. They discovered that ACE-2 receptors may be found in both the exocrine and endocrine pancreatic tissues. Another study by Wang *et al* [14] focused on 52 Covid-19 pneumonia patients and found increased serum amylase and/or lipase levels (17.3%). McNabb-Baltar *et al* [15] reported hyperlipasemia in patients (12.7%) with confirmed Covid-19 (the mean lipase level was 148.4-151.8 U/L). Some subjects (2.8%) had lipase levels that were more than three times the normal limit (>180 U/L) despite the absence of clinical symptoms of acute pancreatitis. There were some patients with digestive symptoms,

including anorexia (66.7%), nausea (55.6%), diarrhoea (55.6%), and abdominal discomfort (33.3%). Barlass *et al* [16] studied 294 admitted Covid-19 patients, 83 of whom had high serum lipase (16.8%) and some with serum lipase levels three times higher than normal.

The current data show that the SARS-CoV-2 infection manifested in extrapulmonary organs such as the GI tract. We conclude that increased amylase and/or lipase levels in Covid-19 patients are not always indicative of pancreatic injury. These elevated enzymes might be also be found in other clinical conditions, which may not be caused only by pancreatic injury or inflammation. Additionally, hyperamylasemia may be found in conditions such as alcoholism, lactic acidosis, anorexia nervosa, bowel perforation, and diarrhoea. The Covid-19 patients may present with acidosis and diarrhoea, resulting in elevated serum amylase. Diarrhoea or intestinal inflammation increases amylase and lipase absorption in the bowel lumen, resulting in the further elevation in the blood. Amylase is eliminated from the body by RES

and kidneys [17-19], hyperamylasemia may be found in kidney injury. Further studies should be carried out to determine pancreatic injury or clinically relevant pancreatitis in Covid-19 patients.

Conclusion

The present study showed that serum amylase and lipase were significantly elevated in Covid-19 survivors compared to control subjects. These findings suggest that the Covid-19 patients had a substantially higher mean level of serum amylase and lipase than the control subjects. These patients are prone to severe respiratory illness including pancreatic injury and the increased amylase and/or lipase in Covid-19 patients is not always indicative of pancreatic injury and which may also be found in other clinical conditions.

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Author contributions

NU: data collection and analysis, drafted the manuscript. MA: conception or design of work, analysis and interpretation of results. SK: conception or design of work, analysis and interpretation of results. MMK: analysis and interpretation of results. HA: conception or design of work, drafted the manuscript, critically revised and proofread the manuscript. SP: analysis and interpretation of results. RA: conception or design of work, analysis and interpretation of results. All authors approved the final version of the manuscript for submission and publication.

Declaration of competing interest

The authors declare that there is no conflict of interest.

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