ORIGINAL ARTICLE

Impact of COVID-19 Pandemic on the incidence of acute pancreatitis due to delay in laparoscopic cholecystectomy

Uzma Shamim Seth, Mohammad Taha Kamal, Dileep Kumar, Munira Murtaza Khomusi, Sadia Lateef, Maha Kamal

Abstract

Objective: The goal of this study was to evaluate the prevalence of acute pancreatitis (AP) in cholelithiasis patients who were scheduled for laparoscopic cholecystectomy (LC) and were postponed because of the pandemic.

Material and Methods: The study was carried out at the Jinnah Post Graduate Medical Centre Surgical Unit 1, Ward 3 and was a cohort observational study. The study was conducted from June 2022 to March 2023 for the duration of nine months. A total of 383 patients were included in the study. Patient demographics, co morbidities, serum amylase and lipase levels and results of the CT scan were examined and recorded.

Results: The majority of the patients (75.5%) were female, with an average age of 54, according to information gathered from 383 patients enrolled in the study. The most common co-morbidities were hypertension and diabetes mellitus. Analysis of the CT scan results revealed relationships between the number of stones and side effects such as fluid accumulation and pancreatic enlargement. Male patients and those without diabetes or high blood pressure had greater serum levels of amylase and lipase. The study also showed a strong correlation between pancreatitis severity grading methods (Ranson and APACHE II Scores) and the CT Severity Index.

Conclusion: This study clarifies the frequency of acute pancreatitis in individuals with cholelithiasis whose scheduled laparoscopic cholecystectomy was postponed because of the pandemic. Our results provided crucial information about the co-morbidities and demographics of the patient group, particularly the prevalence of females and the link to hypertension and diabetes mellitus.

Keywords: laparoscopic cholecystectomy, cholelithiasis, acute pancreatitis

Received
Date: 31st August, 2023
Accepted
Date: 18th December, 2023

Jinnah Postgraduate Medical Centre, Karachi
US Seth
D Kumar
MM Khomusi
S Lateef
M Kamal

Civil Hospital, Karachi
MT Kamal

Correspondence:
Dr Uzma Shamim Seth
Department of General Surgery, Jinnah Postgraduate Medical Centre, Karachi.
email: uzma_shamim1@hotmail.com

Introduction:

The Covid-19 epidemic caused a delay in elective procedures. Patients experienced acute pancreatitis as a result of the postponement of their procedures. A rapid pneumonia outbreak hit Wuhan City, China, in December 2019. After extensive investigation, a novel coronavirus was identified as the cause of this outbreak. On February 11, 2020, the World Health Organization designated this virus as COVID-19. This highly dangerous virus quickly spread throughout China and many other countries. The virus continues to spread globally as a pandemic, posing a serious threat to public health globally.[1,2] The global reorganization of medical services has also been adversely impacted by the COVID-19 epidemic. The diagnosis and treatment of patients that required surgery were guided by the understanding of COVID that came with the evolution of the epidemic. However, there was a delay in procedures because of the pandemic condition, which would have harmed patients' health outcomes.[3-6]

Inflammation of the pancreas and loss of acinar cells are symptoms of acute pancreatitis (AP),

which can have local or systemic repercussions.[13] The clinical combination of LC and untreated gallstones is already well-established.[14] The gall bladder produces a stone, which escapes and plugs the ampulla of Vater, which is where the bile and pancreatic ducts pour their fluids into the intestines. AP and gallstones are closely related to one another. The most frequent (74%) cause of AP is gallstones.[15]

In Pakistan, gallstones are detected in 8% of individuals aged 40 and in 20% of those aged 60 or older.[9] Cholelithiasis ranks as the third most frequent reason for hospital admissions in Karachi, Pakistan.[7] In clinical practice, the primary approach to managing gallstone disease typically involves cholecystectomy, along with endoscopic or medical treatments to address any complications that may arise. The preferred method of treatment for symptomatic gallstones is laparoscopic cholecystectomy (LC), the gold standard. Through a very small abdominal incision, the gallbladder is surgically removed during LC. The removal of a damaged gallbladder is accomplished by a minimally invasive surgical procedure.[3] LC is a safe procedure with a speedy recovery time. After the procedure, most hospitals only require a 23-hour stay, and if the patient is doing well, they may let them go on medication.[10] Within a week of the development of acute cholecystitis or gallstone pancreatitis, cholecystectomy is advised by NICE.[12] If not, the condition will result in the first symptoms and perhaps prolonged hospitalization.

Numerous medical procedures had been changed, including the redistribution and risk of intraoperative viral transmission brought on by Covid-19. Non-urgent, non-cancer surgical procedures had fallen behind emergency and cancer surgeries. These were a few of the most typical ailments that required urgent surgery and hospitalizations. As a result of their symptoms, people with gallstone disease frequently have cholecystectomy. The COVID-19 pandemic caused surgery to be postponed, increasing the likelihood of AP in cholelithiasis. Based on the aforementioned information, we created a study with the objective of determining the incidence of AP in patients who presented to the ER with cholelithiasis due to delayed elective LC.

Material and Methods:

The study was designed as a cohort observational study and conducted at the Jinnah Post Graduate Medical Centre, specifically in Surgical Unit 1, Ward-3. 383 patients were enrolled in this study. The research focused on patients who had previously registered for elective surgery before the COVID-19 pandemic. Inclusion criteria for participants encompassed individuals who were hypertensive, diabetic, and diagnosed with acute pancreatitis. Exclusion criteria consisted of patients with acute pancreatitis attributed to causes other than the specified criteria, those with hyperlipidemia, hypercalcemia, or a history of endoscopic surgery, as well as individuals who were COVID-19 positive, pregnant, lactating mothers, or either very young below 25 or above 60 years of age.

The sample size for this study was determined using the World Health Organization's sample size calculator, taking into consideration that approximately 46% of patients return for surgery after prior registration. To achieve a 95% confidence interval with a 5% margin of error, the sample size was calculated using the following formula: n = z^2 * p * (1 - p) / e^2, where 'z' represents 1.96 for a confidence level of 95%, 'p' denotes the proportion expressed as a decimal (0.46), and 'e' signifies the margin of error (0.05). The result was a required sample size of 382 participants for the study.

Data collection was commenced after approval from Institutional Review Board No. F.2-81/2022 GENL/195/JPMC. It involved the use of a predesigned proforma as the data collection tool, which was selected for its validity and reliability. The study enrolled patients who presented to the Emergency Department with acute pancreatitis secondary to gallstones, specifically those who had pre-existing cholelithiasis and had previously registered for elective surgery before the COVID-19 lockdown. All patients who met the inclusion criteria and provided both written and verbal informed con-

Table 1: The demographic data of pancreatitis patients admitted to the hospital

	No of cases	%
Gender		
Male	94	24.5%
Female	289	75.5%
Total	383	100.0%
Age (mean)	54	
Diabetes Mellitus		
Yes	206	53.8%
No	177	46.2%
Hypertension		
Yes	221	60.2%
No	146	39.8%
Other Co-morbidities		
Asthma	13	3.4%
Hepatitis B	15	3.9%
Hepatitis C	16	4.2%
None	339	88.5%

Table 2: A comparative analysis of patient characteristics and CT scan findings against gender

CT Scan Findings		**Quantity of Stones**			**p-value**
		Single	Multiple	Total	
Pancreas Enlargement	Yes	33 (53.2%)	208 (65.2%)	241	0.084
	No	29 (46.8%)	111 (34.8%)	140	
Fluid Collection	No	14 (22.6%)	66 (20.7%)	80	0.609
	Single	11 (17.7%)	75 (23.5%)	86	
	Multiple	37 (59.7%)	178 (55.8%)	215	
Degree of Necrosis	5-10%	12 (19.4%)	73 (22.9%)	85	0.281
	10-20%	8 (12.9%)	33 (10.3%)	41	
	20-30%	1 (1.6%)	4 (1.3%)	5	
	30-40%	4 (6.5%)	14 (4.4%)	18	
	> 40%	5 (8.1%)	8 (2.5%)	13	
	None	32 (51.6%)	187 (58.6%)	219	
Necrosis Site	Body	12 (48%)	48 (41.7%)	60	0.651
	Tail	13 (52%)	67 (58.3%)	80	
CT Severity Index	0-3	0	11 (3.5%)	11	0.806
	4-6	36 (58.1%)	165 (52.9%)	201	
	7-10	26 (41.9%)	136 (43.6%)	162	

sent were included in the study. Data recorded on the predesigned proforma included patient demographics, clinical signs and symptoms, medical history, and reinvestigation results, including serum amylase, serum lipase, CT scan, and ultrasound findings.

Data Analysis:

The data was analysed usingthe SPSS Version 1.0.0.1406 (2021) and MS Excel Sheet for graph and figure tabulation. Quantitative variables, such as age, number of episodes of cholecystitis, number and size of stones were described using mean and standard deviation. Qualitative variables, including gender, diabetic status, hypertension, and other comorbidities, were presented as frequencies and percentages. To control for effect modifiers, stratification was implemented. Post-stratification Chi-square tests were applied to assess the influence of outcomes, with statistical significance set at a p-value of ≤ 0.005. This rigorous approach to data collection and analysis ensures the reliability and validity of the study's findings, contributing valuable insights into the impact of delayed elective surgeries on patients with acute pancreatitis. Various Artificial intelligence tools were utilized for literature review process and manuscript review including Quill bot, Sci Space and Semantic Scholar.

Results:

The study shows a comprehensive demographic overview of patients admitted to the hospital with pancreatitis. Among the 383 individuals included in the study, a majority, comprising 75.5%, were female, while the remaining 24.5% were male. The average age of these patients was 54 years, shedding light on the typical age range associated with pancreatitis cases within this cohort. Notably, 53.8% of the patients had diabetes mellitus, indicating a substantial presence of this comorbidity among those diagnosed with pancreatitis. Additionally, a significant proportion, amounting to 60.2%, had hypertension, underlining the prevalence of this condition within the pancreatitis patient group. The Table 1 provides insights into other comorbidities. However, most patients, encompassing 88.5%, did not have any of these specified comorbidities.

The gender-based differences among participants also show interesting findings. Notably, there is a significant contrast in the mean ages of male and female patients, with males having a

Table 3: The comparison of the quantity of stones with CT scan findings of pancreatitis patients

CT Scan Findings		Quantity of Stones			p-value
		Single	Multiple	Total	
Pancreatic Enlargement & inflammation	Yes	33 (53.2%)	208 (65.2%)	241	0.084
	No	29 (46.8%)	111 (34.8%)	140	
Fluid Collection	No	14 (22.6%)	66 (20.7%)	80	0.609
	Single	11 (17.7%)	75 (23.5%)	86	
	Multiple	37 (59.7%)	178 (55.8%)	215	
Degree of Necrosis	5-10%	12 (19.4%)	73 (22.9%)	85	0.281
	10-20%	8 (12.9%)	33 (10.3%)	41	
	20-30%	1 (1.6%)	4 (1.3%)	5	
	30-40%	4 (6.5%)	14 (4.4%)	18	
	> 40%	5 (8.1%)	8 (2.5%)	13	
	None	32 (51.6%)	187 (58.6%)	219	
Necrosis Site	Body	12 (48%)	48 (41.7%)	60	0.651
	Tail	13 (52%)	67 (58.3%)	80	

Table 4: The comparison of the quantity of stones with CT scan findings of pancreatitis patients

	Serum Lipase	p-value	Serum Amylase	p-value
Gender				
Male	868±1071	0.107	386±243	0.01
Female	658±1105		328±168	
Diabetes Mellitus				
Yes	323±298	0.107	277±123	0.01
No	925±1299		379±207	
Hypertension				
Yes	753±864	0.107	395±259	0.01
No	495±437		342±182	
Incidence of co-morbidities				
Asthma	427±245	0.662	364±232	0.709
Hepatitis B	753±864		395±259	
Hepatitis C	495±437		342±182	
None	729±1148		340±186	

notably higher average age of 58 years compared to females, who have an average age of 52 years ($p = 0.0001$). Additionally, pancreatic stone size varies significantly between genders, with males exhibiting larger stones (mean size of 1.3) than females (mean size of 1.1) ($p = 0.006$). In terms of stone distribution, males tend to have more single stones (n 25) compared to females (n = 37), while females show a significantly higher prevalence of multiple stones. Moreover, gender plays a substantial role in the prevalence of diabetes mellitus and hypertension, with both conditions being more prevalent among females than males ($p < 0.0001$ for both). Interestingly, asthma also exhibits gender-related differences, with a higher incidence among males than females ($p = 0.023$). The data is shown in Table 2.

The CT scan findings was also evaluated in relation to various parameters, allowing for an insightful analysis of the data. Firstly, when examining pancreatic enlargement and inflammation, it appears that a higher percentage of patients with multiple stones (65.2%) experience these issues compared to those with single stones (53.2%), although the difference is not statistically significant ($p = 0.084$). This suggests that while there is an association between stone quantity and these complications, it may not be strong enough to reach statistical significance. Next, it's interesting to note that the majority of patients with multiple stones (59.7%) exhibit fluid collection, whereas a smaller percentage of those with single stones (17.7%) have this complication. However, the p-value of 0.609 indicates that there is no statistically significant difference between the two groups.

The degree of necrosis in the pancreas was also assessed, with varying levels of necrosis categorized by percentage. There doesn't seem to be a significant association between the quantity of stones and the degree of necrosis ($p = 0.281$). However, it's worth noting that patients with no necrosis predominantly have multiple stones (58.6%). Moreover, there was no significant difference between patients with single or multiple stones regarding the site of necrosis ($p = 0.651$).

The comparison of serum lipase and serum amylase levels concerning CT scan findings in pancreatitis patients. The CT scan findings include pancreas enlargement, fluid collection (categorized as single or multiple), necrosis site (pancreatic body or tail), and the degree of necrosis (ranging from 5-10% to more than 40%). Interestingly, the p-values associated with these comparisons are somewhat variable. For some

Table 4: The comparison of the quantity of stones with CT scan findings of pancreatitis patients

	Serum Lipase	p-value	Serum Amylase	p-value
Pancrease Enlargement				
Yes	681±1184	0.618	337±182	0.01
No	739±913		344±194	
Fluid Collection				
Single	793±1790	0.033	296±137	0.001
Multiple	771±821		371±209	
No	420±595		301±150	
Necrosis Site	753±864	0.107	395±259	0.01
Pancreatic Body	1008±2010	0.753	389±177	0.339
Pancreatic Tail	925±1083		420±199	
Degree of Necrosis				
5-10%	961±1705	0.005	386±204	0.00001
10-20%	836±1206		413±190	
20-30%	953±597		450±129	
30-40%	1293±1255		510±145	
More than 40%	522±415		424±68	
None	533±678		286±167	

Table 6: Comparison of Ranson's and APACHE II's scores with CTSI

		CT severity Index (CTSI)			
		Mild (0-3)	Moderate (4-6)	Severe (7-10)	p-value
Ranson Score	0-2	11	71	2	< 0.0001
	3-5	0	36	19	
	> 5	0	94	141	
APACHE II Score	0-2	0	1	0	< 0.0001
	3-5	6	6	0	
	> 5	2	174	159	

parameters, such as pancreas enlargement and fluid collection, the differences in enzyme levels are not statistically significant, as indicated by higher p-values. In contrast, the degree of necrosis has very low p-values, signifying a significant impact on enzyme levels. These findings underscore the importance of CT scan results in assessing pancreatitis severity and its correlation with enzyme levels.

The relationship between the CT severity index (CTSI) and two scoring systems, the Ranson Score and APACHE II Score, was used to assess the severity of acute pancreatitis. The CTSI is categorized into Mild (0-3), Moderate (4-6), and Severe (7-10). The Ranson Score, designed for acute pancreatitis assessment, is divided into three categories - 0-2, 3-5, and > 5, while the Apache Score, used for critically ill patient evaluation, also has three categories - 0-2, 3-5, and > 5. The p-values in the table are all highly significant, suggesting strong statistical associations. Notably, both Ranson and APACHE II Scores exhibit significant associations with CTSI, indicating their effectiveness in predicting the severity of acute pancreatitis. However, the Ranson Score appears to have a slightly stronger association in the "Moderate" and "Severe" categories, as indicated by higher values.

Discussion:

During a study in Bangalore, India, after the first episode has subsided, performing a cholecystectomy on the same day can considerably reduce hospital stays, length of stays, and recurrent pancreatitis without major morbidity. As a result, it was determined from the results above that same admission laparoscopic cholecystectomy is the recommended plan for cholecystectomy for all patients with mild gallstone pancreatitis.[26] Similar to our study, which demonstrated that a delay in LC increased AP severity and length of hospital stay. The findings made it abundantly evident that during the COVID pandemic, the rate of surgery considerably decreased. Decreases were reported in laparoscopic cholecystectomy, elective treatments, and surgeries performed just for biliary colic. Although it rose throughout COVID, the trend of the primary diagnosis, excluding pancreatitis, was non-significant.[27] The delayed LC in the COVID pandemic also raised the incidence and severity of AP in our investigation.

Acute pancreatitis can be brought on by a number of different circumstances, including gallstones, alcohol consumption, high triglyceride levels, high calcium levels, surgical operations, infections, autoimmune illnesses, hereditary susceptibility, chronic use of medications, and physical trauma.[16] Numerous microorganisms, such as bacteria, viruses, fungi, and parasites, have been related to pancreatitis.[17] Examples include the measles, mumps, coxsackie, and hepatitis viruses. The diagnosis of acute pancreatitis

requires the presence of two of the three following criteria, which include sudden onset of severe upper abdominal pain suggestive of the condition, a threefold increase in serum amylase or lipase levels compared to the upper normal limit, and distinctive findings on imaging studies.[18] In contrast to our findings, which found that more females than males were diagnosed with acute pancreatitis, a study conducted in Faisalabad in 2012 examined the significance of age and sex in patients with gallstone disease and surgical complications. The study found that males were more likely than females to develop acute pancreatitis.[9]

When compared to numerous clinical indices and diagnostic results, the comparison of serum lipase and serum amylase levels among individuals with pancreatitis also revealed intriguing results. According to the results, male and female patients had noticeably different levels of serum lipase and amylase, with male patients typically having higher levels of both enzymes. The p values associated with these differences are statistically significant for both amylase and lipase, indicating that gender plays a significant role in enzyme levels among pancreatitis patients. In contrast to our findings, the study found that the quantities of lipase and amylase were not influenced by pancreatic necrosis or other variables.[18–20] The findings also showed how diabetes mellitus and hypertension affect enzyme levels, with statistically significant variations between patients with diabetes and those without it as well as between those with hypertension and those without it. The literature[21] makes clear that both type 1 and type 2 diabetic individuals have decreased levels of amylase and lipase. According to the evidence, these comorbidities may have an impact on the enzyme levels in pancreatitis. It has been reported that lower glucose levels are negatively associated with the enzyme levels and it can be a good prognostic marker to assess acute pancreatitis.[22] It is unusual to detect a substantial correlation between serum lipase and serum amylase levels in pancreatitis patients when it comes to several clinical indicators and diagnostic results. They direct attention to how gender, comorbidities, and CT scan results affect enzyme levels, assisting medical personnel in better comprehending and treating pancreatitis situations depending on these variables.

Overall, this data highlights the usefulness of both scoring methods in determining the seriousness of the pancreatitis, offering important direction to medical researchers and practitioners. The severity of pancreatitis can also be predicted by the results of the CT scan; for this, Ranson and APACHE II scores are typically assessed. Our research revealed a direct correlation between the moderate and severe CT scan findings and high Ranson and APACHE II score.The strong association and high significance are also mentioned in other studies.[23–25] Patients who have experienced cholecystitis in the past who haddelayed laparoscopic cholecystectomy experienced more severe pancreatitis in the future. To lower the recurrence rate of biliary tract-related events, current recommendations advise laparoscopic cholecystectomy for biliary pancreatitis.[28] Patients with moderate acute gallstone pancreatitis can have an early cholecystectomy safely and effectively within 48 hours of admission, with a shorter hospital stay and fewer recurrent biliary episodes.[29] As seen in this study, cholecystectomy delays led to an increase in AP severity.

Conclusion:
The findings of this study provide a thorough demographic summary of hospitalized individuals with gall stone pancreatitis. The information showed a connection between the number of stones and their side effects. Additionally, it demonstrated the connection between the severity of acute pancreatitis and the grading systems. This sets the foundation for efficiently controlling and providing care for patients suffering from benign conditions like gallstones during the pandemic. As elective treatments are postponed in these situations, complications like gall stone pancreatitis are inevitable and increase morbidityof the patients and the strain on hospitals.

Conflict of interest: None

Funding source: None

Role and contribution of authors:

Uzma Shamim Seth, collected the data, referenecs and did the initial writeup.

Mohammad Taha Kamal, helped in collecting the data and also helped in introduction writing.

Dileep Kumar, helped in collecting the references and also helped in abstract writing.

Munira Murtaza Khomusi, helped in collecting the data and also helped in discussion writing.

Sadia Lateef, critically review the article and made final changes.

Maha Kamal, collected the references and also helped in material and methods writing.

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