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Original Article

Etiology of Pancreatitis in Patients at a Tertiary Care Center

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ABSTRACT

Objective: To compare etiological frequencies in patients of acute pancreatitis presenting to our setup with international data.
***Study Design*:** Cross-sectional study
***Place and Duration of Study*:** Department of Gastroenterology, Pakistan Emirates Military Hospital & Combined Military Hospital, Rawalpindi Pakistan, from Aug 2020 to Jan 2022.
***Methodology*:** Patients over 12 years suffering from pancreatitis were recruited using a convenience sampling technique based upon predefined criteria for diagnosis of pancreatitis on a questionnaire. Relevant basic lab tests, including chemistries and imaging, including Ultrasound abdomen and CECT abdomen, were analyzed to establish aetiology. Data were continuously uploaded into an electronic data sheet. International Consensus Diagnostic Criteria (ICDC) algorithms were applied to diagnose autoimmune pancreatitis.
***Results*:** Out of 120 patients, 74(61.7%) were males, and 46(38.3%) were females. Biliary pancreatitis was the most common aetiology 50(41.7%), followed in descending order by idiopathic 36(30%), drug-induced pancreatitis (DIP) 9(7.5%), Post ERCP Pancreatitis (PEP) 8(6.7%), tumours 5(4%), Autoimmune pancreatitis (AIP), Hypertriglyceridemia and alcohol-induced pancreatitis each 2(1.7%).
***Conclusion*:** Biliary pancreatitis has the highest frequency, followed by idiopathic and drug-induced pancreatitis.

Keywords: Etiological frequencies, AIP/DIP, Post COVID pancreatitis.

How to Cite This Article: *Haider MFB, Ali I, Zafar H, Ahsan M, Shah SZH, Sher F. Etiology of Pancreatitis in Patients at a Tertiary Care Center. Pak Armed Forces Med J 2023; 73(2): 575-578. DOI: https://doi.org/10.51253/pafmj.v73i2.8771*

INTRODUCTION

Acute pancreatitis is a major reason for admission to Gastroenterology practice worldwide and is an essential consideration in the differential of acute abdomen.[1] Because of a variety of unidentifiable causes, it risks misdiagnosis and mismanagement leading to a considerable increase in morbidity and mortality. The global incidence ranges from 20-40%/100,000 population and is on the rise.[2] National data on its incidence are not available. Worryingly, only a limited number of local studies are available dealing with its etiological and clinical aspects.[3]

Drug-induced pancreatitis (DIP) is suspected 4 to 8 weeks after initiation of a drug.[4] Its reported incidence is (<5%).[5] Differentiating DIP from autoimmune pancreatitis is not straightforward, as both possibilities exist in the case of Inflammatory bowel disease (IBD).[6] Resorting to International Consensus Diagnostic Criteria for Autoimmune Pancreatitis (ICDC) facilitates the diagnosis of Autoimmune pancreatitis (AIP), which is mostly associated with Crohn's disease. Using steroids During the COVID-19 pandemic makes distinguishing steroid-induced pancreatitis from COVID-19-induced pan-creatitis difficult.[7,8] This diagnostic difficulty in DIP vs. AIP and Post COVID pancreatitis has yet to be specifically addressed in the literature. Failure to identify the cause and premature labelling of cases as idiopathic carries the risk of recurrent pancreatitis attacks with increased morbidity and mortality.[9,10] Henceforth, the present study was conducted with a rationale to define the etiological spectrum of acute pancreatitis at our setup, enabling us to compare it with international data (during COVID times and highlighting COVID-induced pancreatitis in our community). This is intended as an analysis of the accuracy of our diagnostic approach and to make recommendations if needed, with the overall objective of improving patient care.

METHODOLOGY

The Cross-sectional study was conducted at the Department of Gastroenterology PEMH Rawalpindi and Combined Military Hospital, Rawalpindi Pakistan from August 2020 to January 2022. The Hospital Ethical Committee approved the study (ERC/PEMH/104522/20 dated 1/8/20). The sample size was calculated using a WHO sample size calculator, taking the reported prevalence of acute pancreatitis of 0.05%.[7]

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Received: 23 May 2022; revision received: 15 Oct 2022; accepted: 21 Oct 2022

Inclusion Criteria: Patients of either gender, aged 12 to 100 years, presenting in Indoor or Outpatient Departments with acute pancreatitis, were included in the study.

Exclusion Criteria: Children below 12 years of age were excluded from the study.

A case of acute pancreatitis was defined by any 2 of the following: Epigastric (Abdominal) pain consistent with acute pancreatitis, raised serum Amylase /lipase to more than or equal to the thrice upper limit of normal, and/or findings on imaging consistent with acute pancreatitis.[11] Based on the common etiological factors, a bedside questionnaire was designed to screen causes on history rapidly. After the focused history, work-up at our centre starts with preliminary, followed by advanced investigations. Tests in the former include serum calcium, triglycerides, complete blood count, C reactive protein, liver function tests, renal function tests, electrolytes and USG abdomen. Advanced tests include serum IgG4, CT imaging, Magnetic resonance cholangiopancreatography (MR-CP), and Endoscopic ultrasound (EUS). Data shows that most patients with idiopathic acute and recurrent acute pancreatitis have underlying complex genetic risk profiles. A consultant radiologist reported imaging tests. Consultant gastroenterologists did EUS at the Department of Endoscopy, PEMH. All available diagnostic tests were analyzed for patients to confirm acute pancreatitis and establish the cause. The diagnostic work-up was appropriately expanded wherever possible to reach an etiological diagnosis in each case. Follow-up was done telephonically and using digital apps. We used International Consensus Diagnostic Criteria (ICDC) algorithms to screen for autoimmune pancreatitis.[12] Cases in which a specific etiological cause could not be identified were classified as idiopathic.

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 23.00. Mean±SD were calculated for the continuous variable. Frequency and percentage were calculated for categorical variables. The Chi-square test was applied for comparison between groups. The *p*-value of ≤0.05 was considered significant.

RESULTS

Out of 120 patients, 74(61.7%) were males, and 46(38.3%) were females. Mean age of patients was 46.00± 16.00 years. Etiological frequencies are shown in Table-I. Biliary pancreatitis was the most common aetiology, 50(41.7%), followed in descending order by idiopathic 36(30%), drug-induced pancreatitis (DIP) 9(7.5%), Post ERCP Pancreatitis (PEP) 8(6.7%), tumours 5(4%), Autoimmune pancreatitis (AIP), hypertriglyceridemia and alcohol-induced pancreatitis each 2(1.7%). The Breakdown of miscellaneous cases is shown in Table-II. The overall difference in frequency between genders was significant (p=0.001) (Table-III). Comparison of own with international data also showed a significant frequency difference (p<0.001) (Figure).

Table-I: Etiology of acute pancreatitis cases (n=120)

	n(%)
Biliary Pancreatitis	50(41.7)
Idiopathic	36(30.0)
Drug Induced Pancreatitis	9(7.5)
Post ERCP Pancreatitis	8(6.7)
Tumor	5(4.2)
Alcohol Induced Pancreatitis	2(1.7)
Hypertriglyceridemia	2(1.7)
AIP-2/ DIP	2(1.7)
Misc (SPECIFY BREAKUP)	6(5.0)
Total	120(100)

Table-II: Breakdown of Miscellaneous Cases

Condition	Number of cases	Gender
AIP (NOS)	1	female
Choledochal cyst	1	female
Eosinophilic pancreatitis	1	male
Hypercalcemia	1	male
Pancreatic divisum	1	female
Post COVID 19	1	male

Table-III: Gender wise distribution of cases (n=117)

Gender	Etiology									Total
	Biliary	Idiopathic	Drug Induced	Post ERCP	Tumor	Hypertriglyceridemia	AIP-2/ DIP	Misc.	Alcohol	
Male	21(28.4%)	31(41.9%)	5(6.8%)	4(5.4%)	5(6.8%)	2(2.7%)	1(2.7%)	3(4.1%)	2(2.7%)	71(100.0%)
Female	29(63.0%)	5(10.9%)	4(8.7%)	4(8.7%)	0%	0%	1(2.2%)	3(8.7%)	0%	46(100.0%_

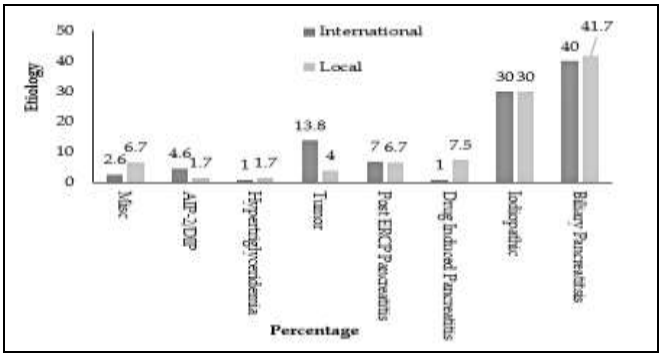

Figure: Comparison of Frequencies with International Studies

DISCUSSION

Our pattern of gender distribution was similar except for autoimmune pancreatitis, where our study has shown female predominance (male to female ratio 1:2) in contrast to 2.9:1 quoted in study.[8] Biliary pancreatitis is the most common cause of acute pancreatitis, accounting for 40 to 70 percent of cases.[12] Post-ERCP pancreatitis (PEP) is seen in 7% of therapeutic ERCP cases. We have 30% idiopathic cases, 83% males, 17% females: median ages 43(males) and 34 (females). Our frequency of idiopathic cases matches that of 30% in published literature.[13] A meta-analysis found that cholecystectomy after an episode of idiopathic acute pancreatitis reduces the risk of recurrent pancreatitis, implying that current diagnostic approaches can label a biliary cause as idiopathic. Endoscopic ultrasonography (EUS) followed by MRCP with secretin administration is suggested to pick micro lithiasis and dynamic obstruction, respectively. Drug-induced pancreatitis (DIP) is suspected 4 to 8 weeks after initiation of a drug.[1] Its reported incidence is (<5%).[14] A study classified pancreatitis-causing drugs into four groups based upon latency (time from initiation to development of disease) and re-challenge (recurrence of disease after re-initiation of a drug).[15] Our higher frequency (7.5%) could be explained by our actively seeking out DIP or insufficient evidence in favour of other causes. No other study in our setup has categorized individual drugs as a cause of AP. In our study, Mesalamine and Valproic Acid belong to class-1a, while Azathioprine, Dexamethasone and Losartan are in class-1b. Distinguishing AIP from DIP in a case of inflammatory bowel disease (IBD) is difficult as stopping the drug on the presumed diagnosis of DIP can aggravate underlying IBD and/or AIP, and continuing it may predispose to further AP attacks in case it is DIP.[16] We introduced a hybrid category AIP/DIP, in uncertain cases. Western studies have favoured AIP over DIP in IBD cases with AP. In other studies, the risk of developing DIP due to azathioprine was higher in women than men and higher in those with Crohn's Disease (CD) than with Ulcerative colitis (UC).[17] Mesalamine-induced AP may occur from 2 days to 2 years after the start of mesalamine, with most cases occurring within six weeks.[18] Consistent with the literature, our cases were diagnosed with IBD when they developed AP.

Valproic acid was used in young males for epilepsy. One was on long-term treatment, while the other was on short-term treatment (<3 months). The former had been having recurrent pancreatitis for years without a definitive diagnosis despite extensive work-up. That underscores the need to consider DIP in AP cases. The drug was immediately stopped in both of them. AP in COVID-19 may be reported at the beginning or after several days of the disease. Usually, it is associated with pneumonia. All known etiological factors, including drugs used in COVID-19 disease, should be ruled out to recognize AP secondary to COVID-19. All the reported cases of COVID-19 pancreatitis developed acute pancreatitis or pancreatic injury in due course or during recovery from viral pneumonia.[19] Reports of steroid-induced DIP are very rare. There is 1 case report in the literature of dexamethasone-induced acute pancreatitis two days after administration of high-dose dexamethasone.[15] Dexamethasone DIP has short latency (<5 days), and COVID has undefined latency, so 2 of our cases probably had Post COVID pancreatitis, but more evidence is needed to establish exact causality.[20]

Our study showed two untypable AIP and one non-specific AIP (AIP-NOS) case with an overall frequency of 2.5%. Diagnosis is challenging because of the lack of standardized diagnostic criteria. It may progress rapidly to end-stage chronic pancreatitis and become indistinguishable from other chronic pancreatitis1. Our patient, a 42-year male, was under evaluation for recurrent unexplained attacks of AP for two years. He had an eosinophil count of 6% and a high IgE of 150IU/mL (<144). In contrast to a series of 3 cases published in the literature.[21] which presented with jaundice, our patient presented with recurrent episodes of abdominal pain. We suggest that absolute eosinophil count and serum IgE panel be added to the work-up algorithms for idiopathic AP cases. Pancreas divisum and choledochal cysts are rare causes of AP.

LIMITATIONS

It was an on-job resource and time-constrained study done during the COVID-19 pandemic. The absence of E-records made follow-up easier. The high turn-around time of IgG4 levels was an additional constraint. Autoimmune workup and tissue diagnosis for both autoimmune and neoplasm were not possible.

CONCLUSION

Consistent with international literature at our setup, gallstones are the commonest cause of acute pancreatitis, followed by idiopathic cases. However, we have a higher incidence of DIP and Hypertriglyceridemia and a lower incidence of AIP, alcohol-induced pancreatitis and tumours.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MFBH: Supervision, Conception, Study design, analysis and Interperitation of data, Critically reviewed manuscript & approval for the final version to be published.

IA & HZ: Co-supervision, Data entry, analysis and interpretation, manuscript writing & approval for the final version to be published.

MA: Critically reviewed, Drafted manuscript & approval for the final version to be published.

SZHS: Data colllection, Entry and analysis of data, preparation of rough draft & approval for the final version to be published.

FS: Data collection and entry & approval for the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investi-gated and resolved.

ACKNOWLEDGEMENTS

We thank Professor Farrukh Saeed, Principal of Army Medical College, Rawalpindi and Dr Muhammad Hafeez, Head of the Department of Gastroenterology.

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