ACUTE PANCREATITIS;
A COMPARATIVE STUDY TO ASSESS THE CLINICAL OUTCOME OF ACUTE PANCREATITIS IN RELATION WITH MAJOR ETIOLOGIES.

Anwar Hussain Abbasi[1], Shahab Abid[2]

1. MBBS, FCPS (Medicine)
   Assistant Professor
   Department of Medicine,
   Rawal Medical College,
   Rawal Institute of Health sciences,
   Islamabad.
2. MBBS, FCPS (Medicine, PhD
   Professor
   Department of Medicine
   The Aga Khan University Hospital,
   Karachi.

Correspondence Address:
Dr. Anwar Hussain Abbasi
Assistant Professor
Department of Medicine
Rawal Medical College,
RIHS, Lehtrar Road, Islamabad.
anwar30pk@yahoo.com

ABSTRACT... Objectives: To determine the clinical outcome of acute pancreatitis in relation with major etiologies (Gallstones, Alcohol, and Drugs). **Study Design:** Cross sectional hospital based study. **Setting:** Aga Khan University Hospital. **Period:** 16 years (from 1st January 2001 to 30th June 2016). **Methods:** All patients with acute pancreatitis admitted. Major risk factors of pancreatitis such as gallstones, alcohol, and drugs were evaluated and outcomes assessed for the development of complications and mortality. **Results:** We evaluated 3049 patients with acute pancreatitis, the causative agents found, 80.35% (N = 2450), followed by Alcohol 13.05% (N = 398) and drugs 6.59% (N = 201), respectively. Patients with alcohol abuse were relatively older 53.74 years compared to patients with gallstones 39.54 years and drugs induced 43.26 years AP. Among them, the overall complication rate was 5.05% (N = 155). The most common complication was development of sepsis 45.8% (N = 71) and the overall mortality rate observed was 0.91% (N = 28). **Conclusions:** Gall stones are the leading cause of acute pancreatitis while drugs are the rare cause, however in significant number of patients cause remained obscure. Based on the above results patients with drug induced pancreatitis have good outcome as compared to gall stones and alcohol induced acute pancreatitis, however further studies warranted.

Key words: Acute Pancreatitis, Major Etiologies, Prognosis, Pakistan.

INTRODUCTION

The burden of acute Pancreatitis (AP) is not lower and epidemiological studies observed its incidence is around 5 – 80 per person per 100,000 in a population. The prevalence of AP is quite variable throughout the world and even huge difference can be seen in different areas of a given country. Acute pancreatitis is an acute inflammatory disorder of the pancreas that involves the pancreas and peripancreatic tissues but can sometimes affect other organ system too. The rate of complication among these patients varies between 10% and 20% and if not treated immediately the mortality can rise up to 25% but most of the patients resolved spontaneously.[1,2] The most common causes of acute pancreatitis are gall stones and alcohol abuse, accounting for 70-80% of case. Other risk factors include hypertriglyceridemia, hypercalcemia, drugs, infections, trauma, post ERCP, tumors, pancreatic

divism, and some cases are also idiopathic.[3,4]

Drugs are considered to be the rare cause of acute pancreatitis. However 525 different drugs are listed in the World Health Organization (WHO) which may leads to AP. Many of them are widely used to treat highly prevalent diseases, the causality for many of these drugs remains elusive and causality of only 31 among 525 drugs was well established.[5] The determination of the incidence of drug induced pancreatitis is complicated as diagnosing drug induced pancreatitis is very difficult. Its incidence has been estimated between 0, 1-2% in some older studies but in more recent studies its incidence rose up to 5.3%.[6,7]

Determination of underlying etiologies which causes the development of acute pancreatitis is crucial and has a great importance on assessing

the prognosis at the time of presentation and during hospitalization. Different studies have documented the prognosis of acute pancreatitis patients in relation to underlying etiological factors; every study has shown different statistics in their region.[8,9] Developed countries like USA, UK, Japan, and china where alcohol consumption is higher than the developing countries are also linked to higher mortality rates in alcohol associated pancreatitis because chronic consumption of alcohol predispose the patients with liver cirrhosis and pancreatitis which affects the outcome in these patients and leads to poor prognosi. On the other hand, some of the studies also observed that pancreatitis caused by gallstones has more severe and insidious onset and is associated with higher mortality than alcohol induced AP. While, there are studies which has shown no difference among these two etiologies.[10-12] In Pakistan, no such study has been conducted till now with a larger sample size to observe the association between major etiological factors (Gallstones, Alcohol, and Drugs) on the outcome of patients with acute pancreatitis.

PATIENTS & METHODS
This cross sectional hospital based study was conducted at Aga Khan University Hospital, Karachi for a period of sixteen years (from 1st January 2001 to 30th June 2016) in all patients admitted in a gastroenterology unit and surgical unit as a diagnosed case of acute pancreatitis through a consecutive sampling technique. The Hospital Ethical Committee approved the study, and all the patients provided written informed consent.

All diagnosed admitted cases of acute pancreatitis with age more than 18 years of either gender managed conservatively or through surgical intervention were enrolled under this study. The diagnosis of acute pancreatitis was made based on patient's clinical presentation with abdominal symptoms and along with atleast 3-fold elevated levels of serum amylase or lipase.

The diagnosis of acute pancreatitis was made using multifactorial clinical scores (APACHE II

> 7; Glasgow-Imrie > 2; MODS > 2); and peak C-reactive protein value of >150 mg/L; and/or pancreatic necrosis of ≥30% as defined by contrast enhanced computed tomography (CECT) scan; and (5) alcoholic or biliary SAP. Patients reporting alcohol consumption shortly before the onset of symptoms, having no gallstones in the gallbladder or bile ducts as defined by abdominal ultrasound (US) and/or CT scan were included in the alcohol induced AP group, whereas patients with gallbladder and/or bile duct stones on abdominal US and/or CT scan, elevated serum bilirubin and/or liver enzymes, and no history of recent alcohol intake were included in the biliary AP group.

Statistical package for social science SPSS version 17 was used for data entry and final analysis. Frequencies and percentages were calculated for qualitative variables like age, risk factors of AP, and outcome of AP. Mean will be calculated for Quantitative variables like age and BMI.

RESULTS
A total of 3049 patients of acute pancreatitis were included in our study after meeting the inclusion and exclusion criteria. The overall frequency of three different etiological factors was mentioned in a Table-I. Gallstones was the most common cause of acute pancreatitis 80.35% (N = 2450), followed by Alcohol 13.05% (N = 398) and drugs 6.59% (N = 201), respectively. Patients with alcohol abuse were relatively older 53.74 years compared to patients with gallstones 39.54 years and drugs induced 43.26 years AP. The mean age and BMI of acute pancreatitis associated with different etiologies are mentioned in table number 1 along with other demographics.

When observing the co-morbid conditions, hypertension and diabetes were the most common co-morbid conditions in patients with gallstone induced and drug induced AP while prevalence of liver cirrhosis was relatively higher alcohol induced AP. The complete statistics in mentioned in Table-I.

The overall complication rate was 5.05% (N =

155). Figure-1 shows outcome of patients with different etiological factors. More than 96% of the patients recovered completely in patients with gallstone induced AP while more than 92 % of the patients with drug induced AP and more than 85% of the patients with alcohol induced AP recovered completely without any complication. The complication rate and the worst outcome were observed in patients with alcohol induced AP 9.79% and 4.02%, respectively. Amongst all patients with AP, the better outcome was observed in patients with drug induced AP. The overall mortality rate observed was 0.91% (N = 28). The most common complication was development of sepsis 45.8% (N = 71), shown in Figure-2.

DISCUSSION

Acute pancreatitis is a fascinating disease. In the Pakistan, the most common etiology of acute pancreatitis is gallstones and to some extent less common is excessive alcohol consumption while drug induced AP is rarely observed in daily routine practice.[11]

We have identified some differences between gallstones, alcoholic, and drug associated AP groups in terms of demographic characteristics, course, and outcomes. In the present study majority of patients with gallstones AP were females, whereas older males dominated in the alcoholic and drug induced AP group.

Variables	Gallstones	Alcohol	Drugs
	(n = 2450)	**(n = 398)**	**(n = 201)**
Age - Years			
Mean	39.54	53.74	43.26
Length of Stay - Mean	4.53	7.22	6.14
BMI - Kg/m2	26.44	24.12	24.18
Gender	**N (%)**	**N (%)**	**N (%)**
Male	858 (35.02)	351 (88.19)	112 (55.72)
Female	1592 (64.97)	47 (11.80)	89 (44.27)
Area of Residence	**N (%)**	**N (%)**	**N (%)**
Urban	1412 (57.63)	233 (58.54)	129 (64.17)
Rural	1038 (42.36)	165 (41.45)	72 (35.82)
Co-Morbid Conditions	**N (%)**	**N (%)**	**N (%)**
Hypertension	1090 (44.48)	144 (36.18)	113 (56.21)
Diabetes	1301 (53.10)	161 (40.45)	83 (41.29)
Liver Cirrhosis	59 (2.40)	93 (23.36)	5 (2.48)

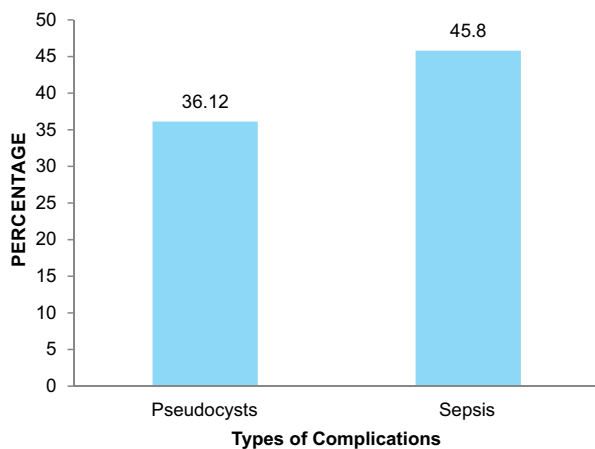**Table-I. Clinical characteristics of patients with acute pancreatitis (N = 3049)**

Figure-1. Types of complications observed in patietns with three major etiologies associated pancreatitis
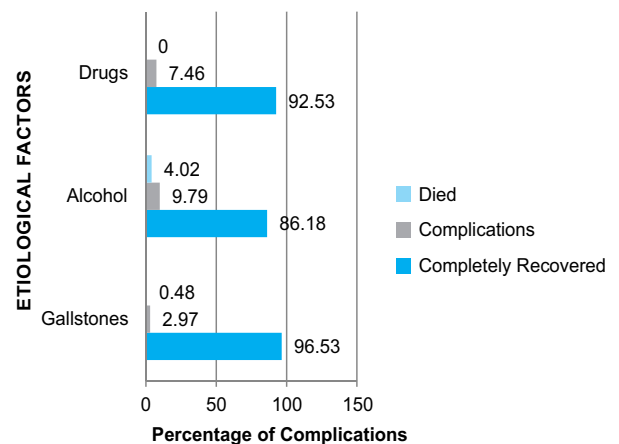

Figure-2. Overall outcome of acute pancreatitis patients in realtion to different etiolgies

These results are not consistent with data from the other studies showing which sows biliary and alcoholic AP is common in elderly women and in middle-aged men, respectively.[13,14] There are certain factors which may affect the overall incidence rate of AP based on the scientific differences like choosing of sampling technique & study design and other factors like social and cultural issues and facility available where the patients are being managed.

Our study demonstrated that, hypertension and diabetes were the most common co-morbid conditions in patients with gallstone induced and drug induced AP while prevalence of liver cirrhosis was relatively higher alcohol induced AP. On the other hand, larger scaled data also confirm that diabetic patients are two folds more prevalent than non diabetic patients. On the other hand, when comparing the BMI, there is no such increased in BMI among these three groups. The findings of our study are similar to the study conducted previously conducted international study.[15]

Besides etiological factors involved in causing acute pancreatitis is the development of underlying infection which initiates Systemic Inflammatory Response Syndrome (SIRS) which is a compensatory response starts soon after the development of acute pancreatitis by the action of inflammatory markers such as cytokines which progress and may lead to Multiple Organ Failure (MOF). If the patient is not managed properly this SIRS can convert into Sepsis after few days of operation that is why concerning physician and surgeon take this as a challenge and prevent the conversion of SIRS into Sepsis so that the prognosis of these patients can be improved. In our study the most common complication was development of sepsis.[12] In contrast to Sepsis, the development of Pseudocysts is comparatively less common and previously conducted studies mentioned its prevalence around 10% of patients with acute pancreatitis,[16] which is consistent with our study.

However, the data from the previously published literature has demonstrates the variability in hospitalization and outcome in acute pancreatitis patients.[17,18] Some of these studies are also unclear that which etiological factor is highly vulnerable in increased mortality and the mortality range during the early phase ranged between 0% to more than 80%.[19] The overall mortality rate observed in our study was quite lower than the study conducted previously in which the mortality rate was 5%[20] and in another study was 16%.[21]

CONCLUSION

Gall stones are the leading cause of acute pancreatitis while drugs are the rare cause, however in significant number of patients cause remained obscure. Based on the above results patients with drug induced pancreatitis have good outcome as compared to gall stones and alcohol induced acute pancreatitis, however further studies warranted.

Copyright© 15 Dec, 2018.

REFERENCES

1. Garg SK, Sarvepalli S, Campbell JP, Obaitan I, Singh D, Bazerbachi F, et al. **Incidence, admission rates, and predictors, and economic burden of adult emergency visits for acute pancreatitis: Data from the national emergency department sample, 2006 to 2012.** J Clin Gastroenterol 2018 Apr 6.

2. Abu-El-Haija M, El-Dika S, Hinton A, Conwell DL. **Acute pancreatitis admission trends: A national estimate through the kids' inpatient database.** J Pediatr 2018 Mar; 194:147-51.

3. Munigala S, Subramaniam D, Subramaniam DP, Buchanan P, Xian H, Burroughs T, et al. **Predictors for early readmission in acute pancreatitis (AP) in the United States (US) - A nationwide population based study.** Pancreatology 2017 Jul; 17(4):534-42.

4. Uc A, Fishman DS. **Pancreatic disorders.** Pediatr Clin North Am 2017 Jun; 64(3):685-706.

5. Baxter KA, Pucher PH, Berry DP, Elberm H, Abu-Hilal M, Marangoni G, et al. **The effect of non-steroidal anti-inflammatory drugs on severity of acute pancreatitis and pancreatic necrosis.** Ann R Coll Surg Engl 2018 Mar; 100(3):199-202.

6. Kumar S, Ooi CY, Werlin S, Abu-El-Haija M, Barth B, Bellin MD, et al. **Risk factors associated with pediatric acute recurrent and chronic pancreatitis: Lessons from INSPPIRE.** JAMA Pediatr 2016 Jun 1; 170(6):562-9.

7. Pant C, Sferra TJ. **Emergency department visits and hospitalizations in children with chronic pancreatitis in the United States.** J Pediatr Gastroenterol Nutr 2015 Nov; 61(5):568-70.

8. Malli A, Li F, Conwell DL, Cruz-Monserrate Z, Hussan H, Krishna SG. **The burden of systemic adiposity on pancreatic disease: Acute pancreatitis, non-alcoholic fatty pancreas disease, and pancreatic cancer.** JOP 2017; 18(5):365-8.

9. Ho UC, Mu CF, Hsu CY. **Ethnic differences in risk factors of acute pancreatitis.** Ethn Health 2018 Apr; 23(3):321-8.

10. Bonfrate L, Wang DQ, Garruti G, Portincasa P. **Obesity and the risk and prognosis of gallstone disease and pancreatitis.** Best Pract Res Clin Gastroenterol 2014 Aug; 28(4):623-35.

11. McNabb-Baltar J, Ravi P, Isabwe GA, Suleiman SL, Yaghoobi M, Trinh QD, et al. **A population-based assessment of the burden of acute pancreatitis in the United States.** Pancreas 2014 Jul; 43(5):687-91.

12. Spanier B, Bruno MJ, Dijkgraaf MG. **Incidence and mortality of acute and chronic pancreatitis in the Netherlands: A nationwide record-linked cohort study for the years 1995-2005.** World J Gastroenterol 2013 May 28; 19(20):3018-26.

13. Frossard JL, Steer ML, Pastor CM. **Acute pancreatitis.** Lancet 2008 Jan 12; 371(9607):143-52.

14. Yadav D, Lowenfels AB. **The epidemiology of pancreatitis and pancreatic cancer.** Gastroenterology 2013 Jun; 144(6):1252-61.

15. Kim DB, Chung WC, Lee JM, Lee KM, Oh JH, Jeon EJ. **Analysis of factors associated with the severity of acute pancreatitis according to etiology.** Gastroenterol Res Pract 2017; 2017:1219464.

16. Zhang HR, Lei JQ, Lu XR, Yang YF, Liu F. **[Acute pancreatitis complicated with retino-choroidal disease--long-term follow-up study of a case].** Zhonghua Yan Ke Za Zhi 2004 Jul; 40(7):487-9.

17. Mutinga M, Rosenbluth A, Tenner SM, Odze RR, Sica GT, Banks PA. **Does mortality occur early or late in acute pancreatitis?** Int J Pancreatol 2000 Oct; 28(2):91-5.

18. Gloor B, Muller CA, Worni M, Martignoni ME, Uhl W, Buchler MW. **Late mortality in patients with severe acute pancreatitis.** Br J Surg 2001 Jul; 88(7):975-9.

19. Renner IG, Savage WT, III, Pantoja JL, Renner VJ. **Death due to acute pancreatitis. A retrospective analysis of 405 autopsy cases.** Dig Dis Sci 1985 Oct; 30(10):1005-18.

20. Satoh K, Shimosegawa T, Masamune A, Hirota M, Kikuta K, Kihara Y, et al. **Nationwide epidemiological survey of acute pancreatitis in Japan.** Pancreas 2011 May; 40(4):503-7.

21. Wei AL, Guo Q, Wang MJ, Hu WM, Zhang ZD. **Early complications after interventions in patients with acute pancreatitis.** World J Gastroenterol 2016 Mar 7; 22(9):2828-36.

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Anwar Hussain Abbasi	Concept, Data collection, Data Analysis, Discussion.	
2	Shahab Abid	Data analysis, Discussion, Conclusion.	