



## Acute pancreatitis: Demographics, aetiological factors and outcomes

### KEYWORDS

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**ABSTRACT** Background-Acute pancreatitis is a broad spectrum diseases, which vary from parenchymal edema to necrosis. We report our experience of spectrum of aetiologies and outcomes of acute pancreatitis.

*Patients and methods.* Prospective data of patients with acute pancreatitis during June 2011 – December 2014. The causes, complications and mortality rate of the pancreatitis were noted.

*Results.* From June 2011 – December 2014, there were 282 patients with acute pancreatitis- 94 females and 188 males. Median age was 37 years. Episodes of pancreatitis were associated with alcohol consumption in 62% of cases and with gallstones in 14%; 4% with both gallstones and alcohol consumption, 8% with dyslipidaemia and 5% with retroviral disease. 9% of admissions ended in death of the patient.

*Conclusions.* Alcohol was the main cause of pancreatitis. Outcomes in this series are similar to Western studies except that the majority of deaths occurred early, implying that improved supportive care may improve survival.

### Introduction-

Acute pancreatitis (AP) is a common acute medical condition requiring emergent care. Yet, no prevalence data are available from India. Only some idea of incidence can be obtained from patients admitted in tertiary care centers. At the All India Institute of Medical Sciences (AIIMS), New Delhi, 276 patients with AP were hospitalized from January 1997 to June 2002, i.e. about 55 patients per year. This is about the same as in similar centers in England. The incidence of AP has, however, been reported to be much higher in USA, Finland and Scotland (49.3, 46.6 and 41.9 per 100,000 population, respectively)<sup>1</sup> Furthermore, it has been noted that the incidence of AP has been steadily rising during the last decade in European countries<sup>2</sup> and UK.<sup>3</sup> Gallstones and alcohol are the most common causes of AP, gallstones being about twice as common as alcohol in our population. Other causes include hypertriglyceridemia, hypercalcemia, post endoscopic retrograde cholangiopancreatography (ERCP) and drug-induced pancreatitis, but they are much less common. Since the morbidity and mortality of AP differ markedly between mild and severe disease (mild < 5% vs severe 20–25%), it is very important to assess severity as early as possible. Multiple clinical criteria, biochemical parameters and imaging criteria have been used for this purpose.

We prospectively investigated the hospital prevalence, aetiology, disease severity and outcomes of pancreatitis in SKN Medical college and General hospital.

### Patients and methods

During the period June 2011 – December 2014 data were prospectively collected on all admissions of patients to SKN Medical college & General hospital with a diagnosis of pancreatitis.

The diagnosis was established by clinical presentation, together with an elevated serum amylase level (at least twice the upper limit of normal\*) or an elevated urine amylase level >760 U/l.<sup>4</sup> Imaging by ultrasound or computed tomography scan was used as a confirmatory or primary diagnostic investigation where indicated. The pancreatitis was considered to be idiopathic when a cause was not ap-

parent after initial screening.

All patients were assessed using the Glasgow criteria.<sup>5</sup> Organ dysfunction (Atlanta criteria)<sup>6</sup> was evidenced by the presence of shock (systolic blood pressure <90 mmHg), pulmonary dysfunction (PaO<sub>2</sub> <60 mmHg), renal failure (creatinine level >174 μmol/l) or gastrointestinal bleeding (>500 ml/h). A CT scan was an additional diagnostic modality in patients judged to have severe disease, to diagnose and quantify pancreatic necrosis.<sup>7,8</sup> Lipid assays were performed routinely. Patients with pancreatic necrosis and requiring organ support were given piperacillin-tazobactam combination.

The number of patients requiring intensive care unit admission, the duration of ICU and hospital stay, the development of complications and the number of deaths were noted.

### Statistical analysis

Descriptive statistics were used to determine the characteristics of the cohort. These were stated as mean values and range.

### Results

From June 2011 – December 2014, there were 322 admissions (1% of total admissions to the general surgical wards in the same period) of 282 patients with a diagnosis of acute pancreatitis, of whom 94 were female and 188 male. The median age of the patients was 37 years (range 13 - 73 years) and the median hospital stay was 6 days (range 1 - 123 days).

The median serum amylase level was 676 U/l (range 25 - 11 144 U/l) and the amylase level reached the diagnostic cut-off level in 252 admissions (78%). In 53 admissions (16%) an elevated urine amylase level supported the diagnosis where the serum amylase was normal or marginally elevated. In 6 patients with markedly elevated triglycerides and normal or unmeasurable serum or urine amylase. The clinical presentation and the dyslipidaemia were considered supportive of the diagnosis. In 4 patients the diagno-

sis was established at laparotomy. In 2 patients with an elevated amylase level ischaemic bowel was suspected, but in the other 2 the diagnosis was not suspected preoperatively. Ultrasound and CT scan were the sole confirmatory investigations in 7 cases.

The aetiological associations are set out in Table I.

**Table I. Spectrum of aetiologies, ethnic distribution and mortality**

Aetiology	No. (%)	Female	Male	Deaths (%)
Alcohol	198 (61.5)	15	183	15 (7.6)
Gallstones	44 (13.7)	35	9	4 (9.1)
Alcohol/gallstones	14 (4.3)	8	6	4 (28.5)
Idiopathic	21 (6.5)	9	12	1 (4.7)
Dyslipidaemia	26 (8.1)	22	4	3 (11.5)
Retroviral disease	16 (5.0)	13	3	1 (6.3)
Other	3	3	0	0
Total	322	105	217	28 (8.7)

Alcohol and gallstones were the main factors associated with pancreatitis. Sixteen patients were known to have HIV infection. One of these had a possible alcohol association, and in 8 patients on antiretroviral therapy with didanosine and stavudine these drugs were thought to be responsible for the pancreatitis. In the remainder the cause was uncertain. Primary hyperparathyroidism and hereditary spherocytosis accounted for a single case each.

Of the 44 patients with gallstone-related pancreatitis and the 14 with gallstones and alcohol consumption as probable causes, 42 had cholecystectomy within 30 days of the admission, 2 refused surgery and 1 had had a previous cholecystectomy. The others did not honour appointments for cholecystectomy at 6 weeks. Seventeen had endoscopic retrograde cholangiopancreatography-14 for jaundice, 2 for persistent symptoms and 1, who had proven choledocholithiasis during advanced pregnancy. Five patients with pancreatitis associated with gallstones and no jaundice died. ERCP was not performed in any of these patients. Complete assessment using a modified Glasgow Score of 8 criteria was done in 301 of the 322 admissions (93%). The proportions of patients assessed as having severe disease according to the Glasgow criteria and the organ failure criteria of disease severity were similar (Table II).

**Table II. Comparison of severity scores as predictors of outcome in representative series**

Author	Year	No.	Sensitivity	Specificity	PPV	NPV
Glasgow Score						
Larvin <sup>24</sup>	1989	290	61	89	59	90
Wilson et al. <sup>25</sup>	1990	160	71	88	66	91
Tran and Cuesta <sup>26</sup>	1992	259	58	89	68	84
Taylor et al. <sup>27</sup>	2005	49	64	73	67	70
This series	2014	322	57	92	31	94
Organ failure						
This series	2014	322	57	88	31	96

PPV = positive predictive value; NPV = negative predictive value

Of the patients 34 (11%) were admitted to the intensive care unit; 21 of them died, in all of whom the Glasgow criteria had predicted severe disease. The range of stay in the ICU was 1 - 23 days. Seven patients died without ICU admission. The Glasgow criteria had predicted mild disease in 5 of these patients and severe disease in 2. Unfortunately a bed in the ICU was not available in the latter 2 cases. Thirty-three (32%) of the 102 patients who had CT scan assessment had pancreatic necrosis. One was managed with percutaneous drainage and another with open

surgery and lavage. In the other 31 management was expectant as infection of pancreatic necrosis was not established. Ten of these patients developed pseudocysts, 4 a pancreatic abscess and 7 died. Forty-nine patients (15%) developed local complications. Pseudocysts occurred in 29 (9%). Ten had spontaneous resolution, 7 were managed expectantly and 7 were lost to follow-up. Four were drained by endoscopic means and 1 had spontaneous drainage into the duodenum.

Four patients (1%) developed an abscess. Two were successfully treated by percutaneous drainage and open drainage with lavage, but in the other 2 percutaneous drainage resulted in colonic fistula and subsequent death. Transient obstructive jaundice (21 cases, 7%), gastric outlet obstruction (10, 3%) and haemorrhage (3, 1%) resolved with supportive therapy. Portal hypertension developed in 1 case

(0.3%) as a consequence of portal vein thrombosis and a pseudocyst in the region of the head of the pancreas. This resolved after transduodenal endoscopic cyst drainage. There were 28 deaths, of which 71% occurred within 2 weeks. Assessment of severity using the Glasgow Score and organ failure severity assessment score predicted mild disease in 11 of the deaths. The distribution of the deaths according to aetiology is set out in Table I. Dyslipidaemia and a dual aetiology of alcohol and gallstones were associated with the highest proportions of deaths.

## Discussion

Internationally the incidence of pancreatitis is rising. In 1987 there were 108 000 admissions in the USA (excluding Veterans Affairs hospitals), with 2251 death<sup>9</sup>. More recently in a 2006 report this had more than doubled to 220 000 admissions<sup>10</sup>. In the UK a rising incidence by a factor of 10 has been noted from the 1960s to the 1980s, but there is still a wide regional variation from 150 to 420 cases per million population<sup>11,12</sup>. In this cohort alcohol was implicated in two-thirds of the admissions and gallstones in 17%, while 5% were deemed idiopathic (Table I). Table II shows the variation in the aetiologies of acute pancreatitis in US, European and South African settings. In general, Western cohorts have a significantly higher prevalence of gallstone aetiology. Patients were not routinely counselled for HIV testing, so only those with known disease were identified. Pancreatitis in patients infected with HIV is most frequently associated with antiretroviral medication and with opportunistic pancreatic infections<sup>13-16</sup>. In this series over half the patients were receiving treatment but none were identified with pancreatic infection. Outcomes have been found to be similar to non- HIV-related pancreatitis<sup>16</sup> and our limited data support this observation. However, pancreatitis has been shown to be associated with an increasing proportion of deaths in patients on highly active antiretroviral therapy (HAART)<sup>17</sup>. HAART has been associated with the development of pancreatitis. The antiretroviral drug most frequently associated with pancreatitis is didanosine, an adenosine analogue<sup>13,15</sup>. Ritonavir, a protease inhibitor, has been associated with severe hypertriglyceridaemia and pancreatitis.<sup>18</sup> Pentamidine, an aromatic diamidine used in the treatment and prophylaxis of *Pneumocystis carinii* pneumonia, also causes pancreatitis by a direct toxic effect.<sup>13</sup>

In view of the over 30% prevalence of HIV in surgical patients in some studies<sup>19</sup> it is important that details of HAART therapy are obtained. HAART can then be modified to reduce the risk of subsequent pancreatitis. Hypercalcaemia is rare, as our single case illustrates, but worth investigating because although primary hyperparathy-

roidism is identified in less than 1 in 400 cases, treatment will be curative for both conditions.<sup>20</sup> In the diagnostic work-up of acute pancreatitis an elevated amylase level is nonspecific as it may be raised in a number of acute abdominal conditions. Thomson *et al.*<sup>12</sup> performed

laparotomies in 7 patients (2%) because of diagnostic doubt. In the present series laparotomy confirmed the diagnosis in 4 cases (1%), ultrasound in 4 (1%) and CT scan in 3 (1%). Of Thomson *et al.*'s series of 378 patients<sup>12</sup> 26 (7%) developed pseudocysts and 11 (3%) pancreatic abscesses, figures similar to the present series, in which we found 29 (9%) pseudocysts and 4 (1%) pancreatic abscesses.

### Mortality

The ability of the Glasgow Score and organ failure severity assessment score to predict severe disease in a number of series is set out in Table II. Figures for the Glasgow Score in the different studies are similar. The specificity is generally in the upper 80s, but sensitivity, i.e. the ability to detect all those with severe disease, is much lower. It was disappoint-

ing that the organ failure severity assessment score did not improve on the sensitivity. These indices are ineffective as clinical management tools because they do not accurately select patients for monitoring in a high-care unit. They are more useful for epidemiological comparison. The mortality rate of 9% in this series is comparable to the mortality reported in some of the cited references.<sup>21-23</sup> Thomson *et al.*<sup>12</sup> reported a mortality of 15%, although only half of the deaths were thought to be directly related to complications of pancreatitis. The mortality due to gallstones

at 9% is comparable to another series, which showed a mortality rate of 6%.<sup>23</sup> The proportions of early and late deaths (with 2 weeks as the cut-off point) in different series are set out in Table III. A larger proportion of patients in this series died early, from systemic inflammatory response syndrome and multiple organ dysfunction syndrome, than in almost any other series. It is interesting to note that 7 of the patients who died early were not admitted to the ICU for monitoring. This again illustrates lack of an effective tool with which to predict the need for ICU admission.

**Table III. Comparison of the frequency of aetiologies, complications and deaths in representative series**

Author	Origin	Number	Alcohol	Gallstones	Idiopathic	Local complications	Mortality		
							Total	Early <2 wks	Late >2wks
Ashley <i>et al.</i> <sup>28</sup>	USA	1 110	NS	NS	NS	NS	2%	29%	71%
Mann <i>et al.</i> <sup>22</sup>	England	631	30%	29%	NS	NS	9%	44%	56%
Toh <i>et al.</i> <sup>23</sup>	England	186	20%	33%	32%	15%	9%	NS	NS
Mofidi <i>et al.</i> <sup>29</sup>	Scotland	759	33%	47%	13%	14%	6%	31%	69%
Thomson <i>et al.</i> <sup>12</sup>	Scotland	378	15%	41%	20%	9%	8%	NS	NS
Carnovale <i>et al.</i> <sup>30</sup>	Italy	1135	6.5%	68.7%	12.3%	NS	5%	51%	49%
Ricci <i>et al.</i> <sup>31</sup>	Italy	125	12%	76%	0%	NS	4%	NS	NS
John <i>et al.</i> <sup>3</sup>	S Africa	136	83%	7%	7%	10%	8%	NS	NS
Funnell <i>et al.</i> <sup>2</sup>	S Africa	99	74%	14%	7%	NS	13%	NS	NS
This series	India	322	62%	14%	7%	16%	9%	79%	21%

### Conclusion

This series reaffirms that alcohol is the major factor associated with acute pancreatitis followed by gallstone in Indian context. It needs to be kept in mind that both HIV and HAART are possible aetiological factors, as the latter can be altered to reduce the risk. Severity indices are poor

practical management tools owing to their low sensitivity. The mortality rate is similar to norms elsewhere, but the majority of deaths occur in the first 2 weeks. Improved selection for and availability of early supportive management have the potential to reduce mortality

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