ACUTE PANCREATITIS IN NORTH-EASTERN PENINSULAR MALAYSIA: AN UNUSUAL DEMOGRAPHIC AND AETIOLOGICAL PATTERN

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ABSTRACT

A survey of 142 cases of acute pancreatitis was undertaken in two major hospitals serving the state of Kelantan in Malaysia. Females outnumbered males by a ratio of more than 3:1. The incidence among females peaked in the third decade of life. Twenty-one percent (23/109) of the females were pregnant. Ultrasonography revealed gallstones in only 9.4% (13/138). However, abnormalities of serum transaminases were found in 35% (35/100), suggesting that occult gallstones or microlithiasis may be the cause in a significant proportion of patients. Alcohol was virtually absent as an aetiological factor. There was a higher frequency of Ascaris infection in this group than a control hospital population (11/35 vs 33/242; p<0.02) suggesting that ascariasis may be an important cause of acute pancreatitis in Kelantan. Only 8.4% fell into the category of severe pancreatitis. The overall mortality rate was 2.1%.

Keywords: *acute pancreatitis, Malaysia, ascariasis, occult gallstones, pregnant.*

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INTRODUCTION

Most standard textbooks state that the incidence of acute pancreatitis peaks between the fifth and seventh decades of life, and that the two most common causes are gallstones and alcohol[1,2]. Although many other aetiological agents are recognised such as hyperparathyroidism, severe hypertriglyceridaemia, drugs, viruses and ascariasis; these are generally thought to account for only a minority of cases[1-9]. We have observed in the course of our clinical practice in Kelantan that the demographic and aetiological pattern of the disease differ in many respects from the standard textbook description. Kelantan is a state of 1.2 million people in North-eastern Peninsular Malaysia, comprising predominantly of a rural Muslim Malay population. The aim of this study was to describe the demographic, aetiological and clinical pattern of acute pancreatitis in the state.

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METHODS AND PATIENTS

This study was jointly conducted at the Universiti Sains Malaysia (USM) Teaching Hospital and Kota Bharu General Hospital, the two largest hospitals in Kelantan. The study began with a retrospective survey of patients with acute pancreatitis admitted to USM hospital between March 1987 and September 1990. Retrieval of case records was facilitated by the fact that the diagnosis of all admissions are recorded on computer. To eliminate the possibility of obtaining a false picture due to discrepancies in referral patterns, a prospective study was then undertaken involving both hospitals between October 1990 and March 1992. This had the twin advantage of providing a more representative sample of patients with acute pancreatitis and allowing larger numbers to be studied over a short period. The diagnosis of acute pancreatitis was made on the grounds of a compatible clinical picture and raised serum amylase. The level of serum amylase which is generally accepted as diagnostic is four times the upper limit of the normal range[10-13]. Serum amylase in the two participating hospitals was measured using two different commercially available kits (Abbott and Bio Merieux), with a variation of 45 i.u./l in the upper limit of the normal range. In order to ensure that all patients studied had true pancreatitis, a cut-off point of 500 i.u./l was taken as diagnostic. This level was more than 4 times the upper limit of normal at both hospitals. The diagnosis of acute pancreatitis in the retrospective group was critically reappraised. As much information as possible was obtained from the history and investigations pertaining to aetiology. The eventual clinical outcome was recorded as severe or non-severe using previously described criteria[8].

The main imaging modality of the gallbladder and biliary tree was abdominal sonography. If the gallbladder was not visualised, the examination was recorded as inadequate. Abnormalities of early liver function tests (LFTs within 48 hours) were recorded; as elevated transaminases have been reported to have a positive predictive value in the order of 80-90% in predicting the subsequent detection of gallstones in patients

presenting with acute pancreatitis[11,13,14-17]. An indirect assessment of the importance of ascariasis in our area was made by making a comparison between the rate of ascaris infection in patients with pancreatitis and the infection rate in a control group of patients admitted to an internal medicine ward at USM hospital. The latter group was part of a previously published study[18] done in 1989-1990 and served as a control. Serology for enterovirus was done using a complement fixation test[19] (Behringwerke AG, Germany) which detects antibodies to Coxsackie virus B1, B2, B3 and A3; as well as ECHO virus 4, 6, 9, 12, 14, 24 and 30. Serology done on a single blood sample taken during admission was considered significant if the titres exceeded 1:100[20].

Statistical methods

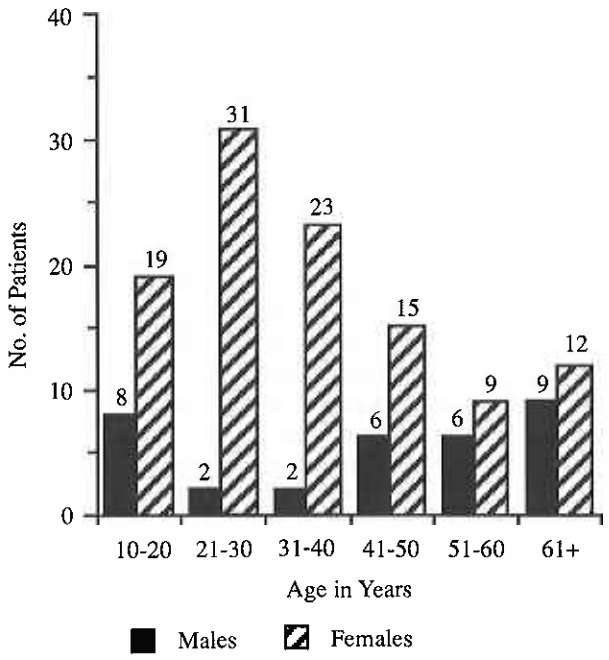
The x^2 test was used to detect differences in proportions between the two groups and a p value of less than 0.05 was taken as significant.

RESULTS

Demographic characteristics

There were 142 patients in the series of which 52 were in the retrospective cohort and 109 (77%) were female. The age distribution is shown in Fig 1. The median age was 35 years (range 10 - 76 years). Sixty percent of the patients were below the age of 40 years. Twenty-one percent (23/109) of the female patients were either pregnant or in the immediate post-partum period. Ninety-six percent (136/142) of the group were Malays and the rest were Chinese.

Fig 1 – Age distribution of the patient population



Biochemistry

Serum lipids were done on 102 patients; only one of whom had severe hypertriglyceridaemia due to a rare inborn error of metabolism (Apo C II deficiency). Serum calcium was measured in all but 11 patients and was not elevated in any patient. Serum transaminase levels at index admission were available in 100 patients. Thirty-five percent (35/100) of these patients had a serum alanine transaminase (ALT) or aspartate transaminase (AST) of greater than 60 iu/l; median ALT being 151 iu/l (range 62 - 1848 iu/l) and median AST being 177 iu/l (range 70 – 1606 iu/l). Forty percent (8/20) of the pregnant patients whose LFTs were checked had an ALT/AST of greater than 60 iu/l; median ALT being 135 iu/l (range 72 - 223 iu/l) and median AST being 115 iu/l (range 77 - 151 iu/l).

Imaging

Satisfactory ultrasonographic studies were done on 138 patients and gallstones were detected in 9.4% (13/138). Two patients were subjected to endoscopic retrograde cholangiopancreatography (ERCP). An Ascaris worm was detected in the common bile duct on ERCP in one of these patients.

Infection with *Ascaris Lumbricoides*

Stool specimens were examined for Ascaris ova in 135 patients (25%) and found to be positive in 11 patients. Twelve other patients (3 stool negative, 9 stool not examined) gave a history of having recently vomited or passed Ascaris worms. It was noted that a substantial number of patients had not been specifically questioned about Ascaris worms. Of the 35 patients whose stools were examined for Ascaris ova, only 6 had given a history of having vomited or passed worms. In at least one patient the history of vomiting worms was obtained only after a stool specimen was examined. This indicates that there was unlikely to have been a bias towards examining the stool only in patients with a positive history of having expelled worms. The stool positive rate of 31% (11/35) in this group was significantly higher than the 14% (33/242) stool positive rate in the control group of patients admitted to the internal medicine wards ($p<0.02$)[18].

Alcohol and drug ingestion

Alcohol was incriminated as the aetiological agent in only 2 patients. One patient was on the oral contraceptive pill. Two patients were being treated for lymphoma with steroids and chemotherapy.

Enterovirus serology

Twenty-two sera (15%) were tested. None showed significant titres.

Clinical course and outcome

Three patients died within 72 hours of admission. One of these patients developed pancreatitis after admission during the course of a septicaemic illness. The other 2 deaths were directly caused by acute pancreatitis, one of whom developed circulatory collapse and died within 10 hours of admission; the other developed acute respiratory distress syndrome (ARDS) and died in the intensive care unit. Four patients developed respiratory distress with associated pleural effusions but settled on oxygen therapy administered by face mask and did not require mechanical ventilation. Three other patients developed transient hypotension (systolic blood pressure below 100 mg Hg) early in the course of hospital stay which responded to conservative measures. One patient was readmitted with septicaemia a few days after discharge. Pseudocysts were detected in 2 patients, none of whom required surgical intervention. Indeed, no patient underwent surgery either for complications during the acute attack or for late complications. Apart from the patients who died, 5 patients were hospitalised for more than 20 days. In 2 of these patients the prolonged hospital stay was for reasons other than acute pancreatitis (ie chemotherapy in one case, obstructive uropathy and paraplegia in the other). In total, 12 patients (8.4%) were classified as having suffered severe pancreatitis. Although only 4 patients had documented evidence of having been admitted to either hospital with recurrent episodes, 22 other patients gave a history of previous bouts of similar pain suggestive of past

attacks.

DISCUSSION

The marked female preponderance and younger age distribution are unusual features. The ethnic composition is a reflection of the population of Kelantan. The low incidence of alcoholic pancreatitis reflects the low consumption of alcohol in this predominantly Muslim community. Despite the fact that ultrasound was performed by trained radiologists and examinations were repeated if the gallbladder was not at first visible, stones were detected in only 9.5% of cases. If the gallbladder is visible, ultrasonography is reported to be 90% accurate in detecting gallstones[21,22]. Abnormalities of LFTs described as markers of gallstones in patients with acute pancreatitis[15] were found in 35% of our cases; a figure which is higher than the 9.5% with ultrasonographically visible gallstones. One explanation is that many patients in our study may harbour biliary microliths which are now thought to be the aetiological agent in cases previously regarded as idiopathic[12,13]. Pregnant females were overrepresented in this study. Biliary sludge which occurs more commonly in pregnancy[23-25] may be the aetiological link between pregnancy and pancreatitis. Thirty percent (11/35) of patients whose stool specimens were examined for Ascaris ova were positive. Another 12 patients gave a history of having vomited or passed Ascaris worms; a probable underestimate as many patients were not specifically questioned about Ascaris infection. Although stool examination for Ascaris eggs was built into the protocol of the prospective study, results were not available for many patients, largely because of poor patient compliance in providing stool samples and the logistic problems arising as a result of the shortage in nursing staff, a problem afflicting many hospitals in the country. Notwithstanding, the 35 patients whose stool samples were examined were probably representative of the whole group. It is unlikely that there was a bias towards selecting for stool examination those who gave a positive history of having expelled worms. This is supported by the fact that of the 35 patients only 6 gave a history of having passed worms. The pancreatitis group had a higher stool positive rate than the control group which represented a sample of a hospital population of comparable age[8]. Although the sex ratio of the control group[8] was equal unlike the study group, the infection rates among women and men within the control population was the same, indicating that infection rates in our population at least appear to be independent of sex. Eosinophil counts as surrogate markers of worm infection were not done as they are not specific for ascariasis, especially in an area like ours which has a high prevalence of mixed worm infections. Although ascariasis has long been reported as a cause of acute pancreatitis, the evidence is derived largely from case reports and small series[26-31], the exception being a large series from Kashmir, India[32]. Our observations provide further indirect evidence that Ascariasis may be an important cause of acute pancreatitis in endemic areas. The presumed mechanism of Ascaris-induced pancreatitis is migration of the worm into the bile duct causing temporary obstruction at the sphincter of Oddi[33]. It is noteworthy that one of the two patients subjected to ERCP had an Ascaris worm in the bile duct. Drugs known to cause acute pancreatitis were detected in only a minority of our cases. The low frequency of the use of the oral contraceptive pill (a known cause of acute pancreatitis) is consistent with the prevailing religious and cultural beliefs. Coxsackie virus does not seem to be an important aetiological agent in our area, although the number of patients tested were relatively small. Viral serology should ideally have been done on paired sera. However complement fixing antibodies usually reach high titres in an acute infection[20], and none of the patients who were tested attained such levels. The 8.4% rate of severe pancreatitis is somewhat lower than that reported in the West and in Hong Kong[8,9] suggesting that the disease tends to follow a more benign course here. A potential pitfall however is that severe cases may present with a variety of systemic manifestations resulting in underdiagnosis[34].

In summary, acute pancreatitis in Kelantan has a strikingly different demographic and aetiological pattern as compared to that described in the standard textbooks. Investigation for Ascaris should be considered in any patient presenting with acute pancreatitis in an endemic area. It behoves the clinician dealing with acute pancreatitis to be wary of occult gallstones even if initial ultrasonography does not reveal stones. A diligent search for gallstones by repeated ultrasonography and/or ERCP is probably merited. There may be as yet unidentified aetiological agents which are operational in our area.

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