

Chapter 8

**Profile of chronic pancreatitis in North Kerala –  
A retrospective descriptive study**

Varghese Thomas, Harish K

## **Summary**

*Chronic calcific pancreatitis is a disease initially described in the middle and southern parts of Kerala. We describe our experience with chronic pancreatitis from North Kerala. Pain was the commonest presenting symptom. A minority, nevertheless a significant proportion (29%) of our subjects, consumed cassava. Recurrent hypoglycemia was the most common metabolic complication in these subjects. We also suggest that further studies be conducted to determine the link between chronic pancreatitis and low intake of vegetables/fruits.*

## **Introduction**

In Kerala, chronic calcific pancreatitis (CCP) has been considered as a disease of middle and southern parts of the state. There are only a few cases of chronic pancreatitis described from north Kerala so far. The present study aims to present the epidemiological and clinical data of patients with CCP seen in a tertiary care in north Kerala over the past two decades.

## **Materials and methods**

Patients with chronic pancreatitis who were attending the departments of gastroenterology, medicine, surgery and the diabetic clinic of Medical College, Calicut were included in the study for a period from 1982-2004. Chronic calcific pancreatitis is defined for the purpose of this study as any patient with radiological / ultrasonologic/ CT scan/ ERCP evidence of pancreatic parenchymal calcification or ductal calcification. Inclusion criteria: Patients above the age of 12 years with chronic calcific pancreatitis (patient with radiological / ultrasonologic/ CT scan/ ERCP evidence of either pancreatic parenchymal or ductal calcification.).

## **Exclusion criteria**

Definite evidence of hyperparathyroidism, patients with pancreatic diabetes without evidence of pancreatic calcification and definite evidence of hereditary pancreatitis. Subjects and sample size: 230 patients above the age of 12 years seen in outpatient and inpatient departments of gastroenterology, medicine, surgery and the diabetic clinic of Medical College Hospital, Calicut during the study period November 1982 to November 2004 with a diagnosis of chronic calcific

pancreatitis were included in this study. The study on profile of patients with chronic pancreatitis was a departmental objective from 1982 onwards and a standard proforma was used to collect data whenever a patient with chronic pancreatitis was seen by any member of the department. All demographic, clinical and investigation details were entered in the proforma and periodically updated as and when patients returned to our department. Between May 1996 and April 1998, the diet history a group of 31 patients were studied in detail with special reference to cassava intake. Tropical calcific pancreatitis (TCP) was diagnosed only after exclusion of indulgence in alcohol. Alcoholic chronic pancreatitis (ACP) was diagnosed in patients having a long history of significant alcohol consumption either on a daily basis or several times per week (exceeding 80g/day).

## Results

### General observations

A total of 230 patients with chronic calcific pancreatitis were included in this study. Two hundred and seven patients satisfied the criteria for inclusion in the TCP group. The geographical location of these patients is given in Table 1. The age, sex and religion wise distribution of patients with chronic pancreatitis is given in Table 2. Tables 3 to 5 describe the clinical, radiological and calculi-related features of the patients.

**Table 1: Geographical location**

District	Number	(%)
Kozhikode-urban	27	13
Kozhikode-rural	74	35.7
Malappuram	45	21.7
Kannur	21	10
Palakkad	12	5.8
Thrissur	6	2.9
Wyanad	6	2.9
Kottayam	4	1.9
Kasargod	3	1.4
Miscellaneous	9	4.3
<b>Total</b>	<b>207</b>	

**Table 2: Age, sex, religion of 230 cases of chronic pancreatitis**

	<b>Alcoholic calcific pancreatitis</b>	<b>Tropical calcific pancreatitis</b>
Number of patients	23	207
Male : Female	23:0	148: 59 (ratio – 2.2 : 1)
Hindu	19 (83 %)	129 (62.3%)
Muslim	1 (4.3 %)	67 (32.4 %)
Christian	3 (13 %)	11 (5.3 %)
Mean age of onset of symptoms (range)	47.2 yr (23-71)	35.7yr (9-65)

**Table 3: Presenting symptoms in TCP**

<b>Symptoms</b>	<b>No. of cases (Total 207)</b>
Abdominal pain	98 (47.34%)
Diabetes mellitus	74 (35.7 %)
Steatorrhoea	23 (11.1%)
Jaundice	12 (5.8%)

**Table 4: Radiological investigations**

(CT scan / Ultrasonogram / plain x-ray of abdomen))

<b>Abnormalities</b>	<b>No. of cases 207</b>	
Dilated main pancreatic duct	56	27 %
Psuedocyst	44	21.3%
Dilated biliary system	10	4.8%
Ascites	9	4.3%
Mass head of pancreas	6	2.9%
Pancreatic calcification	204	
Equivocal findings	3	

**Table 5: Size of pancreatic calculi on plain x-ray of abdomen (48 cases)**

Size of calculi	ACP n =17	TCP n = 31
>1cm	2 (11.76%)	20 (64.51 %)
0.5-1cm	7 (41.17%)	9 (29%)
<0.5 cm	8 (47%)	2 (6.45)

### **Complications**

Ten patients with TCP presented with obstructive jaundice and 6 were found to have mass lesion in the region of head of pancreas (2.9%) and four patients had benign stricture of lower end of bile duct. Pseudocyst of pancreas was seen in 44 patients (21.3%) with TCP in comparison with 8 patients with ACP (34.7%). Pancreatic ascites was seen in 9 patients with TCP (4.3%). The pain became intractable in 13 (6.28 %) patients and they were subjected to surgical procedures. Severe protein calorie malnutrition with kwashiorkor like skin changes were observed in one patient (14 years) who also had evidence of a large pseudocyst. (Fig 1)

### **Familial clustering**

Presence of TCP in other members of the family was observed in 4 patients (2 siblings, and 2 identical twins).

### **Cassava consumption and alcohol intake**

Detailed diet history was obtained from 31 patients with TCP. History of daily consumption of cooked cassava was obtained in 9 patients (29%). The mean daily cassava intake was 222.22g (range 100 to 500 g) for a mean duration of 12 years (range 7 – 12). In 11 (35.8%) patients, the mean cassava intake was 126 g weekly and 11 patients never had taken cassava (35.48%). The mean daily intake of vegetables in these patients were 20 g/day. The mean calorie intake was 1830 kcl/day.

Three patients with TCP with long history of abdominal pain and diabetes mellitus in young age also gave a history of significant alcohol intake.

They had noticed symptoms of pancreatitis much before they took to the habit of regular alcohol intake. The mean alcohol intake in 23 ACP patients were 141.1 g per day and the mean duration was 19 years (range 14-30 years)

## **Discussion**

Ninety percent of subjects in our group belonged to the category of TCP and only 10% belonged to the ACP group. All patients in ACP group were males and 83% of patients were Hindus where as only 4 % of the ACP patients belonged to the Muslim community. The low occurrence of ACP among muslim patients may be due to the low prevalence of alcoholism in that community. Among the 207 patients with TCP, the male : female ratio was 2.2: 1. Various other studies <sup>1,2</sup> indicated male preponderance of 1.63 - 3: 1 but a field study <sup>3</sup> in 1988 revealed higher incidence among females, M: F – 5:8.

Forty nine percent of our patients with TCP belonged to Kozhikode district, 35.7 % to Kannur District and 21.7 % belonged to the Malappuram District. Overall 167 patients from these three adjacent districts together contributed to 81% of cases of TCP. It is intriguing to note that only 3% of patients belonged to the Wyanad district with geographical features and dietary habits similar to the Kottayam District in middle Kerala where the disease was described in large numbers earlier by Geevarghese<sup>1</sup>. It is all the more interesting to note that large number of people belonging to the Wynad district are either migrants or descendants of migrants from the same belt in middle Kerala where TCP was noted in large numbers earlier. In our study, there were only 4 migrants from Kottayam District who had settled in north Kerala during their childhood days.

One previous study<sup>4</sup> has pointed out about the occurrence of pancreatitis in Calicut region and it was stated that the disease is more common in the migrants from central Kerala. However, our present study clearly showed that TCP is prevalent more in the native population of north Kerala than in the migrants from central Kerala region who had settled predominantly in Wynad District. The religion wise distribution of patients roughly corresponded to the census data of religions. Less

number of cases are reported from the northern most district of Kasargod, which could be due to the proximity with Manipal, where Kasturba Medical College is situated.

Classically, a vast majority of cases with TCP are diagnosed between 11 and 30 years of age. The remaining cases are detected in the fourth decade<sup>5, 6</sup>. The mean age at onset of symptoms in our study was 35.37 years with a range of 9 to 65 years. Eighty-seven patients (42%) were found to be above 40 years, compared with 3.25%, 7.25%, 16.4 % and 33 % above 40 years age reported from south Kerala, Madras, Pune and Central Kerala respectively.

The mean age at onset of symptoms in ACP patients in our study was 47.2 years with a range of (23-71) years. The average age of intake of alcohol was 141.17 g day and mean duration of drinking was 19.7 years with a range of 12-30 years. Various studies have shown that daily intake of 150 g alcohol for a minimum duration of 5 - 6 years is required to produce alcoholic calcific pancreatitis. Our study revealed that average intake of alcohol was almost similar to other studies, but the minimum duration of drinking was 12 years.

Among the 31 patients with TCP in whom a detailed diet history was available, only 9 patients gave a history of consumption of cooked cassava as staple diet daily, with an average intake of 222.2 g for a mean duration of 12 years. Eleven patients (35.48%) never had consumed cassava. The average daily intake of calories in these patients was 1830 kJ. Both ACP and TCP patients in our study had a predominantly rice based diet rich in carbohydrates. A study of cassava consumption in patients having TCP at Kottayam showed that the intake of cassava was 373.3g /day among those with TCP and 167.3 g among those without the disease.

Geevarghese had presented epidemiological data to suggest a positive correlation between cassava intake and incidence of TCP in several geographic areas. Cyanogenic glycosides contained in cassava are considered to be the toxic factors. Although in north Karnataka and Pune there is scope to incriminate an alternate cyanide containing staple diet (sorghum), no such factor can be suggested in Tamil Nadu, Andhra

Pradesh, Orissa and West Bengal. Tuescher et al<sup>7</sup> failed to find cases of TCP in a West African population with high cassava consumption. Experimental studies have not conclusively proven the role of cassava in TCP yet.

Four patients in our study had a sibling with TCP of whom two were identical twins, and another an elder brother. Fewer numbers of familial clustering may indicate that environmental factors may be playing a greater role in the causation of TCP than genetic factors.

Many of our patients belonged to the poor or lower middle class socio-economic category. There were some patients who belonged to a rich background. Over 80% of patients seen in hospitals in Trivandrum and in Cuttack were poor or very poor. However, patients with TCP detected at private or paying clinics do not belong to poor socio-economic group.

Complications of diabetes mellitus were seen in 32 out of 74 of our patients (43.2%) with TCP. Most common complication was recurrent hypoglycemia. Long-term complications of diabetes (neuropathy, myopathy, retinopathy) were noticed in 12 patients (16 %). The incidence of overt diabetes was seen in 34% of 404 ACP patients studied by Howard and Jordan <sup>8</sup> from 118 reports on the subject and 45% in the series of Marks and Bank from South Africa, whereas in TCP the incidence of diabetes had been reportedly quite high, even up to 90%<sup>9</sup>.

Abdominal pain was present in 89% of our TCP patients. This is comparable with various other reported studies. Steatorrhoea as a complaint was seen in 11% of our patients with TCP. However, one study had shown that 76% of patients had steatorrhoea when a standard fecal fat estimation was done. Our patients with steatorrhoea complained of passing greasy stools and dripping of oil from anus during defecation. This description of steatorrhoea in TCP is in sharp contrast to the textbook description of steatorrhoea characterized by profuse, frothy and foul smelling stools. This specific complaint of passing of oil per anus occurs especially after a fatty meal and this is highly diagnostic of exocrine pancreatic failure. Therefore this type of steatorrhoea is to be clinically distinguished from classic steatorrhoea seen in small bowel disease, and a new term of *oilorrhoea* is proposed to be used to describe the

steatorrhoea in exocrine pancreatic dysfunction.

Ten patients in our study presented with obstructive jaundice and in 6 cases a mass was found in the head region of pancreas (2.9%). It is estimated that patients with tropical pancreatitis are at least 8 times more at risk of developing pancreatic cancer compared to controls. In a recent follow up of 266 patients with TCP studied over 8 years period in Kerala, 22 patients (8.3%) had pancreatic carcinoma and their mean age was 46.8years.

Another observation is that 64.5% of our TCP patients had calculi >1cm size where as 47% of ACP patients had calculi <0.5 cm in size in plain X ray abdomen. TCP is characterized by the frequent occurrence of large, discrete, dense calculi. Patients with alcoholic calcific pancreatitis have typically small, speckled calculi with irregular hazy margins. This finding is consistent with earlier observations by Chari et al<sup>10</sup>

The diagnosis of tropical pancreatitis in the absence of calcification is difficult. In our series we have not included non-calcific pancreatitis i.e. patients who are juvenile diabetics with unequivocal exocrine or morphological changes in the pancreas. This might explain the low incidence of diabetes mellitus in our series. Another observation in our series which warrant further studies is the low intake of vegetables and fruits in TCP patients.

### **New hypothesis**

In this context it is worthwhile to explore the possibility of other environmental agents in the causation of TCP. Alcohol is a definite risk factor for chronic pancreatitis. Ethyl alcohol is produced by fermentation of carbohydrates. It has been proven beyond doubt that ethyl alcohol even though in small quantities is produced in human intestinal tract by bacterial and fungal fermentation. There are studies, which have suggested a role for endogenous alcohol in the causation of non-alcoholic steatohepatitis<sup>r</sup>. Both cassava and rice are rich in starch and the epidemiological association of cassava with TCP may be linked through endogenous production of alcohol like substances. It is possible that some chemicals similar to ethyl alcohol is produced by fermentation

of carbohydrates in the intestinal tract and this substance is not detoxified properly in patients with TCP which may lead to pancreatic damage. This defect in detoxification may be genetically determined. Further studies are required in this direction to prove or disprove this hypothesis

### **Summary**

With better understanding of the illness it seems that the natural history of TCP previously described by Geevarghese as pain between the ages of 6-10 years, diabetes by the age of 20 years and death before age of 30 years had definitely changed. In north Kerala, the disease is less common in the hilly regions and the role of cassava seems to be less important. Familial clustering of TCP is infrequent in north Kerala. The search for the role of other environmental factors should continue.

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