# INCIDENCE OF FIBROCALCULOUS PANCREATIC DIABETES IN CHATTOGRAM

Mayin Uddin Mahmud[1]* Mohammad Ahsanul Abedin[2] Shah Md. Zakir Hossain[3] Roksana Reza[4]

## Abstract

**Background :** Fibrocalculous Pancreatic Diabetes (FCPD) is a unique form of diabetes secondary to chronic pancreatitis usually found in tropical countries of the world. Fibrocalculous pancreatic diabetes affects young individuals and runs an aggressive course to reach the endpoints of diabetes, pancreatic calculi and exocrine pancreatic dysfunction (Steatorrhoea) in the majority of cases. There are characteristic features of FCPD clinically, radiologically, ultrasonographically which distinguish it from diabetes of other causes and also from chronic pancreatitis of other aetiologies seen in temperate zones, e.g. alcoholic chronic pancreatitis. To observed the incidence of FCPD among the patients attending at the hospital.

**Materials and methods:** We conducted this study among 487 patients over a period of January 2016 to December 2017 in different wards of Chittagong Medical College Hospital which is the largest hospital in Chattogram, Bangladesh. FCPD was diagnosed based on the standard criteria.

**Results:** The incidence of fibrocalculous pancreatic diabetes is 0.61% among the diabetic patients in Chattogram. Mean age of the patients is 39.7 ± 10 years. Mean age of onset of diabetes is 37.3±15 years.

**Conclusion:** This study reports the incidence of fibrocalculous pancreatic diabetes in Chattogram district, the second largest city in Bangladesh.

**Key words :** Fibrocalculous Pancreatic Diabetes; Diabetes mellitus; Chattogram.

## Introduction

Fibrocalculous Pancreatic Diabetes (FCPD) is a form of diabetes secondary to nonalcoholic, chronic, calcific pancreatitis. It is seen in tropical, developing countries of the world.[1] FCPD is characterized by insulin requiring diabetes and presence of pancreatic calculi or other evidence of chronic pancreatitis, e.g dilated pancreatic ducts and mutations in the SPINK gene.[2] Several terms have been proposed for this syndrome, including tropical calcific pancreatitis, tropical chronic pancreatitis, tropical pancreatic diabetes, nutritional pancreatitis and endemic pancreatic syndrome.[3] For sake of uniformity and international agreement, it was adopted as fibrocalculous pancreatic diabetes proposed by the WHO Study Group Report on Diabetes when this entity was introduced as a subtype of Malnutrition-Related Diabetes Mellitus (MRDM).[4] In the recent Expert Committee on Classification of Diabetes, the entity known as "malnutrition-related diabetes mellitus" was deleted and FCPD is now classified as a "disease of exocrine pancreas" under the category of "Other types of diabetes". The commonly used suffix "tropical" may not be appropriate as the disorder has been recently reported from temperate zones in migrants from tropical countries.[5]

Zuidema from Indonesia was the first to describe diabetes associated with pancreatic calculi and severe malnutrition.[6] Reports from several tropical parts of the world including Uganda, Nigeria, other parts of Africa, Brazil and several countries in Asia including Thailand, Bangladesh and Sri Lanka indicated the widespread occurrence of this syndrome.[7-11]

The aetiopathogenic mechanisms for FCPD remain unclear. Clinical evidence of malnutrition at the time of diagnosis of FCPD suggested that malnutrition could be a factor in the aetiology of FCPD.[12] However, malnutrition at presentation may well be secondary to severe exocrine and/or endocrine pancreatic deficiency.[13] Protein–calorie malnutrition has been shown to produce pancreatic changes as well as glucose tolerance and insulin deficiency in experimental animals.[5] McMillan and Geevarghese observed the geographical occurrence of FCPD in areas where the tuber cassava

1. Resident Surgeon of Surgery
Chittagong Medical College Hospital, Chattogram.
2. Assistant Professor of Surgery
Chittagong Medical College, Chattogram.
3. Medical Officer of Nephrology
Bangabandhu Sheikh Mujib Medical University, Dhaka.
4. Post Graduate Student of MPhil (Pharmacology)
Chittagong Medical College, Chattogram.

***Correspondence:** **Dr. Mayin Uddin Mahmud**
*E-mail: dr.mayin@gmail.com*
*Cell : 01712 05 53 98*

*Submitted on : 16.06.2020*
*Accepted on : 14.07.2020*

(Tapioca, manihot) is consumed as a staple food and suggested a causative role for cassava in the aetiology of this condition.[14] But cassava consumption is not habituated in Bangladesh. Familial clustering of FCPD has been described by several workers.[12,15,16]

The cardinal triad of FCPD is abdominal pain, pancreatic calculi and diabetes.[1] The patient usually present with abdominal pain, thirst, polyuria and features of gross pancreatic insufficiency resulting steatorrhoea and malnutrition.[10] Despite excellent clinical descriptions of the disease, until recently no criteria had been established for the diagnosis of FCPD. Mohan et al were the first to propose a set of criteria for the diagnosis of FCPD, based on an extensive review of the literature.[13,16,17] These criteria (Table I) have been generally accepted by other workers in the field.[3,18] To our knowledge, there is no population based study on the incidence of FCPD in this region. This paper reports the incidence of FCPD among the patients attending at the only tertiary hospital in Chattogram, the second largest city in Bangladesh.

## Materials and methods

This study was conducted in Chittagong Medical College Hospital from January 2016 to December 2017. 487 patients were recruited from the indoor patients in different wards. Individuals aged 20 years or more suffering from Diabetes Mellitus were recruited based on a systematic random sampling technique. Patients with renal and cardiovascular complication of Diabetes Mellitus were excluded from this study. A questionnaire elicited demographic, socioeconomic, behavioral and past medical history of the study subjects and included specific questions related to chronic pancreatitis such as the history of recurrent abdominal pain and/or passing greasy or oily stools. All respondents underwent a plain abdominal X-ray as well as abdominal ultrasonography to rule out pancreatic calculi. FCPD was diagnosed based on the following criteria : i) Presence of pancreatic calculi on abdominal X-ray and evidence of ductal dilation on ultrasonography ii) Absence of alcoholism, or other known causes of chronic pancreatitis iii) Evidence of diabetes i.e fasting plasma glucose equal to or greater than, 7.0 mmol/L (126 mg/dL) or random plasma glucose greater than 11.1 mmol/L (200 mg/dL) or subject on drug treatment of diabetes. After collection of data, they were processed, analyzed and interpreted both manually and by SPSS for Windows version 20.0 software.

## Results

A total of 487 diabetic patients fulfilling the inclusion criteria participated to this study. FCPD was diagnosed in 3 diabetic subjects, yielding a prevalence of 0.62% among the total diabetic subjects. The remaining diabetic patients are categorized as diabetes of other cause. The mean age of FCPD patients is 39.7± 10 years whereas the mean age of diabetes of other cause category is 54.3± 10 years. Among them all of the FCPD patients are male whereas there is 43.2% male in diabetes of other cause group (Table II). 105 patients (21.7%) in the diabetes of other cause group is smoker whereas 1 patient (33.3%) in FCPD group is smoker (Fig 1). None of the patients in FCPD group is alcoholic. On the other hand 188 patients (38.8%) in the diabetes of other cause group is alcoholic (Fig 2). Recurrent abdominal pain was present in 2 patients (66.67%) in FCPD group whereas it was present in 25 patients (5.2%) in the other group. Passage of oily stool was present in 2 patients (66.67%) in FCPD group and it was present in only 18 patients (3.7%) in the other group. All of the patients (100%) in FCPD group were diagnosed as type 2 diabetes mellitus. On the other hand 298 patients (61.6%) were diagnosed as type 2 diabetes mellitus in the other group. Mean

**Table I :** Criteria for Fibrocalculous Pancreatic Diabetes (FCPD).[13,16,17]

i) The patient should originate from a "tropical" country

ii) Diabetes should be present

iii) Evidence of chronic pancreatitis must be present: Pancreatic calculi on abdominal X-ray or at least three of the following:
   (a) Abnormal pancreatic morphology on sonography/CT scan
   (b) Recurrent abdominal pain since childhood
   (c) Steatorrhoea
   (d) Abnormal pancreatic function test

iv) Absence of other causes of chronic pancreatitis, i.e alcoholism, hepatobiliary disease, primary hyperparathyroidism etc.

age at onset of diabetes was 37.3±15 years in FCPD group and it was 49±10 years in the other group. Mean body mass index in the FCPD subjects was 15.6 ±4.6 kg/m$^2$ whereas in other subjects it was 26.4±5.2 kg/m$^2$. In FCPD subjects the mean waist circumference was 74.2 ± 9 cm and on the other hand it was 90.3±10 cm (Table III).

**Table II :** Particulars of the responders.

| Variable | FCPD n= 3 | Diabetes of other cause n= 484 | |
|---|---|---|---|
| Age (Mean ± SD) | 39.7 ± 10 | 54.3 ± 10 | p<0.031 |
| Gender (%) | | | |
| Male | 3 (100%) | 209 (43.2%) | |
| Female | 0 | 275 (56.8%) | |

SD : Standard Deviation

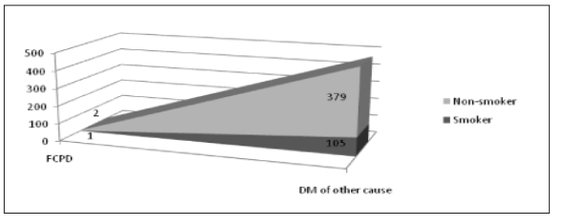


**Fig 1 :** Distribution by smoking habit.

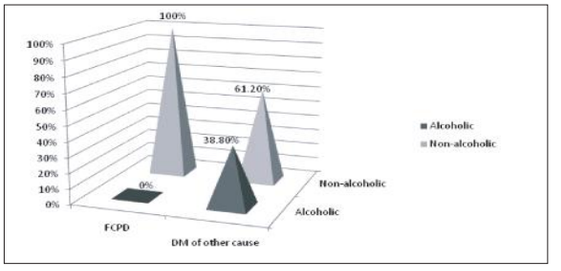


**Fig 2 :** Distribution by alcohol consumption.

**Table III :** Clinical characteristics of the responders.

| Variable | FCPD n= 3 | Diabetes of other cause n= 484 | |
|---|---|---|---|
| Recurrent abdominal pain | 2 (66.7%) | 25 (5.2%) | |
| Passing greasy/oily stools | 2 (66.7%) | 18 (3.7%) | |
| Type of Diabetes | | | |
| Type 1 | 0 | 186 (38.4%) | |
| Type 2 | 3 (100%) | 298 (61.6%) | |
| Age at onset of diabetes (Mean ± SD years) | 37.3±15 | (49.0±10) | p<0.041 |
| Body mass index (Mean ± SD kg/m$^2$) | 15.6 ± 4.6 | 26.4 ± 5.2 | p<0.001 |
| Waist circumference (Mean ± SD cm) | 74.2±9.0 | 90.3±10.0 | p<0.001 |

SD : Standard Deviation

## Discussion

This is first study on incidence of FCPD in this area. Our study shows that 0.61% of the diabetic patients have FCPD. This study was conducted among the diabetic patients in the only tertiary hospital in Chattogram. This result reflects the overall situation of incidence of fibrocalculous pancreatic diabetes among the diabetic patients in this area. The highest prevalence of FCPD in the world appears to be in southern India, where 1700 cases have been documented by Geevarghese alone.[19] At the M.V. Diabetes Specialties Centre (MVDSC) at Chennai (Madras) a large referral centre for diabetes, about 50 patients with FCPD are registered annually, which constitutes about 1% of all diabetic patients and 4% of "young" diabetic patients (Defined as onset below 30 years of age).[13] During the 1980s at the S.C.B. Medical College Hospital at Cuttack, in Orissa, FCPD constituted 2.5% of all diabetic patients while at Trivandrum in Kerala it comprised 7% of all diabetic patients.[20,21] Recently, there appears to have been a decline in the number of patients seen at most centers. In a study conducted on prevalence of FCPD in Chennai in South India, prevalence of FCPD was shown 0.36% among the known diabetic patients.[1] Balakrishnan et al. in a nationwide prospective study in India on chronic pancreatitis based on clinical and radiological criteria, reported a prevalence of 3.2% for FCPD, 38.7% for alcoholic pancreatitis and 60.2% for 'idiopathic pancreatitis'.[15] Our study shows the similar incidence of FCPD as Chennai. More population studies are needed on the prevalence/incidence of FCPD in different parts of the world. In our study FCPD patients are younger (39.7 ± 10 years vs. 54.3 ± 10 years, p<0.031). The mean age is slightly lower than other study (41.4±18.4 years vs. 51.7±10.7 years, p=0.032).[1]

In our study history of recurrent abdominal pain was present in 66.7% of the FCPD patients. Other study shows that history of abdominal pain is given only in 10–20% of patients, while on direct questioning up to 70–80% of patients may recall a childhood history of pain.[3] History of passage of oily stool was present in 66.7% of FCPD patients in our study. Whereas in other study it was shown that when the fat content of diet is experimentally increased, steatorrhoea becomes evident in 90% of the patients.[15]

Mean age at onset of diabetes in FCPD patients was 37.3±15 years in our study. In other study it is shown that in the majority of patients the diagnosis of diabetes is made between the ages of 20 and 40, but onset in childhood, in infancy and at older age groups is not uncommon. Zabeen et al. reported a series of FCPD patients among Bangladesh children and adolescents. They report that 106 (25%) of a series of 429 children and adolescents with diabetes diagnosed below 18 years of age had FCPD.[10]

In our study mean body mass index (15.6 ± 4.6 kg/m2 vs. 26.4 ± 5.2 kg/m2, p<0.001) and mean waist circumference (74.2 ± 9 vs. 90.3 ± 10 cm, p<0.001) are significantly lower compared to diabetic patient of other cause. This is probably due to undernutrition of the FCPD patients. At M.V. Diabetes Specialties Centre (MVDSC) at Chennai overt malnutrition was observed only in 25% of patients, although 70% were lean.[22] In Orissa, the majority of FCPD patients were poor and many were malnourished.[20,23]

**Limitations**

This study was conducted in a single centre of a district and the duration of the study was short. The course of the disease and its complications should be sorted out.

**Conclusion**

FCPD is a type of idiopathic chronic pancreatitis that occurs in the tropics, but is also seen in Bangladesh. Although this study includes only the Chattogram district, it may reflect the actual situation in the whole country. Our study shows that 0.61% of diabetic subjects had FCPD. It affects young patients. Its diagnosis is established by clinical evaluation and imaging, particularly plain film of the abdomen, ultrasound and/or CT scan of the abdomen showing pancreatic calculi. Many etiological factors have been suspected but genetic mutations appear as the most likely cause. Although the prevalence of FCPD is low, this entity must be kept in mind in countries where its occurrence has been reported. The clinical significance of FCPD is that its therapy would include, in addition to control of diabetes, management of the pain of pancreatitis, long term pancreatic enzyme replacement and periodic screening for pancreatic adenocarcinoma.

**Recommendations**

A large population based study should be conducted throughout a long duration to report the incidence of FCPD in Bangladesh. The exact aetiological factors for this disease should be ruled out. More studies should be conducted to establish a management plan of this disease.

**Acknowledgement**

We would like to pay our heartiest gratitude to all the patients included in this study without whom the study would not be possible. We thank to the Head of the Department of Surgery for his continuous support. We would like to thank the doctors and all other stuffs of surgery outpatient department of our institute for their tremendous support for managing the patients.

**Contribution of authors**

MUM-Conception, design, acquisition of data, manuscript writing & final approval.

MAA - Interpretation of data, critical revision & final approval.

SMZH - Data analysis, critical revision & final approval.

RR - Data analysis, manuscript writing & final approval.

**Disclosure**

All authors declared no competing interest.

**References**

**1.** Mohan V, Farooq S, Mohan D. Prevalence of Fibrocalculous Pancreatic Diabetes in Chennai in South India, JOP. J Pancreas (Online). 2008; 9(4):489-492.

**2.** Chandak GR, Idris MM, Reddy DN, Bhaskar S, Sriram PV, Singh L. Mutations in the pancreatic secretory trypsin inhibitor gene (PSTI/SPINK1) rather than the cationic trypsinogen gene (PRSS1) are significantly associated with tropical calcific pancreatitis. J Med Genet. 2002; 39:347-351.

**3.** Bhat JA, Bhat MH, Misgar RA, Bashir MI, Wani AI, Masoodi SR et al. The clinical spectrum of fibrocalculous pancreatic diabetes in Kashmir valley and comparative study of the clinical profile of fibrocalculous pancreatic diabetes and type 2 diabetes mellitus. Indian J Endocr Metab. 2019;23:580-584.

**4.** WHO study group report on diabetes mellitus. WHO Technical Report Series No. 727. WHO, Geneva. 1985.

**5.** Unnikrishnan R, Mohan V. Fibrocalculous Pancreatic Diabetes. Curr Diab Rep. 2020;20(6):19.

**6.** Zuidema PJ: Cirrhosis and disseminated calcification of the pancreas in patients with malnutrition. Trop Geogr Med. 1959;11:70–74.

**7.** Shaper AG: Chronic pancreatic disease and protein malnutrition. Lancet ii. 1960; 1223–1224.

**8.** Akanji AO: Malnutrition related diabetes mellitus in young adult diabetic patients attending a Nigerian diabetic clinic. J Trop Med Hyg. 1990;93:35-38.

**9.** Dani R, Penna FJ, and Nogueria CED: Etiology of chronic pancreatitis in Brazil: A report of 329 consecutive cases. Int J Med. 1976;6:316–320.

**10.** Zabeen B, Nahar J, Tayyeb S, Nahar N, Azad K, Donaghue K. Fibrocalculous pancreatic diabetes in Bangladeshi children and adolescents : A not so rare form of secondary diabetes. Int J Diabetes Dev Ctries. 2018;38(2):153-157.

**11.** Ilangosekara V: Malnutrition related diabetes mellitus in Sri Lanka: Fact or fiction? J Ceylon Coll Phys. 1995;18:16–25.

**12.** Praveen G, Mohan V: Fibrocalculous pancreatic diabetes-current scenario in developing countries. Int J Diabetes Dev Ctries. 2018;38(2): 131–132.

**13.** Mohan V, and Premalatha G: Fibrocalculous pancreatic diabetes. Int J Diabetes. 1995;3:71–82.

**14.** McMillan DE, and Geevarghese PJ: Dietary cyanide and tropical malnutrition diabetes. Diabetes Care. 1979;2:202–208.

**15.** Balakrishnan V, Unnikrishnan AG, Thomas V, Choudhuri G, Veeraraju P, Singh SP et al. Chronic pancreatitis. A prospective nationwide study of 1,086 subjects from India. JOP. 2008;9:593–600.

**16.** Mohan V, Chari ST, Hitman GA, Suresh S, Madanagopalan N, Ramachandran A and Viswanathan M: Familial aggregation in tropical fibrocalculous pancreatic diabetes. Pancreas. 1989; 4:690–693.

**17.** Mohan V and Alberti KGMM: Diabetes in the tropics. In International Textbook of Diabetes Mellitus. 1991; 177–190.

**18.** Consensus Statement from the International Workshop on Types of Diabetes Peculiar to the Tropics, 17–19 October 1995, Cuttack, India. Acta Diabetol Lat. 1996; 33:62–64.

**19.** Geevarghese PJ: Calcific Pancreatitis. Varghese Publishing House, Bombay. 1985.

**20.** Tripathy BB: Epidemiology of tropical calcific pancreatitis. In Tropical Calcific Pancreatitis, Kumar N and Acharya SK, Eds. Roussel Scientific Institute, Trivandrum. 1994;12–28.

**21.** Balakrishnan V: Tropical pancreatitis, epidemiology, pathogenesis and etiology. In Chronic Pancreatitis in India, Balakrishnan V, Ed. Indian Society of Pancreatology, Trivandrum.1987;81–85.

**22.** Mohan V, Mohan R, Susheela L, Snehalatha C, Bharani G, Mahajan KU, Ramachandran A, Viswanathan M, and Kohner EM: Tropical pancreatic diabetes in South India: heterogeneity in clinical and biochemical profile. Diabetologia. 1985; 28: 229–232.

**23.** Tripathy BB, and Samal KC: Chronic calcific pancreatitis with diabetes in the young in Orissa. In Chronic Pancreatitis in India, Balakrishnan V, Ed. Indian Society of Pancreatology, Trivandrum. 1987;87–96.