

# Non Insulin Dependent Diabetes Mellitus in Young – Overlap with Malnutrition Related Diabetes Mellitus

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## Abstract

Diabetes in the tropics although not a homogenous entity, does have certain distinctive characteristics of its own. Genetic, nutritional dietary, and other environmental factors seem to be responsible for some of the differences noted between diabetes in tropical countries and diabetes in the West. Recent studies have highlighted the common factors which are shared by both non- insulin dependent diabetes in the young (NIDDDY) and malnutrition related diabetes mellitus (MRDM) such as a low body mass index, lower age at onset, variable metabolic responses in response to changes in nutritional status and male predominance. Evidence in favour of familial aggregation with evidence of vertical transmission of disease from parent to offspring in fibrocalculous pancreatic diabetes (FCPD) has been put forward. The genetic predisposition to FCPD shares similarities with both IDDM and NIDDDM. Prevalence of vascular complications, particularly those of microvascular origin are common in MRDM as in NIDDDY and increases with duration of diabetes.

## KEYWORDS

Body Mass Index, Familial Aggregation, Genetic Aetiology, Malnutrition at Diagnosis, Microvascular Complications, Nutritional Factors, Tropical Diabetes

Diabetes in the tropics shows distinct variations in several respects from that seen in Western countries [1]. In non-insulin dependent diabetes mellitus

(NIDDDM) there is a reversal of the sex ratio and a lower prevalence of obesity [2]. Maturity onset diabetes of the young (MODY), also referred to as non-insulin dependent diabetes of the young (NIDDDY), is more common among Asian Indian patients than in the Western population. In addition there are special forms of diabetes associated with malnutrition. Two subclasses of malnutrition related diabetes mellitus (MRDM) have been identified by the WHO study group report [3] namely fibrocalculous pancreatic diabetes (FCPD) and protein deficient diabetes mellitus (PDDM).

Several earlier studies from India [4-6] have reported on the clinical features of these tropical forms of diabetes but few have used the modern criteria for the diagnosis of diabetes. In a recent review on MRDM [7] the authors have rightfully stressed on the need for more organised studies on the epidemiological, clinical, biochemical and aetiological aspects of these tropical forms of diabetes.

Recent studies have pointed out the possibility of overlap between NIDDDM in the young and FCPD. In our own study on a group of 10,000 consecutive diabetic patients seen at the Diabetes Research Centre at Madras during a three year period we found that 545 patients were young diabetics (YD) defined as those with an age at diagnosis of 30 years or less [8]. Table 1 shows the clinical characteristics of the study groups. Out of the total 545 YD patients, 314 were classified as NIDDDY (57.7 per cent), 119 as IDDM (22 per cent) and 22 as MRDM (5 per cent, FCPD:4 per cent, PDDM:1 per cent).

**Table 1 : Clinical Characteristics of the 461 Young Diabetics who could be classified[Ref. 8]**

DIABETES TYPE	NUMBER	PER CENT	SEX RATIO M : F	BMI (kg/m <sup>2</sup> )	AGE (years)	AGE AT DIAGNOSIS (years)	DURATION OF DIABETES (years)
NIDDDY	314	(57.7)	188:126	23.6 ± 4.8	36 ± 8	26 ± 3	9 ± 2
IDDM	119	(22)	73:46	17.4 ± 4.2	23 ± 20	21 ± 10	5 ± 4
FCPD	21	(4)	17:4	18.8 ± 3.5	30 ± 6	26 ± 5	5 ± 4
PDDM	7	(1)	6:1	15.9 ± 1.6	23 ± 6	22 ± 4	3 ± 2

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The features shared by both NIDDM and MRDM patients were the lower but similar age at onset and the male predominance. Though the body mass index (BMI) was the lowest in the patients with PDDM, only a very small percentage of NIDDM patients were obese. Leanness (BMI < 18 kg/m<sup>2</sup>) was not a characteristic feature of the MRDM group as 70 per cent of the IDDM were also lean. A recent survey conducted by us in a rural area around Madras city showed that both men and women in the rural population had mean BMI < 18 kg/m<sup>2</sup>. Nevertheless the prevalence of NIDDM was fairly high at 2.6 per cent [9]. Malnutrition at diagnosis is considered to be the most important point of differentiation of MRDM from other classes of diabetes. Recent studies [10, 11] have shown that considerable heterogeneity exists in the clinical presentation of FCPD with overt malnutrition being seen in only a smaller percentage of the patient population suggesting that much significance cannot be attached to the nutritional state at diagnosis for classifying diabetic patients. Furthermore, in contrast to several earlier reports it has been shown that MRDM patients also hail from middle and even upper income groups.

### **Familial Factors**

It is already well established that there is a high degree of familial aggregation in NIDDM [12]. A positive family history of NIDDM has been found to be a hall-mark of NIDDM. However till recently very little information on the genetic factors associated with FCPD was available. Geevarghese [13] had reported that 8 per cent of his 1700 cases of tropical pancreatitis had "familial pancreatitis". In a study by Pitchumoni [14] only one family with FCPD in a parent and offspring was reported. Balakrishnan [15] reported the occurrence of the disease in three pairs of twins and several siblings but again only one instance of disease in a parent and offspring was mentioned.

In a systematic screening of 98 first degree relatives of FCPD patients using sensitive techniques such as GTT, X-ray films, ultrasonography and exocrine pancreatic function tests, Mohan et al [16] showed that there is a familial aggregation of FCPD with evidence of vertical transmission of the disease from parent to offspring in some families. Support for a genetic aetiology of FCPD has also come from a recent study [17] in which an association of FCPD with the HLA-DQ beta gene located on chromosome 6 as well as with the hypervariable region near the insulin gene located on chromosome 11 has been demonstrated. Thus, the genetic

predisposition to FCPD shares similarities with both IDDM and NIDDM. However, definitive evidence for a genetic aetiology for FCPD can only be obtained by linkage studies of genetic markers with the disease which are currently in progress.

### **Biochemical Factors**

One of the important clinical characteristics of both forms of MRDM is that despite requiring insulin for control of diabetes, patients do not become ketotic on withdrawal of insulin. It has been suggested that the ketosis resistance in FCPD may be a result of partial preservation of beta cell function [18]. Those with the highest C-peptide levels responded to oral hypoglycaemic agents thus resembling the NIDDM patients in this respect [19]. Another explanation offered for this phenomenon of ketosis resistance is the post prandial glucagon suppressibility seen in the FCPD patients [20].

Abdul Kadir in his investigation on ketosis proneness of his PDDP patients after nutritional rehabilitation has observed that improved nutrition allowed some of his patients to be controlled with oral hypoglycaemic agents. These studies highlight the variability in metabolic responses in MRDM patients with change in nutritional status.

Insulin resistance is a common feature observed in patients with NIDDM [19]. Reports of insulin resistance in FCPD patients reported earlier are not borne out in recent studies on FCPD. Yajnik [21] has reported that the high insulin dose required by these patients in the initial stages comes down considerably once these patients settle down after an initial phase of polyphagia, excessive food intake and rapid weight gain.

### **Vascular Complications**

Contrary to earlier belief, recent studies have shown that microvascular complications are as common in MRDM as in NIDDM with an increasing prevalence of complications with increasing duration of diabetes (Table 2). In one study [22] it was shown that the two severe sight-threatening forms of retinopathy, namely maculopathy and proliferative retinopathy do occur in FCPD. Nephropathy and renal insufficiency were also common [8, 10]. Nerve conduction studies show that the occurrence of neuropathy in FCPD was comparable to that of NIDDM [23]. The occurrence of macrovascular disease [24] and peripheral vascular disease though not common in young patients was dependent on

duration of diabetes and were shown to occur in elderly onset FCPD patients.

**Table 2 : Vascular Complications in Young Diabetics [Ref. 8]**

	NIDDM (314)	IDDM (119)	FCPD (21)	PDPD (7)
<i>MICROAVASCULAR</i>				
BDR	56*	13	7	1
PDR	12	4	2	0
NEUROPATHY	75	25	7	3
NEPHROPATHY	31	14	2	0
<i>MACROVASCULAR</i>				
IHD	19	3	2	0
PVD	1	1	0	0

\* P < 0.05

Figures are actual numbers of patients; Figures in brackets are the total number studied; BDR = Background Diabetic Retinopathy; PDR = Proliferative Diabetic Retinopathy; IHD = Ischaemic Heart Disease; PVD = Peripheral Vascular Disease

### Concluding remarks

Tropical diabetes although not a homogenous entity, does have certain distinctive characteristics of its own. Genetic, nutritional, dietary and other environmental factors seem to be responsible for some of the differences noted in tropical diabetes compared with diabetes in the West. Available evidence in the literature points to certain similarities between young subjects with NIDDM and MRDM. MRDM continues to provide a fascinating area for research. Several questions about this entity still remain unanswered. Further studies in this field could throw more light on the understanding of not only MRDM but also other types of diabetes as well.

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