Profile of Childhood Onset Diabetes in Orissa

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ABSTRACT

Among 5112 patients seen during a 5-year period (1983-88), 93(1.81%) had onset of diabetes by 15 years of age. Three among them were infants. Of the rest, 54 had Insulin dependent diabetes mellitus (IDDM), 25 protein deficient diabetes mellitus (PDDM) and 11 fibrocalculous pancreatic diabetes (FCPD). Clinical character as well as biochemical and hormonal data on these three categories are presented. Analysis indicates that it is easy to classify childhood onset diabetics into these categories as their features are quite distinctive.

INTRODUCTION

In spite of strong genetic basis, diabetes is much less frequent in children than among the middle aged and the elderly. Clinical manifestion and susceptibility to certain complications may vary with age of onset. Childhood diabetes, in particular , is encumbered with special problems such as rapid onset of symptoms, urgency of treatment , maintenance of somatic growth and sexual development as well as need for regulating their social behaviour and psychic status. Hence, inspite of low incidence, there are special reasons for close analysis of diabetes in children.

Classically, the term juvenile diabetes is applied when the disease manifests before 15 years of age. In the West, almost all such patients are characterised by proneness to develop ketosis. The term juvenile or juvenile onset diabetes (JOD) remained unchallenged till last decade, although it was realized that almost all patients with onset of diabetes up to age of 20 years, a large majority with onset by 30 years and a few with onset at later age could have all the metabolic characteristics of juvenile diabetes. Further, reports from developing countries indicated that all patients of juvenile age group may not be dependent on insulin for prevention of ketosis and prolongation of life. Hence the National Diabetes data group (1979) (1) and WHO Expert Committee on Diabetes (1980) (2) promulgated the use of the term insulin dependent diabetes mellitus (IDDM) to classify patients previously known as juvenile onset diabetes (JOD).

IDDM is known to occur in all populations but is relatively uncommon except in those of North European extraction. Diabetes in childhood, other than IDDM, may be due to a variety of very rare genetic syndromes, but in several developing countries may belong to now recognised classes of Malnutrition-related diabetes mellitus (MRDM), either protein deficient diabetes mellitus (PDDM) or fibrocalculous pancreatic diabetes (FCPD) (3).

MATERIAL AND METHODS

In order to access the incidence and clinical pattern of childhood-onset diabetes in this part of the country, records of all diabetic patients observed between 1983-88 at the Department of Endocrinology, S.C.B. Medical College, Cuttack are analysed. In a sense it may be considered to be a prospective study as records are maintained with the specific purpose of determining the clinical type of all diabetics along with special studies in those with early onset of the disease.

A total of 5112 cases were observed at the diabetic section during the 5 year period. Among them 93(1.81%) had onset of diabetes below 15 years of age. In 3 patients, diabetes occurred during infancy. Clinical characteristics of the rest (90) are analysed . Presence of ketones in urine, when untreated, was considered as the hall mark of IDDM and radiographic/ultrasound evidence of pancreatic calculi that of FCPD. PDDM was diagnosed when there was no ketosis or pancreatic calculi inspite of very severe diabetes . Further unambiguous history of prolonged undernutrition in early childhood was essential for diagnosis of PDDM.

Results

The relative incidence IDDM, PDDM & FCPD among 90 childhood onset diabetics, together with their age and sex distribution are presented in Table 1. IDDM was the predominant type, accounting for 60 percent of the total.

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In contrast, analysis of distribution of clinical types among diabetics with onset by 30 years of age revealed PDDM to be more common (55%) than the other two types. This indicates that there is a sharp rise in incidence of PDDM between 15 to 30 years of age.

The data on the habitat (rural/urban) and socio-economic status are presented in Table 2 and those on their physical status in Tale 3 . Height and weight values are classified according to percentile chart furnished by the ICMR (4).

Severity of diabetes, as judged from FBG and HbA_1 in the three clinical types, are shown in Table 4. Hyperglycemia was severe or very severe in patients of IDDM and PDDM , while it was mild to moderate in FCPD.

Table 5 indicates the serum protein ad lipid values in the three clinical types.

Table-1
Incidence, Age and Sex distribution of three clinical types of childhood onset diabetes

	Total	Clinical Types		
		IDDM	PDDM	FCPD
Number	90	54 (60%)	25 (27.8%)	11 (12.2%)
Sex (M:F)	51 : 39	31 : 23	13 : 12	7 : 4
Age at onset				
< 5	3	3	-	-
5-10	14	12	1	1
11-15	73	39	24	10
	100%	60%	27.8%	12.2%
	275			
Onset by 30 years	100%	19%	55%	26%

Table-2
General information of three clinical types of childhood onset diabetes

	Total	CLINICAL	TYPES	
	(%)	IDDM(%)	PDDM(%)	FCPD(%)
Habitat				
Urban	32.3	55.5	0.00	22.0
Rural	67.7	44.5	100	78.0
Socio Economic Status				
Very poor (Upto Rs. 500/- PM)	24.0	9.0	68.0	-
Poor (Rs. 500/- - 1000/- PM)	32.0	21.0	32.0	90.0
Middle income (> 1000/- PM)	44.0	70.0	-	10.0

Insulin requirement was higher in PDDM compared to IDDM and FCPD (Table 6). Incidence of complications such as Ketosis, infection, neuropathy and vasculopathy in the 3 clinical types are shown in Table 7. Both infection and neuropathy were more common in PDDM and FCPD compared to IDDM. Ketosis was conspicuous by it s total absence in PDDM in spite of very severe hyperglycemia and presence of infection in some.

Serum insulin, C-peptide, hGH (table 8) T3,T4, r T3, TSH, both basal and response to TRH (table 8A), prolaction, LH, urinary 17 ketosteroids and serum cortisol have been measured (Table 8B) in a cross section of patients of all 3 clinical types. Urinary 17 Ketosteroid and T3, T4 were significantly lower and TSH higher in PDDM compared to IDDM.

Table-3
Physical status of three clinical types of childhood onset diabetes

STATURE		Total	Clinical Types		
		%	IDDM(%)	PDDM(%)	FCPD(%)
HEIGHT	PERCENTILE				
Stunted	< 15th	35	26	68	-
Short	16th-50th	61.5	67	32	100
Average	51th-85th	3.5	7	-	-
Tall	86th +	-	-	-	-
WEIGHT	PERCENTILE				
Emaciated	< 15th	30	15	64	27
Very lean	15th-50th	70	80	36	63
Lean	51th-85th	-	-	-	-
Standard	8th +	-	-	-	-
BMI					
Very lean	< 14	84.4	78	100	82
Lean	14-19	15.6	22	-	18
Standard	19 +	-	-	-	-

Table-4
Severity of diabetes in three clinical types of childhood onset diabetes

SEVERITY		TOTAL	CLINICAL TYPES		
		No.	IDDM(%)	PDDM(%)	FCPD(%)
Mild	FBG < 150 mg/dl	3	-	-	27
Moderate	150-200 mg/dl	8	-	-	73
Severe	201-250 mg/dl	1	-	4	-
Very severe	250 + mg/dl	78	100	96	-
Ketosis		33	59	-	9
HbA	8-10%	4	-	-	36
	11-14%	32	11	24	64
	14 +	54	89	76	-

DISCUSSION

Diabetes mellitus is the most common endocrine disorder encountered during childhood beyond infancy. In our study of childhood onset diabetes seen during a 5 year period (1983-88) we encountered 3 cases of diabetes in infancy which is reported to be quite uncommon on global basis constituting of about 1.0-2.5% of childhood onset diabetics (5). None of the three patients had family history of diabetes, all were males and their birth weight was reported to be normal. Age at diagnosis was between 4 and 9 months. All of them had gradual onset of symptoms with enuresis and polyuria. Hyperglycaemia was of moderate degree. Ketosis was not evident at time of diagnosis . At start, insulin requirement was between 1.5 to 3 u/Kg. No case of true congenital diabetes was seen during the period of observation.

In trying to classify the rest of the patients, it was found that the distinction between IDDM, PDDM & FCPD were quite obvious. Proneness to ketosis indicated by ketonuria easily distinguished IDDM from the other two types. Presence of pancreatic calculi isolated FCPD from the rest. PDDM was not necessarily diagnosed by exclusion. History of severe under-nutrition in early childhood was considered as a moot point for diagnosis.

Table-5
Serum protein and lipid profile of three clinical types of childhood onset diabetes

Lipids		Total No.	CLINICAL TYPES IDDM (%)	PDDM (%)	FCPD (%)
Protein	< 5 mg/dl	38	7.4	100	82
	5-7 mg/dl	50	88.8	-	18
	7 +	2	3.8	-	-
Cholesterol					
	< 150 mg/dl	12	11	56	18
	150-250 mg/dl	72	78	44	82
	250 +	6	11	-	-
Triglycerides					
	< 100 mg/dl	39	44	52	18
	100-150 mg/dl	24	22	24	55
	150 +	27	34	24	27
HDLC					
	< 40 mg/dl	4	-	12	9
	40-50 mg/dl	48	44	76	45.5
	50 +	38	56	12	45.5
HDL-C/TC			0.25 ± 0.06	0.32 ± 0.05	0.28 ± 0.02

Table-6
Insulin requirements in three clinical types of childhood onset diabetes

Insulin requirements u/day	Total No	CLINICAL TYPES IDDM(%)	PDDM(%)	PCPD(%)
< 40	36	56	-	55
40-60	28	44	-	36
60 +	26	-	100	9

Table 7
Incidences of complications of three clinical types of childhood onset diabetes

Complications	Total	CLINICAL TYPES		
	No	IDDM	PDDM	FCPD
Ketosis	33	32 (59.2)	-	1 (9)
Infection				
Dental	2	2 (3.7)	-	-
Lungs	11	4 (7.4	7 (28)	-
U.T.I.	1	1 (1.8)	-	-
Skin	19	7 (12.9)	9 (36)	3 (27.2)
Vascular				
Nephropathy	3	2 (3.7)	1 (4)	-
Retinopathy	9	4 (7.4)	2 (8)	2 (18.2)
Neuropathy				
Peripheral	24	9 (16.6)	11 (44)	4 (36.3)
Autonomic	3	-	3 (12)	-
L J M	2	1 (1.8)	1 (4)	

Figures in parenthesis indicate percentage

Table 8
Hormonal profile of clinical types of childhood onset diabetes

Tests	Units (mean)	Control	CLINICAL TYPES		
			IDDM	PDDM	FCPD
Insulin	μU/ml				
Basal		12.2 ± 4.6	2.7 ± 0.71	3.46 ± 1.12	4.49 ± 1.10
Post Mixed meal (2h)		36.5 ± 4.85	4.79 ± 1.16	16.26 ± 0.61	9.68 ± 3.52
Post Glucose (2h)		58.16 ± 11.94	5.57 ± 2.49	13.12 ± 1.16	17.11 ± 1.16
C-peptide	ng/ml				
Basal		0.82 ± 0.14	0.39 ± 0.04	0.34 ± 0.08	0.86 ± 0.24
Post Mixed meal (2h)		1.78 ± 0.18	0.79 ± 0.14	0.54 ± 0.28	1.32 ± 0.31
Post Glucose (2h)		2.90 ± 0.16	0.88 ± 0.11	0.61 ± 0.10	1.78 ± 0.35
hGH	ng/ml				
Basal		3.4 ± 0.8	3.1 ± 0.30	8.82 ± 3.19	6.89 ± 2.44
Post Glucose (1hr)		3.4 ± 0.2	4.6 ± 0.36	10.2 ± 2.74	10.42 ± 3.68
Post Glucose (2hr)		2.3 ± 0.1	4.6 ± 0.31	13.21 ±1.64	12.31 ± 2.18

Table 8A
Hormonal profile of three clinical types of childhood onset diabetes

Tests	Units	Control	CLINICAL TYPES		
			IDDM	PDDM	FCPD
Tri-iodothyronine (T3)	ng/ml	0.7 ± 0.09	0.61 ± 0.12	0.57 ± 0.16	0.60 ± 0.30
Thyroxine (T4)	ug/dl	7.6 ± 2.6	6.2 ± 1.1	4.28 ± 2.3	7.30 ± 2.86
TSH (Basal)	mlu/ml	3.5 ± 1.2	2.82 ± 1.26	3.6 ± 1.08	3.88 ± 1.40
TRH Stimulation	mlu/ml	42.5 ± 7.5	17.26 ± 2.2	14.8 ± 2.3	15.2 ± 1.40
r-T3	ng/ml	0.1 ± 0.02	0.19 ± 0.08	0.20 ± 0.05	0.19 ± 0.05

All those who had no ketonuria or pancreatic calculi had positive history of malnutrition. This, along with very severe hyperglycaemia, were the criteria for establishing the diagnosis of PDDM.

Insulin dependent diabetes mellitus

The 54 cases of IDDM constituted 1.06% of the total 5112 cases. This incidence is higher than 0.45% (32/7025) cases of Juvenile onset IDDM (JIDDM) reported by Krishnaswami and Co-workers (6) from Madras, but lower than 1.2% (6 out of 500) seen by Dash et al at Chandigarh (7). Only in 5 out of 54 onset was by 5 years while 39 had onset between 11 and 15 years. There was no obvious seasonal variation in the incidence. Apparently, the incidence of juvenile onset IDDM in Orissa is gradually on the increase. Six years back it constituted 0.6% of all diabetes compared to 1.06% in the present series. Thirty two patients had frank ketonuria at presentation. The rest were already under treatment. Majority of the patients with IDDM were from the urban sector and from middle income group (Table 2). Yet only 7% were of average height while the rest were either short or very short in stature according to Indian standards (Table 3).

Weight-wise, 85% of the patients were very lean, and 15% even emaciated (Table 4). Serum protein was mostly in the normal range, while cholesterol was normal to high in 89% of the cases with a mean of 195.8 ± 38.3 mg/dl. Mean Triglycerides level was 107.1 ± 38.5 mg/dl and HDLC/TC (0.25 ± 0.06), both within normal limits (Table 5). Insulin requirement was within 40 u/day in the majority of the patients and between 40-60 u/day in the rest (Table 6).

In newly diagnosed cases of IDDM, insulin levels at fasting and in response to meals and glucose was found to be low. C-peptide levels were not very low at fasting but rise in response to glucose was negligible, showing very poor insulin reserve. Basal growth hormone levels were within normal limits. In general the features were more or less similar to IDDM seen in other parts of the country.

Table 8B
Hormonal profile of three clinical types of childhood onset diabetes

Tests	Units	Control	CLINICAL TYPES		
			IDDM	PDDM	FCPD
Prolactin	mlu/ml	275 ± 76	872.0 ± 18.4	672.0 ± 16.3	694.3 ± 22.2
LH	mlu/ml	8.5 ± 2.5	9.16 ± 0.60	10.1 ± 0.9	10.14 ± 4.43
Plasma cortisol	μg/dl	14.0 ± 3.1	22.0 ± 2.3	15.0 ± 2.8	14.8 ± 3.9
24 hours Urinary 17 Ketolsteroid.	mg/24 hrs	6.4 ± 1.3	8.8 ± 2.8	5.9 ± 2.3	6.5 ± 1.9

Protein deficient diabetes mellitus

Young patients with very severe diabetes who are aketotic inspite of remaining untreated for long periods (Ketosis resistant young, 'J' type) are quite common in this part of the country (8). All such patients are of rural orgin and belong to families of very poor economic status. History of chronic protein energy under-nutrition could be elicited in each case. Most patients were between 12 to 30 years of age. More recent studies (1981) (9) at the same centre revealed no alternation in clinical spectrum as observed initially in early 60s. In the present analysis PDDM('J' type) is found to constitute 27% of the patients with childhood onset diabetes, whereas 55% of diabetics with onset by 30 years belong to this category (Table 1). Out of 25 patients, only one had onset before 11 years of age; the rest between 11 and 15 years (Table 1).

Above two thirds (68%) came from very poor socioeconomic stratum. All the cases had retarded growth, with either stunted or very short stature. Further all were either emaciated or very lean with BMI (Kg/M^2) abdomen or ultra sonography revealed any calculi or deformity in the pancreas at screening or at subsequent repeat examinations. That is why WHO 1985, the nomenclature protein deficient pancreatic diabetes" (PDPD) needed to be altered to the now acceptable term Protein deficient diabetes mellitus (PDDM).

Ketosis was conspicuous by its absence, in spite of severe hyperglycaemia and high Hb A_1 (Table 4). Mean serum protein was low (3.23 ± 1.28 g/dl). Lipid profile showed hypertriglyceridemia in 24%, hypercholesterelemia in none (Mean 160.17 ± 33.95 mg/dl) while HDLC/TC (Mean 0.32 ± 0.05) was in a higher range. All had insulin requirement, more than 60 u/day. Nearly half (44%) had peripheral neuropathy while only 1 had evidence of limited joint mobility.

The basal serum insulin was low (Mean 3.46 ± 1.12 µu/ml), and rise in response to meals or glucose was of low order (Table 8). Measurement of C-peptide revealed a much-compromised functional status of B cells. Growth hormone levels were high at basal state (Mean 8.82 ng/ml ± 3.19) and rose significantly after administration of glucose. These were reminiscent of high hGH in patients with frank protein energy malnutrition (10).

From these observations, it is evident that PDDM is definitely a separate entity and cannot be considered to constitute one or the other end of the clinical spectrum of either FCPD, IDDM or NIDDM.

Fibrocalculous pancreatic diabetes

Plan skiagram of abdomen and ultrasonography revealed calculi, ductal dilatation and structural abnormality of the pancreas in around 12% of patients with childhood onset diabetes. There was male preponderance and all but one had onset of diabetes between 11 and 15 years of age (Table 1). Seventy eight percent of cases came from rural area and 90% were of poor socio-economic startum (Table 2). All of these had height and weight less than the 50^{th} percentile. Only 2 had BMI above 14 (Table 3). Hyperglycaemia was less severe than other 2 forms of diabetes in children (Table 4). The lipid profile was unremarkable with mean cholesterol 176.62 ± 24.84 mg/dl, triglyceride 139.46 ± 42.76 mg/dl and HDLC/TC (0.26 ± 0.02) at safe range (Table-5). Insulin requirement was less than 40 u/day in over half of the cases. Skin infection and peripheral neuropathy were frequent complications occurring in 27 and 36% of patients.

Compared to PDDM, although fasting serum insulin appeared similar (mean 4.49 ± 1.10 µu/ml, the C-peptide levels (ng/ml) were higher (0.34 ± 0.68 VS 0.86 ± 0.24 in FCPD), indicating less severe diabetic state. High basal hGH and lack of suppression by hypeglycemia suggested a state of underlying undernutrition.

Out of these 11 cases, 2 were subjected to surgery, as one had severe abdominal pain and the other failed to thrive in spite of good diabetes control. Stones were removed from the dilated ducts and pancreatic-jejunostomy done to drain pancreatic juice to a loop of jejunum. Post-operatively, at 3 weeks the mean insulin requirement fell from 40 to 15 u/day . Subsequently there was significant gain in weight and improvement in quality of life (11).

From the above observations, it is apparent that childhood onset diabetes, although uncommon, is not rare. All diabetes centres in this country must be facing the problems of juvenile onset IDDM, possibly more in the north west than in the south. As in other parts of the world, the incidence of

JIDDM may be on the rise, hence exchange of knowledge, at all levels, on its management cannot be neglected. In addition, in our country, there must be awareness of occurrence of other clinical types among children with diabetes. After exclusion of cases of diabetes in infancy, the rest of the patients could be clearly categorised into three clinical types. Such was also the case with young diabetics with onset by 30 years of age. All the cases of PDDM and large majority with FCPD were rural and poor compared to majority of IDDM from urban middle class. With similar grade of hyperglycaemia, ketonuria was conspicuous in IDDM, but not in PDDM. Growth and general health was poorer in PDDM, insulin requirement higher and neuropathy more prevalent. HDLc/TC was high (0.3), similar to that reported by us in undernourished diabetics of other categories (12). Serum insulin and C-peptide were higher in PDDM and FCPD compared to IDDM , possibly accounting for the lack of ketosis. Raised basal growth hormone levels, paradoxically rising after glucose administration, further supports the view that these types are causally related to malnutrition. There was no overlap between cases of PDDM and FCPD. The latter were milder, required less insulin and revealed evidence of exocrine pancreatic disease in X-ray, ultrasonography and function tests. Thus, the expressions of doubts regarding the existence of a separate clinical entity as PDDM are totally unfounded.

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