

Studies on Youth Onset Diabetes (Below 30 Years of Age At Onset) Regarding Phenotypic Presentations, Complications Associations Including Thyroid Dysfunction

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Abstract

Introduction: Diabetes mellitus (DM) is one of the most common chronic diseases in children and adolescents. The clinical presentations of youth onset diabetes (<30 year) in Tropical Countries differ from those in Western Countries in some respect.

Apart from Type 1 and type 2 diabetes some others type of diabetes seen only in Tropical country like Malnutrition modulated diabetes Mellitus (MMDM) and Fibrocalculous pancreatic diabetes (FCPD). **Aim and Objective:** To document the prevalence of young diabetes (<30 year of age at onset among the diabetic patient, to categorised the patient, find out the associations and complications as the worldwide prevalence of diabetes has raised dramatically over the past two decades and around 10% of diabetic in India have onset below 30 years of age. **Material and methods:** This institution based cross sectional study was conducted on consecutive 63 cases of diabetic patients whose onset of diabetes was less than 30 years, who attended the the outpatient department of the Endocrine, Nutrition and Metabolic diseases in Calcutta school of tropical medicine (CSTM) and in patient of Carmichael hospital for Tropical disease (CHTD), Kolkata from January 2012 to January 2013. **Results:** Among 63 patients the most commonly identified diabetes was T1DM (68.25%). The other types of diabetes seen are T2DM (14.28%), FCPD(14.28%), MMDM(03.17%). Most of the patients (69.84%) were rural population and majority (52.38%) had disease onset between the age of 10 -20 years of age. Major group of study subject (n = 29) presented with general weakness whereas Polyuria, Polydipsia with these presenting symptoms were 14 and 10 subjects respectively. The most common association was infection which was detected in 27 people. Dyslipidemia, Dimness of vision, Heart disease, HTN and Thyroid dysfunction were detected 22, 23, 03, 13 and 8 subjects respectively. Diabetic Retinopathy was detected in 18, nephropathy in 10, neuropathy in 22 and coronary artery disease were seen in 2 study subjects. **Conclusion:** Type 1 diabetes still the most prevalent form of young onset diabetes of India. Prevalence of type 2 diabetes is increasing among young Indian with metabolic syndrome. There is sharp decline of prevalence of MMDM but FCPD is still persisting.

Key word: Tropical country, Young diabetes- associations and complications.

Introduction:

The incidence of diabetes in youth is increasing worldwide, posing a serious challenge to health care providers. There is a consensus that long term complications are related not only to quality of metabolic control but also disease duration. Careful longitudinal studies in both low- and high incidence populations have shown a 3% annual increase in incidence of type 1 diabetes¹.

Criteria for diagnosis of diabetes².

1. Symptoms of diabetes and casual plasma glucose ≥ 200 mg/dl (11.1 mmol/L) casual is defined as any time of day without regard to time since last meal. Or
2. FPG ≥ 126 mg/dl (7.0 mmol/L) Fasting defined as no caloric intake for at least 8 hours. Or
3. Plasma glucose ≥ 200 mg/dl (11.1 mmol/L) during an OGTT. The test should be performed as describe by the world health Organisation using glucose load containing the equivalent 75 gms anhydrous glucose dissolved in water.

(In case of children 0.75 gm/kg B.W.)

Around 10% of the diabetic patient have onset below 30 year of age³. The clinical presentations of youth onset diabetes (<30 year) in Tropical Countries differ from those in Western Countries in some respect. Apart from Type 1 and type 2 diabetes some others type of diabetes seen only in Tropical country like Malnutrition modulated diabetes Mellitus (MMDM) and Fibrocalculous pancreatic diabetes (FCPD).

Type 1 diabetes remains the predominant clinical subset in young people in India and may account for 90% of diabetic children⁴. In rural Socio-economically backward populations the peak age of onset of type 1 diabetes has been reported delayed compared to affluent urban population⁵. It may have acute onset mainly in children and slowly progressive type 1 diabetes in adult⁶. Those with slowly progressive form present with

insidious onset of lethargy, asthenia, weight loss and polyuria. Those with rapidly progressive form present with subacute onset of thirst, polyuria, rapid weight loss progressing to ketonuria and ketoacidosis. Acute metabolic complications and chronic Microvascular complication are usual sequelae of many of Type 1 diabetes in India.

Prevalence of type 2 diabetes in young increasing sharply and also the age of presentation is falling due to change in life style, lack of exercise changes in food pattern. Young obese person also prone to develop type 2 diabetes⁷. They present with variable hyperglycemia, normal weight or over weight and good response to life style modification and/or oral hypoglycemic agent (OHA)⁸. Two types of type 2 diabetes in young Indian - the classical maturity onset diabetes in young (MODY) presentation with dominant multigenerational inheritance patterns⁹ and other without multigenerational pattern inheritance⁸. Foetal under nutrition followed by good catch up growth could lead to obesity and type 2 diabetes in later life¹⁰ problem is compounded when foetal under nutrition is followed by postnatal over nutrition¹⁰.

The proposed diagnostic criteria for FCPD are¹¹ – i) origin should be from tropical country, ii) diabetes should be present, iii) evidence of chronic pancreatitis must be present in the form of pancreatic ductal dilation with or without pancreatic calculi which can be demonstrated by radiological examinations and pancreatic exocrine function test are often abnormal and there will be no other causes of pancreatitis like alcoholism hepatobiliary disease etc. Apart from the above criteria some other features are frequently present i.e onset below 30 years of age, chronic under nutrition, insulin requirement for control, ketosis resistant even on prolonged interruption of insulin therapy, low C-peptide level, HLA DR₃ association^{12,13}.

MMDM is often confused with slowly progressive type 1 diabetes. They usually come from rural or

semi rural areas with poor socio-economic background and history of long standing under nutrition. These patients suffer from severe hyperglycemia (FPG \geq 200mg/dl) but are not prone to develop ketoacidosis even on prolonged interruption of insulin therapy. Radiological evaluation does not show any pancreatic calculi. There is no response to oral hypoglycemic drug and insulin is necessary for control. Pyogenic and fungal infection of skin and soft tissues and peripheral neuropathies are most common complication¹⁴. Metabolic complications like ketosis and non ketotic hyperosmolar coma usually do not occur in spite of infections and very severe hyperglycemia¹⁵. Common complications in younger age group are psychological problems, limited joint mobility, microalbuminuria and peripheral and autonomic neuropathy Diabetic ketoacidosis and hypoglycemia are very common in lower age group and decreases with age and self involvement in the treatment.

Back ground non- proliferative retinopathy neuropathy and nephropathy are common than macrovascular complications.

Other autoimmune disorder that occur with an increased frequency in children with Type 1 diabetes: thyroid disorder, adrenal insufficiency and celiac disease. Hypothyroidism co exist with type 1 DM with prevalence estimate between 7 – 24% depending on race age and geographical distribution¹⁶ and affect women more frequently than man¹⁷. The rare associated abnormalities in young diabetes are positive gastric parietal cell antibody, hypogonadism, osteopenia etc.

Materials and Methods:

This institution based cross sectional study was conducted on consecutive 63 cases of diabetic patients whose onset of diabetes was less than 30 years, who attended the the outpatient department of the Endocrine, Nutrition and Metabolic diseases in Calcutta school of tropical medicine (CSTM) and in patient of Carmichael hospital for Tropical disease (CHTD), Kolkata from January

2012 to January 2013. The only exclusion criteria were pregnancy and those patients or parent of the patients (in case of minor) unwilling to give consent. After clinical evaluation and investigation patients were categorized in following types:

I. Type -1 Diabetes

Those patients who were insulin dependent, ketoacidosis or ketonuria on insulin withdrawal, no history of chronic pain abdomen and steatorrhoea (features of chronic pancreatitis) no detectable pancreatic calculi on radiological examination are categorized in type -1 diabetes.

II. Diagnostic criteria for MMDM¹⁸

Clinical Features	Score
1. Age of onset (10 – 30 years)	1
2. Leanness BMI <16.0	2
BMI 16.0 – 18.0	1
3. History of malnutrition in childhood	2
4. Stigma of malnutrition clinical past /present	1
5. Severe hyperglycemia (FPG \geq 250 mg/dl)	1
6. Lack of proneness to ketosis (absence of ketonuria on withdrawal of insulin for long period)	3
7. Insulin requiring (over 60u/day i.e \geq 3 u /kg body weight)	2
8. Absence of x-ray or USG evidence of pancreatic calculi and ductal dilation	3
Total Score	16
Diagnostic Score – 13	Suggestive - 12

III. Diagnostic criteria for FCPD (Mohon et al)¹⁹

1. A patient should originate from a tropical country
2. Diabetes should be present
3. Evidence of chronic pancreatitis must be present

Pancreatic calculi on x-ray abdomen or at least three of following

- a. Abnormal pancreatic morphology on sonography/C.T. Scan.
 - b. Recurrent abdominal pain since childhood
 - c. Steatorrhea
 - d. Abnormal pancreatic function test
4. Absence of other causes of chronic pancreatitis i.e. alcoholism, hepatobiliary disease, primary hyperparathyroidism etc.

IV. Type -2 Diabetes

Those patients whose phenotypic presentation did not match with type 1, Malnutrition modulated diabetes mellitus (MMDM), Fibrocalculous pancreatic diabetes (FCPD) as per previously mentioned criteria and who were well controlled with oral anti diabetic agents were categorized as a type 2 diabetes.

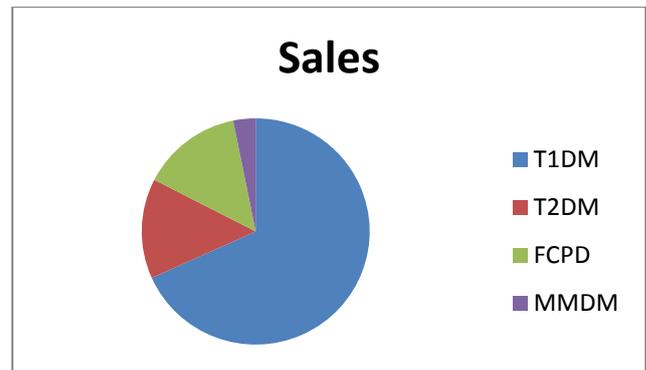
Features of Metabolic Syndrome and Maturity onset diabetes in young (MODY) were sought in all young Type -2 subjects.

Results:

Over all 63 young diabetes (age of onset <30 years) were evaluated. Among these 63 subjects, 37 were male and remaining 26 were female (male: female ratio 1.42:1). Most patients were in the age group of 15 to 35 year. Among them 44 were resident of rural area and remaining 19 were from urban area and 44 of study subjects came from poor socio economic condition, 17 people

were from middle class and only 2 subjects were from affluent society.

Among 63 patients the most commonly identified diabetes was T1DM (68.25%). The other types of diabetes seen are T2DM (14.28%), FCPD(14.28%), MMDM(03.17%).



Most of the patients (69.84%) were rural population and majority (52.38%) had disease onset between the age of 10 -20 years of age. Major group of study subject (n = 29) presented with general weakness whereas Polyuria, Polydipsia with these presenting symptoms were 14 and 10 subjects respectively. The most common association was infection which was detected in 27 people. Dyslipidemia, Dimness of vision, Heart disease, HTN and Thyroid dysfunction were detected 22, 23, 03, 13 and 8 subjects respectively. Diabetic Retinopathy was detected in 18, nephropathy in 10, neuropathy in 22 and coronary artery disease were seen in 2 study subjects.

Distribution of complications in study population according to different types of diabetes and sex.

Complication	Type – 1		Type – 2		FCPD		MMDM		Total
	M	F	M	F	M	F	M	F	
Ratinopathy	9	6	0	1	1	0	1	0	18
Nephropathy	3	4	0	1	2	0	0	0	10
Neuropathy	10	3	1	2	3	2	1	0	22
CAD	1	0	0	1	0	0	0	0	2
Stroke	0	0	0	0	0	0	0	0	0
Total	23	13	1	5	6	2	2	0	52

Distribution of study population according to thyroid dysfunction and different type of diabetes and sex.

Type of Diabetes	Euthyroid		Hypothyroid		Hyperthyroid		Total
	M	F	M	F	M	F	
Type-1 DM	26	7	0	5	0	0	38
Type-2 DM	1	3	0	3	0	0	07
FCPD	4	5	0	0	0	0	09
MMDM	0	0	0	0	0	0	0
Total	31	15	0	8	0	0	54

Metabolic syndrome were detected in 13 study subject. Four were from type-1 DM (Male = 2, Female = 2), six from type-2 DM (Male = 1, Female = 5) and three were FCPD (Male = 1, Female = 2) patients.

Discussion:

Youth onset diabetes is an emerging problem throughout the world, more so in India.

Prevalence of type-2 diabetes in young is increasing probably due to changes in life style like sedentary habits, use of junk food, inclination to avoid all sorts of exertion. Studies on FCPD group were done in our institute regarding their

predisposition, complication and liver dysfunction^{5,13,20}.

This study focussed on current status of different type of young diabetes (i.e., Type 1, Type 2, FCPD and MMDM) regarding clinical presentation, complication and association. Prevalence of thyroid dysfunction was also carried out in these groups.

In our study, the most commonly identified diabetes was T1DM (68.25%). The other types of diabetes seen are T2DM (14.28%), FCPD(14.28%), MMDM(03.17%). Our study well correlated with the study conducted in North India by Goswami R et al²¹ in which T1DM seen in majority cases(37%) but Jyotsna VP et al²² found most common diabetes is FCPD constituted 32.9%.

Type 2 diabetes was found in 14.28% (9) of study population. Goswami R et al⁷⁴ found type 2 diabetes in 13% of their study subjects which is fairly comparable to present study (14.28%).

Fibrocalculous pancreatic diabetes (FCPD) was detected in present study subjects (14.2%) that was also comparable to Goswami R et al Study²¹ which was 11%.

Malnutrition modulated diabetes mellitus (MMDM) was found in only 2 cases which comprise 3.17% of study population. Prevalence of MMDM was found to be much less in present study in comparison to two earlier studies which may be due to marked reduction in the incidence of severe childhood undernutrition particularly Kwashiorkor or marasmic Kwashiorkor.

Microvascular complications of diabetes were seen in majority patients, with peripheral neuropathy being the commonest (42.30%). These findings were consistent with the study by Jyotsna VP et al²² in which peripheral neuropathy was 43.5%.

Clinical and sub-clinical hypothyroidisms were diagnosed in 8 study population. All of them were females. Female preponderance of thyroid

dysfunction was found by K Vondrall et al²³ in their follow up study in type 1 diabetes.

Conclusion:

Type 1 diabetes still the most prevalent form of young onset diabetes of India. Prevalence of type 2 diabetes is increasing among young Indian with metabolic syndrome. There is sharp decline of prevalence of MMDM but FCPD is still persisting. Microvascular complication was the most common complication among the study subjects. Neuropathy was the commonest complication. Thyroid dysfunction in the form of clinical and sub-clinical hypothyroidism was found in significant number of female study subjects.

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