

## Study of clinical profile of type 1 diabetes mellitus cases attending tertiary care hospital in northern Kerala

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### Abstract

**Background:** The type 1 diabetes should consider an important disease both in diagnosis and management. Its prevalence in India is 0.26/1000 population according to a study conducted in 1992. A study conducted in south India, Karnataka (4/100000) it is found out that higher incidence while comparing other Asian countries. This study conducted to know clinical profile of type 1 diabetic patients attending Diabetic clinic Government Medical College Calicut. **Objective:** To study the clinical profile of type 1 diabetes mellitus, with special reference to the aetiology and complications: A case series study. **Methods:** This study is a case series study of 52 diabetes cases purely on insulin and less than 25 years of age attending diabetic clinic in MCH and IMCH under treatment in medicine and paediatrics respectively in Govt Medical college Kozhikode. Data were collected by taking detailed history and checking medical records with the patients. **Results:** The age of onset of DM 73.1% of patients were between 5 and 15 years of age. Female showed higher incidence compared to males (F:M 1.6:1). In this study no relation to consanguineous marriage and father of 9 patients were diabetic and mother of only one patient was diabetic. While probing to the antenatal history of patients only one mother has gestational diabetes. No relation found in the incidence of type 1 DM and maternal age at the time of delivery. Birth weight and incidence could not find out a relationship. Significant relation could not find out with weaning of breastfeeding and other food products. (for example cow milk or gluten sensitive products). No vaccine related aggravation of incidence in all cases polyuria and polydipsia were predominant symptoms. 60% of them present with diabetic ketoacidosis. **Conclusion:** In total 52 cases studied most of them have age of onset between 5 and 15 years of age. Antenatal history, family history, birth weight, immunisation, viral or other infections during early childhood could not find out any relation with disease. Most of them present with polydipsia, polyuria and polyphagia and 60% had DKA at first presentation. Further studies are required to find out etiology, to prevent the disease, to manage properly and to delay complication of type 1 DM.

**Keywords:** Type 1 diabetes mellitus (DM), diabetic ketoacidosis (DKA), birth weight, polydipsia, polyphagia, polyuria, antenatal history.

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### Introduction

Type 1 diabetes mellitus is one of the chronic endocrine disorders starting from childhood due to beta cell destruction in the pancreas either due to immune-mediated or idiopathic aetiology [1]. We know that Diabetes mellitus is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia. The incidence of childhood T1DM varies worldwide [2]. The highest reported incidences of T1DM occur in Finland and Sardinia (37 to 65 per 100,000 children younger than the age of 15 years) [3]. From India, Chennai has reported an urban incidence of 10.5/100,000 population in 1996 [3]. The Karnataka state T1DM registry listed an incidence of 3.7/100,000 in boys and 4.0/100,000 in girls over 13 years of data collection [4]. The age of presentation of childhood onset type 1 DM has a bimodal distribution with one peak at four to six years of age and a second in early puberty (10 to 14 years of age) [5]. Against the most of the autoimmune diseases are common in females regarding the type 1 DM has an autoimmune factor in aetio-pathogenesis many of the international studies show the male preponderance and ratio being 3.2:1 male to female [6]. Regarding aetio-pathogenesis both genetic and environmental factors contribute. Close relatives of type 1 patients had high susceptibility if both parents are type 1 there is a 30% chance to affect the offspring [7]. Monozygotic twins 30% within 10 years of diagnosis of the first

twin [8]. Most of the cases there is no family history. Genetically susceptible individuals in contact with many of the environmental factors can trigger an autoimmune response that can later lead to the development of type 1 diabetes. Mainly following environmental factors seem to be associated: viral infections like mumps, respiratory and enteroviral infections [9], immunizations, diet, higher socioeconomic status, obesity [10], vitamin D deficiency, perinatal factors like maternal age, history of pre-eclampsia and neonatal jaundice. Some studies showed low birth weight decreases the risk, while high birth weight for gestational age and lower gestational age at birth may increase the risk for T1DM [11]. Hyperglycemia without acidosis is the most common presentation of childhood T1DM in most populations. Patients typically present with the following symptoms: polyuria, polyphagia and polydipsia are classic symptoms. Most of them have weight loss explained by their increased catabolism and weight loss. If it is not diagnosed appearance of these symptoms patient goes for diabetic ketoacidosis an acute medical emergency (second commonest presentation). Diabetes is diagnosed when fasting blood sugar goes more than 126 mg/dl or random blood sugar more than 200 mg/dl and Hb1AC more than 6.5% (based on ADA guidelines). Regarding other important investigations as far as type 1 DM concerned are Insulin C-peptide levels (High fasting insulin and C-peptide levels suggest T2DM. Levels are inappropriately low or in the normal range relative to the concomitant plasma glucose concentration in T1DM) as we know main aetiology of type 1 DM is autoimmune destruction of pancreatic beta cells as part of investigation following serum antibody tests are carried out T1DM is suggested by the presence of circulating, islet-specific,

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pancreatic autoantibodies against glutamic acid decarboxylase 65(GAD65),the 40K fragment of tyrosine phosphatase (IA2),insulin, and/or zinc transporter 8 (ZnT8)[12].Insulin deficiency in T1DM most commonly results from autoimmune destruction of pancreatic beta cells and is referred to as type 1A diabetes (approximately 85 percent)[13]. Patients with clinical features of T1DM but without detectable autoantibodies are categorized as having type 1B diabetes (approximately 15 percent)

#### Material and methods

This study is a case series study of diabetic cases purely on insulin and less than 25 years of age patients attending diabetic clinics under department of medicine and paediatrics in Govt medical college Kozhikode in northern Kerala.After getting an informed consent following data were collected sociodemographic features like age, sex,economic status,family history of parents,detailed ante natal history,details of feeding habits in child hood (breast feeding ,weaning history and diet),immunization details, and details of infection and other insults from neonatal period to age of presentation were studied. Investigations like CBC with ESR,fasting blood sugar blood urea serum creatinine serum calcium serum phosphorus serum alkaline phosphatase,fasting lipid profile,urine alb/creatinine ratio, were obtained.A descriptive analysis was done by SPSS software and results are expressed in percentages,scatter charts,linear charts,column charts and pie charts.

#### Observations

These observations were made by studying 52 cases of type 1 diabetes mellitus.Total 52 cases studied 42.3% between 11 and 15 years (22/52) 30.8% between 5 and 10years (16/52) 17.3% between 16 and 20 years (9/52) and 9.6% age group below (5/52).Age of onset of 73.1% of patients was between 5 to 15 years.Regarding gender distribution 32 cases out of 52 (61.5%) were females and 20 cases (38.5%) were males.female to male ratio 1.6:1.on probing into consanguinity of parents of patients 92% were non consanguineous. Fathers of 9 patients were diabetic,two of them had onset of them had onset of disease before 30 years.Mother of one patient had diabetes.There was no history of type 1 diabetes for their parents. None of siblings were twins,siblings of three patients have type 2DM.Antenatal history for gestational DM reported in one case only .25 % of mothers of patients had hyperemesis gravidarum.Only 10 cases had complications during delivery 3 cases with delayed crying one with meconium aspiration ,three cases of breech deliveries and three cases of pregnancy induced hypertension. Regarding birth weight of 31% of cases below 2.5 kg and 69% above 2.5kg (47% between 2.6 and 3 kg)one patient was had microcephaly with hydrocephalus intelligence was normal but marked motor development delay. Another patient with gross developmental delay and poor scholastic performance. On studying the breastfeeding of children out of 52 cases 39 cases had exclusive breastfeeding till 4th month, only 2 of them never got the breast milk. Relationship with weaning and starting of cow milk in 39 cases in 5th month. The pattern of immunization 7 childrens were not immunised all remaining patients were immunized for age.Following chart will give the information regarding infections in childhood

Table 1:Cases and numbers

CASES	NUMBERS
Recurrent respiratory tract infections	8
Measles	6
Mumps	5
Bronchial asthma	5
Eczema	4
Pulmonary tuberculosis	3
Acute diarrhoeal disease	3
Failure to thrive	2
Febrile seizure	2
jaundice	2
Poliomyelitis 8th month/ fully recovered (long term steroids)	1
Rubella	1
Chronic diarrhea	1
Whooping cough	1
Hypothyroidism	1

Evaluation of chest deformity (rickety rosary ribs)	1
Poor milestone development and poor scholastic performance	1
Chicken pox	1
Rheumatic heart disease	1

Another important observation were multiple problems in one patient and age presentation showed following findings

**Table 2:Problems in patient and age of presentation**

Multiple problems in same patient	Age of presentation
RTI and Measles	12
RTI and Eczema	11
Mumps and primary complex	13
Mumps and bronchial asthma	17
Diarrhea and bronchial asthma	13
Jaundice one year back of onset of diabetes	13
A girl taking some ayurvedic medicine for 2 years for improving appetite	3
Measles mumps whooping cough and non immunised	12
History of three times parotitis 7,8 and 10 years(? mumps)	12
ADD (2years) and PTB(8YEARS)	14
Poliomyelitis and bronchial asthma	20
ADD ,measles and rubella	9

Food habits before onset of symptoms all of them were taking a mixed diet but it was inadequate in proteins ,fruits and vegetables. Ongoing to symptoms of presentation polyuria and polydipsia were predominant symptoms .90% had polyphagia, 87% had weight loss 67 % had a history of fever and 60% presented with diabetic ketoacidosis as presenting symptom.On checking fasting blood sugar values only 18% showed values less than 100mg/dl and 82% had values more than 100mg/dl. On testing FLP of these patients serum cholesterol level was 74% of them values were less than 200mg. triglyceride values found less than 150 mg/dl in 82% of patients, regarding the HDL it was found more than 40 mg/dl in 73% cases.

**Discussion**

Total 1708 diabetic patients attending our diabetic clinic around 70 cases are diagnosed as type 1DM in which 52 cases below 25 years are studied in the present study similar study in Kolkata shows comparable incidence[14] 73.1 % of patients .of patients had their onset of disease between 5 and 15 years.this study are similar to study conducted in united states in which 61% belong to the same group and another study conducted in chile the present study also shows that highest incidence less than 15 years of age. Girls exhibited a slightly higher incidence rates than boys in the 11 to 15 years of age group comparable to study conducted in sudan most of the population based studies showed it occurs frequently in males in a ratio 3:2 .A study conducted in finland shows higher incidence in male but in current study it is not population based study ratio shows

slightly more in females than males 1.6:1 In this study fathers of 9 cases out of 52 were diabetic in this group 2 of them diagnosed before 30 years of age and on oral anti diabetic drugs. Type 1 DM showed higher incidence when parents are suffering from type 1 but in this study could not find a strong family relation of type 1DM . None of them were twins, siblings of three patients have diabetes all of them had disease onset after 40 years. According to studies type 2DM was not frequent among parents and siblings of type 1 DM than in general population Regarding the antenatal and perinatal history, mothers of 25% had hyperemesis gravidarum and only one case have gestational DM studies showing no relationship between these factors. Only 10 cases had complications during delivery like delayed crying one with meconium aspiration ,three cases of breech deliveries, and three cases of pregnancy induced hypertension. Different perinatal factors like maternal age, history of pre eclampsia and neonatal jaundice. Are associated with increased incidence of type 1DM.in this study 48.78% of mothers age was more than 25 years.Birth weight of neonates in present study shows 69% had above 2.5 kg Some studies showed low birth weight decreases the risk ,while high birth weight for gestational age and lower gestational age at birth may increase the risk for T1DM.39 cases out of 52 (75%) exclusively breast fed up to 4 months many studies shows exclusive breastfeeding important factor in decreasing the incidence of type 1DM.Like exclusive breastfeeding weaning with cow milk is an important factor it has been proposed that some

component of albumin in cows milk (bovine serum albumin) the basis of most infant milk formulas may trigger an autoimmune response. It is found a strong relationship with starting dairy products at younger age and high milk consumption in childhood increases the levels of cow milk antibodies and that IgA antibodies to cow's milk formula independently associated with increased risk of Type 1 DM. But in present study we are not able to study the antibody titers due to high cost and 75 percentage of our children cow milk started from 5th month onwards. Present study even though we are not able to find out any statistical significant relationship probably due to small number of cases. Type of weaning in 48% of the them with Ragi, normal home food in 29%, baby food in 11%, banana 8 percentage and in 4 percentage provided only kanji (rice based). There is a significant relationship between early cereal exposure and development of Type 1 Diabetes especially gluten containing cereals. Children initially exposed to cereals between ages 0 and 3 months and those who were exposed at 7 months or older had increased incidence compared with those who were exposed during the fourth month. One case of chronic disease and two cases of food induced diarrhoea (greenish coloured) one aggravated following milk ingestion and in other cases induced with wheat and ragi ingestion. Vitamin D deficiency has a proven role in development of Type 1 Diabetes in many studies conducted world wide and in this study could not find out any clinical features suggestive of vitamin D deficiency. One girl evaluated her chest deformity and received vitamin D supplementation. Finland, one country with maximum incidence, one study with supplementation of vitamin D showed marked reduction of incidence of Type 1 Diabetes and a large multicenter trial covering many different European settings consistently showed a protective effect of vitamin D supplementation in infancy. In this study included serum calcium, serum Phosphorus and serum Alkaline phosphatase but none of values were suggestive of vitamin D deficiency one thing is most of our patients in growing age marked elevation of SAP requires to prove vitamin D deficiency but all values being in normal range. More studies are required with estimation of serum vitamin D levels in our patients to prove this association. Regarding Immunization fully immunized for age in 45 (86.5%) cases in present study and non immunized or not completely immunized in 7 cases (13.5%). There are studies showing increased incidence of Type 1 DM in immunized children. Further studies confirmed no evidence of any clustering of cases 2 to 4 years after vaccination with any vaccine and the result do not support a causal relation between childhood vaccination and Type 1 Diabetes (22). One case in this study non immunized for age had history of measles, mumps and whooping cough in childhood his age of onset was at 12 year. Another case one girl fully immunized gave history of parotitis 3 times (first in 7th year unilateral second in 8th years bilateral involvement and third in 10th years bilateral involvement) possibly mumps and age of onset was 12 years. Requires further studies in our population. The viral diseases with proven association are with enteroviruses group A and group B viruses and poliovirus mainly coxsackievirus B virus infection causing meningitis in children but none of our cases had meningitis. But one had history of poliomyelitis in 8th month recovered with minimal disability. Other viruses like varicella, epstein-barr virus, mumps, measles, rubella, rotavirus and cytomegalovirus are also considered as a aetiological factor. In the present study 6 cases of measles, 5 cases of mumps, 3 cases diarrhoea, one case of rubella and chickenpox each. Three cases had pulmonary tuberculosis; 4 cases had Eczema, one case had rheumatic heart disease on penicillin prophylaxis. 8 cases with history of recurrent respiratory tract infections in a frequency of 2 to 3 episodes per month. In some cases we noticed the occurrence of different diseases in the same patient like measles and diarrhoea in one case, RTI and measles in one case, measles, mumps and whooping cough occurring non-immunized patient before 3 years (age of onset of diabetes was 12 yrs) acute diarrheal disease, measles and rubella in one case, mumps and pulmonary tuberculosis in one

case, mumps and bronchial asthma in one case mumps, one female fully immunized had a history of mumps 3 times and age of onset was 12 years and in one case jaundice one year before the onset of diabetes [22-24]. One patient had hypothyroidism before the onset of diabetes and is on thyroxine. 2 to 5% of patients with Type 1 Diabetes develop autoimmune hypothyroidism. Up to 20% of patients with Type 1 Diabetes have positive anti thyroid antibodies (anti thyroid peroxidase and anti thyroglobulin) [25]. In all cases polyuria and polydipsia were predominantly symptoms. The most common presenting clinical findings in children with Type 1 Diabetes are polyuria, polydipsia and weight loss. (26) 90.38% cases had history of polyphagia at the time of presentation. Weight-loss accounted in 87% of patients. Many other studies showed 34% of weight loss [20]. An Irish study of 283 children polyuria, polydipsia were present in 70% of patients and weight loss in 34%. and in one indian study 19.4% [27]. In present study DKA at the onset in 31 cases (60%). In Irish study DKA in 25% of patients [26] and in one Indian study 19.4% [27]. FBS less than 100 mg/dl in only 18% and it was more than 100 mg/dl in 82% since most of our patients are low socioeconomic status; majority of them depend on the insulin provided from our institution. Total S. cholesterol less than 200 mg/dl in 74% of cases and 3% of cases it is more than 300 mg/dl (28). In 82.5% of cases triglyceride found less than 150 mg/dl many studies showed lipid profile with normal or decreased values (28) 73 percentage of cases showed HDL more than 40 mg/dl.

#### Conclusion

Age of onset of 73.1% of patients were between 5 and 15 years and girls exhibited slightly higher incidence rates than the boys in the 11 to 15 year age group. 61.5% were females. Study shows some female trend towards disease and autoimmune nature of the illness should be studied. There was no family history of Type 1 Diabetes among the patients studied. Fathers of 9 patients and mother of one patient had features of type 2 diabetes which is controlled with Anti diabetic drug. There are many controversies regarding association of birth weight and development of diabetes. Recent study showed increasing birth weight will increase incidence. In this study 69% was more than 2500 gram and 31% came below 2500 gram could not find out any correlation with age of presentation. 75% of patients exclusively breastfed up to 4 months and majority of them using cereals for weaning. No definite evidence of vitamin D deficiency was detected among these patients and further studies are required to find out aetiological association of vitamin D deficiency. Around 40% of them had a history of viral infections like measles, mumps, rubella, chickenpox and acute diarrhoeal disease in childhood and most of their age of onset of diabetes was at or after 12 years further studies are required to prove the etiological association. Body mass index of the patients showed a decline tendency towards 25 years that lies below 25th percentile than expected suggest a growth failure as age advances. Polyuria, polydipsia, polyphagia and weight loss were the predominant symptoms in this study. There is a high incidence (60%) of diabetic ketoacidosis as the first presentation in our patients compared to other studies. Majority of patients had FBS values more than 100 mg/dl (82%) since our patients depend on insulin provided by diabetic clinic which may not be adequate to meet the total required dose. They require further support and empowerment. Majority of their lipid profile is in the normal range may be explained by insulin deficiency and lack of obesity. Further studies are required to find out etiology to prevent the disease to manage properly and to delay complications of Type 1 Diabetes.

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