# Clinico-Epidemiological Study of Type I Diabetes Mellitus in Children in a Tertiary Care Center

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**ABSTRACT**

**BACKGROUND**

T1DM accounts for about 10% of all cases of diabetes. This represents a more than 400-fold variation in the incidence per 100 population. It is estimated that of the 400,000 total new cases of type 1 diabetes occurring annually in all children under age 14 yrs. in the world, about half are in Asia even though the incidence rates in that continent are much lower, because the total number of children in Asia is larger. We wanted to assess the incidence of Type 1 Diabetes Mellitus and study the demographic details, biochemical and metabolic alterations in these patients.

**METHODS**

50 children aged between 0 to 12 years admitted to the Department of Paediatrics at a tertiary care centre were analysed in the study. The study was conducted for a 2-year period.

**RESULTS**

The incidence was 1.3 /1000 Paediatric admissions in this study. The mean age was 9.7 years. However, the mean age of onset of T1DM was 7.8 years. Most of the children belonged to low socio-economic group and the consanguinity was also high in this study. There was a wide distribution of clinical presentations in the children with T1DM. Children also presented with mild, moderate and severe diabetic ketoacidosis. 2 children died in our study due to DKA.

**CONCLUSIONS**

The incidence of T1DM is increasing. All children with type 1 diabetes should have access to appropriate insulin therapy as most of the children had missed insulin injections that lead to severity of the disease and the children presented with DKA.

**KEYWORDS**

Demography, Incidence, Biochemical and Metabolic Alterations, Type 1 Diabetes Mellitus (T1DM)

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*DOI: 10.18410/jebmh/2020/232*

*Financial or Other Competing Interests: None.*

*How to Cite This Article:*
*Shanigaram K, Polanki R, Varahala AM. Clinico-epidemiological study of type I diabetes mellitus in children in a tertiary care center. J. Evid. Based Med. Healthc. 2020; 7(22), 1073-1079. DOI: 10.18410/jebmh/2020/232*

*Submission 12-04-2020,*
*Peer Review 17-04-2020,*
*Acceptance 14-05-2020,*
*Published 30-05-2020.*

## BACKGROUND

Diabetes mellitus (DM) is a common, chronic, metabolic syndrome characterized by hyperglycaemia as a cardinal biochemical feature. Type 1 diabetes mellitus (T1DM) affects 15 million children in the world and is rapidly increasing in specific regions so that annual increase of 2-5% is reported in Europe, Middle East and Australia.[1,2] The complications include DKA as the primary cause of death in children with T1DM.[1,3,4] Up to 20% of patients with T1DM have positive anti-thyroid antibodies and 2 to 5% patients with T1DM develop autoimmune hypothyroidism.[5,6] Intensive glycaemic controls dramatically reduce the risk of long term vascular complications, growth retardation, puberty delay and also dyslipidaemia.[1,4,7,8,9]

Fraction of glycosylated haemoglobin (HbA1c) could provide a reliable index of glycaemic control. Thus, to obtain a profile of long-term glycaemic control, it is recommended that HbA1c measurements be obtained 3 to 4 times per year. Female gender has been identified as an independent risk factor for poor glycaemic control.[10,11,12,13,14,15]

T1DM is the most common endocrine-metabolic disorder of childhood and adolescence, with important consequences for physical and emotional development. Girls and boys are almost equally affected but there is a modest female preponderance in some low-risk populations. Peaks of presentation occur in 2 age groups i.e. at 5-7 yrs. of age and at the time of puberty. The 1st peak may correspond to the time of increased exposure to infectious agents coincident with the beginning of school; the 2nd peak may correspond to the pubertal growth spurt induced by gonadal steroids and the increased pubertal growth hormone secretion.[16]

### Objectives

1. To assess hospital-based incidence of type 1 diabetes mellitus (T1DM) in children.
2. To study demographic details, presenting features, hospitalization details, complications, Co-morbidities, biochemical and metabolic alterations in these children.

## METHODS

### Study Period

November 2010 to October 2012.

### Subjects

All T1DM children in the study period. 50 Children from 0-12 years with T1DM, attending to department of Paediatrics, Mahatma Gandhi Memorial Hospital, Warangal, Telangana which is a tertiary care centre affiliated to Kakatiya Medical College. Consent from parents was taken to participate in the study.

### Study Design

Cross-Sectional, Descriptive, Analytical study.

Base line variables like, age, sex, region, socio-economic status, other family characteristics, breast feeding details, clinical features, lab investigations, height, weight, BMI, co-morbidities, mortality if any, will be recorded in a predesigned Case record form. Appropriate statistical tests (Mean, S.D., Median t-test for quantitative/continuous variables and proportions, Chi-square/Fisher exact test and odds ratio for qualitative variables) were conducted using Epi info 3.5.1 and MedCalc @ Version 11.4.4.0. Approval of Institutional Ethical Committee was taken.

## RESULTS

Total hospital admissions during present study period were 96419. Total hospital admissions in Paediatric ward excluding neonatal admissions were 14537. 50 cases of T1DM were admitted during the study period. In the present study of 50 admissions, 3 children (6%) were between 1-3 yrs., 4 children (8%) were between 3-6 yrs., 31 children (62%) were between 6-12 yrs. and 12 children (24%) were more than 12 yrs. The mean age at admission was 9.74 ± 3.0 yrs. Youngest child was 1 yr. 9 months and eldest child was 12 years 8 months.

In this present study 34 (68%) were females & 16 (32%) were males. In the present study, mean weight at admission was 25.4 ± 8.2 Kg, the mean height value at admission was 121.0 ± 18.0 cm and mean BMI at admission was 16.9 ± 2. Family h/o of type 2 diabetes was present in 6 (12%) children. In this study 37 (74%) children were products of consanguineous marriage. Consanguinity is a very common practice among tribal community and some communities of backward casts in this area. As per modified Kuppuswamy scale 20 (40%), 23 (46%), 7 (14%) belongs to lower, lower middle, upper middle, respectively. In the present study we noted that 41 (82%) children were breastfed for varying time and 9 (18%) children were top fed. In the present study, mean age at onset of the disease was 7.8 ± 2.8 yrs.

Osmotic symptoms were reported by parents as polyuria 45 (90%), polydipsia 30 (60%), polyphagia 11(22%). Osmotic symptoms in newly diagnosed cases were reported for 2 – 3 wks. duration prior to the diagnosis at admission. In this study most common presentation at admission was vomiting 49 (98%). Deep breathing (Kussmaul breathing) 41 (82%) & pain abdomen 37 (74%) were other frequent symptoms. Altered sensorium was noted in 4 children & two children who died had altered sensorium.

The mean PR at admission was 124/mt in age group of 1-3 yr., 120/mt in 3-6 yrs. age group, 103/mt in 6-12 yr. age group and 113/mt in >12 yrs. The mean RR at admission was 51/mt in age group of 1-3 yr., 41/mt in 3-6 yr. age group, 35/mt in 6-12 yr. age group and 37/mt in >12 yrs.

Median Systolic Blood pressure in different age groups was 80 mmHg, 80 mmHg, 90 mmHg, 110 mmHg respectively. Median Diastolic Blood Pressure in different age groups was 60 mmHg, 50 mmHg, 70 mmHg, 60 mmHg respectively. In this study 19 (38%) children were newly diagnosed as T1DM. Another 31 (62%) children were already diagnosed as T1DM previously (in this hospital or other hospitals and referred to this hospital) and they presented with DKA in our study period. H/O insulin dose omission for few doses to few days was present in 30 (96.7%) out of 31 known T1DM cases.

**Routine Investigations**

Haemoglobin status- mean Hb at admission was 11.02 ± 1.38 g/dL and lowest value noted as 8.0 g/dL, highest value noted as 14.8 g/dL. Total RBC 2.8-4.8 million /cumm. Mean RBC 3.9 ± 0.5. Total leukocyte count was 5400-18000/cumm. Mild leukocytosis was noted in 5 children. The means of WBC count was as follows Neutrophils 66 ± 7.8%, Lymphocytes 27.3 ± 7.5%, Eosinophils 2.8 ± 1.8% and Monocytes 3.3 ± 1.4%.

| Sample Size | 50 |
|---|---|
| Lowest value | 274.0000 |
| Highest value | 598.0000 |
| Arithmetic mean | 479.6200 |

***Table 1. Summary Random Blood Sugar***

In the present study, mean blood sugar level at admission was noted as 479 ± 84 mg/dL.

**Metabolic Profile (pH, $pCO_2$ AND $HCO_3$)**

In the present study, the mean arterial pH at admission was 7.13 ± 0.20. The mean pH noted as 7.12 at the time of admission. In the present study, the mean $pCO_2$ noted at admission was 32.4 ± 6.46 mm Hg and lowest value was 15.2 mm Hg, highest value was 45 mm Hg (95% CI 30.56 to 34.28). In the present study, mean arterial bicarbonate level was noted at admission 11.15 ± 5.44 mmol/L. The lowest value was 2.4 mmol/L and highest value was 19 mmol/L.

**Ketoacidosis**

The severity of ketoacidosis at the time of presentation as studied in our patients. 18 (36%) cases presented with mild ketoacidosis, 17 (34%) cases presented with moderate ketoacidosis, & 14(28%) cases presented with severe ketoacidosis. In this study, all the children showed ketone bodies in urine.

**Serum Electrolytes**

In the present study, mean sodium was recorded at admission was 135.6 ± 4.00 mEq/L. Lowest value of Na was 128 mEq/L & highest value was 148 mEq/L (95% CI 134 - 137). Hyponatremia (<135 mEq/L) was noted in 20 (40%) cases. Mean potassium recorded at admission was 4.2 ± 0.86 mEq/L. Lowest value was 2.3 & highest value was 6.3 mEq/L (95% CI 3.99 - 4.48). Hypokalaemia (<3.5) noted in 8 (16%) cases. Hyperkalaemia (>5.5) noted in 3 (6%) cases. Mean chloride value at admission was 99.89 ± 3.33 mEq/L.

**Renal Function Tests**

Creatinine- Mean serum creatinine value at admission was 0.73 ± 0.14 mg/dL. Lowest value was 0.30 & highest value was 1.0 mg/dL (95% CI 0.68 - 0.77).

Blood Urea- Mean blood urea value at admission was 28.4 ± 4.8 mg/dL. Lowest value was 14.0 & highest value was 39.0 mg/dL (95% CI 26.34 - 30.00).

**Liver Function Tests**

SGPT: Mean SGPT value at admission was 34.0 ± 10.0 U/L. Lowest value was 10 & highest value was 57 U/L (95% CI 30.92 - 37.11).

Alkaline Phosphatase

Mean alkaline phosphatase value at admission was 320 ± 93.9. Lowest value was 156 & highest value was 648 (95% CI 292.7 - 347.3).

**Lipid Profile**

Mean HDL value at admission was 39.85 ± 4.8 mg/dL. Lowest value was 25 mg/dL & highest value was 45 mg/dL (95% CI 38.45 - 41.25). Mean LDL value at admission was 84.68 ± 14.11 mg/dL. Lowest value was 52 mg/dL & highest value was 109 mg/dL (95% CI 38.45 - 41.25). Mean Triglycerides value at admission was 131.08 ± 31.80 mg/dL.

**HbA1c**

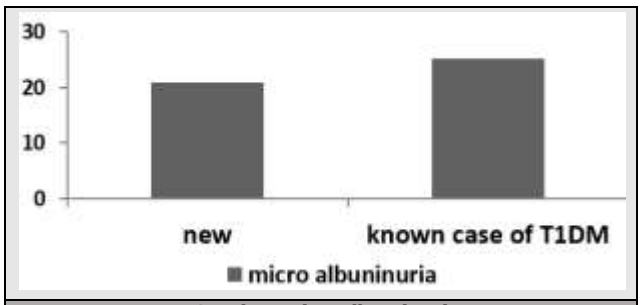
Mean HbA1c value at admission was 9.72 ± 1.97%. Lowest value was 6.8% & highest value was 17.3%. Relation between sex and HbA1c values was also observed in our study. In our study glycaemic control was poor in females. The mean HbA1c in males as 8.71 whereas in females was 9.62.

| Severity | Mean HbA1c |
|---|---|
| Mild | 8.72 |
| Moderate | 9.14 |
| Severe | 9.74 |

***Table 2. Relation Between Hba1c & Severity of Ketoacidosis***

Risk of ketoacidosis increased with higher HbA1c. In this study we observed that HbA1c is directly proportionate to severity of ketoacidosis. Mean c peptide value at admission was 0.22 ± 0.2. Lowest value was 0.01 & highest value was 1.00 (95% CI 0.15 - 0.28). Mean c peptide value of new cases at admission was 0.27 and in known cases of T1DM at

admission was 0.19. In all cases C peptide levels were significantly low.




***Graph 1. Microalbuminuria***

Microalbuminuria levels are high in known cases of T1DM compare to newly diagnosed cases (Graph 1). In this study we have done fundus for all cases and results were normal.

**Other Endocrine Systems**

Thyroid profile was done in all patients after stabilization, Hypothyroidism was found in 7(14%) cases and all are females. One child was diagnosed as T1DM with hypothyroidism and Addison's. In this study we diagnosed Turners syndrome in a known case of T1DM.

**Duration of Hospital Stay**

Average duration of hospital stay in males is around 13.6 days where as that of females is around 13.8 days.

**Comorbid Conditions**

In this study 9(18%) cases had Urinary tract infection in that 6(12%) were girls, 3(6%) were boys, 3(6%) cases had Pneumonia, 5(10%) cases had vulvovaginitis and 6(12%) cases had pyoderma.

**Mortality**

In this present study (n=50), 48 cases were discharged & 2 cases (4%) died. A 10 yrs. old male child and a 9 yrs. old female child both are known cases of T1DM, with H/O previous 3-4 DKA attacks, brought to the hospital in a very moribund state (altered sensorium, severe dehydration, hypotension, and severe ketoacidosis) and died within 1 day of admission.

## DISCUSSION

The discussion is based on the results obtained in this study compared with review of literature.

**Hospital Incidence**

In this present study incidence of type 1 DM in children was 1.30/1000 paediatric ward admissions. In a study done by Ramachandran A, Snehalatha et al[17] observed that the peak incidence was between 10 and 12 yrs. In another study conducted by same authors Ramachandran A, Snehalatha et al, [18] observed that the prevalence of insulin dependent diabetes is not rare. It is higher than reported from many other Asian countries.

**Age**

In this present study the mean age at admission was 9.7 ± 3.01. In a study done by Aria Setoodeh - Fereydoun Mostafavi et al[19] observed that the mean age of male children at presentation was 9.27 ± 4.02 and in females is 9.83 ± 3.35 yrs. In a study done by Sandeep & et al[20] observed that the mean age of patients at presentation was 7.4 ± 3.9 yrs.

**Sex Distribution**

In this present study (n=50), girls 34 (68%) are more affected than boys 16 (32%). Sandeep & et al[20] observed that boys (27) and girls (28) were equally affected. A Study done by R. R. Jahagiridar & et al[21] (n= 12) observed 8 males, 4 females.

**Weight**

In the present study the mean weight at admission was 25.46 ± 8.22 Kg, whereas in the study done by Sandeep & et al[20] observed that the mean weight at presentation was 17.76 ± 8.38 kg.

**Height**

In the present study mean height at admission was 121.0 ± 18.0 cm. R.R. Jahagiridar, et al[21] noted the median height was 126.3 cm.

**BMI**

In this present study median BMI at admission was 16.9 $Kg/m^2$ and in the study done by R.R. Jahagiridar, et al[21] observed that the median BMI 13.1 $kg/m^2$.

**Family History**

In present study Family H/O of type 2 diabetes was observed in 6 (12%) children.

**Consanguinity**

In this study 37 (74%) children were products of consanguineous marriage. Consanguinity is a very common practice among tribal community and in some communities of backward classes in this area.

**Infant Nutrition Details**

In this study we noted that 41 (82%) children were exclusively breastfed. A study done by Kimpkymaki[22] concluded that Infants who had been breastfed exclusively

for at least 4 months had lower risk of seroconversion risk of positivity for IA-2A or all four auto antibodies than those infants who had breastfed exclusively for less than 2 months.

**Age at Onset of Diabetes**

In the present study we observed that means age at disease onset was 7.82 ± 2.81 yrs. A study done by Aria Setoodeh - Fereydoun Mostafavi et al, [19] observed that the mean age at disease onset was 7.6 ± 3.3 yrs.

**Clinical Features of Children with DKA**

In this present study we observed that vomiting 49(98%) by far the most frequent symptom followed by polyuria 45 (90%), pain abdomen, polydipsia. Study done by R.R. Jahagiridar et al[21] noted that polyuria (83.3%) was the most common symptom, followed by vomiting (50%), pain abdomen and polydipsia. Vomiting, polyuria and pain abdomen was prominent symptoms in all the above studies.

**Vital Data**

The mean pulse rate at admission was 124/min in 1 - 3 yrs, 120/min in 3 - 6 yrs., 103 /min in 6 - 12 yrs., 113/min in>12 yrs. The mean respiratory rate at admission was 51/min in 1 - 3 yrs., 41/min in 3 - 6 yrs., 35/min in 6 - 12 yrs., 37/min in>12 yrs. The Median SBP in different age groups was 80 mmHg, 80 mmHg, 90 mmHg, 110 mmHg 1-3 yrs., 3-6 yrs., 6-12 yrs. & > 12 yrs. respectively. Median DBP in different age groups was 60 mmHg, 50 mmHg, 70 mmHg, 60 mmHg respectively. The blood pressure was normal in all patients, but 3 patients presented with shock. In the study done by R.R. Jahagiridar, et al[21] observed that the blood pressure was normal in all patients, but 1 patient presented with shock.

**Diabetic Ketoacidosis Previous Attacks**

In this study we observed that DKA attacks are more common in female patients. A study done by Aria Setoodeh - Fereydoun Mostafavi et al[19] and they observed that DKA attacks occurred more frequently in females.

**H/O Insulin Omission**

In this present study we noted that Insulin dose omission was noted in 30 cases out of 31 known cases of T1DM and they presented with DKA. Sandeep et al[20] observed that the omission of insulin either deliberately or inadvertently is responsible for DKA in established diabetic children.

**Routine Investigations**

Mean Hb at admission was 11.02 ± 1.38 g/dL and lowest value noted as 8.0 g/dL, highest value noted as 14.8 g/dL. Total RBC 2.8-4.8 millions /cumm. Mean RBC 3.9 ± 0.5. Total leukocyte count was 5400-18000/cumm. Mild leukocytosis was noted in 5 children. The means of WBC count was as follows Neutrophils 66 ± 7.8%, Lymphocytes 27.3 ± 7.5%, Eosinophils 2.8 ± 1.8% and Monocytes 3.3 ± 1.4%.

**Random Blood Sugar**

In this present study Mean blood sugar level at admission was noted as 479 ± 84 mg/dL. A study done by Sandeep & et al[20] observed that mean blood sugar level at admission was 479.4 ± 84.2 mg/dL

| Features | Sandeep et al (Mean ± SD) [20] | Present Study (Mean ± SD) |
|---|---|---|
| Ph | 7.06 ± 0.1 | 7.12 ± 0.2 |
| $pCO_2$(mmHg) | 18.2 ± 7.6 | 32.42 ± 6.4 |
| HCO3(mEq/dL) | 7.1 ± 5.0 | 11.1 ± 5.4 |

***Table 3. Metabolic Profile (pH, $HCO_3$,$pCO_2$)***

**Ketoacidosis**

In this study 18 (36%) presented with mild ketoacidosis, 17 (34%) present with moderate ketoacidosis, & 14(28) presented with severe ketoacidosis. In a study done by Pinkey JH et al[23] found that 26% of T1DM patients presented with DKA among them, 16% were in severe ketoacidosis, 10% had mild to moderate ketoacidosis.

**Urine for Ketone Bodies**

In this study, all the children were presented with positive urine ketone bodies. However ketonuria was not quantitated in the present study. Sandeep & et al[20] observed urine ketone bodies 4+ at the time of admission.

| Serum Electrolytes | Sandeep et al[20] (n=55) | Present Study n=50 |
|---|---|---|
| Hyponatremia (<135 meq /L) | 20 | 20 |
| Hypernatremia (>150 meq /L) | 3.6 | 0 |
| Hypokalaemia (<3.5 meq/L) | 10.9 | 8 |
| Hyperkalaemia (>5.5) | 27.3 | 3 |

***Table 4. Serum Electrolytes***

**Renal Function Tests**

In the present study renal function tests (blood urea, creatinine) were normal, whereas a study done by R. R. Jahagiridar & et al[21] observed that two patients have high blood urea and creatinine levels.

**Lipid Profile**

In this present study lipid profile was normal in male and female patients whereas a study done by Aria Setoodeh - Fereydoun Mostafavi et al,[19] they observed dyslipidemia more frequently in females.

**HbA1c**

Mean HbA1c value at admission was 9.72 ± 1.97%. Lowest value was 6.8% & highest value was 17.3%. In the present study HbA1c significantly higher in females. A study done by Rewers A et al[24] noticed that the incidence of ketoacidosis

was increased with age in girls and the risk of ketoacidosis in children increased with higher HbA1c. A study done by Aria Setoodeh - Fereydoun Mostafavi et al[19] observed HbA1c was significantly higher in females. A study done by Ehehalt S, Gauger N et al[25] stated HbA1c is a reliable criterion for diagnosing type 1 diabetes in childhood and adolescence. Risk of ketoacidosis increased with higher HbA1c. Sensitivity of HbA1c at the onset of childhood type 1 diabetes (T1DM) was calculated to be 100%. Specificity of HbA1c as diagnostic criterion was 100%.

**C Peptide**

In the present study, C peptide levels were significantly low in all the cases. A study done by Ying Xin et al observed that the C Peptide levels were significantly low in most of the patients with diabetic ketoacidosis.[26]

**Microalbuminuria**

A study done by Marcovecchio ML et al[27] observed that HbA1c was independently associated with microalbuminuria.

**Other Endocrine Abnormalities**

In the present study Thyroid profile was done in all patients after stabilisation. A study done by Aria Setoodeh - Fereydoun Mostafavi et al[19] observed that thyroid profile did not show a significant difference between girls and boys whereas in this study 7 (14%) female patients diagnosed as hypothyroidism. One child was diagnosed as T1DM with hypothyroidism & Addison's disease. In this study we diagnosed Turners syndrome in a known case of T1DM.

**Duration of Hospital Stay**

A study done by Sandeep & et al[20] noted the mean stay in the hospital was 11.7 ± 8.59 days. In this study we observed that mean duration of hospital stay was 13 days.

**Other Comorbid Conditions**

A study done by Sandeep Kumar Kanwal & et al[20] UTI seen in 3 cases, pneumonia in 4 cases, acute GE in 6 cases. In this study 9 (18%) cases had Urinary tract infection, 3 (6%) cases had Pneumonia, 5 (10%) cases had vulvovaginitis and 6 (12%) cases had pyoderma. Micro vascular complications were not observed.

**Mortality**

In this present study (n=50), 48 patients discharged & 2 cases (4%) died due to DKA. A study done by Sandeep & et al[20] (n=55), 48 patients discharged & 7 died. Cerebral oedema, renal failure & sepsis accounted for most of the deaths.

## CONCLUSIONS

The hospital incidence of T1DM was 1.3 per 1000 paediatric ward admissions. Girls were more affected than boys with type I diabetes mellitus. Mean age at presentation was 9.7 ± 3.01 yrs. Mean age at disease onset was 7.34 ± 2.81 yrs. Vomiting, osmotic symptoms, pain abdomen were the most common presenting symptoms. Two thirds of children presented with mild to moderate ketoacidosis. Omission of insulin was the precipitating factor for DKA in known cases of T1DM. Poor glycaemic control was observed in girls. Renal and liver function tests were normal in all the cases. C Peptide levels were low in all the cases. Microvascular complications were not observed. Among T1DM children, hypothyroidism was another endocrine abnormality. This is most commonly observed in female patients. DKA is an important cause of morbidity & mortality in children with T1DM. Timely diagnosis, appropriate management, careful monitoring and apprehending complications are critical to ensuring a favourable outcome. Early identification of subjects at risk for long term complications and early implementation of preventive and therapeutic strategies are fundamental in order to reduce the complication of diabetes.

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