



CLINICAL PRESENTATION OF CHILDREN WITH TYPE 1 DIABETES MELLITUS IN A TERTIARY CARE HOSPITAL

Dr. Krishna Sahithi* T MBBS, Third year post Graduate, Pediatrics *Corresponding Author

Dr. Anil Kumar. P DCH, DNB, Fellow in pediatric nephrology. Associate Professor of pediatrics, Department of Pediatrics.

Dr. Jahnavi Sushma. E Post Graduate third year, Pediatrics.

ABSTRACT

Objective: To determine the clinical presentation of children admitted with type 1 diabetes mellitus in a tertiary care hospital. **Methods:** Retrospective study was done in the department of pediatrics, Government general hospital, Guntur, for a time period of 2 years from August 2020 to August 2022 with a sample size of 32 children. **Results:** A total of 32 children below twelve years of age with diagnosis of type 1 diabetes mellitus presented to ESR and OPD were included in the study. The results were discussed based on clinical presentation, age, gender, random blood sugar and HbA1c values. Our study showed that most common clinical presentation for admission was Diabetic keto acidosis. The age of presentation was highest among 10-12 years age group of children with female preponderance. Majority 78% of sample size were hailing from rural areas. 90% of the children had deranged HbA1c values. **Conclusion:** To create awareness through our study regarding early symptoms, prompt diagnosis by screening random blood sugars in children presenting with weight loss, polyuria, polydipsia, pain abdomen and respiratory distress. The necessity of regular treatment to prevent further complications as incidence of Type-1 Diabetes Mellitus is increasing worldwide.

KEYWORDS : Type-1 diabetes Mellitus, DKA, Clinical manifestation, HbA1c levels.

1. INTRODUCTION:

Type 1 DM is the most common endocrine-metabolic disorder of childhood and adolescence with important consequences for physical and emotional development. A study using population-based estimates of diabetes incidence and prevalence showed that approximately 15,000 youths are diagnosed with T1DM each year [1]. T1D Index shines a light on important statistics about the burden of T1D globally. The expected number of people living with T1D in 2040 will be 17.43 million [2]. Type 1 DM accounts for most cases of diabetes in childhood, but it's not limited to this age group new cases can present in adult life. The incidence of type 1 DM is increasing in most populations [3,4]. Modeling suggests that the number of children with type 1 diabetes will nearly triple between 2010 and 2050 [5]. India accounts for most of the children with T1DM in South-East Asia. According to the International Diabetes Federation diabetes atlas, India has 3 new cases of T1DM/100,000 children of 0-14 years and the estimated total number of children with T1DM in India in 2021 is around 1,24,600 [6]. Data from India reveals a significant prevalence of type 1 diabetes (over 10/100,000 population), with certain urban pockets reporting over 30/100,000 population [7].

Individuals with T1DM confront serious lifestyle alterations, including an absolute daily requirement for exogenous insulin, monitoring of blood glucose levels, and the need to pay constant attention to dietary intake. Mortality and morbidity result from a constant potential for acute metabolic derangements and from long term complications [8].

Potential acute complications include development of hypoglycemia related to insulin excess or hyperglycemic keto acidosis from insulin deficiency. T1DM is primarily caused by genetic susceptibility, environmental factors, and disorders of the immune regulatory mechanisms. A combination of all these three can ultimately lead to destruction of pancreatic beta cells leading to hyperglycemia, ketoacidosis and potentially death, if not treated with insulin.

2. AIMS AND OBJECTIVES

To study the clinical manifestations of children presenting with new onset type 1 DM to a tertiary care hospital.

To study the age at the time of presentation

To study the RBS and HbA1C levels at the time of presentation.

3. MATERIALS AND METHODS

Study Design: Retrospective observational study.

Study Setting: Department of pediatrics, Government general hospital, Guntur.

Study Period: 2 Years from August 2020 to August 2022

Study Population:

All the children who have been admitted to ward, intensive care unit with diagnosis of type 1 DM.

Inclusion Criteria:

Children under twelve years of age with diagnosis of type 1 diabetes mellitus, Fasting plasma glucose >126mg/dl (7mmol/L) or 2hour plasma glucose during OGTT >200mg/dl (11.1mmol/L) or HbA1C > 6.5% (48mmol/mol).

Sample Size: 32

4. OBSERVATION AND RESULTS:

Table-I Age

SNO	AGE	No of children	Percentage
1	<5years	3	10
2	5-7years	8	26.6
3	7-9years	7	23.3
4	10-12years	12	40

TABLE-1 shows that children between the age group of 10-12 years accounted for 40% of the total children which corresponds to pubertal age group. Children aged 5-7 years and 7-9 years accounted for 26% and 23% respectively. Children less than 5 years accounted for 10%

Table-II Sex

S.NO	SEX	NO CHILDREN	PERCENTAGE
1	MALE	13	43.3
2	FEMALE	17	56.6

TABLE-II shows that there is female preponderance accounting for 56%

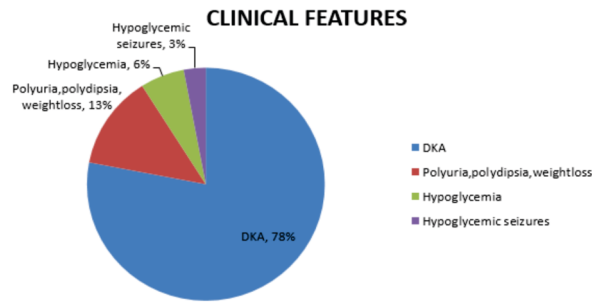


Figure-1 Clinical Presentation Of Children With Type 1 dm

Figure-I shows the most common presentation of children admitted was DKA which constituted 78%, followed by polyuria, polydipsia and weight loss, accounting for 13%. Six percent of children were admitted due to hypoglycemia. Three percent children were admitted due to hypoglycemic seizures.

Table III: Rbs At The Time Of Presentation

Random blood sugar	No.of children	Percentage
>350	24	75
250-350	3	9.3
150-249	2	6.2
50-149	Nil	Nil
<50	3	9.3

Table 3 shows that majority of the children, Seventy five percent of them had RBS levels of more than 350 at the time of presentation 9% of them had RBS value of less than 50 and they had presented with symptoms of hypoglycemia and hypoglycemic seizures.

Out of the total children 78% had no family history, 7% had affected first degree relative, 15% had a second degree affected relative.

In our study the most common presentation for admission was DKA which accounted for 78% of all the children, as our center is a tertiary care government hospital, and most of them were hailing from rural area which indicates the children were brought to medical attention at a very later stage and also lack of awareness regarding early symptoms and treatment.

Children with associated syndromes included one child with Down syndrome and one child with Turner syndrome. Two children had presented with associated nephrotic syndrome. Children with other associated endocrine abnormalities included a child with hypothyroidism.

In study done by Abdulaziz M. Al Rashed et al [9], the most common presentation was polyuria, polydipsia and polyphagia rather than DKA

In study done by Pasi, Rachna et al [10], the common presentation was polyuria, polydipsia and weight loss, DKA accounted for 26% of cases, with male preponderance.

In study done by Sanjay Kalra et al [11] the prevalence of type 1 DM was higher in urban areas and was higher in males compared to females.

In study done by Prasanna Kumar et al [12] the incidence/prevalence of T1 DM (per 100,000 persons) was 3.8. Population-based data from the SEARCH study reflects significant hyperglycemia; nearly 17% of youth with type 1 diabetes have HbA1c >9.5% (>80 mmol/mol) [5].

In study done by Wei Peng et al [13], the presentation of DKA was 50% and incidence of type 1 DM has risen from 39 cases/year in 2009-2010 to 95 cases/year in 2017-2018 (≈2.5-fold increase).

5. DISCUSSION:

T1DM previously called Insulin dependent diabetes (IDDM), or juvenile diabetes is characterized by low or absent levels of endogenously produced insulin and dependence on exogenous insulin. The onset occurs predominantly in childhood with a median age of 7-15 years but it could be present at any age. Natural history includes 4 distinct stages 1. Pre-diabetes 2. Diabetes 3. Honeymoon period 4. Established diabetes with acute/chronic complications [14]

T1DM is characterized by autoimmune destruction of pancreatic islet beta cells. Genetic susceptibility and environmental factors contribute to pathogenesis. There is clear evidence of familial clustering of T1DM with prevalence in siblings approaching 8%. In monozygotic twins the concordance rates range from 30 to 65% and in dizygotic twins 6 to 10%. There is a difference in inheritance pattern between two parents, risk is 3-4% if mother is affected and 5-6% if father is affected, indicating the risk is more when its inherited from father [15]. However, 85% of newly diagnosed T1DM patients don't have family history and hence we cannot solely rely on family history to identify patients at risk of development of T1DM.

Susceptibility to T1DM is genetically controlled by alleles of major histocompatibility complex (MHC) class II genes expressing human leukocyte antigens (HLA). Autoantibodies to beta cell antigens include Insulin autoantibody (IAA), islet cell cytoplasm antibody (ICA), glutamic acid decarboxylase antibody (GADA), islet antigen 2 (IA-2A), zinc transporter 8 (ZnT8A). They can be detected in the serum of the patient's months to years prior to the clinical onset of T1DM. It has been postulated that 90% of the destruction of β-cells occurs before the disease manifests clinically.

Pre-diabetes is the phase prior to the onset of T1DM, which could provide an opportunity for early intervention. Various therapies using steroids, immunosuppressants, and cyclosporins have been tried during the prediabetes phase but there is no proven evidence for their application. At the time of diagnosis if viable beta cells are still present and produce insulin, there may be a partial remission of the disease (honeymoon period) but over time more beta cell mass is destroyed, and the patient becomes totally dependent on exogenous insulin for survival. Various environmental factors, possible viral infections, congenital rubella syndrome, enteroviral infections, mumps virus have been postulated to play a role in the mediation of destruction of pancreatic beta cells [16].

In some children with apparent T1DM the beta cell destruction is not immune mediated, this subtype is seen in African and Asian origin patients and is distinct from known causes of beta cell destruction such as drugs, viruses, mitochondrial gene defects and ionizing radiation, these individuals have extensive periods of remission with variable insulin deficiency, like T2DM.

Peak of presentation occurs in two age groups, 5-7 years of age and at the time of puberty. The first peak corresponds to the time of increased exposure to infectious agents coincident with beginning of the school. The second peak might correspond to the pubertal growth spurt induced by gonadal steroids and increased pubertal growth hormone secretion which antagonizes insulin [16]

The classic clinical manifestations of new onset diabetes in children reflect the hyperglycemic and catabolic state which

include polyuria, polydipsia, polyphagia and weight loss. In the advanced disease they present with symptoms and signs of DKA which include dehydration, nausea, vomiting, lethargy, altered mental status and in extreme cases coma. Although most symptoms are nonspecific the most important clue is an inappropriate polyuria in any child with signs of dehydration and poor weight gain. There may be opportunities to reduce time to diagnosis for up to one third of cases, by up to two weeks. In most cases the initial progression occurs over weeks rather than months. Signs and symptoms of advanced ketoacidosis include Kussmaul respirations, fruity odor, prolonged corrected QT interval, diminished neurocognitive function and coma.

Fasting plasma glucose > 126mg/dl(7mmol/L) or 2hour plasma glucose during OGTT >200mg/dl(11.1mmol/L) or HbA1c > 6.5%(48mmol/mol). ADA recommends an HbA1c target of <7.5% (<58 mmol/mol) for children aged <18 years [17] Many of the studies have shown that most of the children fail to meet glycemic targets and also the current care fails to prevent severe hypoglycemic episodes. In 2015, the T1D Exchange found that up to 6% of individuals had reported a seizure or loss of consciousness attributable to hypoglycemia [18].

Diagnostic opportunities might be maximized by measures that improve access to primary care, and public awareness of T1DM [19]. In India and especially in the rural settings the diagnosis of type1 DM is inadvertently being delayed due to lack of awareness of early symptoms and the children are presenting at late stages with DKA. There is a need for creation of awareness among the treating pediatricians for earlier diagnosis and also there are many lapses in regard to adherence to treatment in these children. It is very important in educating the care givers of the children regarding strict dietary management, regular monitoring of blood glucose and insulin delivery. However in most of the children especially in the younger age groups dietary restriction is a big issue and also many children hailing from rural areas don't have enough access for monitoring blood glucose levels due to financial issues. Storage and adherence to insulin treatment is another constraint in them, leading to many of them landing up in complications especially DKA.

There have been many advances in the monitoring of blood glucose levels and delivery of insulin. From intermittent monitoring of glucose to usage of minimally invasive continuous monitoring devices which could facilitate better glucose control. There have been advances in the development of newer technologies which integrate glucose monitoring with automated insulin delivery as a result could have a significant impact on the glycemic control preventing hyperglycemia as well as hypoglycemia, there by reducing the burden of care in children with type1 diabetes mellitus [20].

Certain studies have shown that children with T1DM could have evidence of cognitive dysfunction and structural changes within the central nervous system. Children diagnosed with type 1DM before the age of 6 years have shown to had performed poorly on cognitive tests including learning and memory while some of them are also likely to meet criteria for clinically significant impairment [21].

6. CONCLUSION:

The incidence of type1 DM has been increasing worldwide, the importance of awareness of the early symptoms and prompt diagnosis and initiation of treatment, regular glucose monitoring and adherence to treatment is essential for the prevention of grave complications associated with the disease. Routine screening of random blood sugar in patients presenting with symptoms like polyuria with signs of

dehydration, weight loss can help in early diagnosis, prevention of DKA and associated long term complications.

Financial Support And Sponsorship

NILL

Conflict Of Interest

There are no conflicts of interest

7. REFERENCES:

1. Das AK. Type 1 diabetes in India: Overall insights. *Indian J Endocrinol Mehtab.* 2015 Apr;19(Suppl 1): S31-3. Doi: 10.4103/2230-8210.155372. PMID: 25941645; PMCID: PMC4413384
2. <https://www.tlindex.org/#global>. Accessed September 28, 2022.
3. Mayer-Davis EJ, Lawrence JM, Dabelea D et al, SEARCH for Diabetes in Youth Study. Incidence Trends of Type 1 and Type 2 Diabetes among Youths, 2002-2012. *N Engl J Med.* 2017 Apr 13;376(15):1419-1429. doi: 10.1056/NEJMoa1610187. PMID: 28402773; PMCID: PMC5592722.
4. Dabelea D, Mayer-Davis EJ, Saydah S, et al SEARCH for Diabetes in Youth Study. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. *JAMA.* 2014 May 7;311(17):1778-86. doi: 10.1001/jama.2014.3201. PMID: 24794371; PMCID: PMC4368900.
5. Imperatore G, Boyle JP Thompson TJ, Case D, et al SEARCH for Diabetes in Youth Study Group. Projections of type 1 and type 2 diabetes burden in the U.S. population aged <20 years through 2050: dynamic modeling of incidence, mortality, and population growth. *Diabetes Care.* 2012 Dec;35(12):2515-20. doi: 10.2337/dc12-0669. PMID: 23173134; PMCID: PMC3507562.
6. idf.org/aboutdiabetes/what-is-diabetes/facts-figures. Accessed September 28, 2022
7. Kalra S, Dhingra M. Childhood diabetes in India. *Ann Pediatr Endocrinol Metab.* 2018 Sep;23(3):126-130. Doi: 10.6065/apem.2018.23.3.126. Epub 2018 Sep 28. PMID: 30286567; PMCID: PMC6177665.
8. (1993). The Effect Of Intensive Treatment Of Diabetes On The Development And Progression Of Long-Term Complications In Insulin-Dependent Diabetes Mellitus. *The New England Journal of Medicine*, 329 (14), 977-986. doi: 10.1056/NEJM199309303291401.
9. Al Rashed AM. Pattern of presentation in type 1 diabetic patients at the diabetes center of a university hospital. *Ann Saudi Med.* 2011 May-Jun;31(3):243-9. Doi: 10.4103/0256-4947.81529. PMID: 21623052; PMCID: PMC3119963.
10. Pasi, Rachnal ; Ravi, Kumar Satish2, Type 1 diabetes mellitus in pediatric age group: A rising endemic. *Journal of Family Medicine and Primary Care: January 2022 - Volume 11 - Issue 1 - p 27-31* Doi: 10.4103/jfmpc.jfmpc.975_21
11. Kalra S, Kalra B, Sharma A. Prevalence of type 1 diabetes mellitus in Karnal district, Haryana state, India. *Diabetol Metab Syndr.* 2010 Mar 9; 2:14. Doi: 10.1186/1758-5996-2-14. PMID: 20214794; PMCID: PMC2844357.
12. Kumar P, Krishna P, Reddy SC, Gurappa M, Aravind SR, Munichoodappa C. Incidence of type 1 diabetes mellitus and associated complications among children and young adults: results from Karnataka Diabetes Registry 1995-2008. *J Indian Med Assoc.* 2008 Nov;106(11):708-11. PMID: 19368094.
13. Peng W, Yuan J, Chiavaroli V, et al 10-Year Incidence of Diabetic Ketoacidosis at Type 1 Diabetes Diagnosis in Children Aged Less Than 16 Years From a Large Regional Center (Hangzhou, China). *Front Endocrinol (Lausanne).* 2021 Apr 27;12:653519. doi: 10.3389/fendo.2021.653519. PMID: 33986725; PMCID: PMC8112199.
14. Skyler JS, Bakris GL, Bonifacio E, et al Differentiation of Diabetes by Pathophysiology, Natural History, and Prognosis. *Diabetes.* 2017 Feb;66(2):241-255. doi: 10.2337/db16-0806. Epub 2016 Dec 15. PMID: 27980006; PMCID: PMC5384660.
15. Hämeläinen AM, Knip M. Autoimmunity and familial risk of type 1 diabetes. *Curr Diab Rep.* 2002 Aug;2(4):347-53. doi: 10.1007/s11892-002-0025-2. PMID: 12643195.
16. David R, Weber, Nicholas Jospe, Type1 Diabetes Mellitus, Nelson Textbook of Pediatrics, 21th edition 2020. ch-607.
17. American Diabetes Association Professional Practice Committee. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2022. *Diabetes Care.* 2022 Jan 1;45(Suppl 1):S17-S38. doi: 10.2337/dc22-S002. PMID: 34964875.
18. Miller KM, Foster NC, Beck RW, et al, T1D Exchange Clinic Network. Current state of type 1 diabetes treatment in the U.S.: updated data from the T1D Exchange clinic registry. *Diabetes Care.* 2015 Jun;38(6):971-8. doi: 10.2337/dc15-0078. PMID: 25998289.
19. Lee JJ, Thompson MJ, Usher-Smith JA et al, Opportunities for earlier diagnosis of type 1 diabetes in children: A case-control study using routinely collected primary care records. *Prim Care Diabetes.* 2018 Jun;12(3):254-264. doi: 10.1016/j.pcd.2018.02.002. Epub 2018 Mar 13. PMID: 29548694.
20. Kahan Ovitz, Patrick M, Russell Steven J et al, Type 1 Diabetes—A Clinical Perspective. *Point of Care: The Journal of Near-Patient Testing & Technology: March 2017 - Volume 16 - Issue 1 - p 37-40* Doi: 10.1097/ POC. 0000000000000125
21. Gaudieri PA, Chen R, Greer TF, et al, Cognitive function in children with type 1 diabetes: a meta-analysis. *Diabetes Care.* 2008 Sep;31(9):1892-7. doi: 10.2337/dc07-2132. PMID: 18753668; PMCID: PMC2518367.