Original Research Paper

Volume-9 | Issue-2 | February-2019 | PRINT ISSN - 2249-555X

Diabetology

PROFILE OF CHILDREN PRESENTING WITH DIABETIC KETOACIDOSIS IN OUR SET UP

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ABSTRACT In our study, 34 children of type 1 diabetes mellitus were taken who presented to our set up with diabetic ketoacidosis. Maximum number of children with diabetes mellitus who presented with diabetic ketoacidosis were in the age group of 10 – 18 years(64.70%) followed by age group of >5 – 10 years of age(26.47%) and minimum number of children were in the age group of 2 – 5 years(8.82%) with mean age of presentation is 11.3 years(n=11.3). Number of female cases outnumbers the number of male cases(55.88% vs 44.11%). RBS levels were on the higher side in all the presenting cases(n=366 mg/dl) and corresponding HbA1c levels were also on the higher side(n=10.8). 64.70% children of diabetic ketoacidosis presented to us with respiratory distress as their presenting complaint, 35.29% children presented with fever, 26.47% children presented with polyuria and polydipsia, 20.50% children presented with pain abdomen, 14.70% children presented with vomiting as their presenting complaint. With insulin therapy both lab profile and clinical improvement ensues. RBS level reduces to <250 mg/dl within few hours(n=6.2 hours). Mean time taken to shift the patients from iv to sc insulin was 19.2 hours(n=19.2 hours).On further study of cases, association were found between type 1 diabetes mellitus and celiac disease(10%), and with hypothyroidism(6%). 10% of children presented to our department with diabetic ketoacidosis were having both celiac disease and hypothyroidism. It took several days for the children presenting with diabetic ketoacidosis for their discharge(n=13.7 days).Parental understanding regarding the disease and treatment has a worthwhile effect while children of ignorant parents are seen having multiple number admissions with diabetic ketoacidosis in these 9 months of study.

KEYWORDS : Random blood sugar, Glycosylated hemoglobin, Type 1 diabetes mellitus, Diabetes ketoacidosis.

INTRODUCTION

Diabetic ketoacidosis is the main cause of increased morbidity and mortality in children with type 1 diabetes mellitus. Type 1 diabetes mellitus is an immune mediated disease that triggers, as a final consequence, the complete or partial loss of pancreatic cells, decreasing the production of endogenous insulin, and thus generating a dependence of the affected patient on the exogenous insulin administration to maintain adequate energy production.[1]

GENETICS

Genetics plays a role in progression to clinical disease. Class II HLA genes are the ones most strongly associated with the risk of type 1 diabetes mellitus. Some of the known associations include HLA DR3/4-DQ2/8 genotype.[2]

PATHOPHYSIOLOGY

The metabolic disorder itself is hyperglycemia with increase in ketones circulating in the body leading to ketoacidosis.[3]

Pathophysiology of diabetic ketoacidosis involves autoimmune destruction of beta cells in the pancreas and the subsequent lack of insulin. Severe hyperglycemia and systemic inflammation associated with DKA have been shown to further deplete functional pancreatic islets.[4]

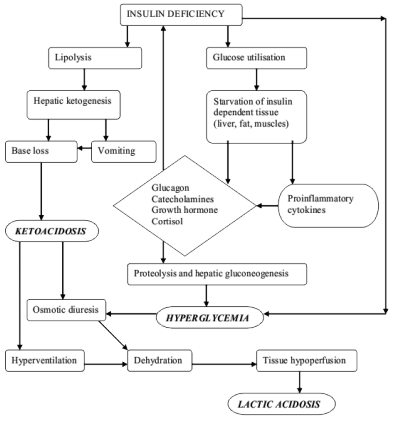

Figure 1

Absolute or relative insulin deficiency decreases glucose utilization in insulin sensitive tissues and promotes lipolysis. Energy deficiency in these tissues is a stress, stimulating counter regulatory hormones (glucagon, catecholamines, growth hormone, cortisol) and proinflammatory cytokines, which also stimulate these hormones. The counter regulatory hormones in turn enhance lipolysis and proteolysis, providing a substrate for hepatic ketogenesis and hepatic and renal gluconeogenesis, all of which results in ketoacidosis, osmotic diuresis, dehydration and tissue hypoperfusion, adding lactic acidosis to metabolic acidosis from accumulated ketones and loss of base in urine.[5]

Formation of ketone bodies[6]

The process includes the following steps-

- Beta oxidation of fatty acids to acetyl CoA.
- Formation of acetoacetyl CoA.
- Conversion of acetoacetyl CoA to 3-hydroxy-3-methylglutaryl CoA (HMG CoA) and then to AcetoAcetate
- Reduction of AcetoAcetate to 3-hydroxybutyrate.

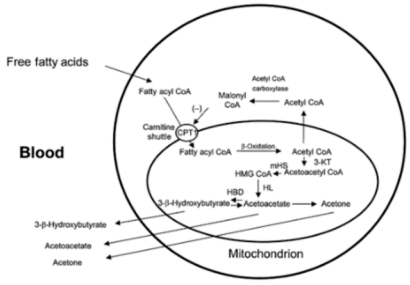

Figure 2

SIGNS AND SYMPTOMS

Diabetic ketoacidosis consists of triad of hyperglycemia, ketosis and academia. An arterial ph less than 7.35, serum bicarbonate (HCO3) value of less than 15 mEq/L, and a blood glucose level of greater than 250 mg/dl with a moderate degree of ketonemia and/or ketonuria are necessary for diagnosis of diabetes ketoacidosis.[7]

These factors have their own distinguished sign and symptoms;

hyperglycemia causes polyuria, polydipsia and dehydration. Shortness of breath, tachypnoea and kussmaul breathing are distinct features of ketosis; severe acidosis may include abdominal pain, decreased sensorium and intruding focus.[8]

COMPLICATIONS[9]

- Cerebral oedema

Diabetic ketoacidosis carries a substantial risk of life threatening complications such as cerebral edema and is the commonest cause of diabetes related death in children.[10] In young children cerebral and other autoregulatory mechanisms may not be well developed. Hence, great severity at presentation in younger children together with less maturity of autoregulatory systems combine to predispose children to cerebral edema.[11]

- Exogenous insulin induced hypoglycemia.
- Iatrogenic hypokalemia
- Abrupt discontinuation of intravenous insulin therapy after resolution of DKA without overlapping subcutaneous insulin coverage may precipitate hyperglycemia
- Hypoxemia and Non cardiogenic pulmonary oedema

Due to falling colloid osmotic preesure and subsequent increase in lung water content and diminished lung compliance.

- ARDS
- Vascular thrombosis

TYPE OF STUDY

Prospective study

STUDY DESIGN

INCLUSION CRITERIA

34 children of age between 2 to 18 years of age of either gender.

EXCLUSION CRITERIA

Children less than 2 years of age and more than 18 years of age.

MATERIALS AND METHODS

34 children presenting to intensive care department of pediatrics, government medical college and rajindra hospital patiala with diabetic ketoacidosis with age ranging from 2 years to 18 years were subjects of study. For the purpose of study, children were divided into age group of 2 – 5 years, >5 – 10 years, >10 – 18 years respectively. Name, age, gender, address, clinical examination and serial lab profile, response to treatment was recorded on a pre-designed and pre-tested proforma. Data so obtained was subjected to analysis for the purpose of study.

OBSERVATION

- Distribution according to age and gender

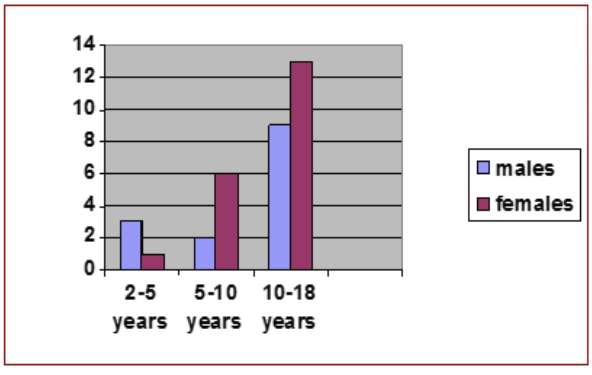

Table 1

In our study, number of female patients outnumbers the number of male patients which depicts that there is a modest female preponderance.

Maximum number of children are between the age group of 10-18 years which include cases who presented with the first episode of diabetic ketoacidosis as well as cases having repeated episodes.

- Distribution according to RBS levels

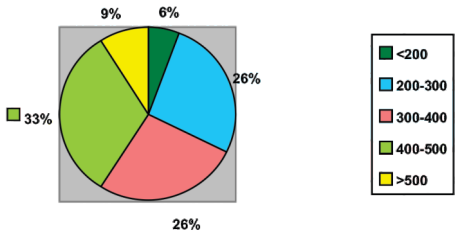

Figure 3

Children were categorized according to their presenting RBS levels. Here RBS levels are depicted in mg/dl. Mean RBS level at presentation was 366 mg/dl (n=366).

- Distribution of children according to their HbA1c levels at presentation

HbA1C Levels (%)	7-8	8.1-9	9.1-10	10.1-11	11.1-12	12.1-13	13.1-14	14.1-15	15.1-16	16.1-17	17.1-18
No. of children	4	7	3	6	4	4	-	1	2	2	1

Table 2

HbA1c levels were raised in every child presented with diabetic ketoacidosis in our set up. Mean HbA1c level was found to be 10.8 (n=10.8).

- Distribution of children according to presenting complaints

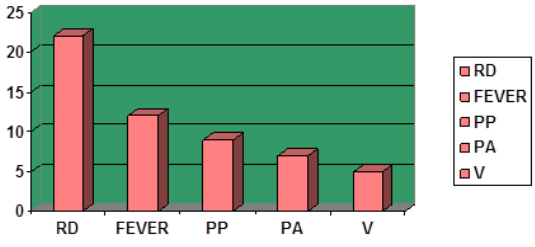

Figure 4

Main presenting complaint of children with diabetic ketoacidosis in our set up is respiratory distress. 22 out of 34 children were having respiratory distress as their chief complaint, followed by fever, polyuria and polydipsia, pain abdomen and only 5 out of 34 children presented with vomiting as their presenting complaint.

- Association with celiac disease and hypothyroidism

Association have been found between celiac disease, hypothyroidism and type 1 diabetes mellitus . 3 out of 34 children were having celiac disease along with type 1 diabetes mellitus whereas 2 children out of 34 children were having hypothyroidism along with type 1 diabetes mellitus. 3 children were having both celiac disease and hypothyroidism along with type 1 diabetes mellitus.

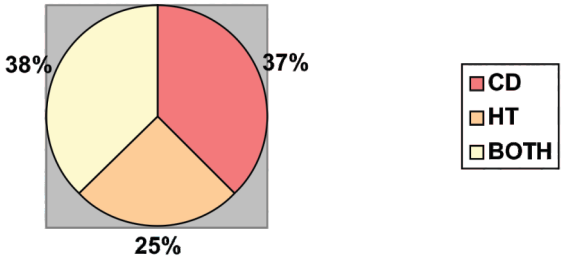

Figure 5

Of all the children who are having associated autoimmune diseases, children having celiac disease or children having both celiac disease and hypothyroidism along with type 1 diabetes mellitus are more common than isolated hypothyroidism alongwith type 1 diabetes mellitus.

- Response of the children to insulin therapy

Insulin therapy was started in every case of type 1 diabetes mellitus presented with diabetic ketoacidosis. Continuous iv infusion was started initially. With insulin therapy both lab profile and clinical improvement ensues. Depending upon the clinical improvement and serially monitored RBS levels of the child iv infusion was tapered, stopped and child was shifted to sc insulin.

Time taken to shift the child from continuous iv insulin to sc insulin varies from case to case with minimum time in our study was 12 hours and maximum time taken was 30 hours with the mean of 19.2 hours (n=19.2).

- Distribution of children as per average number of days of admission

No. of days of hospital admission	No. of children
<5	0
5-10	7
11-15	18
16-20	6
21-25	2
>25	1

Table 3

RESULTS

In our study, maximum number of children with diabetes mellitus who presented with diabetic ketoacidosis were in the age group of 10 – 18 years(64.70%) followed by age group of >5 – 10 years of age(26.47%) and minimum number of children were in the age group of 2 – 5 years(8.82%) with mean age of presentation is 11.3 years(n=11.3). Number of female cases outnumbers the number of male cases(55.88% vs 44.11%). RBS levels were on the higher side in all the presenting cases (n=366 mg/dl) and corresponding HbA1c levels were also on the higher side (n=10.8). 64.70% children of diabetic ketoacidosis presented to us with respiratory distress as their presenting complaint, 35.29% children presented with fever, 26.47% children presented with polyuria and polydipsia, 20.50% children presented with pain abdomen, 14.70% children presented with vomiting as their presenting complaint. With insulin therapy both lab profile and clinical improvement ensues. RBS level reduces to <250 mg/dl within few hours(n=6.2 hours). Mean time taken to shift the patients from iv to sc insulin was 19.2 hours(n=19.2 hours).On further study of cases, association were found between type 1 diabetes mellitus and celiac disease(10%), and with hypothyroidism(6%). 10% of children presented to our department with diabetic ketoacidosis were having both celiac disease and hypothyroidism. It took several days for the children presenting with diabetic ketoacidosis for their discharge(n=13.7 days).Parental understanding regarding the disease and treatment has a worthwhile effect while children of ignorant parents are seen having multiple number admissions with diabetic ketoacidosis in these 9 months of study.

DISCUSSION

In our study, a total of 34 patients presenting to the emergency with diabetes ketoacidosis were taken. Most of the children were undiagnosed cases of type 1 diabetes mellitus. While some of the children were known case of type 1 diabetes mellitus, presented with diabetic ketoacidosis. Main presenting complaint in our set up was respiratory distress. This is because most of the patients who came to our set up belong to rural background with ignorant attitude. These people ignore vague symptoms like nausea and vomiting, thus seek medical advice when the child develops respiratory distress.

When interviewed, they knew route and advised dosage of sc insulin. These people were aware of the diet which should be avoided but on further questioning it is found that most of the people were not strictly following the diet plans. Most of the children in our study were school going and they were active in outdoor sports and knew the importance of workout in diabetes mellitus. However most of these children were not following any fixed exercise schedules. All this was also responsible for the high presenting RBS levels.

Analysis of HbA1c was done in all 34 subjects and found to be raised in each and every case presented with diabetic ketoacidosis. Analysis of glycated hemoglobin (HbA1c) in blood provides evidence about an individual's average blood glucose levels during the previous two to three months, which is the predicted half-life of red blood cells.[12] Recent glycemia has the largest influence on HbA1c value, with 50% of HbA1c formed in the month prior to sampling and 25% in the month before that.[13] HbA1c levels may be altered by factors other than glycemic conditions. In particular factors that affect erythrocyte turnover and hemoglobinopathies (such as malaria, chronic anemia, large quantities of blood loss, hemolysis, uremia, pregnancy, smoking and various infections).[14]

In a study it was observed that administration of initial bolus dose of insulin was not associated with reduced time to resolution of DKA, when compared to patients not administered an insulin bolus.[15] In our set up every child admitted with diabetes ketoacidosis was given continuous iv infusion of insulin along with iv fluids to correct dehydration. Regular monitoring of RBS levels were done. RBS levels falls gradually to <250 mg/dl within few hours(n=6.2 hours). However clinical improvement ensues after improvement of lab profiles with the mean of 19.2 hrs.

Diabetes associated autoantibodies are often measured at diagnosis and include islet cell autoantibodies (ICAs), antibodies against GAD (GADAs) and insulin autoantibodies (IAAs). Clinical onset of type 1 diabetes may also be accompanied by other organ specific autoantibodies such as thyroperoxidase antibodies (TPOAs) and endomysial antibodies (EMAs). They are associated with thyroid disease and celiac disease respectively.[16] Being a genetic cause of the disease, type 1 diabetes mellitus is related to autoimmune diseases inc. celiac disease and hypothyroidism. Two inflammatory disorders, type1 diabetes mellitus and celiac disease, cosegregate in population, suggesting a common genetic origin. Since both diseases are associated with the HLA class II genes on chromosome 6p21.[17] In our study it is found that celiac disease is more commonly related to type 1 diabetes mellitus(10% of cases). than hypothyroidism(6% of cases). Occurance of all of the 3 autoimmune diseases together is also common(10% of cases).

A defined protocol is being followed by our hospital for treatment of children presenting with diabetes ketoacidosis before these children are being discharged. IV continuous regular insulin infusion along with iv fluids were started in each and every case. After clinical improvement iv regular insulin is switched to regular sc insulin TDS before each meal. Regular RBS monitoring done. After RBS level falls within normal limits, regular sc insulin is being switched to sc mixtard (combination of intermediate acting and long acting insulin). So it takes several days before the child is discharged with the mean stay of child in our set up is 13.7 days (n=13.7 days).

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