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Original Research Article

"A STUDY ON ANALYSIS OF THE OUTCOME OF THE DIABETIC KETOACIDOSIS TREATED CHILDREN WITH MODIFIED PROTOCOL AND TO ASSESS THE PREDICTORS OF PROGNOSIS."

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ABSTRACT:

Background: DKA is identified by three clinical features: Hyperglycemia, Ketonuria or Ketonemia and Acidosis. Many patients with diabetes may present with hyperglycemia; however, DKA is not diagnosed without the other two clinical features being present. Children being treated for DKA develop clinically important neurological compromise about 0.2 – 1% of the time[5].

OBJECTIVES: To analyze the outcome of children with DKA treated with a modified protocol and to assess the predictors of prognosis based on clinical and laboratory parameters.

MATERIAL & METHODS: Study Design: Prospective hospital based comparative study. **Study area:** Department of PAEDIATRICS, in a tertiary care hospital. **Study Period:** 1 year. **Study population:** All the children presented in DKA during this period are taken for the study. Age group ranged between 4 months and 13 years. **Sample size:** study consisted a total of 35 cases. **Sampling method:** Simple Random sampling method. **Study tools and Data collection procedure:** The Care takers will be explained about the purpose of the study and a written assent will be taken. Data will be collected in a pre –designed, pre-structured, questionnaire which will include demographic details of patients such as Name, Age, Sex, Education, Per capita Income, Social Class, Residence, Signs & Symptoms. These aspects of the clinical parameters are stressed upon in our study.

Results: Out of 35 cases hospitalized, 32 cases(91.4%) recovered without any complications of DKA. Average recovery time in these patients is 23.15hrs. 2 cases died due to uncontrolled septicaemia despite of good glucose control and stabilization of their ketoacidosis state. 1 case which is admitted with history of missing 2 doses of insulin the previous day with head injury expired 16 hrs after admission (CT – scan brain not done as the patient condition is not stable to mobilize him from PICU.)

CONCLUSION: In our study it has been shown that the altered level of consciousness at the time of presentation is correlated well with the serum osmolality than with blood glucose and pH. But it has also been shown that, when DKA is managed in a PICU setting using modified

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standard protocol the outcome is rewarding in children and is associated with no complications.

Keywords: Diabetic Ketoacidosis, Bicarbonate buffers, mortality rate

INTRODUCTION:

Juvenile onset diabetes can affect any one of any age but is more common in people under 30 years and tends to develop in child hood, hence its name. Other names for Juvenile onset diabetes include Type 1 diabetes or Insulin dependent diabetes mellitus.

Type 1diabetes is being increasingly reported from many centres in India and the rise in incidence could be apparent due to improved diagnostic facilities such as routine use of glucometer or it could be a reflection of true increase in the incidence as seen in the western world[1]. Diabetic ketoacidosis (DKA) is one of the major complications of Type 1 diabetes in childhood associated with increased risk of morbidity and mortality due to electrolyte and acid-base disturbances if left untreated. About 25-40% of newly diagnosed diabetic patients present with DKA especially under the age of 5 years[2]. A mortality rate of about 5% has been reported[3,4].

DKA is identified by three clinical features: Hyperglycemia, Ketonuria or Ketonemia and Acidosis. Many patients with diabetes may present with hyperglycemia; however, DKA is not diagnosed without the other two clinical features being present. Children being treated for DKA develop clinically important neurological compromise about 0.2 – 1% of the time[5].

DKA results from an absence or reduced effect of insulin and an excess of the counter regulatory hormones glucagon, cortisol, growth hormone and catecholamines. These hormones counteract the glucose lowering effect of insulin and are released in response to stress and other stimuli. In DKA carbohydrate and fat metabolism are affected. Reversal of DKA is associated with inherent risk of hypoglycemia, hypokalemia, cerebral edema. Correction of ketosis takes longer time than correction of blood glucose levels, so low insulin drip is continued for further correction of ketosis. Ketogenesis continues until fatty acid substrates already in the liver are depleted. Bicarbonate buffers regenerated by the distal renal tubule and by metabolism of ketone bodies steadily repairs acidosis once ketoacid production is controlled. Bicarbonate is not used for correction of acidosis in DKA.

Tracer studies have found that during the first four hours of therapy for DKA, up to 80 percent of the decline in glucose concentration may be caused by rehydration[6]. Insulin must be given at the beginning of therapy to accelerate movement of glucose into cells, to subdue hepatic glucose production, and to halt the movement of fatty acids from the periphery to the liver.

Low insulin infusion rates (0.02 – 0.05 U/kg/h) are usually sufficient to stop peripheral release of fatty acids thereby eliminating the flow of substrate for ketogenesis. Therefore, the initial infusion rate may be decreased if blood glucose levels go below 150mg/dL despite the addition of glucose to the infusion. Potassium levels must be closely followed and electrocardiographic monitoring continued until DKA is substantially resolved. If needed, the parenteral potassium can be increased to 80mEq/L or an oral supplement can be given if there is no emesis. Rarely, the IV insulin must be temporarily stopped. Studies of patients with a pH level of 6.9 or higher have found no evidence that bicarbonate is beneficial,[7] and some

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studies have suggested bicarbonate therapy may be harmful for these patients. There is no role of routine use of bicarbonate in DKA[8].

Hence the present study was undertaken to analyze the outcome of children with DKA treated with a modified protocol and to assess the predictors of prognosis based on clinical and laboratory parameters.

OBJECTIVES: To analyze the outcome of children with DKA treated with a modified protocol and to assess the predictors of prognosis based on clinical and laboratory parameters.

MATERIAL & METHODS:

Study Design: Prospective hospital based comparative study.

Study area: Department of PAEDIATRICS, in a tertiary care hospital.

Study Period: 1 year.

Study population: All the children presented in DKA during this period are taken for the study. Age group ranged between 4 months and 13 years.

Sample size: study consisted a total of 35 cases.

Sampling method: Simple Random sampling method.

Inclusion criteria: All the children presented in DKA during this period are taken for the study. Age group ranged between 4 months and 13 years.

Exclusion criteria: Severe ill children, children without DM and who did not want to participate in the study.

Ethical consideration: Institutional Ethical committee permission was taken prior to the commencement of the study.

Study tools and Data collection procedure:

The Care takers will be explained about the purpose of the study and a written assent will be taken. Data will be collected in a pre –designed, pre-structured, questionnaire which will include demographic details of patients such as Name, Age, Sex, Education, Per capita Income, Social Class, Residence, Signs & Symptoms. These aspects of the clinical parameters are stressed upon in our study.

1. Duration of illness prior to admission
2. Glasgow coma scale EMV score at presentation
3. Severity of dehydration.

LABORATORY PARAMETERS MEASURED:

1. Blood glucose
2. Urinary ketones
3. Serum electrolytes (Serum sodium, Serum potassium)
4. Blood urea
5. Blood urea nitrogen (BUN) = Blood urea/2.14
6. Serum creatinine
7. Arterial Blood Gas (ABG) analysis
8. Infection screen (in some cases)

Treatment given:

1. Fluid therapy
2. Insulin therapy
3. Correction of ketoacid accumulation
4. Serum potassium correction

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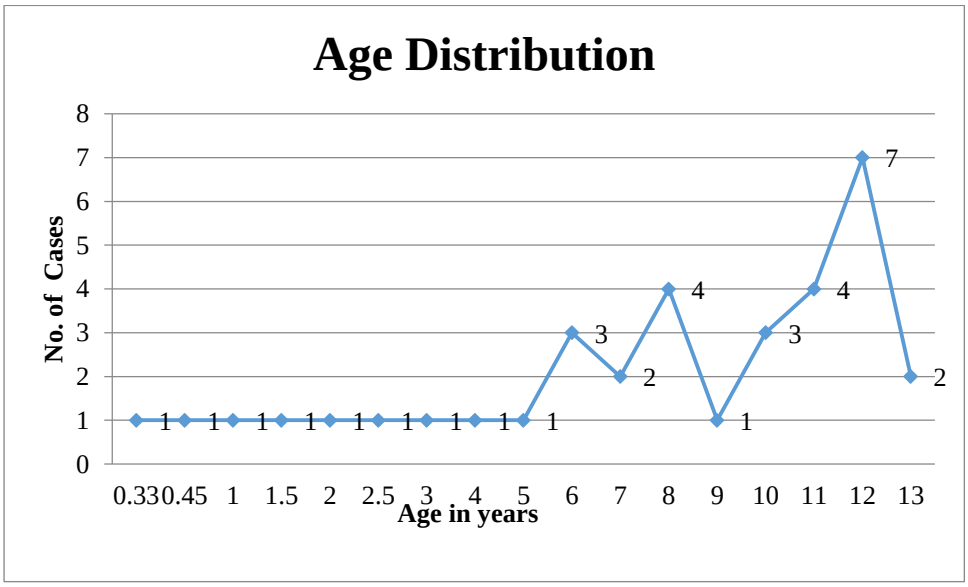
5. Bicarbonate therapy.

Statistical analysis:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test or Mann Whitney U test was used as test of significance to identify the mean difference between two quantitative variables and qualitative variables respectively. P value <0.05 will be a statistically significant study.

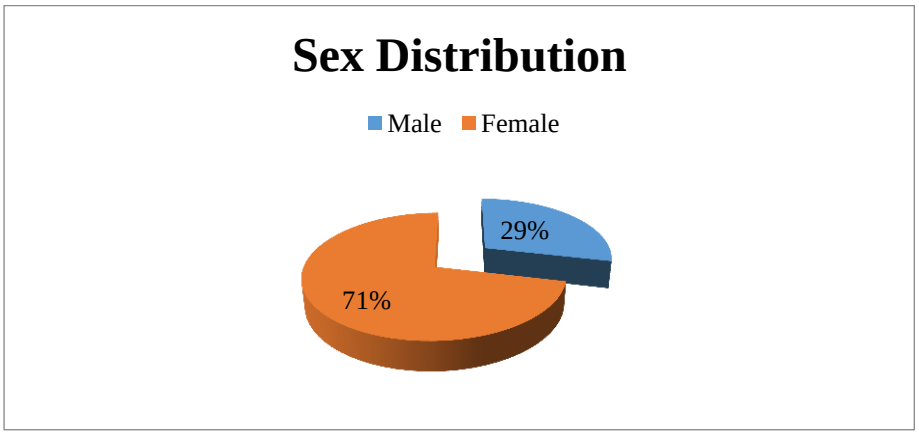
OBSERVATIONS & RESULTS:

Figure 1: Age Distribution



Age group ranged between 4 months and 13 years with mean age of 5.63 years. Out of these 35 patients 2 (5.7%) patients were infants, 26 (74.28%) patients were above 6 years.

Figure 2: Sex Distribution



Out of these 35 study population 10 (29%) were male and 25 (71%) were female.

Figure 3: Symptoms at Presentation

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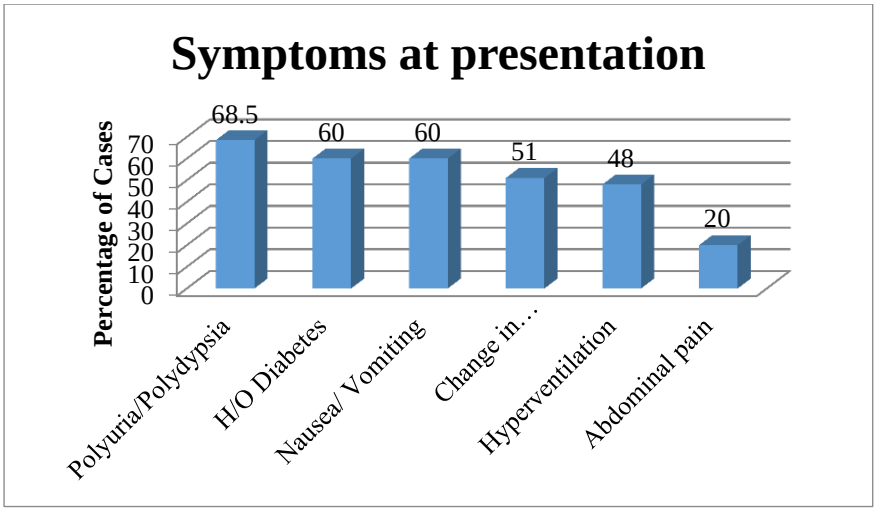
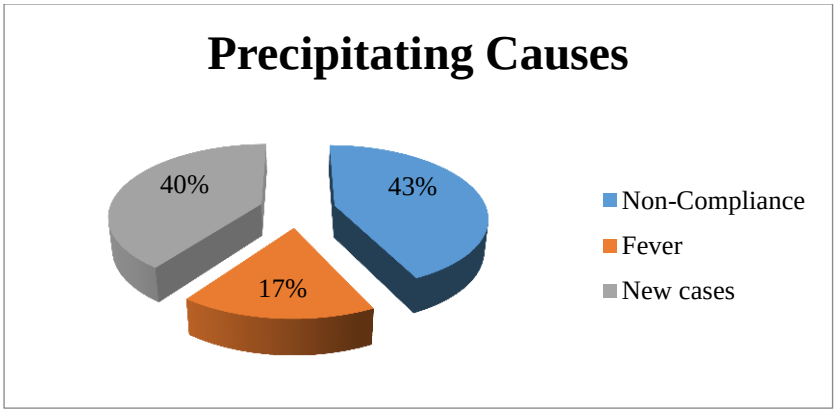


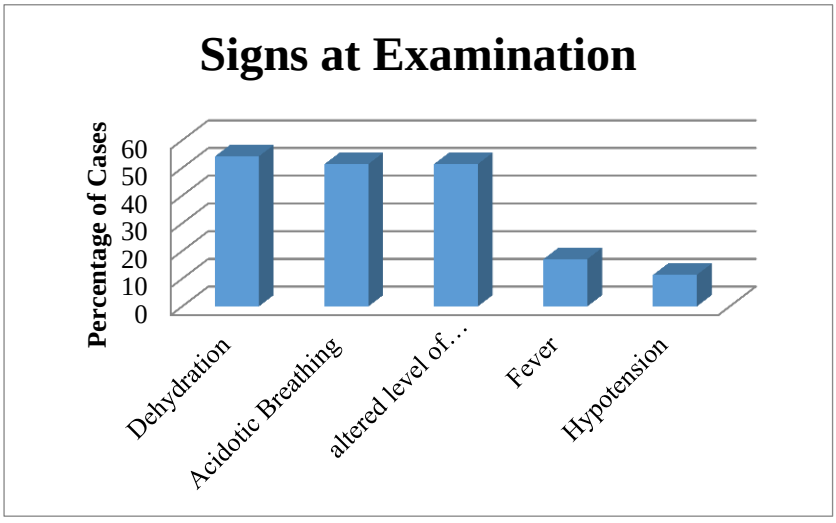
The most common symptoms that were elicited in patients either just prior to admission or at the time of diagnosis of ketoacidosis. Diabetes mellitus was newly diagnosed at presentation in 40% (14 cases) of cases, 43% (15 cases) of cases were due to non compliance and 17% (6 cases) were due to fever (stress). The presenting symptoms were polyuria/polydypsia (68.5%), Nausea/vomiting (60%), Change in sensorium (57%), Hyperventilation (48%) and Abdominal pain (20% with out any specific underling cause).

Figure 4: Precipitating Causes



Diabetes mellitus was newly diagnosed at presentation in 40% (14 cases) of cases, 43% (15 cases) of cases were due to non compliance and 17% (6 cases) were due to fever (stress).

Figure 5: Signs at Examination



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The clinical findings at admission which were 54.2% (19 cases) of cases had dehydration, 51.4% (18 cases) of cases had acidotic breathing, 51.4% (18 cases) of cases had altered level of consciousness, 17.1% (6 cases) of cases had fever and 11.4% (4 cases) of cases had Hypotension.

Blood sugar levels at admission varied between 315mg % and 1046mg %. The mean blood sugar was 566.51%. The mean blood sugar in those who had altered sensorium compared to those who did not was 310.48 (18 cases) and 298.6 (17 cases) respectively. The calculated Fisher 't' test value is 1.34 which is less than the tabulated 't' value 2.10. $p > 0.05$ even at 95% confidence intervals, so the observed difference is due to chance.

Blood gas analysis revealed, mean pH to be 7.06 (range 6.8 to 7.25). The mean pH in those who had altered sensorium compared to those who did not was 6.99 (18 cases) and 7.14 (17 cases) respectively. The calculated Fisher 't' test value is 1.25, which is less than the tabulated 't' value 2.10. $p > 0.05$ even at 95% confidence intervals, so the observed difference is due to chance.

Patients with disturbed conscious level had a mean serum osmolality of 310.48 (18 cases) while those who did not manifest this sign had mean osmolality of 298.6 (17 cases). This difference is statistically significant ($p < 0.05$) as the calculated Fisher 't' value is 3.98 which is more than the tabulated 't' value 2.10. High Serum osmolality at the time of presentation correlated well with the altered level of consciousness.

In the search for a precipitating cause for the DKA it was observed that missing doses of insulin was noted to be dominating the clinical picture. 40% of cases were newly diagnosed as diabetic and 18% of cases are presented with fever. The patients had stopped insulin for variety of reasons including depression, being "fed up", unable to purchase and feeling that they were well enough not to require insulin.

Out of 35 cases hospitalized, 32 cases(91.4%) recovered without any complications of DKA. Average recovery time in these patients is 23.15hrs. 2 cases died due to uncontrolled septicaemia despite of good glucose control and stabilization of their ketoacidosis state. 1 case which is admitted with history of missing 2 doses of insulin the previous day with head injury expired 16 hrs after admission (CT – scan brain not done as the patient condition is not stable to mobilize him from PICU.)

DISCUSSION:

The incidence of DKA in our hospital is (0.12%). Diabetic ketoacidosis continues to be common with a relatively constant incidence in the western countries despite improvement in general medical care[9]. Incidence of 35 cases over a 12 months period seen in one medical unit certainly highlights the extent of the problem.

In this series 40% of patients never knew they had diabetes mellitus and were diagnosed for the first time during an acute presentation. The typical symptoms related to uncontrolled hyperglycemia that dominate the clinical presentation. Even after the patients recovered from their ketoacidosis state, they were unable to recall all their symptoms. Slightly more than half of the patients had nausea and vomiting. Abdominal pain as presenting feature in Diabetic ketoacidosis is not uncommon, occurring in about 20% [10, 11, 12] of cases. Hyperventilation could reflect one of two possibilities – one of which is compensation for metabolic acidosis and the other is pneumonia. The clinically detectable dehydration is due to large fluid losses.

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In DKA, patients may lose fluid easily through osmotic diuresis, vomiting, fever and hyperventilation.

The lack of biochemically demonstrable hypokalemia in patients with DKA is not unexpected. Despite their total body potassium deficit, studies have shown that only in 4 – 10% of patients is the plasma potassium less than normal [3, 4]. In our study 11.4% of cases presented with hypokalemia.

The high mean serum osmolality at presentation is not surprising in view of the marked dehydration in most of these cases. This study also documents previous observations that disturbance of conscious is most closely linked to the degree of dehydration [3, 13]. We had mortality of about 8.57% which compares with the average mortality of about 0 – 20% described in diabetic literature[12]. Despite achieving good blood sugar levels and correction of metabolic acidosis we lost 3 patients of these 2 were due to uncontrolled septicemia and 1 due to head injury.

Majority of the cases (42%) presented in our institute are due to poor compliance. 40% of cases are newly diagnosed. Of these newly diagnosed cases, 5.7% (2 cases) of cases who were infants, presented in severe respiratory distress, thought to be severe bronchopneumonia had come out to be DKA. So, high index of suspicion is necessary on the part of the clinician.

Occurrence of cerebral edema from developing countries has been found to be as high as 26% among a cohort of children admitted at a pediatric intensive care unit in north India. Literature on reasons for such high incidence of cerebral edema from developing countries is very scarce. Studies by Tiwari et al[14] from Chandigarh-India have identified fluid refractory shock, higher volume of fluids at admission and respiratory failure requiring ventilation to be significant risk factors for cerebral edema in DKA. However only fluid refractory shock, azotemia and younger age were identified to be significant risk factors for cerebral edema in multivariate analysis[14].

Hence recommendations regarding fluid therapy based on guidelines from developed countries where sepsis and shock are not major factors in children with DKA needs to be addressed for future guidelines when applied to developing countries. Whether there is a need for more liberal fluid therapy in DKA in developing countries where sepsis, shock and renal failure have been identified to be risk factors for mortality needs to be addressed by multicentric trials.

Jayashree et al[15] in 2004 from India published their retrospective study in DKA. They reported that among 64 children with DKA 30 children had foci of infection. Respiratory infection in 10, soft tissue infection in 10, meningitis in 3, hepatitis in 2, peritonitis, chronic suppurative otitis media, tonsillitis, ethmoiditis and oral and vulval candidiasis in one each. Cerebral edema and complicating sepsis were reported to result in poor outcome in children with DKA. In their series, sepsis was the triggering factor in one third of cases.

Kanwal et al[16] from India have documented in their study on 55 DKA children, incidence of shock to be 18.1%, 10.9% were due to hypovolemia and 7.25% were due to septic shock.

CONCLUSION:

In our study it has been shown that the altered level of consciousness at the time of presentation is correlated well with the serum osmolality than with blood glucose and pH. But it has also been shown that, when DKA is managed in a PICU setting using modified

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