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ORIGINAL ARTICLE

Rhabdomyolysis in Children Under Treatment for Diabetic Ketoacidosis at National Institute of Child Health

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ABSTRACT

Objectives: To determine the frequency of rhabdomyolysis in children under treatment for Diabetic Ketoacidosis (DKA) at National Institute of Child Health (NICH).

Materials and Methods: Total 100 patients who were suffering from DKA were enrolled. Blood and urine samples were collected from of each child in aseptic conditions in sterilized container and sent for base line labs, urine ketone and serum creatinine kinase (CK) levels. All the demographic details and duration of diabetes mellitus and DKA and its treatment were recorded on a predesigned data collection proforma.

Results: Out of 100 patients, 43 were male and 57 were female with mean age of 9.79±3.26 years. Seventy percent of the patients were aged 7.1-14 years, followed by 25.0% patients were aged 1-7 years and only 5.0% patients were aged of 14.1-18 years. The Mean duration of DM and DKA were 3.89±2.75 years and 9.72±4.65 hours respectively. Mean RBS, Urea and Creatinine level were 404.9± 99.1, 35.70±27.5 mg/dl and 0.73±0.75 mg/dl respectively. Mean hemoglobin and WBC level were 13.61±14.3 g/l and 16.33±11.8 respectively. The mean Na level was 137.79±5.64 mmol/l, mean K level was 4.01±0.89 mmol/l, mean Phosphorus level was 27.6±42.0 mg/dl and mean Cl level was 106.8±6.3 mmol/l. The mean PH was found 7.1±6.49 and mean Bicarbonate was 7.56±3.01 mmol/l. Fifty two percent patients were treated for more than 24 hours and 48.0% patients were treated for less than 24 hours. 7% patients under treatment for DKA were suffered from Rhabdomyolysis and expiry was 5%.

Practical implication: In this study we find out that there is very little chance of causing rhabdomyolysis under treatment for DKA but we should take precautionary measures to prevent its progression towards its complications i.e., renal failure and cardiac Arrest which can lead to mortality. This study will lead a positive role in early cure of the DKA patients to avoid further complication.

Conclusion: It is concluded that in DKA patients Rhabdomyolysis is of clinical concern because it can result in significant morbidity and mortality by causing Acute Renal failure, DIC, Cardiac Arrest, Arrythmias, significant electrolyte imbalance, but there is very little chance of causing rhabdomyolysis under treatment for DKA in our setup and it too can be avoided by early and aggressive treatment of DKA.

Keywords: Rhabdomyolysis, Diabetic Ketoacidosis**,** Children, Hemoglobin , Creatinine

INTRODUCTION

Diabetes Mellitus is a life threatening disorder characterized by inadequate control of blood glucose level. [(1)] Rhabdomyolysis is a syndrome caused by muscle breakdown which releases intracellular contents into the blood stream. Rhabdomyolysis can manifest from the range of being asymptomatic to the range of being a life-threatening condition causing acute kidney injury and severe electrolyte abnormalities. It has been stated that the incidence of DM would be 69.9 million in Indian population and 11.6 million in Pakistani population by 2025. [(2, 3)] Diabetic ketoacidosis (DKA) is a serious, potentially lethal and acute complication of type 1 DM in children, which is associated with increased morbidity and mortality. It is caused by insulin deficiency. Globally, diabetic ketoacidosis vary between 12-80%.[(4)] In Pakistani population there are approximately 75.83% children with diabetic ketoacidosis in type 1 diabetes. [(5)]There is an association between DKA and rhabdomyolysis. The exact mechanism of this association has yet to be documented.[(6)] Rhabdomyolysis is a potentially life-threatening syndrome, characterized by rapid breakdown and leakage of skeletal muscle content such as electrolytes, myoglobin, creatine kinase and other sarcoplasmic proteins into the circulation.[(7-9)]

Hyperosmolar state is an extremely rare cause of rhabdomyolysis. The causes of rhabdomyolysis are broadly categorized into three groups: traumatic, nontraumatic exertional, and nontraumatic nonexertional. [(10)] A number of factors are responsible for the onset of rhabdomyolysis in children, including infection, muscle injury, drugs, toxins, hyperthermia and metabolic disorder.[(6, 11, 12)] But the most important and leading causes of rhabdomyolysis in children are infection, trauma, and exercise.[(6, 13)]

A release of cell products in the bloodstream and extracellular space follows and CK is massively elevated. Serum sodium, serum osmolality, and blood glucose are the major determinants and are involved for rhabdomyolysis in children.[(6, 14)] An association between diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state (HHS), and rhabdomyolysis has been documented; however, the exact mechanism of this association has yet to be established.[(14)] It has been proposed that the metabolic disturbances associated with HHS predisposes to destruction of muscle cells, mainly by disrupting the Na/K ATPase pump.[(6)] Serum sodium, serum osmolality, and blood glucose were the major determinants for rhabdomyolysis in adults with diabetes.

This study was conducted in pediatric population, as very little work done in children and adolescents, to achieve a current frequency of Rhabdomyolysis affecting children with DKA, so that we can do urgent measures to prevent its progression towards its complications i.e., renal failure and cardiac Arrest which can lead to mortality.

Objective: To determine the frequency of rhabdomyolysis in children under treatment for DKA at NICH.

MATERIALS AND METHODS

Study Design and setting: The Prospective Cross-sectional study was conducted in endocrinology department of National institute of child health (NICH) Karachi.

Duration of the study: Duration of the study was 9 months (January 2022 – September 2022).

Sample Size: Sample size of 100 was calculated by using Online Open Epi Sample size calculator taking the following parameter.

Anticipated population=6.98% [(15)]
Confidential interval= 95%
Margin of error= 5%

Inclusion Criteria:

- Children of either gender with age 1-18 years.
- All children with type 1 diabetes admitted at NICH presenting with DKA.

Exclusion Criteria:

- Children presenting with DKA along with chronic cardiac disease or chronic renal failure.
- Parents of children not willing to participate in study.

METHODS

After the permission of Institutional Ethical Review Board of NICH, a total of 100 patients were enrolled and written informed consent for the study was obtained from the caregivers of children. Demographics data of all the enrolled patients were obtained either from parents or from medical file including name, age and gender. Details about duration of diabetes mellitus and DKA and its treatment were also be noted. Detail history for the symptoms including dark urine, muscle aches, muscle weakness, fever, cough or fatigue was taken. Blood sample and urine sample were collected from of each child in aseptic conditions in sterilized container and sent to laboratory of the hospital for random blood sugar (RBS), serum urea, serum creatinine, serum electrolytes (Sodium (Na), Potassium (K), Phosphorus (Ph) and Chlorine (Cl), complete blood count (CBC, hemoglobin (Hb), white blood cells (WBC), platelets count), arterial blood gas (ABG), serum creatine kinase (CK) and ketones. A predesign questionnaire was used to collect data.

Statistical Analysis: SPSS (version 25.0) was used for the analysis of data. The data was presented in the form of table and graph. The paired Student's t-test was applied.

RESULTS

Out of total 100 patients, 43 children were male and 57 children were female (Table 1, Fig 1-0). Age of the patients were ranged from 1 year to 18 years (mean age of 9.79±3.26 years). Seventy percent of the patients were aged 7.1-14 years, followed by 25.0% patients were aged 1-7 years and only 5.0% patients were aged of 14.1-18 years (Table 2-0). The Mean duration of DM and DKA were 3.89±2.75 years and 9.72±4.65 hours respectively. Mean RBS, Urea and Creatinine level were 404.9± 99.1, 35.70±27.5 and 0.73±0.75 respectively. Mean hemoglobin and WBC level were 13.61±14.3 and 16.33±11.8 respectively. By measuring the electrolytes level, the mean Na level was 137.79±5.64 mg/dl, mean K level was 4.01±0.89 mmol/l, mean Phosphorus level was 27.6±42.0 mg/dl and mean Cl level was 106.8±6.3 mmol/l. The mean PH was found 7.1±6.49 and mean Bicarbonate was 7.56±3.01 mmol/l.

Table 1-0: Clinical characteristics of patients (n=100)

Variable	Mean	SD
Age (Years)	9.79	3.26
Duration of DM (Years)	3.89	2.75
Duration of DKA (Hours)	9.72	4.65
RBS	404.9	99.1
Urea (mg/dl)	35.70	27.59
Creatinine (mg/dl)	0.73	0.75
HB (g/l)	13.61	14.3
WBC	16.33	11.8
CK ((IU)/L)	216.77	452.4
Ketone	2.91	0.40
Electrolytes:		
Na (mmol/l)	137.79	5.64
K (mmol/l)	4.01	0.89
Ph (mg/dl)	27.6	42.0
Cl (mmol/l)	106.8	6.3
ABG:		
PH	7.1	6.49
Bicarbonate (mmol/L)	7.56	3.01

HB= Hemoglobin, RBC= Red blood cells, WBC= White blood cells, CK= Creatine kinase, ABG= Arterial blood gas, Ph= Phosphorus, PH= power of hydrogen

The patients were distributed and it was found that 65.0% patients fell in moderate category of DKA followed by severe category in which 31.0% patients and in mild category there are only 4.0% patients. Fifty two percent patients were treated for more than 24 hours and 48.0% patients were treated for less than 24 hours. In this study 5% patients were expired. 7% patients under treatment for DKA were suffered from Rhabdomyolysis (Table 2-0). Stratification was done on the basis of different variables as shown in Table 3-0.

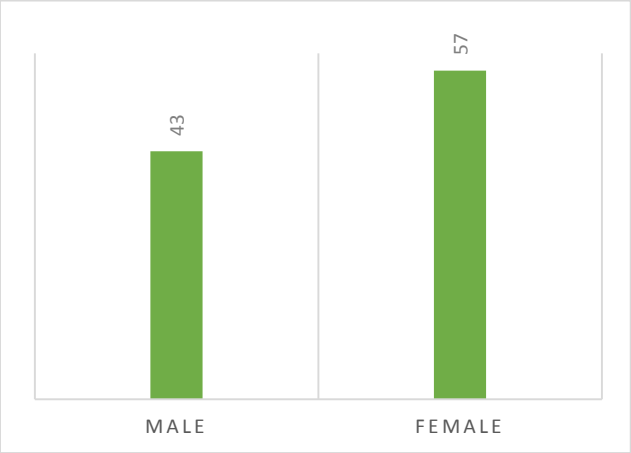

Figure 1-0: Graphical Representation of gender

Table 2-0: Distribution of Patients on The Basis of Different Variables (n=100)

Variables	Frequency	Percentage
Age Group (Years):		
1-7	25	25.0
7.1-14	70	70.0
14.1-18	5	5.0
Gender:		
Male	43	43.0
Female	57	57.0
Severity of DK:		
Mild	4	4.0
Moderate	65	65.0
Severe	31	31.0
DK treatment:		
<24 hour	48	48.0
>24hour	52	52.0
Outcome:		
Alive	95	95.0
Expired	5	5.0
Rhabdomyolysis:		
Yes	7	7.0
No	93	93.0
Total	100	100.0

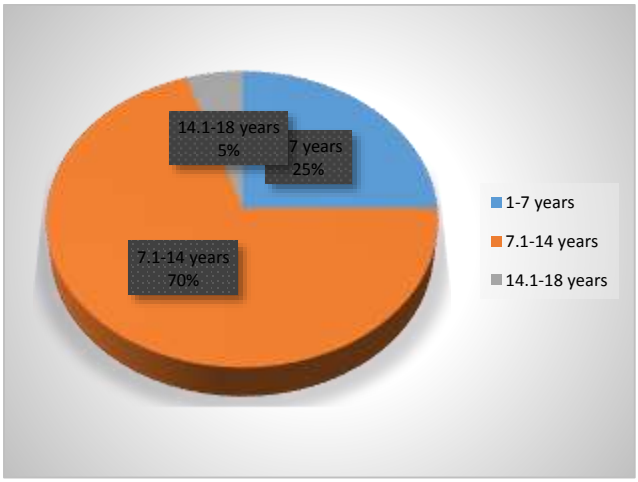

Figure 2-0: Graphical Representation of Distribution Of Patients According To Age Group (n=100)

Table 3-0: Stratification Was Done on The Basis of Different Variables (n=100)

Rhabdomyolysis			
Variable	Yes	No	P- Value
Gender			
Male	2	41	0.35
Female	5	52	
Age group			
1-7 years	1	24	
7.1-14 years	6	64	0.61
14.1-18 years	0	5	
Severity of DK			
Mild	0	4	
Moderate	5	60	0.83
Severe	2	29	
DK treatment			
<24 hour	3	45	0.54
>24hour	4	48	

DISCUSSION

Rhabdomyolysis is of high concern in children with DM as it can lead to significant morbidity or mortality. This study was conducted in order to determine the frequency of rhabdomyolysis in children under treatment for DKA. Because there is an association between DKA and rhabdomyolysis. In a study titled "Rhabdomyolysis in Diabetic Emergencies," conducted by L.-M. Wang et al. stated that there were 44 (16%) patients of rhabdomyolysis out of 265 patients.[10, 16] This showed that rhabdomyolysis in diabetic patients did occur more frequently than assumed. But in our study as compared to this very few patients (7%) were affected from rhabdomyolysis during treatment for DKA.

In our study the mean RBS value was very high. Electrolyte abnormalities are noticeable features of rhabdomyolysis because the electrolyte abnormalities such as hypernatremia, hypokalemia and hypophosphatemia seen in high RBS state are responsible for rhabdomyolysis [10, 17]. In rhabdomyolysis patients the phosphorus level is elevated because during the disruption of muscle cells, the phosphoric components of the body are dissolved and released into the plasma, leading to hyperphosphatemia [18]. In our study we found very high mean phosphorus level as a complication of DKA.

The clinical symptoms were reliant on the severity of the rhabdomyolysis. Since the breakdown of muscle content such as myoglobin, creatine phosphokinase (CPK), electrolytes (Na, Ph, Cl and K), proteins and non-protein substances were released and lead to high content level of these substances in the plasma.(18) The detection of these content in plasma may contribute to the early diagnosis of rhabdomyolysis.[19, 20] In rhabdomyolysis patients the disturbances of electrolyte balance and metabolic acidosis take place. When muscle injury and weakness take place, it leads to too much intracellular influx of Na^+ and Ca^{2+}. That results in to draws water into the cell and interrupts the intracellular space integrity. [21, 22]

It has been stated that the level of creatine kinase (CK) is elevated in the case of rhabdomyolysis. The Laboratory finding in our study shows that the mean serum CK is in normal range. An elevated CK level is the most sensitive and important clinical laboratory test for assessing an injury to muscle that has the potential to cause rhabdomyolysis.[22, 23]

Most of the symptom were observed during 12-24 hours after the initial muscle damage. The color of urine is converted in to dark, term as "tea-colored", because the kidney fails to work and the production of urine become diminished, usually 12-24 hours after the initial muscle damage. So, it is very helpful to treat such patients within 24 hours.

CONCLUSION

It is concluded that in DKA patients Rhabdomyolysis is of clinical concern because it can result in significant morbidity and mortality by causing Acute Renal failure, DIC, Cardiac Arrest, Arrythmias, significant electrolyte imbalance, but there is very little chance of causing rhabdomyolysis under treatment for DKA in our setup and it too can be avoided by early and aggressive treatment of DKA.

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