Risk Factors and Outcome of Acute Kidney Injury in Children with Diabetic Ketoacidosis

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Abstract:

Background: *Children with diabetic ketoacidosis (DKA) suffer from several complications. Among them acute kidney injury (AKI) is one of the grave complications.*

Objectives: *To determine the risk factors for development of AKI in children (age <15 years) with DKA and observe the outcome of these children.*

Method: *An observational study was done in Department of Paediatrics, BIRDEM General Hospital, Dhaka, Bangladesh from January 2019 to December 2020. During study period, we observed all children with DKA who developed AKI. Data of clinical and biological variables were taken from hospital records and analysed. The parameters of children with AKI were compared with children with DKA who did not develop AKI. Then outcome of the children with AKI were measured. Statistical analysis was done by using SPSS version 23.*

Results: *Among 73 children with DKA, 16 (21.9%) children developed AKI. Children were divided into two groups, DKA with AKI and DKA without AKI. No statistically significant differences were found in demographic features of children in both groups. We observed that, delay in initiation of treatment, low Glasgow Coma Scale (score-<8), haemodynamic failure, severe acidosis and sepsis were significant risk factors of developing AKI. Out of 16 children with AKI, 9(56.2%) patients needed peritoneal dialysis and 7(43.7%) responded to fluid resuscitation. Complete resolution occurred in 13(81.2%). Total mortality in DKA children was 13(17.8%). Among them 84.6% children died due to AKI.*

Conclusions: *This study documented that 21.9% of children with DKA developed AKI. Among them mortality was 84.5%.*

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Introduction:

Diabetic ketoacidosis (DKA) is a life-threatening complication of type 1 diabetes. Globally about 15-70% of children with diabetes mellitus (DM) present with DKA as their first presentation.[1] Mortality due to DKA in children varies from 0.15% to 0.35% in developed country, but percentage is high in developing countries (3.4%-13.4%).[1,2] There are several complications of DKA that are responsible for morbidity and mortality, among them AKI is one of the serious complications.[2] The incidence of AKI in children with DKA range from 35 to 56.5%[3-5] in various study. In a study conducted at Canada showed that about 64.2% of children with DKA developed AKI.[6] In DKA, children undergo varying degree of dehydration and electrolyte imbalance due to osmotic diuresis.[4,5,6] As in children compensatory mechanism for dehydration is not well established so they are more vulnerable to volume depletion which leads to acute tubular necrosis and AKI.[4,5,6] Symptoms of AKI in DKA are sometimes masked due to osmotic diuresis. Delay in initiation of treatment, hyperglycaemia, severe acidosis, haemodynamic failure are the common risk factors which may contribute to development of AKI in children with DKA. If risk factors can be addressed earlier the

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mortality in children with DKA as well as the risk of development of chronic kidney disease in later life can be reduced.[5]

The objective of the study was to determine the rate of acute kidney injury (AKI) in children (age <15 years) who presented with DKA, to identify the associated risk factors related to the development of AKI and to determine the outcome of children in DKA with AKI.

Methodology:

An observational study was undertaken in department of paediatrics, BIRDEM General Hospital, Dhaka from January 2019 to December 2020. Institutional Review Board, BADAS approved this study. During this period total 73 children with type 1 DM with DKA were admitted. Among them, some patients were previously diagnosed as DM and on treatment were defined as known DM. Those who had recently diagnosed as DM and treatment was not started defined as new DM. DKA was defined by some clinical and biochemical criteria such as dehydration, rapid deep sighing breathing (Kaussmaul respiration), nausea, vomiting and abdominal pain, progressive obtundation, loss of consciousness, hyperglycemia (BG: >11 mmol/L, ~ 200 mg/dL), venous blood pH <7.3 or HCO_3 <15mmol/L and ketonaemia or ketonuria.[2] According to the degree of acidosis severity of DKA is classified as mild, moderate and severe. In case of severe DKA venous pH is < 7.1 and/or HCO_3 < 5mmol/l along with hyperglycaemia.[2] Vital signs and haemodynamic status were monitored, intake-output were measured. Child with cold clammy skin, prolonged capillary refilling time, rapid thready pulse and low/non-recordable blood pressure was defined as having haemodynamic failure.[3,4] GCS < 8 was taken as low GCS. Sepsis was confirmed by blood culture report which was sent on the day of admission. Delay of initiation of treatment of DKA was defined when commencement of treatment did not occur on the same day of diagnosis.[5] Bedside blood glucose level was monitored hourly and urinary sugar & acetone were monitored 6 hourly and other relevant investigations like complete blood count, serum electrolytes, urea, creatinine, blood gas analysis and septic screening and urine routine examinations were done. All medical records from admission till discharge were collected in a separate questionnaire for each patient including investigation profile and detail management. Management of all DKA children were done according to ISPAD Consensus Guideline 2018.

Acute kidney injury (AKI) was defined according to pRIFLE criteria depending upon decreased urinary output and/or increased serum creatinine level.[3,4,6] Based on presence or absence of AKI, children with DKA were divided into two groups. Those who developed AKI on admission or during the course of treatment were classified as 'AKI group' and those who did not develop any features of AKI were classified as 'No AKI group'. Baseline characteristics and clinically relevant variables of these children of both groups were compared.

Statistical analysis

Data were expressed as mean, number and percentage. Comparison of baseline characteristics and clinically relevant variables of patients with and without AKI was done by using chi-square tests. To identify the predictors of AKI on admission, logistic regression model was carried out using the following variables: delay in initiation of treatment, Glasgow coma scale, hemodynamic failure, acidosis, sepsis and blood glucose. Correlations were made with a simple linear regression test. We considered $p<0.05$ as statistically significant. Data analysis was done by using SPSS version 23.

Results:

During this study period 73 children were admitted with DKA. Among these children with DKA, 16 (21.9%) children had AKI at admission. Children were divided into two groups: AKI group and no AKI group.

The comparison of demographic, clinical parameters (Table I) & biochemical profile (Table 2) among the

Table I

Comparison of demographic and clinical profile between the two groups (N-73)

	AKI (n-16) %	No AKI (n-57)	P-value
Mean Age (year)	8.06 ± 2.8	8.57 ± 2.3	0.59
Male : Female	1:3	1:1.5	0.24
Known DM	06 (37.5%)	22 (38.5%)	0.47
New DM	10 (62.5%)	35 (61.4%)	0.58
Urban: Rural	1:1.2	1: 1.9	0.18
Severe DKA	16 (100%)	25 (43.8%)	0.001
Haemodynamic failure	16 (100%)	22 (38.5%)	0.001
Sepsis	06 (37.5%)	03 (5.2%)	0.002

Table II
Comparison of biochemical profile between the two groups (N-73)

	AKI (n-16) %	No AKI (n-57)	P-value
Severe Acidosis	13 (81.2%)	21 (36.8%)	0.001
HCO_3 (mmol/l)	6.9 ± 4.2	8.5 ± 4.5	0.002
Glucose (mmol/l)	35.2 ± 4.5	30.5 ± 5.9	0.004
Creatinine(mg/dl)	6.26 ± 1.79	0.80± 0.21	0.00
Na (mmol/l)	137.8 ± 6.54	136.5 ± 6.73	0.50
K (mmol/l)	5.0 ± 1.42	4.1 ± 0.89	0.01
Chloride (mmol/l)	108.3 ± 10.1	105.5 ± 7.1	0.21

Table III
Risk Factors of AKI:

	AKI (n-16)	No AKI (n-57)	Odds Ratio (95% CI)	p-value
Delay in initiation of Rx	12	13	1.99 (1.32-3.01)	0.001
Low GCS score on admission (GCS <8)	14	11	2.45 (1.55-3.86)	0.002
Haemodynamic failure	16	22	1.72 (1.32-2.26)	0.001
Severe acidosis (pH <7.1/ HCO3 <5 mmol/l)	15	11	2.36 (1.50-3.70)	0.001
Sepsis	06	03	2.53 (0.99-6.41)	0.002
High blood glucose (>15mmol/l)	11	29	1.17 (0.92-1.48)	0.14

two groups were observed. In no AKI group there was 57 children and in AKI group there was 16 children. In Table 1 it was shown that, mean age of AKI and no AKI group was 8.06 ± 2.8 and 8.57 ± 2.3 respectively. No significant difference were seen regarding age, sex and known DM or new DM in both group. All of the children in AKI group presented with severe DKA with haemodynamic failure, however in no AKI group 43.8% developed severe DKA and 38.5% developed haemodynamic failure. Sepsis was also significantly prevalent in children with AKI (37.5%).

Regarding biochemical profile (Table 2), children with AKI had severe acidosis with significantly reduced bicarbonate, higher blood glucose and higher potassium.

Then we analyse the possible risk factor of AKI. The analysis showed that delay in initiation of treatment, low GCS score, haemodynamic failure, sepsis and severe acidosis were the significant risk factor for AKI for children with DKA (Table III).

Out of 16 children with AKI, 9(56.2%) patient needed peritoneal dialysis and 7(43.7%) responded to fluid resuscitation. Complete resolution occurred in 13(81.2%). Total mortality in DKA children was 13(17.8%). Among them 84.6% children died due to AKI. None of them progressed to chronic kidney disease after 18 months.

Discussion

In this present study, 21.9% of children who presented with DKA, developed AKI at presentation or during the course of treatment. Majority (62.5%) of them were newly detected DM with DKA. As they remained undiagnosed prior to referral or inappropriately treated, most of them tended to present as severe DKA. These children are prone to develop several complications like AKI, cerebral oedema etc.[2]

AKI is acute and reversible deterioration of renal function. The cause of AKI in DKA is assumed to be prerenal.[4,6] Hypoperfusion of kidney results from hypovolemia due to osmotic polyuria and sometimes gastrointestinal losses leads to renal injury. However, accurate assessment of volume depletion is difficult in these patients. Acute kidney injury can be determined by oliguria and/ or raised serum creatinine level. [3-6] pRIFLE criteria are used to classify the risk of AKI in children. [3-6]

The incidence of AKI in children with DKA ranges from 35% to 64%.[3-6] In a study held in a korean center,

found that 90 episodes of DKA in 58 children, 77.8% presented with AKI.[7]

This study also showed that children who had severe DKA along with severe acidosis and haemodynamic failure at presentation were at risk in developing AKI, which correlate with other studies.[8,9] A study conducted at British Colombia Children Hospital at Canada, concluded that AKI was associated with marked volume depletion and severe acidosis in DKA patient.[6]

Regarding other possible risk factors, delay in initiation of treatment & low GCS score on admission were also found significant in this study; which were consistent with other studies. [5,8,9]

Sepsis was one of the complications of DM which contributes in development of DKA in children.[10] In most of the cases sepsis remain indolent in DKA patient. Here we observed that children with DKA and sepsis were one of the risk factors of development of AKI and it was statistically significant.

Several study had found that hyperchloremia as an important risk factor in children admitted with DKA with AKI, [11,12] but in this study no significant associations was found with serum chloride level.

Close monitoring & control of blood glucose, meticulous fluid resuscitation are the mainstay of management of these children with DKA and AKI. In some cases peritoneal dialysis are also required. In this study. 7(43.7%) responded to fluid resuscitation and 9(56.2%) patient needed peritoneal dialysis. Complete resolution occurred in 13(81.2%). All of them were kept on follow up. None of them developed chronic kidney disease till date. During the study period 13(17.8%) children with DKA died. Among them 11(84.6%) died due to AKI. Other than AKI, 2(15.3%) children died due to cerebral oedema. In a study in Chandigarh, India, they found about 13% death in children with DKA with AKI.[12,13]

Conclusions

Acute kidney injury is a significant complication for children with DKA which is responsible for increase mortality and morbidity of these children. Delay in initiation of treatment, haemodynamic failure, severe acidosis and sepsis are possible risk factors. In most of the cases AKI is transient and respond to correction of dehydration. Early recognition and prompt initiation of management may reduce the risk of development of AKI in children with DKA.

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