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Hemolytic uremic syndrome in children: Seizure disorders and mortality rate

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Abstract

Background and Objective: Hemolytic Uremic Syndrome (HUS) is a thrombotic microangiopathy that contains hemolytic anemia, thrombocytopenia, renal failure and other organ involvement including central nervous system. Frequency of neurologic complications in patients with HUS is high and important cause of mortality. This study was performed to determine seizure disorders in term of acute neurologic complications in children with HUS.

Methods: In this descriptive, cross sectional study, 46 children with diagnosis of HUS were admitted to the Nephrology ward of Ali-Asghar Children's Hospital from 2010 to 2015. They were evaluated about age, sex, neurologic complications including seizure, diarrhea, PICU admission and mortality rate.

Results: In this Study,46 patients were enrolled. Twenty-five (54.3%) patients were male. Mean age was 4.65±4.2 (range from 4month to 15 year). Acute neurologic complications were seen in 16(34.8%) of patients including seizures in 8(17.5%) of cases. Diarrhea was seen in 21(46%) of cases and 18(39%) of patients admitted in PICU. Four (9%) cases died and two of them had seizures. There was no relationship between seizure disorders and age, sex, diarrhea and mortality rate. There was a significant association between mortality and age (p value =0.049, CI=95%, lower = -8.60, upper= -0.02) and between mortality and PICU admission (p=0.009).

Conclusion: In children with HUS neurologic complications such as seizure is common. Mortality rate is higher in younger patients specially with early admission in PICU.

Keywords: Child, HUS, Mortality, Seizure

Introduction

Hemolytic uremic syndrome (HUS) is a common cause of renal failure in childhood period. It occurs in all races –rare in blacks, with equal frequency in male and female and more in preschool-school age children. Its triad includes thrombocytopenia, microangiopathic hemolytic anemia and acute renal insufficiency. Characteristic of HUS is microvascular injury and endothelium cell damage (1). Through the literature two major types of HUS is identified: typical and atypical forms. In typical HUS, syndrome is presented by a diarrheal prodrome and vascular injury mediated by Shiga toxin producing Escherichia Coli (STEC 0157:H7) (2,3). Atypical HUS is defined as diarrhea-negative disease and some nontoxic heritable factors such as ADAMTS 13 (von willebrand factor cleaving-protease) deficiency, complement system defects (H, I, B factors deficiencies) and abnormal metabolism of vitamins are responsible for its manifestations. Atypical HUS has another subtype that is named as neuraminidase triggered by Pneumococcal infections (4-7). Many diseases with microvascular injury can lead to HUS including systemic lupus erythematosus, phospholipid syndrome and malignant hypertension. Also, some drugs including Cyclosporine and Tacrolimus and organ transplantation may have trigger HUS (8,9).

Table 1. Comparison between patients with and without acute seizures

Characteristics	With seizure 8(17.5%)	Without seizure 38(82.5%)	*P* value
Age			
≤1 year	4(9%)	7(15%)	0.06
>1year	4(9%)	31(67%)	
Sex			
Male	3 (6.5%)	22(48%)	0.29
Female	5(11%)	16(34.5%)	
Diarrhea			
Yes	6 (13%)	15 (32.5%)	0.07
No	2 (4.5%)	23 (50%)	
Death			
Yes	2 (4.5%)	2 (4.5%)	0.07
No	6 (13%)	36(78%)	
Mean blood sugar (mg/dl)	92.63±33.1	89.04±19.9	0.68
Mean Serum Sodium (meq/l)	136.00±6.35	137.95±4.82	0.33
Mean Serum Calcium (meq/l)	8.73±1.3	9.10±0.9	0.35
Hypertension			
Yes	3(6%)	10(22%)	0.67
No	5(11%)	28(61%)	

Clinical manifestations of HUS are from mild to multiple organs dysfunction due to renal insufficiency, hemolysis, hypertension, volume and electrolyte imbalances. Other complications may occur such as heart failure, colitis, pancreatitis and central nervous system (CNS) involvement. Patients with HUS present neurologic manifestations with lethargy, coma, focal or generalized seizures, brain edema and structural brain damage due to thrombotic stroke. CNS manifestations as major causes of mortality and morbidity (10,11).

Pathophysiology of CNS involvement are metabolic insults such as hyponatremia, hypocalcemia and uremia. Other causes include toxin mediated injury of vascular endothelium and cerebral ischemia with microthrombi formation (10).

This study was designed to determine demographic features, acute neurologic complications including seizures and mortality rate in patients with HUS.

Methods

This descriptive, cross sectional study was performed on admitted children with diagnosis of HUS in Ali-Asghar Children's Hospital in Tehran, Iran from 2010 to 2015.The project was approved by ethical committee of the Iran University of Medical Sciences. Forty-six patients 4months to 15 years old enrolled the study. Data about age, gender, diarrhea, acute neurologic complications including seizures, serum electrolytes and blood sugar, hypertension, PICU admission and mortality were recorded from medical files. The collected data was analyzed by software of SPSS (version 22). Descriptive statistics such as frequency, mean and standard deviation and analytic statistics including Chi-square and t-test were calculated. P values less than 0.05 was considered significant.

Results

During the study, 46 patients with diagnosis of HUS were admitted to our center. Of these patients, 25(54.3%) were male; mean age was 4.65±4.2 (ranged from 4 months to 15 years) and 11 (24%)of cases were under 12 months of age. Acute neurologic complication was seen in 16 (34.8%) patients including acute seizure disorders in 8(17%), altered level of consciousness–from lethargy to coma and delirium- in 6(13%), headache in 3(7%), increased intracranial pressure in 1(2%)of cases. In patients with seizure, hypertension in 3 cases, fever in 2 cases and hypocalcemia in one case were found. Two cases did not have any cause for seizure. Hypertension was recorded in 13(28%) of patients. Diarrhea was seen in 21(46%) of cases. Eighteen (39%) of patients had early admission in pediatric invasive care unit (PICU). Four (9%) cases died and two of them had seizures. Between two groups with and without seizures there was no relationship from point of age, sex, diarrhea, death and predisposing factors of seizure such as changes in blood sugar, serum electrolytes, and hypertension (Table 1). There was a significant association between mortality and age (p=0.049 CI=95%, lower= -8.60, upper= -0.02) and between mortality and PICU admission (p=0.009).

Discussion

Hemolytic uremic syndrome is a clinical syndrome that specified with hemolytic anemia, thrombocytopenia, renal failure and multiple or-

gans involvement including CNS. It is usually presented by diarrhea. CNS complications is common as 30percent and major cause of mortality during acute phase of HUS. Neurologic manifestations include lethargy, irritability, seizures and in severe cases paresis, coma, brain edema, blindness, ataxia and rigidity can occur (2,10). Major injury is due to cerebral microangiopathy, metabolic changes and hypertensive encephalopathy. Brain imaging defined foci of infarction, edema, hemorrhage specially in basal ganglia (10,12)

Present study showed mean age of patients was near to 4.5-year-old. Adams et al demonstrated this syndrome was frequently seen in children under 15-year-old particularly in 1-4-year-old age group (13).

Acute neurologic complication was 35% in our study and included seizures, altered level of consciousness (lethargy, coma and deliriums), headache and increased intracranial pressure.

Otukesh et al evaluated 92 cases with HUS that had 22(24%) seizure disorders, 18(19.5%) coma and 11(24.5%) irritability. Relationship between seizure disorders and mortality rate was detected (1).

In Nathanson et al study,52 patients with HUS associated diarrhea and neurologic complications were evaluated. Neurologic complications included altered level of consciousness (44cases), seizures (37cases), pyramidal (22 cases) and extrapyramidal (27 cases) syndromes (14). Also Steinborn et al study showed acute neurologic complications in near to30% of patients with HUS (12).

In present study, syndrome was started after a diarrheal disease in 46% of cases but there was no relationship between diarrhea and neurologic manifestations and seizure occurrence.

In Micheletti et al study, 22 children with HUS-with and without diarrhea-assessed from point of neurologic manifestations. Drowsiness and seizure was seen in 18% of patients and it was equal

in each group with and without diarrhea (15).

In our study mortality rate was 9%(4 cases) and two cases had acute refractory seizures. It means 12.5% mortality rate in cases of HUS with neurologic complications. In a study, 90 cases with HUS were evaluated. Twenty-six percent had neurologic manifestations including coma, seizure and 1.1% of cases died (16).

In Eriksson et al study, 22 children had HUS and acute neurologic complications included seizure, coma, hemiparesis or aphasia. Mortality rate was 23 percent (10). Lower rate of mortality may be due to have newer techniques of diagnosis, intensive cares and treatment plans in mentioned centers.

Major predisposing factors of neurologic complications including seizure are hypertensive encephalopathy, electrolyte imbalances and brain edema (10). In our study, patients with seizure had hypertension, fever and hypocalcemia. It is suggested that better handling of common problems in children with HUS –such as hypertension, infections and electrolyte abnormalities-can decrease risk of seizures in these patients.

In this study our limitations were small size sampling and incomplete personal records.

Conclusion

According to present study, acute neurologic manifestations were seen in more than one third of cases that most of them were seizure disorders and altered level of consciousness. Mortality rate was higher in younger patients especially in those with early admission in PICU.

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Conflicts of interest: None declared.

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