Outcome of Hemolytic Uremic Syndrome in Iraqi Children a Single Centre Experience in Baghdad

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ABSTRACT:

BACKGROUND:

Hemolytic uremic syndrome (HUS) is important cause of acute kidney injury (AKI) and chronic kidney disease (CKD) in children. Proposed prognostic features are controversial.

OBJECTIVE:

Our objective was to study the characteristics of HUS and determine short-term outcome and risk factors for prognosis in children followed in a single center in Baghdad city.

PATIENTS AND METHODS:

We reviewed, retrospectively, the records of children with HUS seen at child welfare Teaching hospital, Baghdad(April2015- April 2017and studied outcome and some prognostic risk factors.

RESULTS:

Thirty-three children with HUS were recorded; 40% had diarrhoea positive (D+) and 60% diarrhoea negative (D−) HUS. The mean age was 47.8 40.4 months and males were 63.6%. At the acute phase seizures and hypertension were present in 33.5%, and 66.7% respectively. Severe anaemia, thrombocytopenia, and leukocytosis were present in 87.9%, 96.6%, and 27.2% respectively. Clinical and laboratory features were not significantly different in D+ and D− cases ($P > 0.05$ for all parameters). Dialysis was undertaken forall patients. Demographic, clinical and laboratory features were not significant risk factors for adverseoutcome. At short-term follow up (mean period ± SD of 18.54 ± 13.21 months), 42.2% had complete renal recovery, 35.4chronic kidney disease, and 24.2% died.

CONCLUSION:

In spite of institution of dialysisand supportive therapy for all patients, our data showed less favorable outcome of HUS.

KEYWORDS: Children, Hemolytic uremic syndrome, Outcome

INTRODUCTION:

Hemolytic uremic syndrome (HUS) is important causeof acute kidney injury (AKI) and chronic kidney disease (CKD) in children [1]. The disease characterized by micro-angiopathic hemolytic anaemia, thrombocytopenia and AKI [2].. Hemolytic uremic syndrome (HUS) is a severe condition which accounts for 0.2 to 4.28 per 100,000 cases of pediatric acute renal failure globally.(3) became 3

D+ HUS has been used for HUS preceded by diarrhoea, which is usually due to Shiga-toxin producing Escherichia coli mostly 0157:H7 (STEC), whereas atypical HUS (aHUS) or D− has been used for the non STEC associated type [1]. D+ HUS is the commonest, has a benign course, not relapse [3].

The aHUS or D− is less common, with tendency to relapse, and has a high risk of renal damage and death [4-6]. aHUS or D− may be primary or familial due to complement dysregulation) or secondary to infectious or non-infectious causes [7]. the overall prognosis of HUS is poor with high risk of CKD and death [8, 9]. High acute mortality rate, short and long term prognosis have been attributed to different risk factors including demographic, clinical, laboratory findings and types of management [10-11]. Data about HUS in Iraq isstill scanty.

OBJECTIVES:

Our objective was to study the characteristics of HUS and determine short-term outcome and risk factors for prognosis in children followed in a single center in Baghdad city.

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PATIENTS AND METHODS:

We retrospectively reviewed the records of all children with HUS who have been followed at the pediatric renal unit in Child welfare Teaching Hospital, Baghdad , between April 2015and April 2017, diagnosis of HUS were based on the presence of the clinical triad of micro-angiopathic hemolytic anaemia, thrombocytopenia and AKI [2]. Patients with incomplete records were excluded. Data were abstracted from the records using standard data collection sheet. Personal data, history, height, weight, blood pressure, clinical course and outcome were recorded. Laboratory data including complete blood count, serum creatinine, blood urea, serum electrolytes were recorded. All relevant data were recorded at admission, discharge and at last follow up clinic visit. Results of the haematological data (Hb, WBCs, and platelets count) and biochemical data (blood urea, serum creatinine) were recorded as low or high levels if below or above the age gender-specific values respectively [13]. Acute kidney injury (AKI) was diagnosed on the basis of serum creatinine levels ≥1.5 above normal levels for age and oliguria (≤ 0.5 ml/Kg per hour for 6 hours) and/or occurrence of acidosis, and/or urea, phosphate and potassium outside the normal range for age [14]. Severe anemiahemoglobin equal or less than 7 g/dl(15)
Chronic kidney disease (CKD)was defined as glomerular filtration (GFR) < 60 ml/min/1.73 m^2 for ≥3 months and CKD5 requiring Renal replacement therapy as GFR < 15 ml/min/1.73 m^2 [16]. Glomerular Filtration rate (GFR) was calculated from the Schwartz formula [17]. Hypertension was defined as blood pressure higher than 95th percentile for age based on data from the Fourth Task Force Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescence [18].
Facilities for isolating STEC and performing compliment abnormalities were not available in our center.
The cases divided into D+ HUS and D− according to preceded by diarrhea or not .
Ethical considerations:
Approval was taken from Iraqi Board for Health Specializations.
All the information was digitally saved without children names.
Limitations of the study
-Short duration of the study(mean period ± SD of 18.54 ± 13.21 months).
-Single center study.
Statistical analysis
All patients' data entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 22 was used. Descriptive statistics presented as (mean ± standard deviation) and frequencies as percentages. Kolmogorov Smirnov analysis verified the normality of the data set. Chi square test was used for comparison between categorical data (Fishers exact test was used when expected variable was less than 20% of total. Independent sample t-test was used to compare between two means and one way ANOVA analysis was used to compare between more than two means. In all statistical analysis, level of significance (p value) set at ≤ 0.05. Statistical analysis of the study was done by the community medicine specialist.

RESULTS:

A total of 33 children with HUS (21 males; 63.6%) were recorded with a mean age ± SD at diagnosis of 47.8 ± 40.4 (range 4-168) months. Infants constituted 17.1% and those below five years 48.7% (Table 1). (42.4%) of cases were referred from rural areas.
HUS preceded by a prodrome of diarrhoea (D+) was found in 13 cases (39.4%), D− in 20 (60%). The mean duration of symptoms ± SD was 11 ± 8.2 (range 1-28) days. Table -2- show demographic, clinical and laboratory features and outcome during the acute phase in D+ and D− HUS
D+ patients had lower age at presentation than D− and that was statistically significant, P = 0.003. However, there was no statistically significant gender difference, P = 0.440. Seizures and hypertension were present in 33.5%, 66.7% respectively. Severe anaemia (Hb< 5 gm/dl), thrombocytopenia, and leukocytosis were detected in 87.9%, 96.9%, and 27.2% of cases respectively.
The mean haemoglobin ± SD was 5.6 ± 1.2 (range 3.6-9.5) gm/dl and the mean serum

creatinine ± SD was 4.4 ± 3.4 (range 1.9-15) mg/dl respectively. Clinical and laboratory features were not significantly different in D+ and D− (P > 0.05 for all parameters), table 2. Dialysis was undertaken in 100% and Dialysis modality was peritoneal dialysis (PD) in 29 patients(87.87%), hemodialysis (HD) in 2 patients (6.1%)and both modalities in 2 patients (6.1%) .Supportive therapies used were transfusion of packed RBCs ± plate lets in 84.6% and fresh frozen plasma (FRP) in 12.8% ,plasmaphresis in 6,1 %.

Risk factors for acute mortality were assessed (Table 3).

There was no statistically significant association between acute mortality and demographic, clinical and laboratory features. Outcome at short-term follow up (mean period ± SD was 18.54 ± 13.21 months) is shown in table 4. Complete renal recovery, with a mean GFR of 110.82 ± 24.91 ml/min/1.73 m^2, was recorded in 42.4 %, CKD with a mean GFR of 27.08 ± 10.82 ml/min/1.73 m^2 in 42, 2%, and death in 24.2%. There was no statistically significant association between hypertension at admission and the risk of adverse outcomes (CKD5 or death), P = 0.336; Relative Risk [RR] = 1.81; 95% confidence interval [95% CI]; 0.49-6.68.

Table 1: Age distribution of children with hemolytic uremic syndrome in the study.

Age inmonths	Number	Percent
<12	12	36.4%
13–60	8	24.2%
>60	13	39.4%
Total	33	100.0%

Table 2: Demographic, clinical, and laboratory features of hemolytic uremic syndrome at admission.

Characteristic	Study group (n = 33)	D+ HUS (n = 13)	D− HUS (n = 20)	P value
Mean age (months)	47.8±40.4	45.54 ± 44.73	84.12 ± 45.28	0.003*
Male/Female ratio	21/12 (1.75:1)	8/5(1.6:1)	13/7(1.8:1)	0.440
Seizures	11 (33.5%)	6 (46.1%)	5 (25.0%)	0.939
Hypertension at admission	22 (66.7%)	10 (76.9%)	12 (60%)	0.802
Severe anaemia	29 (87.9%)	12 (92.3%)	17 (85%)	0.270
Leukocytosis	9 (27.2%)	4 (30.4%)	5 (25.0%)	0.711
Thrombocytopenia	32 (96.9%)	12 (95.6%)	20 (100%)	0.398
Mean high s. creatinine (mg/dl) at admission	4.4 ± 3.4	4.36 ± 2.31	5.00 ± 3.70	0.578

*P value is statistically significant.
D+ HUS – Diarrhea positive hemolytic uremic syndrome, D− HUS – Diarrhea negative hemolytic uremic syndrome.

Table 3: Short term follow up outcome of patients with hemolytic uremic syndrome (n = 33).

Outcome	D+ HUS	D− HUS	Total	Percent
Complete renal recovery	9	5	14	42.4%
no recovery go to CKD	2	9	11	33.4%
Death	2	6	8	24.2%
Total	13	20	33	100.0%

CKD – Chronic kidney disease, D+ HUS – Diarrhea positive hemolytic uremic syndrome, D− HUS – Diarrhea negative hemolytic uremic syndrome

Table-4- Risk factors for mortality in hemolytic uremic syndrome patients

Variable	Recovery		Persistent or(CKD)		Death		P
	No.	%	No.	%	No.	%	
Pallor							
Yes	12	85.7	9	81.8	8	100	0.4*
No	2	14.3	2	18.2	0	-	
Hypertension							
Yes	9	64.3	8	72.7	5	62.5	0.8*
No	5	35.7	3	27.3	3	37.5	
Convulsion							
Yes	3	21.4	3	27.3	5	62.5	0.1*
No	11	78.6	8	72.7	3	37.5	
Hematuria							
Yes	6	42.9	6	54.5	2	25	0.4*
No	8	57.1	5	45.5	6	75	
Lab. Manifestations	**Recovery**		**Persistent**		**Death**		**P value***
Hb at admissionMean±SD	8.05±2.5		7.49±1.7		7.75±1.7		0.8
Plt. at admissionMean±SD	98.5±78.9		131.7±58.2		69.7±47.3		0.1
WBC at admissionMean±SD	13.7±9.2		11.7±5.5		10.6±4.1		0.5
Creatinine at admissionMean±SD	6.4±1.5		3.9±1.9		5.06±3.7		0.2
Management	**Recovery**		**Persistent**		**Death**		**P value***
	No.	**%**	**No.**	**%**	**No.**	**%**	
Peritoneal dialysis	17	51.51	6	18.18	6	18.18	0.4*
hemodialysis	2	6.1	0	-	0	-	
Peritoneal dialysis and hemodialysis	0	0	2	6.1	0	-	

DISCUSSION:

The outcome ofHUS in children were not adequately defined in pediatric patients in Iraq. This may be due to lack of resource and data collection infrastructure. We took the opportunity to study the short term outcome of children with HUS admitted to Child welfare Teaching Hospitaland the probable risk factors for prognosis.

Over the last Two years, we managed 33 children with HUS in our pediatric nephrology unit in child welfare Teaching Hospital .

In this study, males were predominantly affected and D+ patients were younger than D− which is similar to other studies [19].

We diagnosed D− in 60% of patients compared to 25%-18.5% in other countries [10, 20,]. This may be due to lack of data about STEC or complement abnormalities tests.

The demographic, hematological and biochemical findings in this study were comparable to other studies [10]. Our acute mortality rate of 24.2% was higher compared to other data (7.4%-1.5%), which may be due to the early detection and institution of supportive therapy in these countries [20, 24,22].

In many studies high acute mortality was related to many factors e.g. late referral (>28 days), leukocytosis, hypertension at presentation, neurological manifestations and need for dialysis [10,21].

In contrast, in our study none of these factors were significantly associated with high acute mortality for all parameters.

At short term follow up, 33.4% of our patients reached CKD. This result is higher than reportsfrom Iran (11%), Brazil (11.1%), and Argentina (16.1%), but comparable to that from South Africa (32%) [10,20,22].

In this study, the overall mortality of 24.4% is far less than reported in other developing countries; Kenya 55% [24].

At short-term follow up we did not find statistical significant association between hypertension, seizure, high serum creatinine in admission or dialysisand the risk of adverse outcomes as shown in other studies (25)

CONCLUSIONS:

In our study, the acute mortality and the adverse outcomes (Chronic kidney disease) were higher than other countries. Our data indicate the need for better facilities and further studies to define other etiologies, especially for D−HUS andthe need for better microbiological facilities because they are not available in our laboratories in Iraq thatcould allow early and better diagnosis and identification of STEC and complement abnormalities.

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