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Original Article

Microalbuminuria in Pediatric Patients Diagnosed with Hemolytic Uremic Syndrome

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Abstract

Background: *Hemolytic uremic syndrome (HUS) is a clinical entity characterized by the classic triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure.*

Objective: *To evaluate renal involvement using the microalbuminuria/ creatininuria ratio in pediatric patients with a previous diagnosis of HUS and normal renal function.*

Patients and method: *A retrospective study of chart analysis was conducted in December 2024, which investigated the existence of microalbuminuria in patients previously diagnosed with HUS between Feb 2018 and end of Jan 2024 who proceeded without hypertension and with normal renal function (clearance > 90 ml/min measured by Schwartz formula).*

Results: *There were no differences in gender distribution, with 54% (n = 13) being female. The mean age of patients at presentation was 2.1 years (range: 1 month - 35 months). Prodromal Diarrheal was present in 91% (n = 22). During hospitalization, 11 patients (45.8%) required renal replacement therapy (RRT), with peritoneal dialysis being the therapy used in all, with a mean duration of 9 days (range: 2 to 30 days). Eight patients (33%) developed persistent microalbuminuria, with a mean value of 68.6 (range: 37 to 287). Of the total number of patients with persistent microalbuminuria, four received enalapril as an antiproteinuric, which normalized the microalbuminuria-to-creatinuria ratio in 100%. Regarding therapy, treatment was arbitrarily prescribed to those patients with proteinuria greater than 50 mg/g creatinine; patients who did not receive treatment had microalbuminuria below 50 mg/g.*

Conclusion: *The percentage of patients with a history of SHU who had chronic microalbuminuria was comparable to what has been reported in the literature; antiproteinuric medication may postpone kidney impairment.*

Keywords: *Microalbuminuria , Pediatric, Hemolytic Uremic Syndrome*

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1. INTRODUCTION

Hemolytic uremic syndrome (HUS) is a clinical entity characterized by the classic triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure (1). It was first described in 1950 by Dr. Carlos Giantonnio at the Hospital Italiano in Buenos Aires, when he observed three cases of children with bloody diarrhea, generalized edema, and seizures (2). It usually occurs in children aged 1 to 5 years and is rare in children under 6 months and adolescents (3,4). HUS represents the most serious complication of STEC (Shigatoxin-producing Escherichia coli) infections ; 90% of cases are associated with a diarrheal prodrome (D+). It is mostly caused by Escherichia coli , although Shigella dysenteriae , Citrobacter freundii , and Streptococcus pneumoniae can also cause it (5,6). The incidence varies from country to country: in Germany and Austria it is 0.7 to 1 per 100,000 children under 15 years of age, and in Argentina it is 22 per 100,000 children under 15 years of age (7). In Latin America, the problem is concentrated in the Southern Cone countries, mainly Argentina and Chile, where cases are reported throughout the year. In Chile the incidence is 3.4 per 100,000 children under 5 years of age (8). Most children recover completely from the acute illness, but up to 25% may develop long-term renal involvement, such as proteinuria, hypertension, and chronic kidney failure; the presence of proteinuria after D+ HUS has been identified as a risk factor for developing chronic kidney damage (8). Microalbuminuria is considered an early indicator of renal involvement due to hyperfiltration and has been considered a predictor of progressive renal damage in various clinical entities; (9) although microalbuminuria was initially used in diabetic patients, its screening role in the pediatric population is now relevant , due to the increase in obesity, high blood pressure (HBP) and childhood metabolic syndrome (10,11). Some studies show a prevalence of microalbuminuria after HUS of 32% at 3 years and 22% at 5 years, respectively; in Argentina, the prevalence of microalbuminuria is 21% in patients who have had HUS; there are no studies on this subject in Iraq. A recent experimental study showed an early increase in microalbuminuria after administration of Shiga toxin type 2 in rats (12-14). Early identification of risk factors for nephropathy progression could allow for early intervention to slow or halt the progressive development of chronic kidney disease.

Aim of the study: To evaluate renal involvement using the microalbuminuria/ creatininuria ratio in pediatric patients with a previous diagnosis of HUS and normal renal function.

2. PATIENTS and METHODS

Design

A retrospective study of chart analysis was conducted in December 2024, which investigated the existence of microalbuminuria in patients previously diagnosed with HUS between Feb 2018 and end of Jan 2024 who proceeded without hypertension and with normal renal function (clearance > 90 ml/min measured by Schwartz formula).

Variables

Microalbuminuria was routinely measured during follow-up visits to these patients starting 6 months after diagnosis, usually in the first sample in the morning; the samples were processed using Roche COBAS C 501 equipment.

Exclusion criteria:

1. Patients with persistent proteinuria defined as a proteinuria/creatinuria ratio greater than 0.21 mg/dl in more than three samples.
2. Children with hypertension defined as systolic or diastolic blood pressure above the 95th percentile for height, age, and sex.
3. Patients with chronic renal failure defined as creatinine clearance less than 90 according to the Schwartz formula.

The following factors were evaluated: demographic factors (age, sex), clinical presentation at the time of diagnosis, use of antibiotics prior to admission, and requirement for renal replacement therapy.

Microalbuminuria was defined as a microalbuminuria-to-creatinuria ratio >30 mg/g of creatinine in a single morning urine sample on at least three occasions, the microalbuminuria-to-creatinuria ratio is routinely performed starting 6 months after HUS diagnosis.

Statistical analysis

Results were expressed as medians, percentages, standard deviations, and ranges for clinical variables. The chi-square test was performed for independent variables. A p-value < 0.05, alpha error 5%, and 95% confidence interval were considered statistically significant. Data were processed using Microsoft Excel Software.

3. RESULTS

During the study period, 40 patients were hospitalized with a diagnosis of HUS; 16 patients were excluded: two due to chronic kidney disease and two due to proteinuria; eleven patients had no follow-up data, and one patient moved to another city, reducing the sample size to 24. The mean follow-up was 6 years (range: 6 months to 11 years); all patients progressed with normal plasma creatinine levels during follow-up. There were no differences in gender distribution, with 54% (n = 13) being female. The mean age at presentation was 2.0 years (range: 1 month 35 months). Prodromal Diarrheal was present in 91% (n = 22). During hospitalization, 11 patients (45.8%) required renal replacement therapy (RRT), with peritoneal dialysis being the therapy used in all, with a mean duration of 9 days (range: 2 to 30 days). Eight patients (33%) developed persistent microalbuminuria, with a mean value of 68.6 (range: 37 to 287). When differentiating by sex, 5/11 (46%) men and 3/13 (23%) women developed persistent microalbuminuria. Of the eight patients with microalbuminuria, six required RRT in the acute phase of the disease (75%). The clinical characteristics of patients with and without microalbuminuria in their evolution are observed in (**Tables 1 & 2**). Of the total number of patients with persistent microalbuminuria, four received enalapril as an antiproteinuric, which normalized the microalbuminuria-to-creatinuria ratio in 100%. Regarding therapy, treatment was arbitrarily prescribed to those patients with proteinuria greater than 50 mg/g creatinine; patients who did not receive treatment had microalbuminuria below 50 mg/g.

Table 1. Characteristics (age and clinical picture) of the group with altered microalbuminuria/creatinuria index

Sex	Age (years, months)	Prodromal diarrheal	Peritoneal dialysis days	Time of onset (age in years)	Antiproteinurics
F	2, 6	Yes	5	7.8	En
M	1, 10	No	32	6.7	No
F	1, 5	Yes	No	6.2	No
M	1, 9	Yes	11	9.2	En
M	2, 9	Yes	No	5.2	En
M	2, 11	Yes	3	4.3	En
F	1, 11	Yes	10	3.71	No
M	1, 7	Yes	11	0.59	No

En: Enalapril (Oral: 0.1-0.5 mg/kg/day PO OD or in 2 divided doses).

Table 2. Characteristics (age and clinical) of the group with normal microalbuminuria/creatinuria index

Sex	Age	Prodromal diarrheal	Peritoneal dialysis
F	3 y	No	No
F	9 m	Yes	Frustrated
F	2 m	Yes	8 days
M	8 m	Yes	11 days
F	1 y 8 m	Yes	No
M	1.5 m	Yes	6 days
F	2 y 10 m	Yes	No
M	1 y 7 m	Yes	No
M	1 y	Yes	No
F	1 y 1 m	Yes	No
F	9 m	Yes	No
M	3 y 3 m	Yes	No
F	2 y 9 m	Yes	No
F	1 y 8 m	Yes	9 days
F	9 m	Yes	No
M	2 y 1 m	Yes	No

y: years, m: months

4. DISCUSSION

HUS continues to be a cause of acute kidney injury in childhood. The outcome of patients with HUS varies; while most recover kidney function, a percentage develops sequelae, the most common of which are hypertension, proteinuria, and chronic kidney disease (15,16). In patients with persistent proteinuria, the use of drugs such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or both has been shown to reduce protein excretion, thereby preserving renal function. A recent publication shows that enalapril reduced urinary protein excretion by 58.8%, and when combined with losartan, the reduction increases to 83.8%; (17) in our study, the therapeutic response was 100% with monotherapy. There are few follow-up studies of patients with microalbuminuria after the diagnosis of HUS; (18) there are no data on this subject in Iraq. Although several studies in recent years have attempted to identify markers

of poor prognosis for the disease, the diversity of factors considered and the different characteristics of the populations analyzed make the results controversial. Patients who develop HUS with prodromal diarrheal, who progress with anuria and who require dialysis treatment in the acute phase, have a higher risk of chronic complications (19). One of the factors associated with impaired renal function has been the need for renal replacement therapy (20). Our study demonstrates the association of microalbuminuria with the use of dialysis therapy. Microalbuminuria has been shown to be a marker of kidney damage in several conditions and may be the first marker of hyperfiltration and kidney damage in this condition; long-term follow-up of these patients is needed to define its significance (21). In our study, the percentage of microalbuminuria is consistent with that described in the literature; unfortunately, due to the small number of patients, our study does not represent the national reality.

5. CONCLUSIONS

The percentage of patients with a history of SHU who had chronic microalbuminuria was comparable to what has been reported in the literature; antiproteinuric medication may postpone kidney impairment.

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Ethical Clearance:

This work was approved by the local Ethics Committee. Informed consent was obtained from each parent/guardian of the participant pediatric patient. Data collection was in accordance with the Ethical Principles for Medical Research Involving Human Subjects, 2013 declaration of WMA.

Conflict of interest: Authors declared none

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