# Childhood Hemolytic Uremic Syndrome in Jordan**

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**Abstract**

Hemolytic Uremic Syndrome (HUS) is the most common cause of Acute Kidney Injury (AKI) in the developed countries. It consists of Microangiopathic Hemolytic Anemia (MAHA), AKI and thrombocytopenia.

**Objective**: To review the outcome of childhood Diarrhea-associated Hemolytic Uremic Syndrome (D+HUS) presenting to the pediatric department at Jordan University Hospital (JUH).

**Patients and Methods**: In this retrospective study we reviewed the medical records of children presenting to JUH between January 1977 and January 2008 with D+HUS.

**Results**: There were 21 patients (15 girls and 6 boys). Age ranged from 6 months to11 years. 8t children (38%) had Entamoeba histolytica infection. 57% needed peritoneal dialysis. Central nervous system manifestations included drowsiness in 8 patients (38.1%), limb weakness in 2 patients (9.5%), seizures in 9 patients (43%), irritability 3 patients (14%), transient blindness in 2 patients (9.5%), and uremic encephalopathy in 1 patient (4.8%).

**Outcome included**: complete recovery in 11 patients (52.4%), chronic kidney disease in 6 patients (28.6%), central nervous system deficit in 2 patients, and death in 2 patients (9.5%). There was no correlation between the outcome and the presence of leukocytosis, thrombocytopenia, severity of renal failure, hyponatremia, or hypertension ($p< 0.05$).

**Conclusion**: Our data highlights the importance of D+HUS in the pediatric age group. In addition, it emphasizes its manifestations, complications, and outcome.

**Keywords**: D+HUS, Entamoeba histolytica, outcome, Jordan.

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## Introduction

The Hemolytic Uremic Syndrome (HUS) is the most common cause of Acute Kidney Injury (AKI) in the developed countries. It consists of the triad of thrombocytopenia, Microangiopathic Hemolytic Anemia (MAHA), and AKI.

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HUS was first described by Gasser in 1955. [1] Presentation may be typical, following a diarrheal prodrome (D+ HUS) and occurring abruptly in epidemics; or atypical without a diarrheal prodrome (D-HUS), occurring insidiously and sporadically. [2]

However, this classification may not be accurate since some cases with D+HUS may not have diarrhea, and others with D- HUS may have. [2]

The majority of children have D+HUS (90%), where the infecting organism is usually enterohemorrhagic Escherichiae coli (E. coli O157:H7) in Western countries, and Shigella dysenteriae Type I in the Developing nations. [3]

There are few reports on D+ HUS from the Arab countries [4-6] and none from Jordan. Herein, we describe our experience over a thirty-one year period at JUH, a tertiary care hospital in Jordan, with emphasis on complications and outcome of this disease.

**Patients and Methods:**

The medical records of children less than 13 years of age admitted to the Pediatric Department at the Jordan University Hospital with the diagnosis of (HUS) from January 1977 to January 2008 were retrospectively reviewed.

Data included: age at presentation, sex, clinical course, laboratory findings, and outcome.

Inclusion criteria: Children that were D+ with the triad of AKI, MAHA, and thrombocytopenia.

Exclusion criteria: patients with diarrhea negative HUS, and secondary HUS.

To determine outcome, patients were classified according to: Complete recovery, chronic kidney disease, central nervous system deficit, and death.

**Definitions**

Microangiopathic hemolytic anemia (MAHA): Hemoglobin < 100 g/l along with fragmented red blood cells on the blood smear.

Thrombocytopenia: a platelet count of < 150000 cells /$mm^3$.

Acute Kidney Injury (AKI): elevation of the serum creatinine above that for age.

Complete recovery: no clinical evidence of residual damage when seen on follow-up.

Chronic Kidney Disease (CKD): Presence of kidney damage, or Glomerular filtration rate < 90ml/1.73$m^2$/min for > 3 months.

Central nervous system deficit: presence of residual damage following the acute illness.

**Results**

**Clinical data**

Twenty one children were included in the study. Fifteen were females (71.4 %) and six were males (28.6%). The mean age was 2.7 years, with a range from 6 months to11 years. Follow- up ranged from 6 months to 10 years.

**Clinical parameters and laboratory results**

Renal system: Oliguria: 6 (28.6%), hypertension 8(38.1%), edema 13(61.9%), and need for peritoneal dialysis 12(57.1%). One patient who had proteinuria 1 year after the acute illness was found to have focal segmental glomerulosclerosis.

Laboratory results: Elevated serum creatinine 17(80.9%), hypokalemia 7 (33.3%), hyponatremia 15 (71.4%), urinary protein 14 (66.7%), and urinary red cells 13 (61.9%).

Central nervous system: drowsiness 8(38.1%), limb weakness 2(9.5%), seizures 9(42.9%), irritability 3(14.3%), transient blindness 2(9.5%), and uremic encephalopathy 1(4.8%) (Died).

Gastrointestinal system: Diarrhea 21 (100%), vomiting 11(52.4%). Two (9.5%) had rectal

prolapse, and one had massive upper gastrointestinal bleeding culminating in death.

Laboratory results: positive stool culture 3 (14.3%): Escherichia coli (1), salmomella (1), and citrobacter (1).

On stool analysis, presence of Entamoeba histolytica in 8(38.1%) was found.

Hematological: Pallor 13 (61.9%), need for blood transfusion 12 (57.1%).

Laboratory results: White blood cell count (WBC)> 20000/$mm^3$ 6(28.6%), hemoglobin (Hb)< 7 g/dL 11(52.4%), platelets< 50000/$mm^3$ 3(14.3%).

There was no correlation between the outcome and the presence of leukocytosis, thrombocytopenia, severity of renal failure, hyponatremia, or hypertension ($p< 0.05$).

**Outcome**

Eleven (52.4%) patients had complete recovery, six (28.6%) developed Chronic Kidney Disease (CKD), two (9.5%) had Central Nervous System (CNS) deficit, and two (9.5%) died during the acute illness.

**Discussion**

The purpose of this study is to report our experience at a tertiary care hospital in a developing country.

HUS is a multiorgan disease, affecting the renal, hematologic, central nervous system, gastrointestinal, endocrine, cardiovascular and the integumentary systems. [7, 8]

In our study, age of onset ranged from six months to eleven years, which is similar to other reports. [9,10]

One third of our patients developed CKD which is similar to literature. [11]

One child with microalbuminuria developed heavy proteinuria secondary to FSGS one year after the acute illness. This histopathologic finding may develop as a late sequelae of D+HUS.[12, 13] Albuminuria is known to occur in children with HUS after an apparent recovery.

Screening for microalbuminuria may help initiate early therapy to halt or delay the progression of CKD. [14, 15]

Hypertension occurred in 38.1% of our cases which is similar to that from South Africa following a shigella epidemic. [10] Hypertension usually results from volume overload, especially following a blood transfusion.

It may [17] or may not [16, 18] be related to a poor prognosis.

In a systematic review, meta-analysis and meta-regression Garg et al. found out that the severity of CNS complications or need for dialysis were associated with a worse prognosis. [19]

The Central Nervous System (CNS) manifestations are common in HUS. The most frequent CNS manifestations in our series were seizures (42.9%) followed by drowsiness (38.1%). Other reported CNS complications in the literature include cortical blindness and exaggerated deep tendon reflexes, ataxia, hypotonia, hemiplegia, pupillary abnormalities, irritability, hallucinations, nystagmus, decerebrate or dystonic posturing. [20, 21] The incidence of seizures in our patients 42.9% is higher than the 14.8% in the HUS post shigella from South Africa. [10]

Gastrointestinal manifestations, other than diarrhea in our series, included rectal prolapse which occurred in 9.5% of patients.

Rectal prolapse occurred in 6.2% of post shigella HUS cases reported by Bhimma et al. from South Africa.

Most of our stool cultures were negative. This is similar to the study from Kuwait. [6]

The prominent presence of Entamoeba histolytica in our patients could be genuine, as the association has been mentioned in the literature, [18, 22] or an incidental finding, especially that ameba infection is prevalent in developing countries. [22]

None of our patients had oral or anal lesions. Ehlayel et al. from Qatar reported four children with mucocutaneous manifestations. One of their cases, which was post shigella flexneri gastroenteritis developed gallbladder hydrops after four weeks of illness before his demise. [4]

The endocrine system is also involved in the form of hyperglycemia or diabetes.

In our series, none of the patients developed diabetes .Other studies reported an incidence of 0-15%. [23] However, diabetes may occur at a later time even after recovery from hyperglycemia.[24]

Regarding follow up and outcome in our series, death occurred in 2 patients (9.52%). One child died from severe CNS involvement, and the other one from massive gastrointestinal hemorrhage.

Death occurred in 9.52% of our cases, which is higher than that reported in the literature [25] but lower than that (17.3%) in the South African epidemic.

## Conclusion

Our data highlights the importance of HUS in the pediatric age group. In addition, it emphasizes its manifestations, complications, and outcome.

## Acknowledgement

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# حالات المتلازمة اليوريمية الإنحلالية عند الأطفال في الأردن

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**الملخص**

تعتبر المتلازمة اليوريمية الانحلالية من اهم اسباب القصور الكلوي الحاد في البلدان الصناعية. هذا وتتكون من اعتلال الاوعية الشعرية مع انحلال كرات الدم الحمراء مصحوباً بقصور كلوي حاد وانخفاض مستوى الصفيحات.

**الهدف:** مراجعة استرجاعية لحالات المتلازمة اليوريمية الانحلالية عند الاطفال الذين ادخلوا إلى مستشفى الجامعة الأردنية.

**المرضى والطريقة:** في هذه الدراسة الرجعية تمت مراجعة ملفات الاطفال المشخصين بالمتلازمة اليوريمية الانحلالية الاولية المسبوقة بالاسهال من عام 1977 الى عام 2008.

**النتائج:** كان هناك 21 طفلاً (15 اناث و6 ذكور ). تراوحت أعمارهم ما بين 6 اشهر الى 11 سنة. احتاج 12 (57%) مريضاً إلى الديلزة الصفاقية، وجد انتان اميبا هستوليتيكا عند 8 (38%) اطفال، اعراض اصابة الجهاز العصبي المركزي في 8 (38%)حالات شملت ضعفاً في الأطراف في 2(9.5%)، تشنجات في 9(43%) مرضى، هيوجة في 3(14%)، عمى مؤقت في 2(9.5%)، واعتلال دماغي يوريمي في 1 (4.8%)

كانت الحصيلة: شفاءً تاماً لدى 11(52.4%) مريضاً، مرضاً كلوياً مزمناً لدى 6(28.6%) ، اعتلال الجهاز العصبي المركزي لدى 2 (9.5%)، و الوفاة 2 (9.5% )

لم تكن هناك علاقة بين الحصيلة ووجود أو عدم وجود ارتفاع كرات الدم البيضاء، هبوط الصفيحات، شده القصور الكلوي، هبوط مستوى الصوديوم بالدم، او ارتفاع ضغط الدم .

**الخاتمة:** نتائج هذه الدراسه تسلط الضوء على اهمية المتلازمة اليوريمية الانحلالية عند الاطفال، وتؤكد اعراضها، مضاعفاتها، وحصيلتها.

**الكلمات الدالة:** المتلازمة اليوريمية الانحلالية، اميبا، حصيبة، الاردن، الجهاز العصبي.