Hemolytic-Uremic Syndrome: A Population-based Study in Washington, DC and Baltimore, Maryland

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Abstract: A population-based study of hemolytic-uremic syndrome (HUS) revealed that 20 child residents of Washington, DC and Baltimore, Maryland were hospitalized with HUS from January 1979 through September 1983. The number of cases peaked during the summer and fall; none occurred during the winter. Incidence of hospitalized cases was higher in Whites and girls than in Blacks or boys, and the average annual incidence was 1.08 cases/100,000 children <5 year old. This study demonstrates that HUS is not unique to the West Coast, as previously suggested. (*Am J Public Health* 1988; 78:64–65.)

Introduction

Hemolytic-uremic syndrome (HUS) is defined by the triad of microangiopathic hemolytic anemia, acute nephropathy, and thrombocytopenia.[1] It is usually preceded by a prodromal gastrointestinal illness or, less commonly, a respiratory illness. Renal failure, often necessitating dialysis, commonly occurs. Several hospital-based studies suggest that HUS occurs primarily in White children <5 years old and with equal frequency in boys and girls.[2–5] The case fatality rate reported in the United States and Canada is 6–10 per cent.[2,3]

Only one of the hospital-based studies[6] of HUS reported[2–5,7–9] has involved efforts to identify and characterize all cases in a single geographic area. To better define the epidemiology of this syndrome, we studied HUS in a well-defined population in Washington, DC and Baltimore, Maryland.

Methods

We identified medical records of patients under 21 years old who had a discharge diagnosis of HUS (ICD-9-CM code 283.1) and/or acute renal failure (ICD-9-CM code 584.9) at any of the 45 hospitals with pediatric services in the standard metropolitan statistical areas (SMSAs)[10] of Washington and Baltimore from January 1979 to September 1983. To detect patients with HUS who resided within the study area but were hospitalized outside it, we contacted pediatric nephrologists and/or infection control nurses at four tertiary care facilities in Virginia. All charts of children identified by these methods were reviewed and abstracted, using a standardized form, by one of the two pediatric investigators (JSK or TPG).

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A case of HUS was defined as disease with either a diagnosis of HUS made by a pediatrician and/or pediatric nephrologist and confirmed by the pediatric investigators, or a primary diagnosis of acute renal failure with clinical and labortory evidence compatible with a diagnosis of HUS.[1] Incidence data for age, sex, and race are based on 1980 census estimates[10] for the SMSAs of Wasington and Baltimore. Rate ratios and their standard errors were used to determine 95 per cent confidence intervals.[11]

Results

Of the 20 children who met the case definition, none had a primary diagnosis of acute renal failure and none were hospitalized outside the SMSA. Eleven of the 14 children residing in metropolitan Washington and all six children residing in metropolitan Baltimore were <5 years old. The average annual incidence of hospitalized cases of children <5 years old residing in metropolitan Washington was 1.20 per 100,000 person years, of those residing in metropolitan Baltimore 0.90, for both areas combined was 1.08; and for all persons <21 years old 0.26.

The 20 children ranged in age from 5 months to 6.5 years. In both areas, the mean age was similar (3.5) and more HUS patients were female than male. The average annual incidence for both areas combined was higher for girls <10 years old (1.0) than for boys (0.24) (rate ratio = 4.2, 95 per cent CI = 1.4–12.5). The combined female-to-male ratio was 4:1. Nineteen children were White and one was Black; the race-specific average annual incidence for White children <10 years old (0.92/100,000) was higher than that for Blacks (0.095/100,000) (rate ratio = 9.7, 95 per cent CI = 1.3–71.9).

Two HUS cases occurred in 1979, four in 1980, six in 1981, four in 1982, and four in the first nine months of 1983. All cases occurred between April and November, with the peak between August and September. No geographic clustering of cases was observed. Patients' symptoms before hospital admission are listed in Table 1.

Since this is a retrospective study, we were unable to conduct a detailed laboratory-based investigation of etiology. However, for two of the patients, we tested acute- and convalescent-phase serum samples for verotoxin-neutralizing antibody titer. Both these two children had bloody diarrhea before the onset of HUS. The serum of one child showed a fourfold rise in verotoxin-neutralizing antibody

TABLE 1—Symptoms before Hospital Admission in 20 Patients with Hemolytic-Uremic Syndrome

Symptom	No. of Patients
Diarrhea	19
Diarrhea with blood	12
Vomiting	12
Abdominal cramps	13
Fever	3
Upper respiratory infection only	1

titer. Antibody titers were 4 and 8 in serum samples collected 8 and 45 days, respectively, after onset of diarrhea in the second patient, which suggests the presence of verotoxin-producing *Escherichia coli* (VTEC) in this patient. No stool specimens were obtained from either child in the initial stages of illness.

All 20 children developed the characteristic microangiopathic anemia (low mean 7.1 g per cent), 13 developed thrombocytopenia (low mean 70,750/mm^3), and all had evidence of nephropathy. Of the 17 children for whom urine output data were available, three were anuric for >48 h, three for <24 h, and 11 never develped anuria or oliguria. During the acute phase of illness, 10 children were treated with dialysis (n = 9) or plasmapheresis (n = 1), four developed seizures, four required treatment for hypertension, one developed encephalopathic coma with a left-sided hemiparesis, and four had no complications. Long-term complications, which occurred in one patient each, were ongoing seizure disorder; chronic renal insufficiency requiring ongoing dialysis and eventually renal transplantation; severe neurologic complications; and nephrotic syndrome. None of the patients died.

Discussion

In the United States, HUS has been reported to be endemic only in California, based solely on studies of large series of hospitalized patients.[3-5,7-9] Our results indicate that HUS is probably endemic in other areas of the United States as well. In a state-wide study conducted in Oregon,[6] which used methods similar to ours, average annual incidence of hospitalized cases was 2.65 cases/100,000 children <5 years old compared with 1.08 cases/100,000 children <5 years old in our study. Our incidence estimate may be conservative since: some patients with HUS may not require hospitalization, some cases may be misdiagnosed, and older pediatric patients with HUS may have been in hospitals without pediatric services. However, these possibilities seem remote.

In our study, as in the Oregon study, we observed a greater average annual incidence among Whites and girls than in Blacks or boys, reasons for which remain unknown.

Seasonality has been reported previously.[3,6,12] Several pathogens with a similar summer-fall seasonality, including Coxsackie A4, A9, B2, and B4,[13] echovirus 22 and 11,[14,15] *Yersinia* sp.,[16] *Campylobacter* sp.,[17] and *Shigella* sp.,[18] have been isolated from patients with HUS. Recently, VTEC was associated with HUS in pediatric patients.[19,20] *E. coli* 0157:H7, a rare serotype associated with hemorrhagic colitis, was isolated from patients from the United Kingdom[21] and North Carolina.[22] The seasonality and the age-specific attack rate of this pathogen have not yet been defined. Two of the patients we studied had serologic evidence of recent VTEC infection, the significance of which is unknown.

Although it has been suggested that this syndrome is endemic in California and other West Coast states, the results of our study suggest that HUS is also endemic in two large metropolitan areas on the East Coast. Population-based studies in other areas of the country and outbreak investigations that focus on possible infectious causes may help us understand more about this syndrome, its etiology and epidemiology.

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ADDENDUM

Since preparation of this manuscript, two additional reports of the hemolytic uremic syndrome have appeared:

Neil MA, Tarr PI, Clausen CR, Christie DL, Hickman RO: *Escherichia coli* 0157:H7 as the predominant pathogen associated with the hemolytic uremic syndrome: a prospective study in the Pacific Northwest. Pediatrics 1987; 80:37–40.

Tarr PI, Hickman RO. Hemolytic uremic syndrome epidemiology: a population-based study in King County, Washington, 1971 to 1980. Pediatrics 1987; 80:41–45.