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Investigation of an outbreak of bloody diarrhea complicated with hemolytic uremic syndrome

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Abstract In July—August 2009, eight patients with bloody diarrhea complicated by hemolytic uremic syndrome (HUS) were admitted to hospitals in Tbilisi, Georgia. We started active surveillance in two regions for bloody diarrhea and post-diarrheal HUS. Of 25 case-patients who developed HUS, including the initial 8 cases, half were ⩾15 years old, 67% were female and seven (28%) died. No common exposures were identified. Among 20 HUS case-patients tested, Shiga toxin was detected in the stools of 2 patients (one with elevated serum IgG titers to several *Escherichia coli* serogroups, including O111 and O104). Among 56 persons with only bloody diarrhea, we isolated Shiga toxin-producing *E. coli* (STEC) O104:H4 from 2 and *Shigella* from 10; 2 had serologic evidence of *E. coli* O26 infection. These cases may indicate a

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previously unrecognized burden of HUS in Georgia. We recommend national reporting of HUS and improving STEC detection capacity.

1. Introduction

Shiga toxin-producing *Escherichia coli* (STEC) can cause illness ranging from mild diarrhea, to bloody diarrhea, to the hemolytic uremic syndrome (HUS) — a life-threatening condition that manifests with a triad of: microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure [1]. HUS develops in approximately 6% of patients with STEC O157:H7 infection [2], but other non-O157 STEC strains have been implicated, particularly in the European region [3—7]. STEC are found in the intestinal tracts and excrement of a variety of animals, especially ruminants. Outbreaks of STEC infection are frequently associated with meat products, such as ground beef, as well as raw produce, dairy products, contaminated water, or contact with ruminant mammals or ill persons [8].

The national communicable disease surveillance system of Georgia monitors diarrheal diseases. National regulation mandates notification of diarrhea cases within 24 h after registration. More than three epidemiologically-linked cases trigger an investigation [9]. Lack of laboratory capacity, especially in rural areas, limits detection of enteric pathogens in patients with diarrheal illness. STEC infection complicated with HUS has never been officially reported in Georgia.

Between July and August 2009, eight patients with bloody diarrhea complicated by HUS were admitted to hospitals in Tbilisi, Georgia; two of those patients died. Stool samples of all patients were sent to the laboratory of the National Center for Disease Control and Public Health of Georgia (NCDC). After conducting bacterial culturing and serological testing, the laboratory of the NCDC reported seven possible *E. coli* O157 isolates from the eight hospitalized patients. An investigation was initiated to determine if these cases represented an outbreak, to identify the etiologic agent(s) and, if possible, to identify the source(s) of infections.

2. Materials and methods

2.1. Active surveillance

On 24 July 2009, active surveillance, case finding and data collection for bloody diarrhea and HUS was initiated at nine clinics in the two most affected regions: Tbilisi (5 clinics) and Shida Kartli (4 clinics). Most affected regions were identified based on analysis of line listing data and communication with the main regional clinics of Georgia. All nine clinics were located in hospitals with the capacity for dialysis or treatment of patients with diarrhea and that are major regional or central level clinics. Active surveillance efforts ceased on December 11, 2009.

Patients were identified based on clearly defined case definitions: a case of bloody diarrhea was defined as $\geqslant 3$ patients reported loose stools in 24 h containing visible blood. A case of HUS was defined as laboratory-confirmed anemia and kidney damage (elevated creatinine, hematuria, or proteinuria) occurring within 21 days after diarrheal illness [10].

Each of the nine selected surveillance clinics were provided with stool and serum collection kits and detailed instructions for specimen collection and storage. HUS and bloody diarrhea clinical description and patient management information were provided to physicians and supervisors of infectious disease and/or dialysis departments. At all nine clinics, a focal point was nominated for daily phone calls. These calls were for identification and reporting of any new cases of bloody diarrhea or HUS based on case definitions.

Stool samples were transported in sterile containers containing buffered glycerol saline solution for better preservation during transport. A portion of the stool sample was also inoculated into Buffered Peptone Broth (0.2% final concentration) for selective enrichment of *E. coli* and *Salmonella* spp. Samples (stool and stool inoculated in broth) were stored at 2—8 °Celsius (C) and picked up from collection sites in coolers containing cold packs. Samples were delivered to NCDC for testing on the same day from Tbilisi hospitals and within a maximum of 48 h from regional hospitals.

2.2. Epidemiologic and clinical data collection

Case-patients or their caregivers were interviewed and demographic, clinical, and exposure information was collected using structured questionnaires. Exposures assessed included food, water sources,