Epidemiological Report

Hemolytic Uremic Syndrome
Historic Series 2010 – 2021

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BRIEF HISTORY OF HEMOLYTIC UREMIC SYNDROME

Hemolytic uremic syndrome (HUS) is a complex and severe, acute-onset disease in which an immune reaction, most commonly after a gastrointestinal tract infection, causes low levels of red blood cells and platelets and kidney damage. The main clinical manifestations are renal failure, which affects the vast majority of patients, pallor, bruising and petechiae. Arterial hypertension and neurological manifestations such as irritability, lethargy, convulsions and coma are present in 25% of patients.

It can occur in individuals of any age, however, it affects more elderly people and children, being one of the most frequent causes of acute renal failure in children, especially those under 5 years of age. Early diagnosis of the disease and advances in treatment, including anemia, have reduced mortality during the acute period, currently between 2% and 3%. However, 5% of children with HUS develop chronic renal failure, requiring dialysis procedures or kidney transplantation within a few years. Another 30% continue with microhematuria and varying degrees of proteinuria, and may develop end-stage renal failure that can last for decades.

Since 2000, hemolytic uremic syndrome has been a disease of immediate compulsory notification in the state of São Paulo (SSP), and since 2004, probable food causes predominated in the records. Nationally, the HUS became an unusual disease of immediate compulsory notification by Ordinance No. 2,472, of August 31, 2010, and Ordinance No. 1,984, of September 12, 2014; previously, the disease had already been the subject of Resolution SS-20, February 22, 2006, and the Sanitary Code – Law 10,083, of September 23, 1998. It must be notified in the Notifiable Diseases Information System (Sinan) using the Notification/Conclusion Form; and, since 2019, the SHU Investigation Form must also be completed, to be sent to the DFWD/ESC.

ETIOLOGICAL AGENT

Shiga toxin-producing *E. coli* (STEC) bacteria, such as *Escherichia coli* O157:H7 and *Shigella sp*, can cause a wide spectrum of diseases, ranging from mild diarrhea to severe cases of hemorrhagic colitis, capable of progressing to severe extraintestinal complications, including hemolytic uremic syndrome and thrombotic thrombocytopenic purpura (TTP).

E. coli O157:H7 causes diarrhea, usually bloody, called hemorrhagic colitis, with severe abdominal pain, and the patient may or may not have a low-grade fever. Approximately 10% of these patients progress to HUS, whose main manifestations are acute kidney damage, thrombocytopenia and microangiopathic hemolytic anemia. Other strains of *Shiga* toxin-producing *E. coli* (STEC) can also

cause diarrhea and hemolytic uremic syndrome. And this production is essential for the development of classical forms of HUS.

The serotypes of the STEC category that are associated with severe disease in human beings, such as O157:H7, O26:H11, O103:H2, O111:H8/H and O113:H21, are termed Enterohemorrhagic *E. coli* (EHEC). Strains O26, O45, O111, O121, O103 and O145 cause approximately 71% of outbreaks not caused by O157:H7. In 2011, the O104:H4 strain was responsible for the outbreak of diarrhea in Europe, with about 4,000 diarrheal cases (12 deaths) and almost 900 HUS (48 deaths).

TRANSMISSION MODE

The main host of STEC bacteria is cattle, and human contamination occurs through the consumption of foods infected with animal feces, especially those prepared with raw or undercooked ground meat and unpasteurized milk. Vegetables can become infected during cultivation, due to contamination of irrigation water and manure.

Person-to-person transmission, via the fecal-oral route, can occur and is favored by the low infective dose and studies indicate that a number as small as ten organisms would be enough to trigger the infection.

Its incubation period varies from three to eight days, with an average of three to four. In the prodromal period, severe abdominal pain, non-bloody diarrhea and short-term fever occur, and vomiting may occur. After two to three days, most cases progress to bloody diarrhea, with the presence of clots and intensifying abdominal pain. From 10% to 15% of patients with hemorrhagic colitis develop HUS within a period of approximately seven days, of which between 10% and 50% remain with some chronic renal impairment, requiring dialysis procedures or even kidney transplantation

EPIDEMIOLOGICAL SITUATION

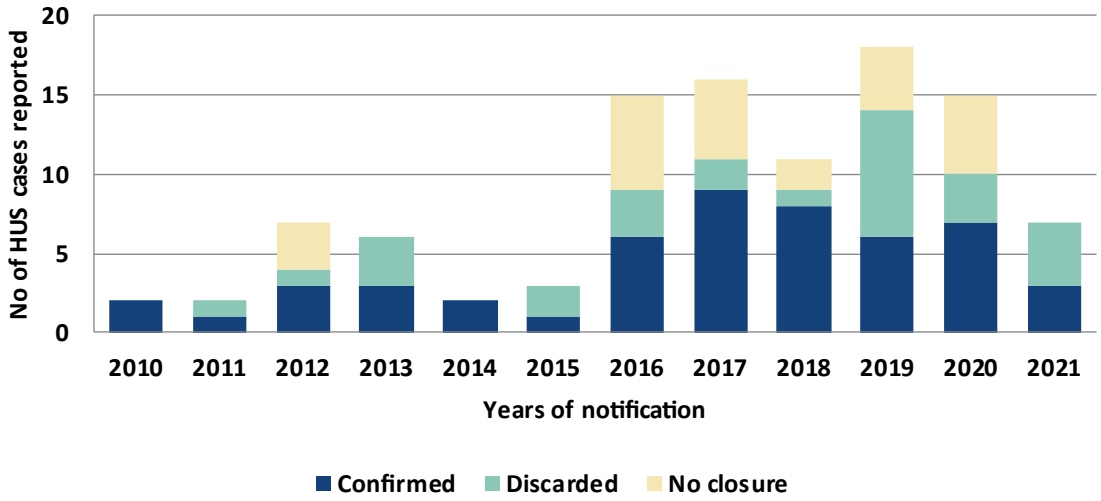
In the SSP, HUS, bloody diarrhea and *E. coli* are part of the active surveillance system for foodborne diseases (FDA), monitoring of acute diarrheal diseases (MADD) and surveillance of outbreaks of FDA.

This system is based on three basic axes: 1) surveillance of bloody diarrhea from its notification by public and private health services to epidemiological surveillance teams; 2) notification of emerging pathogens by public and private laboratories to VE teams, who carry out an active search

in laboratories and health services; and 3) notification of HUS by health professionals and services, public and private, and the respective active search for these specific syndromes.

From this perspective, an analysis of the period from 2010 to 2021 shows that of the 104 cases reported in the SSP, 51 were confirmed, 28 were discarded and 25 were not closed in the system (Graph 1), although the data provided in the investigation allow us to infer that they are ruled out cases. It is noted that 2017, 2018 and 2020 were the years with the highest number of confirmations, respectively with nine, eight and seven cases.

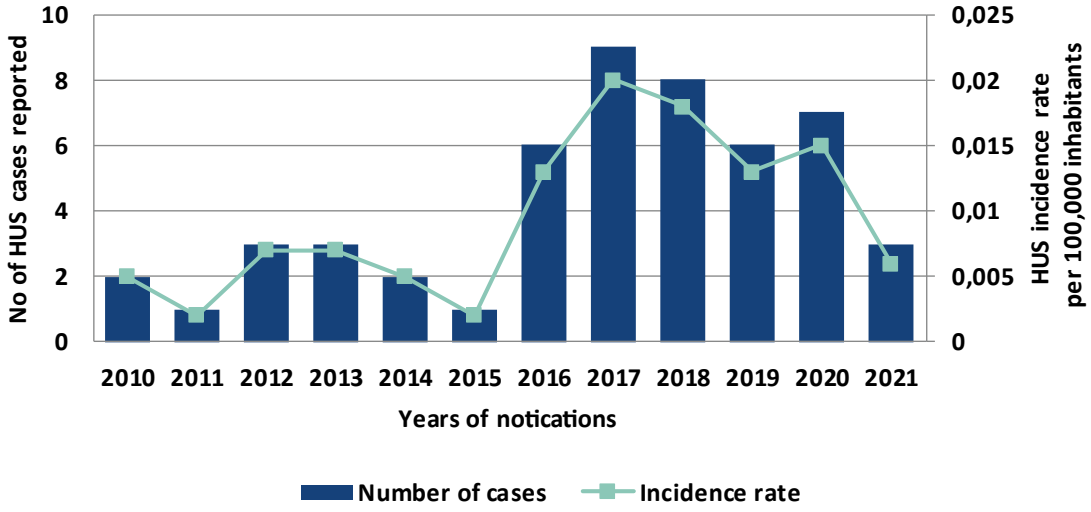
Graph 1. Reported HUS cases by closure classification, SSP, 2010 to 2021.*



Source: DFWD/ESC/DCC/SHD-SP. *Data extracted from Sinan and handled by DFWD on June 10, 2022.

The number of HUS notifications in the state varied over the years. From 2010 to 2014, the highest incidence was only 0.01/100,000 inhabitants, with a variation of one to three positive cases per year (Graph 2). With the inclusion of the HUS in the national compulsory notification list, the increase in the number of reported cases between 2015 and 2021, as well as confirmed cases, has become noticeable, raising the incidence to 0.02/100,000 inhabitants in 2017, still a very low rate when compared to the global incidence, around 0.6/100,000 inhabitants.

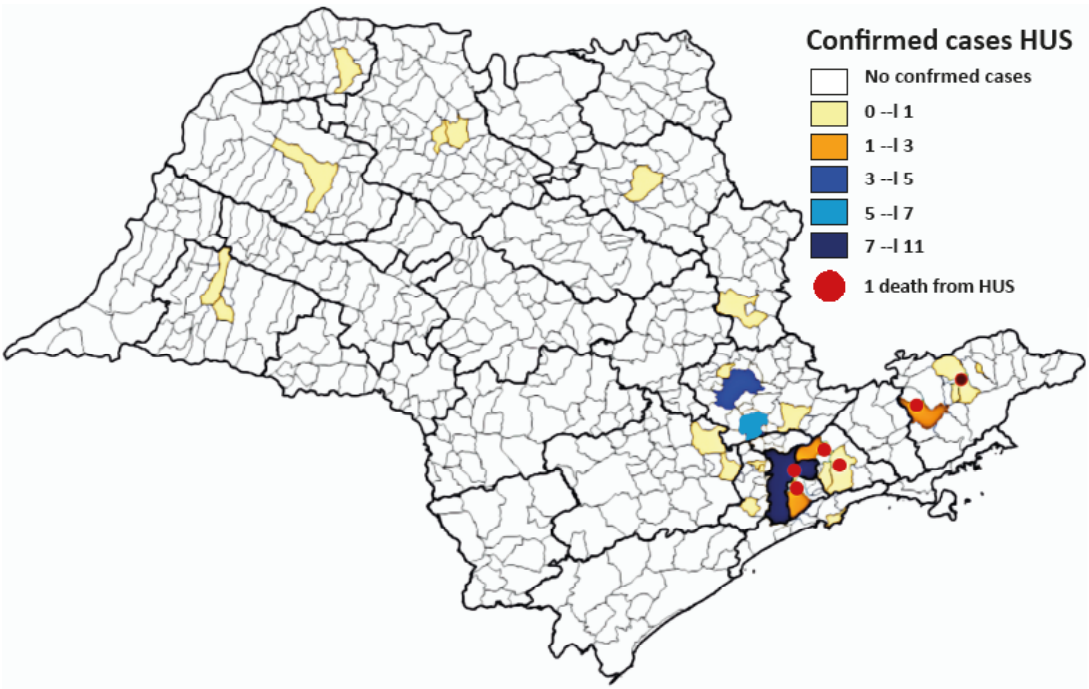
Graph 2. Number of confirmed cases and incidence rate, SSP, from 2010 to 2021.*



Source: DFWD/ESC/DCC/SHD-SP. *Data extracted from Sinan and handled by DFWD on June 10, 2022.

Regarding the occurrence of cases by municipality of residence, the capital of São Paulo had the highest number in the evaluated period (11), followed by Jundiaí (6), Campinas (4), Guarulhos (2), Taubaté (2) and Bernardo do Campo (2) (Figure 1).

Figure 1. Spatial distribution of confirmed HUS cases and HUS deaths, SSP, 2010 to 2021.*

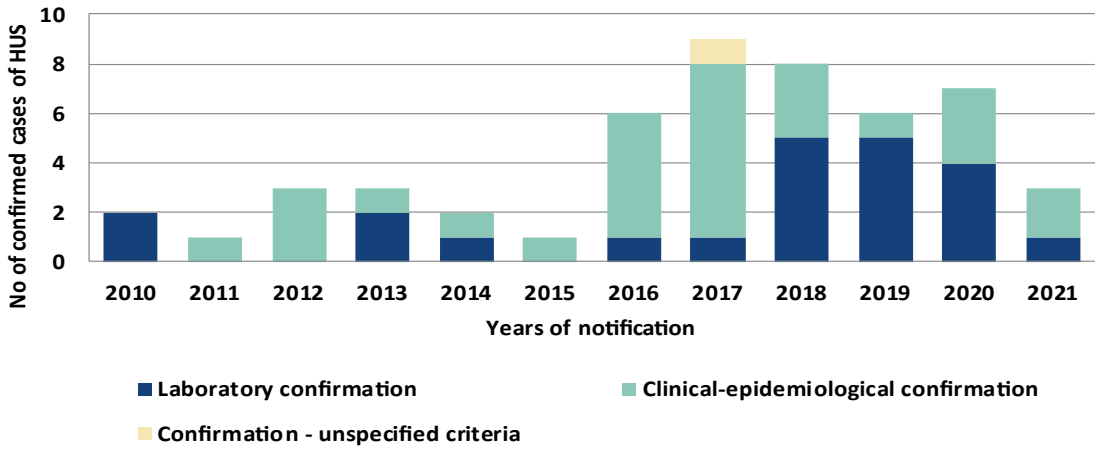


Source: DFWD/ESC/DCC/SHD-SP. *Data extracted from Sinan and handled by DFWD on June 10, 2022.

Thus, of the 51 confirmed cases, 6 evolved to death from HUS: in Arujá and Mogi das Cruzes, in 2012; in Guaratinguetá and São Bernardo do Campo, 2016; in the city of São Paulo, 2017; and Taubaté, 2021.

Among the confirmed cases, 22 were based on laboratory criteria and 28 were clinical-epidemiological; 1 was not specified in Sinan (Graph 3).

Graph 3. Number of confirmed cases by closure criteria, SSP, from 2010 to 2021.*

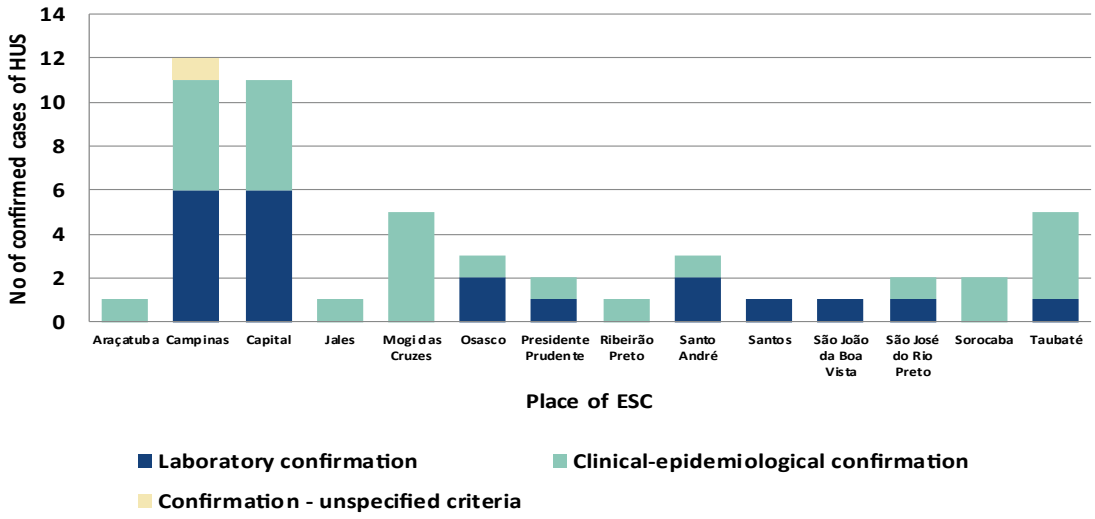


Source: DFWD/ESC/DCC/SHD-SP. *Data extracted from Sinan and handled by on June 10, 2022.

Thus, it is possible to affirm that the ESC (Epidemiological Surveillance Center) Campinas was the one that presented the highest number of confirmations in the evaluated period.

The ESC Santos and São João da Boa Vista, however, had the highest percentages of closure by laboratory criteria (100% of cases), followed by ESC Santo André (67%) and ESC Osasco (67%) (Graph 4).

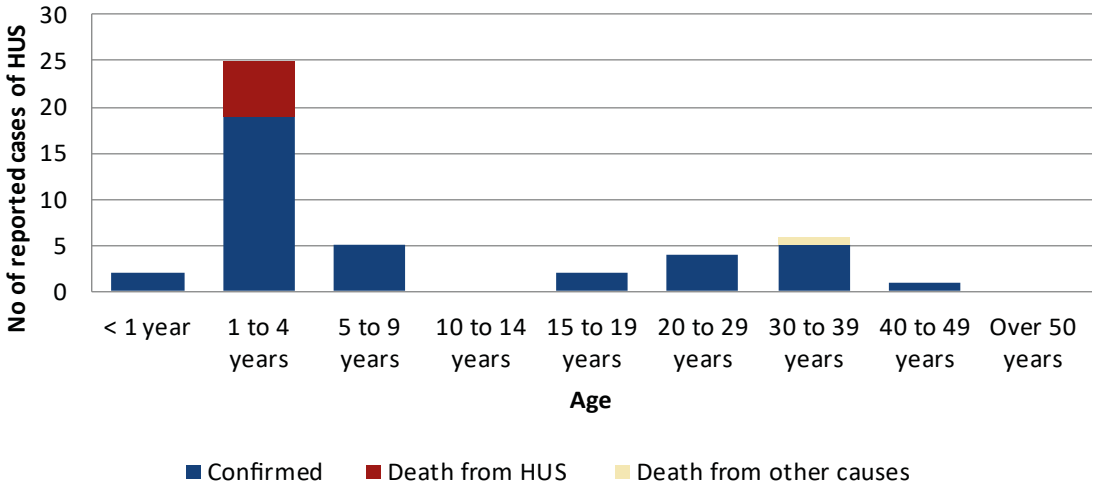
Graph 4. Number of confirmed cases by closure criteria, SSP, from 2010 to 2021.*



Source: DFWD/ESC/DCC/SHD-SP. *Data extracted from Sinan and handled by DFWD on June 10, 2022.

Regarding the age group, the largest number of cases was concentrated between 1 and 4 years of age, similar to what is reported globally, as well as deaths from HUS (Graph 5).

Graph 5. Number of confirmed cases and deaths by age group, SSP, 2010 to 2021.*



Source: DFWD/ESC/DCC/SHD-SP. *Data extracted from Sinan and handled by DFWD on June 10, 2022.

It is essential to detect cases as early as possible in order to provide the necessary assistance, as well as collecting material for laboratory analysis is essential for diagnosis. These actions are a driver in surveillance measures. Therefore, immediate notification of suspected HUS cases and diarrhea

outbreaks is extremely important. In this sense, each and every event of the type reported must be investigated in order to try to determine the source of infection, as well as the possible contacts of the patient.

Regarding these contacts, when an individual has acute diarrhea, it is necessary to take precautions that prevent oral-fecal, person-to-person or foodborne transmission. Therefore, people with diarrhea should not prepare meals or care for children or patients before healing or two successive negative stool results. They need to be away from food handling and receive guidance on hygiene and hand washing measures. Finally, cultures should be collected from contacts that are restricted to food handlers, attendants, and other staff involved in the care of children or patients, as they may be contributing to the spread of infection.

It is noteworthy that in outbreaks detection of the pathogen in food is useful. Furthermore, in the evaluated period, no case belonged to this scenario.

PREVENTION MEASURES

Interrupting transmission, whether through food, water or person-to-person, involves educational and health measures that must be adopted as soon as the diagnosis is suspected and the first evidence of causal factors is available. In this sense, preventive measures capable of reducing the incidence of the disease are:

- surveillance of slaughter conditions to reduce meat contamination by the animal's intestinal contents;
- educating the population on the consumption of properly cooked meat, especially ground meat, which must be cooked until the pink color disappears;
- consumption of juices, milk and their derivatives only pasteurized;
- HACCP procedures in the cultivation of vegetables and fruits and surveillance of the use of animal manure – the use of this untreated material, in particular, has been responsible for the contamination of fruits and vegetables;
- irradiation of meats, mainly ground meat;
- adequate chlorination of all public water supply, for human consumption and filling of swimming pools;

- education of food handlers, housewives and the general population for basic hygiene care and frequent hand washing, before preparing or consuming food, among others; and
- adoption of strict hygiene measures in day care centers, with hand washing after using the bathroom, changing diapers, before meals and when taking care of children, in addition to basic care during the preparation and provision of meals for children and employees, as well as with drinking fountains, toilets, counters, etc.

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