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ORIGINAL

Determinants of Hemolytic Uremic Syndrome in children under five years of age in Argentina

Factores determinantes del Síndrome Urémico Hemolítico en niños menores de cinco años en Argentina

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ABSTRACT

Introduction: hemolytic uremic syndrome (HUS), associated with Shiga toxin-producing Escherichia coli (STEC), is a leading cause of acute renal failure in children under five years of age. In Argentina, its high incidence reflects challenges in access to drinking water, food hygiene and health education.
Objective: to evaluate the determinants of the incidence of HUS in Argentine children, focusing on hygiene practices, food consumption, access to water and knowledge of caregivers.
Method: observational and descriptive study with three phases: literature review, survey to 33 parents of children <5 years old (food habits, hygiene, knowledge of HUS) and comparative analysis with data from the National Epidemiological Bulletin.
Results: 90,9 % of respondents resided in urban areas, with access to treated water (81,8 %) and high hygiene practices (84,8 % hand washing). However, risks persist: 48,5 % consume unpasteurized products, 33,3 % do not use separate cutting boards and 30,3 % do not know about HUS. The Bulletin highlights higher incidence in rural areas with poor infrastructure and in hot seasons. Cross-contamination and food handling in restaurants were factors highlighted.
Conclusions: the incidence of HUS in Argentina is linked to gaps in the rigorous implementation of hygiene practices, unequal access to drinking water and lack of knowledge about prevention. Educational campaigns, improvement of sanitary infrastructure and food controls are recommended, especially in vulnerable areas and during periods of higher risk. The integration of public policies and community education could reduce the burden of the disease in the child population.

Keywords: Hemolytic-Uremic Syndrome; Argentina; Food Ingestion; Child.

RESUMEN

Introducción: el Síndrome Urémico Hemolítico (SUH), asociado a *Escherichia coli* productora de toxina Shiga (STEC), es una causa principal de insuficiencia renal aguda en niños menores de cinco años. En Argentina, su alta incidencia refleja desafíos en acceso a agua potable, higiene alimentaria y educación sanitaria.
Objetivo: evaluar los factores determinantes de la incidencia del SUH en niños argentinos, centrándose en prácticas de higiene, consumo de alimentos, acceso al agua y conocimiento de cuidadores.
Método: estudio observacional y descriptivo con tres fases: revisión bibliográfica, encuesta a 33 padres de niños <5 años (hábitos alimenticios, higiene, conocimiento del SUH) y análisis comparativo con datos del Boletín Epidemiológico Nacional.
Resultados: el 90,9 % de los encuestados residía en zonas urbanas, con acceso a agua tratada (81,8 %) y altas prácticas de higiene (84,8 % lavado de manos). Sin embargo, persisten riesgos: 48,5 % consume productos no pasteurizados, 33,3 % no usa tablas de corte separadas y 30,3 % desconoce el SUH. El Boletín resalta mayor incidencia en áreas rurales con infraestructura deficiente y en temporadas cálidas. La contaminación

cruzada y la manipulación de alimentos en restaurantes fueron factores destacados.
Conclusiones: la incidencia del SUH en Argentina está vinculada a brechas en la implementación rigurosa de prácticas de higiene, acceso desigual al agua potable y desconocimiento sobre prevención. Se recomiendan campañas educativas, mejora en infraestructura sanitaria y controles alimentarios, especialmente en zonas vulnerables y durante períodos de mayor riesgo. La integración de políticas públicas y educación comunitaria podría reducir la carga de la enfermedad en la población infantil.

Palabras clave: Síndrome Hemolítico-Urémico; Argentina; Ingestión de Alimentos; Niño.

INTRODUCTION

Hemolytic uremic syndrome (HUS) constitutes one of the leading causes of acute renal failure in childhood, especially in children under five years of age. This clinical syndrome is characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal damage, and in most cases, is associated with infection by Shiga toxin-producing Escherichia coli (STEC). Transmission of this bacterium occurs mainly through contaminated food -such as undercooked minced meat, unpasteurized dairy products, and raw vegetables- or by direct contact with infected people or animals, with young children particularly vulnerable due to their immature physiology and behavioral habits.[1,2]

In Argentina, HUS represents a serious public health problem. The disease is endemic and disproportionately affects the sectors most exposed to poor sanitary conditions, such as lack of drinking water or inadequate food handling practices. Although the country has had mandatory reporting of HUS since 2000 and a National Prevention and Control Program since 2009, indicators continue to show a high incidence, especially in rural and peri-urban areas and during warm seasons such as spring and summer.

The identification of risk factors is crucial for implementing more effective public health policies. Several studies have pointed out that water quality, food hygiene practices, and caregivers' knowledge about HUS are determining variables that influence the occurrence of new cases. In this context, it is essential to develop studies that integrate official epidemiological data and first-hand information from families to establish precise correlations and promote targeted preventive interventions.

This study aims to provide empirical evidence on the factors that influence the high prevalence of HUS in Argentina's children under five years of age. For this purpose, an observational and descriptive study based on a survey of parents of children in this age group is conducted, complemented by a comparative analysis of data from the National Epidemiological Bulletin. This approach aims to shed light on the daily practices of consumption, hygiene, and access to water, as well as on the degree of knowledge responsible adults have about this disease, to contribute to the design of more effective prevention and health education strategies.

What are the determinants of the high incidence of Hemolytic Uremic Syndrome in Argentina in children under five years of age, and how do hygiene practices, access to drinking water, and caregivers' knowledge of the disease influence it?

General objective

The purpose of this study is to evaluate the determinants of the high incidence of Hemolytic Uremic Syndrome in children under five years of age in Argentina, with emphasis on hygiene practices, food consumption, access to drinking water, and caregivers' level of knowledge.

METHOD

Hemolytic uremic syndrome

HUS is a clinical syndrome involving hemolytic anemia (with fragmented red blood cells), low blood platelet levels (thrombocytopenia), and acute kidney injury (AKI), the latter being the leading infectious cause of AKI in children. The main reason for HUS is endothelial cell injury in microvessels (arterioles, capillaries, and venules), although the etiology and pathogenesis vary.[3] Patients with HUS-STEC present with fatigue, pallor, dizziness, sometimes petechiae and bruising, shortness of breath, edema, and decreased urine volume, all suggestive of HUS-STEC due to the previous episode of bloody diarrhea.

The main virulence factor of STEC strains is the so-called Shiga toxins encoded by the six genes. The adhesin intimin, encoded by the ease gene, is involved in the intimate adherence of bacteria to enterocytes. The Stx gene is encoded in a lysogenic bacteriophage incorporated into bacterial DNA. Stx production depends on the replicative cycle of the Stx phage and its release after bacterial lysis.[4] However, STEC strains lacking this gene can also cause disease in humans. While it has not yet been established which combination of markers defines an STEC strain as pathogenic, the presence of the stx/ease genes is associated with a risk of more severe disease.[5] There are two families of Stx toxins: Stx1 and Stx2, each of which has different variants. Although

all variants have been isolated from patients with diarrhea, not all have the same degree of association with developing the most severe clinical forms.[6,7,8,9,10,11]

In Argentina, as in the rest of the world, cattle are the natural and most important reservoir of E. coli O157:H711. STEC strains have been recovered from fecal samples in 39 % of healthy animals. STECs are transmitted to humans through food and water contaminated with fecal material from carrier animals.[6] Other proposed routes of transmission are associated with direct contact with humans or animal carriers via the fecal-oral route. The infection sources most frequently associated with HUS in our country are food with insufficiently cooked minced meat, apple juice or unpasteurized dairy products, raw vegetables, salami, and blood sausage.[12,13]

The bacterium colonizes the intestine and begins to produce Shiga toxin (Stx), which passes into the circulation and binds to its specific receptor, which is present mainly in the endothelium of the renal glomerulus and tubular epithelium. There, it is internalized and causes cell death.[8]

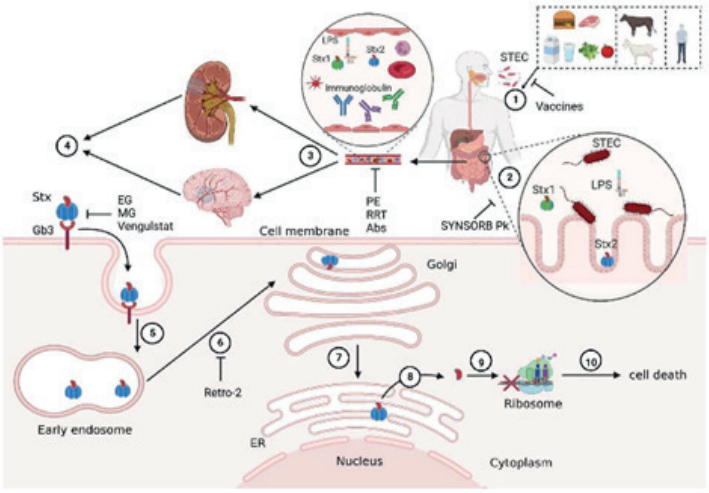

Figure 1. Cell Structure and Components

The incubation period usually ranges from 2 to 12 days, with an estimated median of three days. Incubation can sometimes be more prolonged. The predominant symptom is diarrhea, which is bloody in 60 % of patients. Abdominal pain is more intense than other bacterial gastroenteritis, and most patients infected with O157:H7 do not have fever. Nausea and vomiting are sometimes reported. Diarrhea usually improves within a week and is complicated by hemolytic uremic syndrome in about 15 % of cases (5-10 % of sporadic cases, > 20 % during outbreaks).[3,4,5,6,7,8,9,10,11]

Diagnosis

Clinically, the diagnosis of HUS-STEC is based primarily on possible previous infections or history of exposure, corresponding clinical symptoms, and ancillary tests[7,8] that indicate thrombotic microangiopathy, such as nonimmune hemolytic anemia (hematocrit < 30 %, with fragmented erythrocytes on peripheral blood smear and a negative Coombs' test), thrombocytopenia (platelet count < 150. 000 mm3), and abnormal renal function (a serum creatinine concentration exceeding the upper limit of the reference range for age) with or without hypocomplementemia. If HUS-STEC is suspected, fecal and serologic tests are required to determine if there is evidence of STEC infection.[3,4,5,6,8,9,11]

Treatment

Treatment of HUS-STEC is mainly symptomatic. Patients require hospitalization in specialized services familiar with the management of renal injury and red blood cell transfusions, as well as detection, monitoring, and treatment of hypertension, neurological manifestations, intestinal complications, ischemic cardiomyopathy, pancreatitis). Careful management of intravascular volume is critical in the acute phase.[3,4,5,6,7,8,9,11]

Research objective

The present work uses the PICO format to formulate the research question: What are the determinants of the high incidence of hemolytic uremic syndrome in Argentina in children under 5? Therefore, this thesis aims to Evaluate hygiene practices and food consumption in families with children belonging to the aforementioned age range, analyze the access to drinking water and disinfection practices in each household, and determine the parents' level of knowledge about HUS and its relationship with food hygiene.

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Study design and methodology

This observational and descriptive study seeks to identify risk factors associated with HUS in children under 5 years of age.

The PICO format was used to formulate the research question: What are the determinants of the high incidence of HUS in children under 5 years of age in Argentina?

It is carried out in three phases.

Phase 1: bibliographic review

A bibliographic review was done by analyzing Scielo, Elsevier, and PubMed databases. In the latter, the search filter applied was Mesh (medical subject heading) with the keywords "Hemolytic Uremic Syndrome; renal failure; epidemiology; stec infection; prevention, selecting the most relevant articles on the study of HUS, STEC, and the prevalence of this disease in our country. This allows the selection of relevant articles to theoretically support the study, emphasizing research that relates HUS with environmental and sanitary factors in the Argentinean infant population.

Phase 2: field survey

In this phase, a field survey was designed using a closed multiple-choice questionnaire through the Google Forms platform (https://forms.gle/nUiLanrYhLzjemSL9), in which 33 parents of children under 5 years of age answered the following questions: Demographic data (age, sex, area of residence), consumption habits of meat and dairy products with an emphasis on unpasteurized products, access, and water treatment, knowledge about HUS and its relationship with water and food quality and hygiene practices in the preparation and consumption of food such as hand washing, disinfection of fruits and surfaces and separate use of cutting boards.

The results obtained were collected and organized in a database to calculate the percentages and frequencies of each response.

Phase 3: comparative analysis with the national epidemiological bulletin

The survey data are contrasted with the information provided in the National Epidemiological Bulletin to observe similarities and differences in HUS risk factors in different areas of Argentina. This analysis allows us to identify how risk factors related to water quality and dietary practices are geographically distributed in the country and affect the incidence of HUS in the vulnerable infant population.

For this study, the incidence of risk factors associated with HUS in children under 5 years of age is used as a variable, taking into account the population studied.

Limitations of the study

Among the limitations, the small sample size stands out; the results may not wholly represent the general population.

Due to the time constraint in preparing this work, the sample is mainly composed of urban residents, which could bias the results.

A review of medical records at the Gandulfo Hospital was initially planned, but this was not possible due to access restrictions, which limited the analysis of data obtained on the form and data from public bulletins.

Inclusion and exclusion criteria

Table 1. Inclusion Criteria

Inclusion Criteria	Description
Age of children	Children under 5 years of age
Participation in the questionnaire	Parents of children under 5 years of age who have completed the questionnaire on risk factors associated with HUS.
Area of residence	Residents of Argentina

Table 2. Exclusion Criteria

Exclusion Criteria	Description
Age of children	Children older than 5 years old and children younger than 1 year old.
Residence outside Argentina	Children residing outside of Argentina, since the study focuses on the country's child population
Unrelated medical conditions	Children with chronic medical conditions not related to HUS, to avoid bias in the analysis.

Inclusion and exclusion criteria were chosen based on the results of the form made taking into account the determinants of HUS in Argentina.

RESULTS

Thirty-three parents of children under 5 years of age were surveyed and the following results were obtained:

Demographic profile: 54,5 % of respondents were 5 years old, 60,6 % were male and 90,9 % resided in urban areas.

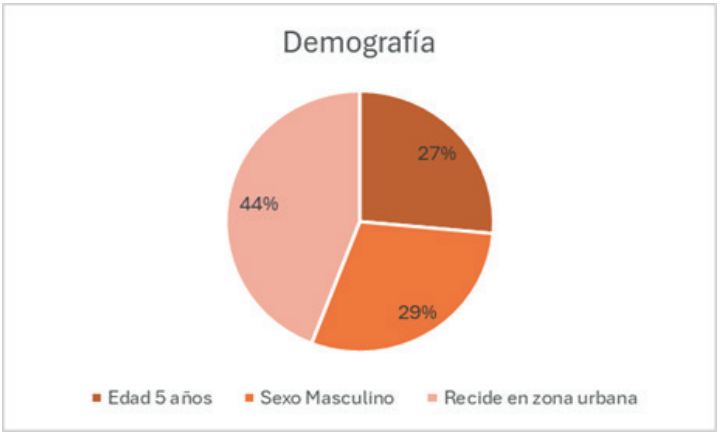

Figure 2. Demographics

Meat and Dairy Consumption: 63,6 % consume beef several times a week, with 100 % stating that the point of cooking is "well cooked". 48,5 % stated that they consume unpasteurized products. As for the attendance to fast food restaurants, although 48 % say that they rarely do it, 63,3 % do it.

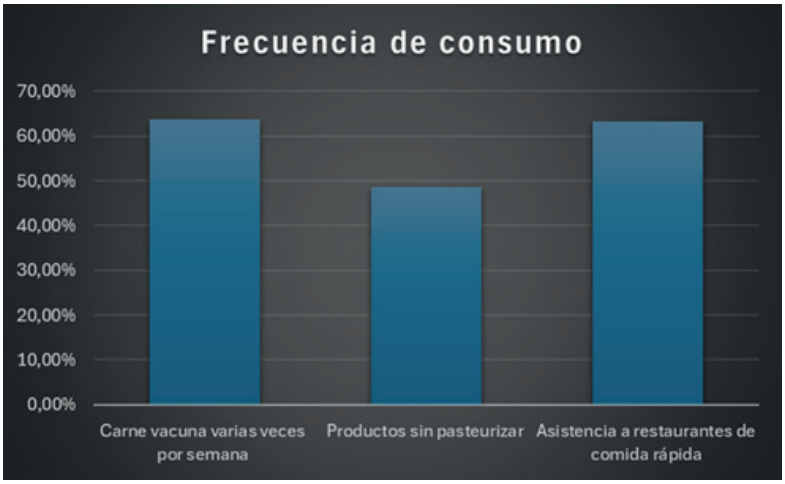

Figure 3. Frequency of consumption

Hygiene practices: 84,8 % reported washing their hands before preparing food, and 90,9 % disinfected fruits and vegetables before consumption. However, only 66,7 % use separate cutting boards for meat and vegetables.

However, only 66,7 % use separate cutting boards for meat and vegetables; while 78,8 % are aware of cross-contamination, 21,2 % are not.

Water Quality and Treatment: 81,8 % treat water before consumption, 33,3 % use bottled water, and 30,3 % use public water.

Knowledge about HUS: 60,6 % of parents know about HUS, while 30,3 % have no information about it but would like to be informed.

Water quality and treatment: 81,8 % treat water before consumption, with bottled water accounting for 33,3 % and public water for 30,3 %

Figure 4 the National Epidemiological Bulletin reports that the incidence of HUS is higher in regions with less access to treated drinking water, especially in rural areas. Although in the study formulated, the majority of respondents reside in urban areas and have access to treated water, a significant proportion still do not apply adequate hygiene measures, which is associated with a high risk of HUS.

Figure 4. Quality of water consumed

Table 3. Prevalence and Awareness of ED in the Child Population

Variable	Description of Responses	Percentage (%)
Child's age	3 to 4 years old, 5 years old, 1 to 2 years old	54,5 % 5 Years, 39,4 % 3 to 4 Years, 6,1 % 1 to 2 Years.
Sex of Child	Female, Male	60,6 % Male, 39,4 % Female
Zone of Residence	Urban, Rural	90,9 % Urban, rest Rural
Cooking of Meat	Well cooked	100 %
Consumption of Unpasteurized Products	Yes, No	48,5 % Yes, the rest No
Attending Fast Food Restaurants	Yes, No	63,3 % Yes, the rest No
Hand Washing Before Food Preparation	Always, Sometimes	Majority Always
Disinfecting Fruits and Vegetables	Yes, No	Majority Yes
Using Different Cutting Boards	Yes, No, I do not use boards	66,7 % Yes, 27,3 % No, the rest do not use.
Cross Contamination Awareness	Yes, No	78,8 % Yes, 21,2 % No.
Day Care or Kindergarten Attendance	Yes, No	Majority Yes
Reporting of HUS Cases in Institution	Yes, No, I do not know	51,5 % No, 48,5 % Don't Know.
Episodes of Vomiting or Diarrhea in 6 Months	Yes, No	57,6 % No, 42,4 % Yes.
Hospitalization for Serious Infections	Yes, No	Majority No
Care for E. coli Infections	Yes, No	Majority No
Familiarity with ED	Yes, No	60,6 % Yes, 39,4 % No.
Perception of Relationship between HUS and Water/Food Quality	Yes, No, Not sure	42,4 % Yes, 45,5 % Not sure, 12,1 % No.

DISCUSSION

The high incidence of hemolytic uremic syndrome (HUS) in Argentina represents a considerable burden to the public health system, especially in children under 5 years of age. Data from the National Epidemiological Bulletin highlight that lack of access to drinking water and inadequate hygiene practices are critical risk factors. In this study, we observed that, although most respondents have access to treated water and adequate hygiene practices, there are still gaps in the rigorous implementation of these measures. An example is the low percentage of respondents using separate cutting boards, which increases the risk of cross-contamination.

Considering that most respondents reside in urban areas, where access to information and hygiene resources is relatively greater, these results may underestimate the situation in rural areas. If this survey were applied nationwide, including areas with less access to health education and hygiene resources, knowledge about practices such as cross-contamination prevention would likely be even more limited, which could reflect an elevated risk in those regions.

On the other hand, among the respondents, we can see a high percentage in the consumption of beef and the incidence of consuming unpasteurized dairy products, being relevant for HUS in the Argentine territory since these products can be vehicles for the Shiga toxin-producing Escherichia coli (E. Coli) bacteria (STEC). As reported in the epidemiological bulletin, this microorganism is one of the primary etiological agents of HUS in

Argentina. Even though 100 % of those surveyed reported consuming well-cooked meat, previous handling and the possibility of cross-contamination, especially in fast-food restaurants, represent a latent risk. Theseibute to the exposure of the pathogen.[1,2,3,4,5]

Regarding water quality, most of the respondents stated that they treat their water before consumption, but there is a low percentage that does not do so; this increases vulnerability to infections that favor the development of HUS and is especially relevant in a country like Argentina, where there are areas with limited access to the quality of tap water. According to the epidemiological bulletin, it has been particularly high in areas where access to drinking water is restricted, or the water treatment infrastructure is not optimal. Public health policies should prioritize improving infrastructure for drinking water and sanitation access, especially in rural and peri-urban areas.

On the other hand, the survey shows that many families consume bottled water, which leads us to presume that access to and choice of water is related to geographic and economic levels.[1,2,10,11]

Safe food handling is crucial for the prevention of HUS. Although the figures in the form report high rates of hand hygiene and disinfection of food, utensils, and surfaces, a percentage of the population does not always follow these practices. This proportion may be sufficient to increase the risk of cross-contamination, especially in handling raw meats, since 33,3 % of people do not use different cutting boards. This practice is the key to preventing STEC transmission, both in the domestic environment and in restaurants. Therefore, it is essential to implement educational campaigns to prevent cross-contamination at home and in restaurants or food trays.

Another aspect to consider is the high incidence rate of visits to fast food restaurants since there is greater exposure to the risks described above.

While 60,6 % say they have information about ED, 30,3 % do not have information about it but would like to have it. This lack of complete knowledge about risk factors and preventive practices may negatively influence decision-making regarding eating habits and hygiene. The epidemiological bulletin reinforces the importance of health education, indicating that the lack of information in specific communities increases the vulnerability of children to this disease.[1,2,8,9,10] Developing awareness campaigns in schools, daycare centers, and community centers is crucial as they could be fundamental to reducing the risk in this vulnerable population group.

A considerable finding is that 54,5 % of the parents have monthly incomes above 600 000 pesos; on the part of the commonwealths, approximately 66,7 % have attained tertiary or university education. These levels may allow access to safe food or good quality water; the current level of education is conducive to good hygiene practices. However, the presence of HUS in communities with higher socioeconomic levels indicates that even if socioeconomic status can reduce some risks, it does not eliminate exposure. This highlights the need to reinforce educational programs at all socioeconomic levels and the fight to eradicate cross-contamination through strict hygienic practices when handling food.[1,2,3,11]

Regarding the geographical distribution of HUS in Argentina, prevalence is more marked in children under 5 years of age. Among the provinces of the Central regions (even more notorious in jurisdictions such as CBA, SFE, and MDZ, among others), there are the highest perceptions of cases reported to health institutions regarding HUS. Seasonalization is a factor that should be considered, as there are peaks of cases in summer and spring, which are associated with increased outdoor activities and the consumption of more perishable foods that could lead to greater exposure to the risk of contamination. Compared with the data reported in the questionnaire, it can be inferred that children in urban environments. However, they have better access to health services and food products and are not exempt from risks due to the behavioral component of those responsible for the children.[1,2,10,11] Therefore, it is advisable to intensify prevention measures during these seasons.

The bulletin emphasizes that lack of education on preventive practices and poor sanitation infrastructure contribute to the high incidence of HUS. This study reveals that, although many respondents are aware of the relationship between HUS and hygiene, there are still gaps in the implementation of these practices in household and food establishments. Another finding provided by the bulletin is the seasonal relationship related to the increase of HUS cases in hot weather, probably due to increased consumption of perishable foods and outdoor activities. This suggests that prevention campaigns should be intensified during these critical periods.

Comparison of these data with the Epidemiological Bulletin reports suggests that the predominant risk factors are linked to health infrastructure, education, and consumption practices. This underscores the relevance of implementing intervention strategies to improve hygiene practices and access to safe drinking water.

In accordance with the bulletin, it is recommended that public health policies focus on Continuing Education Programs, which should include health education modules on ED and hygiene practices in school programs.

Improved Drinking Water Infrastructure: strengthen access to treated water in rural and peri-urban areas to reduce infection vulnerability.

Strengthen Sanitary Controls: implement stricter controls on food handling and sales, whether in tanneries, sausage factories, dairy products factories, or fast food establishments.

Encourage Safe Food Preparation Practices: promote separate utensils for raw food and strict hygiene in food handling.

Encourage Food Handling Practices: promote the care of the food cold chain, ensuring that food is kept in optimal storage conditions to prevent the proliferation of bacteria.

High Season Attention: prioritize food prevention and control campaigns during the highest risk season (spring-summer).

CONCLUSIONS

In conclusion, the research highlights that the incidence of HUS in Argentina depends not only on infrastructural factors but also on hygiene and consumption practices that can be improved through education and sanitary regulation. These strategies, combined, could significantly reduce the risk of HUS in the most vulnerable child population, children under 5 years of age, contributing to the improvement of public health in the country.

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FINANCING

None.

CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

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