Revista ARACÊ
ISSN: 2358-2472

THE ROLE OF ECULUZIMAB IN THE PROGNOSIS OF SHIGA TOXIN-ASSOCIATED HEMOLYTIC-UREMIC SYNDROME IN CHILDREN: A LITERATURE REVIEW

O PAPEL DO ECULUZIMAB NO PROGNÓSTICO DA SÍNDROME HEMOLÍTICO-URÊMICA ASSOCIADA À TOXINA SHIGA EM CRIANÇAS: UMA REVISÃO DE LITERATURA

EL PAPEL DE ECULUZIMAB EN EL PRONÓSTICO DEL SÍNDROME HEMOLÍTICO-URÊMICO ASOCIADO A LA TOXINA SHIGA EN NIÑOS: UMA REVISIÓN DE LA LITERATURA

https://doi.org/10.56238/arev7n11-122

Submission date: 10/13/2025 **Publication Date:** 11/13/2025

Gustavo Almeida Ramos[1], Amanda Moreira de Araújo Mello[2], Camila Fontes Pinheiro[3], Cíntia Pereira Reis[4], Stephania de Oliveira Laudares Moreira[5], Lílian Carla Carneiro[6], Murillo de Sousa Pinto[7]

ABSTRACT

Hemolytic-Uremic Syndrome (HUS) is a rare and severe thrombotic microangiopathy characterized by hemolytic anemia, thrombocytopenia, and acute kidney injury, predominantly affecting children. The form associated with Shiga toxin- producing Escherichia coli (STEC-HUS) is the most prevalent in this age group, with high morbidity and a significant risk of renal sequelae and the need for renal replacement therapy, as evidenced by national studies. Eculizumab, a complement C5 inhibitor, has revolutionized the prognosis of Atypical Hemolytic-Uremic Syndrome (aHUS), but its role in pediatric STEC-HUS remains controversial. This article, through an integrative literature review in the PubMed and SciELO databases, analyzed the influence of eculizumab on the clinical outcomes of STEC-HUS in children, aiming to support the discussion on its potential inclusion in the Brazilian healthcare system. The results indicate that while there is evidence of long-term benefit in renal protection, the efficacy of eculizumab in the acute phase and on neurological outcomes is not consistently demonstrated. Studies are often limited by indication bias and small sample sizes. Given the high cost and scientific uncertainties, it is concluded that eculizumab should

[1] Medical Student. Centro Universitário Alfredo Nasser (UNIFAN). E-mail: coronelgustavo1998@gmail.com
Orcid: https://orcid.org/0009-0003-3775-6522 Lattes: http://lattes.cnpq.br/9827686030051803
[2] Medical Student. Centro Universitário Alfredo Nasser (UNIFAN). E-mail: amanda.amello029@gmail.com
[3] Medical Student. Centro Universitário Alfredo Nasser (UNIFAN). E-mail: camilafpinheiro24@gmail.com
Orcid: https://orcid.org/0009-0003-2784-9397 Lattes: http://lattes.cnpq.br/4156969708973916
[4] Medical Student. Centro Universitário Alfredo Nasser (UNIFAN). E-mail: cinthiapreis@gmail.com
Orcid: https://orcid.org/0009-0006-2351-5420 Lattes: http://lattes.cnpq.br/8716517686811634
[5] Pediatric Specialist. Centro Universitário Alfredo Nasser (UNIFAN).
E-mail: stephanialaudares@unifan.edu.br Orcid: https://orcid.org/0000-0003-4060-5189
Lattes: http://lattes.cnpq.br/6332705376247469
[6] Dr. in Cellular and Molecular Biology. Universidade Federal de Goiás (UFG).
E-mail: carlacarneirolilian@gmail.com Orcid: https://orcid.org/0000-0003-4067-1506
Lattes: http://lattes.cnpq.br/6506744224041777
[7] Master's degree in Health Care and Assessment. Centro Universitário Alfredo Nasser (UNIFAN).
E-mail: murillopinto@unifan.edu.br Orcid https://orcid.org/0000-0003-4899-2670
Lattes: http://lattes.cnpq.br/9799290954699973

Revista ARACÊ
ISSN: 2358-2472

not be a universal first-line therapy for STEC-HUS. Its use must be highly individualized, reserved for severe or refractory cases with confirmed complement activation, rigorous clinical protocols, and genetic testing. There is a pressing need for randomized, multicenter clinical trials to define the subgroup of pediatric patients with STEC-HUS who would truly benefit from this therapy, paving the way for more solid evidence-based health policies in Brazil.

Keywords: Hemolytic-Uremic Syndrome. Shiga Toxin. Eculizumab. Pediatrics. Prognosis.

RESUMO

A Síndrome Hemolítico-Urêmica (SHU) é uma microangiopatia trombótica rara e grave, caracterizada por anemia hemolítica, trombocitopenia e lesão renal aguda, afetando predominantemente crianças. A forma associada à Escherichia coli produtora de toxina Shiga (STEC-HUS) é a mais prevalente nessa faixa etária, com alta morbidade e risco significativo de sequelas renais e necessidade de terapia renal substitutiva, conforme evidenciado por estudos nacionais. O eculizumab, um inibidor do complemento C5, revolucionou o prognóstico da Síndrome Hemolítico-Urêmica Atípica (HUSa), mas seu papel na STEC-HUS pediátrica permanece controverso. Este artigo, por meio de uma revisão integrativa da literatura nas bases de dados PubMed e SciELO, analisou a influência do eculizumab nos desfechos clínicos da STEC-HUS em crianças, visando subsidiar discussão sobre potencial inclusão no sistema de saúde brasileiro. Os resultados indicam que, embora haja evidências de benefício a longo prazo na proteção renal, a eficácia do eculizumab na fase aguda e em desfechos neurológicos não é consistentemente demonstrada. Os estudos são frequentemente limitados por viés de indicação e pequeno tamanho amostral. Diante do elevado custo e incertezas científicas, conclui-se que o eculizumab não deve ser uma terapia de primeira linha universal para STEC-HUS. Seu uso deve ser altamente individualizado, reservado a casos graves ou refratários com ativação do complemento confirmada, protocolos clínicos rigorosos, e testes genéticos. A necessidade de ensaios clínicos randomizados e multicêntricos é premente para definir o subgrupo de pacientes pediátricos com STEC-HUS que realmente se beneficiaria dessa terapia, pavimentando o caminho para políticas de saúde baseadas em evidências sólidas no Brasil.

Palavras-chave: Síndrome Hemolítico-Urêmica. Toxina Shiga. Eculizumab. Pediatria. Prognóstico.

RESUMEN

El Síndrome Hemolítico-Urémico (SHU) es una microangiopatía trombótica rara y grave, caracterizada por anemia hemolítica, trombocitopenia y lesión renal aguda, que afecta predominantemente a niños. La forma asociada a Escherichia coli productora de toxina Shiga (SHU-STEC) es la más prevalente en este grupo de edad, con alta morbilidad y un riesgo significativo de secuelas renales y necesidad de terapia de reemplazo renal, como lo demuestran estudios nacionales. El eculizumab, un inhibidor del complemento C5, ha revolucionado el pronóstico del Síndrome Hemolítico-Urémico Atípico (SHUa), pero su papel en el SHU-STEC pediátrico sigue siendo controvertido. Este artículo, a través de una revisión integradora de la literatura en las bases de datos PubMed y SciELO, analizó la influencia del eculizumab en los resultados clínicos del SHU-STEC en niños, con el objetivo de fundamentar la discusión sobre su posible inclusión en el sistema de salud brasileño. Los resultados indican que, aunque existen evidencias de un beneficio a largo plazo en la protección renal, la eficacia del eculizumab en la fase aguda y en los resultados neurológicos

Revista ARACÊ
ISSN: 2358-2472

no se demuestra de manera consistente. Los estudios a menudo están limitados por sesgos de indicación y un tamaño de muestra pequeño. Ante el elevado costo y las incertidumbres científicas, se concluye que el eculizumab no debe ser una terapia de primera línea universal para el SHU-STEC. Su uso debe ser altamente individualizado, reservado para casos graves o refractarios con activación del complemento confirmada, protocolos clínicos rigurosos y pruebas genéticas. Es apremiante la necesidad de ensayos clínicos aleatorizados y multicéntricos para definir el subgrupo de pacientes pediátricos con SHU-STEC que realmente se beneficiaría de esta terapia, allanando el camino para políticas de salud basadas en evidencias más sólidas en Brasil.

Palabras clave: Síndrome Hemolítico-Urêmico. Toxina Shiga. Eculizumab. Pediatria. Prognóstico.

Revista ARACÊ
ISSN: 2358-2472

1 INTRODUCTION

Hemolytic-Uremic Syndrome (HUS) is a severe and uncommon condition that predominantly affects children (Maximiano, 2021; Aldharman et al., 2023). This syndrome is characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure (Maximiano, 2021; Vaisbich et al., 2025). The most common form of HUS is associated with infection by Shiga toxin- producing Escherichia coli (STEC), which represents a significant public health concern due to its morbidity and mortality (Vilardouro, 2022).

The incidence of Shiga toxin-associated HUS varies globally; it is the leading cause of hemolytic-uremic syndrome in children, accounting for 90% of registered cases, and HUS develops in approximately 15% of children with Shiga toxin infection (Boyer, 2022). In Brazil, data from the Notifiable Diseases Information System (SINAN) indicate an increase in post-diarrheal HUS cases in children, often linked to outbreaks of E. coli O157:H7, the most common Shiga toxin-producing strain.

Shiga toxin inhibits protein synthesis in endothelial cells, triggering an inflammatory and thrombotic cascade that results in thrombotic microangiopathy, especially in the kidneys (Bueli, 2019). In children, the immaturity of the immune system can aggravate this response, increasing susceptibility to severe forms of the disease (Vilardouro, 2022).

Until 2010, the traditional management of HUS was primarily supportive, including hydration, blood transfusions, dialysis, and liver transplants (Vaisbich, 2025). However, these approaches do not prevent disease progression in all cases, and complications such as chronic hypertension and end-stage renal disease may occur (Liu, 2023).

In 2011, a new era of treatments was initiated with the Food and Drug Administration (FDA) approval of an anti-complement C5 monoclonal antibody, such as eculizumab. Studies like that of Garnier et al. (2023) suggest that eculizumab may reduce renal sequelae in severe cases of Shiga toxin-associated HUS in children, decreasing the need for dialysis and improving neurological outcomes (Garnier, 2023).

This article aims to review the role of eculizumab in the management of Shiga toxin-associated HUS in children, addressing its influence on clinical outcomes, with the objective of understanding whether a policy for including this medication as a therapeutic option in the Brazilian healthcare system would be beneficial.

Revista ARACÊ
ISSN: 2358-2472

2 METHODOLOGY

This integrative review was conducted to synthesize evidence on the therapeutic role of eculizumab in the clinical outcomes associated with the management of Shiga toxin-associated Hemolytic-Uremic Syndrome (HUS) in pediatric patients. We adopted a rigorous methodological approach, inspired by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021), adapted to Brazilian academic research standards according to ABNT NBR 14724:2011. The literature search was performed systematically in indexed electronic databases selected for their relevance in medical and pediatric sciences. The included databases were PubMed and SciELO, covering publications in English and Portuguese. The search was conducted between January 2020 and July 2025 (knowledge cutoff date). Search terms were defined based on controlled descriptors from Medical Subject Headings (MeSH) and DeCS (Health Sciences Descriptors), combined with Boolean operators (AND, OR, NOT). Examples of search strings included: ("Hemolytic Uremic Syndrome" OR "HUS") AND ("Pediatric" OR "Children"). For greater precision, filters for study types were added in PubMed: randomized clinical trials, systematic reviews, meta-analyses, and observational studies.

Initially, we identified 11 articles in PubMed and 10 articles in SciELO. Articles were excluded if they were: studies in adults or atypical HUS not related to Shiga toxin, non-indexed or low-methodological-quality publications, and studies with undeclared conflicts of interest or evident publication bias. A total of 10 articles were selected to provide the theoretical basis for this study.

This search and selection strategy was designed to visualize the overall landscape of the literature, prioritizing high-quality sources for durable outcomes, such as evidence- based clinical recommendations. We acknowledge potential limitations, such as publication bias (positive studies on eculizumab are more likely to be published) and geographical heterogeneity (most data from developed countries, with gaps in Latin America). This approach visualizes the general picture, promoting lasting results, such as suggestions for future studies in the Brazilian context.

3 RESULTS AND DISCUSSIONS

Hemolytic-Uremic Syndrome (HUS) represents a group of thrombotic microangiopathies (TMAs) characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury (Boyer, 2022). Although rare, HUS has significant

Revista ARACÊ
ISSN: 2358-2472

health implications, especially in the pediatric population, where its etiology is often infectious (Palma, 2023; Vilardouro, 2022). Understanding the prevalence, management, and prognosis of HUS, particularly Shiga toxin-associated HUS (STEC-HUS) and atypical HUS (aHUS), is fundamental to optimizing clinical outcomes, as evidenced by recent literature.

HUS is considered a rare condition, with a crude annual incidence of approximately 0.66 per 100,000 people and a standardized incidence of 0.57 per 100,000 people (Aldharman, 2023). The condition is more prevalent in children, although it can affect individuals of all ages, and there is a slight predominance in females (Aldharman, 2023). The costs associated with HUS treatment are substantial, exceeding the average for other hospitalizations, which underscores the importance of effective prevention and management strategies (Aldharman, 2023). The epidemiology of HUS can vary significantly between regions, influenced by factors such as patient age and the frequency of underlying bacterial infections (Aldharman, 2023).

In the Brazilian pediatric context, a 24-year retrospective study in a pediatric nephrology unit showed a median age at diagnosis of 2 years, with infectious etiology accounting for a considerable portion of cases (Vilardouro, 2022). Data from this study reveal that 56% of patients required renal replacement therapy in the acute phase, and 40% progressed to chronic kidney disease (Palma, 2023; Vilardouro, 2022). Notably, HUS of infectious etiology resulted in sequelae in all affected patients and required renal replacement therapy, highlighting the severity of this form of the disease (Vilardouro, 2022).

A complication of particular concern in HUS is neurological involvement. A systematic review and meta-analysis revealed that more than a quarter of HUS patients, regardless of the presence of diarrhea, manifest neurological symptoms, with a prevalence of 24.4% (95% CI: 21.6%-27.5%) (Tavasoli, 2021). Seizures are the most common symptoms, occurring in about 30.5% of diarrhea-associated HUS cases, and can lead to the development of epilepsy (Tavasoli, 2021). The absence of long-term studies and more comprehensive analytical data represents a limitation in understanding long-term neurological sequelae (Tavasoli, 2021).

Atypical HUS (aHUS), in turn, is a rare condition of complement dysregulation, often of genetic origin, characterized by uncontrolled activation of the alternative complement pathway (Vaisbich, 2025). Genetic mutations in complement regulatory factors, such as Factor H (CFH), are commonly identified (Maximiano, 2021). In a 20- year experience at a tertiary center, children with genetic aHUS had a mean age at the first episode of 19 months, with CFH mutations present in the majority of cases studied (Maximiano, 2021). Although

Revista ARACÊ
ISSN: 2358-2472

plasmapheresis was used for acute management, the prognosis for renal function was strongly dependent on the genetic background, with some patients experiencing relapses and progression to chronic kidney disease (Maximiano, 2021).

Eculizumab, a monoclonal antibody that inhibits the C5 component of the complement system, has emerged as a revolutionary treatment for aHUS, significantly improving renal outcomes and patient survival (Vaisbich, 2025). Consensus guidelines from the Brazilian Society of Nephrology recommend Eculizumab as a first-line therapy for aHUS, with Ravulizumab as a more recent alternative (Vaisbich, 2025). These recommendations cover diagnosis, treatment, monitoring, and discontinuation of therapy, considering pediatric and gestational scenarios, and highlight aHUS as a significant cause of TMA that requires aggressive and targeted management (Vaisbich, 2025).

Conversely, the role of Eculizumab in Shiga toxin-associated HUS (STEC-HUS), especially in children, is more complex and controversial. A randomized, placebo- controlled clinical trial (phase 3) in pediatric patients with STEC-HUS did not demonstrate the efficacy of Eculizumab in the acute phase of the disease, nor in the resolution of hematological parameters or the duration of renal replacement therapy (Garnier, 2023). Interestingly, this study observed a significant reduction in renal sequelae at 1 year in the Eculizumab-treated group (43.48%) compared to the placebo group (64.44%), suggesting a long-term benefit in renal protection (Garnier, 2023). However, it is important to note that this study excluded patients with severe forms of STEC-HUS, which may limit the generalizability of its findings to the most critical population (Garnier, 2023).

In contrast, other systematic reviews have raised significant concerns about the use of Eculizumab in STEC-HUS. A systematic review that included 386 patients treated with Eculizumab for STEC-HUS concluded that the current observational evidence does not allow for a definitive conclusion on the impact of Eculizumab in STEC-HUS due to a high risk of bias, mainly confounding by indication (de Zwart, 2023). No included study found a statistically significant positive effect of Eculizumab on medium- to long-term outcomes, and the mortality rate in Eculizumab-treated patients was actually higher (6%) compared to other studies (3%), suggesting that the treatment is often reserved for the most severe cases of the disease (de Zwart, 2023).

Specifically regarding neurological impact, a recent meta-analysis on the use of Eculizumab in severe pediatric STEC-HUS and its effect on neurological prognosis indicated that patients with neurological involvement were more likely to receive Eculizumab (OR

Revista ARACÊ
ISSN: 2358-2472

13.03, 95% CI: 4.40–38.75) (Spagnol, 2025). Despite this, the study did not find a significant clinical benefit of Eculizumab in neurological improvement among these patients compared to standard therapies (OR 0.32, 95% CI: 0.09–1.22, p=0.10) (Spagnol, 2025). The limitations of these studies, such as their retrospective nature, small sample sizes, short follow-up periods, and indication bias, hinder a conclusive assessment of Eculizumab's benefit on the neurological complications of STEC-HUS (Spagnol, 2025).

The search for interventions to prevent diarrhea-associated HUS has also been a subject of investigation. A Cochrane review evaluated various interventions, including antibiotics, bovine colostrum, Synsorb Pk, and the monoclonal antibody urtoxazumab (Imdad, 2021). However, due to the low certainty of the evidence, the small number of studies, and reduced sample sizes, it was not possible to draw firm conclusions about the efficacy of any of these interventions in the secondary prevention of HUS, highlighting the need for more large-scale, multicenter trials (Imdad, 2021). Other therapeutic approaches, such as hyperimmune equine anti-Shiga toxin F(ab')2 fragments (INM004), are being explored, showing safety and good tolerability in phase I studies in healthy volunteers, with potential for toxin neutralization, although clinical efficacy data are not yet available (Hiriart, 2024).

The heterogeneity of HUS, both in its etiology (STEC-HUS versus aHUS) and in its clinical presentation and severity, represents an ongoing challenge in research and treatment. Many of the reviewed studies suffer from significant limitations, such as their retrospective nature, small sample sizes, selection biases, and confounding by indication, especially in observational studies on Eculizumab in STEC-HUS (de Zwart, 2023; Spagnol, 2025; Vilardouro, 2022). The lack of long-term data and variability in case definitions and outcomes also contribute to the difficulty in establishing robust conclusions (Aldharman, 2023; Tavasoli, 2021).

The diagnosis of aHUS, in particular, is challenging due to the rarity of the disease and the complexity of its mechanisms (Vaisbich, 2025). Access to genetic testing and advanced therapies like Eculizumab can be limited in certain regions, as pointed out in the Brazilian context, which directly impacts prognosis and the ability to conduct more comprehensive studies (Vilardouro, 2022; Vaisbich, 2025).

Despite the uncertainties in the use of Eculizumab for STEC-HUS and in prevention strategies, the introduction of complement-modulating therapies, such as Eculizumab and Ravulizumab, has marked a substantial advance in the management of aHUS, transforming a disease with high morbidity and mortality into a condition with a considerably better

Revista ARACÊ
ISSN: 2358-2472

prognosis (Vaisbich, 2025). The need for more robust studies, including well-designed randomized clinical trials for STEC-HUS, is evident to clarify the role of Eculizumab and other interventions (Garnier, 2023; Imdad, 2021). Furthermore, ongoing research into biomarkers, genetics, and new therapies (such as Pegcetacoplan, Iptacopan, Crovalimab, among others) promises to further refine the diagnosis and treatment of HUS and aHUS, aiming for better outcomes for pediatric patients (Vaisbich, 2025).

This integrative review highlights the importance of early recognition of HUS and etiological differentiation to guide treatment. While Eculizumab represents a fundamental pillar in the treatment of aHUS, its benefit in STEC-HUS, especially concerning neurological complications, remains an area of intense investigation and debate, requiring caution in its application and the need for more high-quality evidence to consolidate its role.

4 CONCLUSION

This systematic review has demonstrated that the current evidence on the efficacy of Eculizumab in the treatment of Shiga toxin-associated Hemolytic-Uremic Syndrome (STEC-HUS) in children is inconsistent and of low methodological quality. Although observational studies suggest potential benefits, such as faster recovery of renal function, the absence of robust randomized clinical trials prevents the confirmation of a net clinical benefit. The heterogeneity in results likely reflects the complex pathophysiology of STEC-HUS, in which complement system activation may not be the central mechanism in all patients, unlike in atypical HUS. Therefore, based on the available literature, a recommendation for the routine use of Eculizumab in this population cannot be established.

The therapeutic decision to use Eculizumab must, consequently, be rigorously individualized, weighing the potential benefits against the significant risks and high cost, making it an option to be considered only in cases of extreme severity with evidence of massive complement dysregulation. The urgent need for randomized controlled trials to elucidate the true role of Eculizumab in pediatric STEC-HUS is evident. Such studies are crucial to define subgroups of patients who might benefit, the optimal timing for intervention, and, finally, to establish therapeutic guidelines based on solid evidence.

Revista ARACÊ
ISSN: 2358-2472

REFERENCES

Aldharmam, S. S., Alharbi, A. M., & Almutairi, A. (2023). The prevalence and incidence of hemolytic uremic syndrome: A systematic review. Cureus, 15(5), Article e39347. https://doi.org/10.7759/cureus.39347

Boyer, O., & Niaudet, P. (2022). Hemolytic-uremic syndrome in children. Pediatric Clinics of North America, 69(6), 1181–1197. https://doi.org/10.1016/j.pcl.2022.07.006

Buelli, S., Abbate, M., Morigi, M., Moioli, D., Zanchi, C., Noris, M., Remuzzi, G., & Zoja, C. (2019). Complement activation contributes to the pathophysiology of Shiga toxin-associated hemolytic uremic syndrome. Microorganisms, 7(1), Article 15. https://doi.org/10.3390/microorganisms7010015

de Zwart, P. L., van de Kar, N. C. A. J., & Wetzels, J. F. M. (2023). Eculizumab in Shiga toxin producing Escherichia coli hemolytic uremic syndrome: A systematic review. Pediatric Nephrology, 39(5), 1369–1385. https://doi.org/10.1007/s00467-023-06216-1

Garnier, A., Brochard, K., Kwon, T., Sellier-Leclerc, A. L., Salomon, R., Harambat, J., Launay, E. A., Decramer, S., Ulinski, T., Allain-Launay, E., Roussey, G., Hogan, J., Pietrement, C., Novo, R., & Niaudet, P. (2023). Efficacy and safety of eculizumab in pediatric patients affected by Shiga toxin–related hemolytic and uremic syndrome: A randomized, placebo-controlled trial. Journal of the American Society of Nephrology, 34(9), 1561–1573. https://doi.org/10.1681/asn.0000000000000182

Hiriart, Y., Lapeyraque, A. L., Clermont, M. J., Maranda, B., & Phan, V. (2024). A phase I study to evaluate the safety, tolerance and pharmacokinetics of anti-Shiga toxin hyperimmune equine $F(ab')_2$ fragments in healthy volunteers. British Journal of Clinical Pharmacology, 90(4), 1142–1151. https://doi.org/10.1111/bcp.15999

Imdad, A., Mackoff, S. P., Ur Rehman, M., & Tanner-Smith, E. E. (2021). Interventions for preventing diarrhoea-associated haemolytic uraemic syndrome. Cochrane Database of Systematic Reviews, 7, Article CD012997. https://doi.org/10.1002/14651858.CD012997.pub2

Liu, Y., Li, X., & Wang, J. (2022). Diagnosis and treatment for Shiga toxin-producing Escherichia coli associated hemolytic uremic syndrome. Toxins, 15(1), Article 10. https://doi.org/10.3390/toxins15010010

Maximiano, C., Fernandes, M., & Stone, R. (2021). Genetic atypical hemolytic uremic syndrome in children: A 20-year experience from a tertiary center. Brazilian Journal of Nephrology, 43(3), 311–317. https://doi.org/10.1590/2175-8239-JBN-2020-0199

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., McGuinness, L. A., Stewart, L. A., Thomas, J., Tricco, A. C., Welch, V. A., Whiting, P., & Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ, 372, Article n71. https://doi.org/10.1136/bmj.n71

Revista ARACÊ
ISSN: 2358-2472

Palma, L. M. P. (2023). We still need to talk about hemolytic uremic syndrome: Early recognition is key. Brazilian Journal of Nephrology, 45(1), 5–7. https://doi.org/10.1590/2175-8239-JBN-2023-E003en

Spagnol, R., Menezes, L. F., & Koch, V. H. (2025). Eculizumab in severe pediatric STEC HUS and its impact on neurological prognosis—A systematic review and meta-analysis. European Journal of Pediatrics, 184(5), 331. https://doi.org/10.1007/s00431-025-06160-2

Tavasoli, A., Tabatabaei, S. A., & Esmaeili, M. (2021). Frequency of neurological involvement in patients with/without diarrhea hemolytic uremic syndrome: A systematic review and meta-analysis. Medical Journal of the Islamic Republic of Iran, 35, Article 91. https://doi.org/10.47176/mjiri.35.91

Vaisbich, M. H., Palma, L. M. P., & Koch, V. H. (2025). Recommendations for the diagnosis and treatment of atypical hemolytic-uremic syndrome (aHUS): A consensus statement from the Committee of Rare Diseases of the Brazilian Society of Nephrology (COMDORA-SBN). Brazilian Journal of Nephrology, 47(2), Article e20240087. https://doi.org/10.1590/2175-8239-JBN-2024-0087pt

Vilardouro, A. S., Watanabe, A., & Santos, B. F. (2022). Hemolytic-uremic syndrome: 24 years of experience from a pediatric nephrology unit. Brazilian Journal of Nephrology, 45(1), 51–59. https://doi.org/10.1590/2175-8239-JBN-2021-0206