Arch Pediatr Urug 2025; 96(1): e302
doi: 10.31134/AP.96.6

Arcanobacterium haemolyticum infection in pediatrics. Case report

Infección por *Arcanobacterium haemolyticum* en pediatría. Reporte de caso

Infecção por *Arcanobacterium haemolyticum* em pediatria. Relato de caso

Emilia Alonso[1], Eduardo Rompani[2], Adriana Varela[3], Catalina Pírez[4]

Abstract

Arcanobacterium haemolyticum is an agent that causes pharyngitis and rash, especially in adolescents. The maximum incidence occurs between 15 and 18 years of age, and it is suggested to consider this microorganism in the diagnosis of young adults with rash. The typical presentation includes odynophagia, fever, and skin rash, being similar to streptococcal pharyngitis. It can cause invasive infection in both immunocompetent and immunocompromised individuals, particularly in those with diabetes mellitus and malignancies with skin and soft tissue infection. The difficulty in its diagnosis is due to slow growth in cultures, with modern methods such as mass spectrometry facilitating identification. We present the clinical case of a healthy 14-year-old adolescent with odynophagia, headache, asthenia, and skin rash, whose pharyngeal culture revealed *A. haemolyticum* sensitive to penicillin and erythromycin. After treatment, there was improvement within 24 hours. The importance of considering this microorganism in the differential diagnosis of pharyngitis and rash is emphasized, highlighting the lack of case reports. We conclude by highlighting the need for a high level of suspicion to address infections that could go unnoticed and, therefore, avoid complications.

Keywords: Arcanobacterium
Pharyngitis
Rash
Adolescent

1. Médico Pediatra. Asist. Clínica Pediátrica. Unidad Académica "A". Diplomatura Infectología Pediátrica. Facultad de Medicina. UDELAR. Pediatra. Hospital Británico.
2. Médico Pediatra. Hospital Británico.
3. Médico Microbiólogo. Coordinadora Área Microbiología. Hospital Británico.
4. Médico Pediatra. Prof. Clínica Pediátrica. Unidad Académica "A". Diplomatura Infectología Pediátrica. Facultad de Medicina. UDELAR. Directora Depto. Pediatría. Hospital Británico.
Hospital Británico.
Unpublished work.
We declare that we have no conflicts of interest.
This work has been unanimously approved by the Editorial Committee.

Received on: February 10, 2024.
Approved on: June 25, 2024.

Resumen

Arcanobacterium haemolyticum es un agente que causa faringitis y exantema, especialmente en adolescentes. La incidencia máxima se da entre los 15 y 18 años, y se sugiere considerar este microorganismo en el diagnóstico de adultos jóvenes con exantema. La presentación típica incluye odinofagia, fiebre y erupción cutánea, siendo similar a la faringitis estreptocócica. Puede causar infección invasiva tanto en individuos inmunocompetentes como inmunodeprimidos, particularmente en aquellos con diabetes mellitus y neoplasias malignas que presentan infección de la piel y los tejidos blandos. Se destaca la dificultad en el diagnóstico debido al crecimiento lento en cultivos, con métodos modernos como la espectrometría de masas facilitando la identificación. Se presenta el caso clínico de un adolescente de 14 años, sano, con odinofagia, cefalea, astenia y erupción cutánea, cuyo cultivo faríngeo reveló *A. haemolyticum* sensible a penicilina y eritromicina. Tras el tratamiento, hubo mejoría en 24 horas. Se enfatiza en la importancia de considerar este microorganismo en el diagnóstico diferencial de faringitis y exantema, resaltando la escasez de reportes de casos. Se concluye destacando la necesidad de un alto índice de sospecha para abordar infecciones que podrían pasar desapercibidas y evitar complicaciones.

Palabras claves: Arcanobacterium
Faringitis
Exantema
Adolescente

Resumo

Arcanobacterium haemolyticum é um agente causador de faringite e erupção cutânea, principalmente em adolescentes. A incidência máxima ocorre entre 15 e 18 anos, sendo sugerido considerar esse microrganismo no diagnóstico de adultos jovens com exantema. A apresentação típica inclui odinofagia, febre e erupção cutânea, sendo semelhante à faringite estreptocócica. Pode causar infecção invasiva em indivíduos imunocompetentes e imunocomprometidos, particularmente naqueles com diabetes mellitus e doenças malignas que se apresentam com infecção de pele e tecidos moles. A dificuldade no diagnóstico é destacada devido ao lento crescimento das culturas, com métodos modernos como a espectrometria de massa facilitando a identificação. É apresentado o caso clínico de um adolescente hígido de 14 anos com odinofagia, cefaleia, astenia e rash cutâneo, cuja cultura faríngea revelou *A. haemolyticum* sensível à penicilina e eritromicina. Após o tratamento, houve melhora em 24 horas. Ressalta-se a importância de considerar esse microrganismo no diagnóstico diferencial de faringite e exantema, destacando a escassez de relatos de casos. Concluímos destacar a necessidade de um alto índice de suspeição para abordar infecções que poderiam passar despercebidas e evitar complicações.

Palavras chave: Arcanobacterium
Faringite
Erupção Cutânea
Adolescente

Introduction

Arcanobacterium haemolyticum (*A. haemolyticum*) is a non-spore-forming, aerobic, gram-positive bacillus that causes pharyngitis and rash in children and young adults[1,2]. The highest incidence is reported between the ages of 15 and 18, reaching up to 2.5%[2-4].

Among the reported pharyngitis series, a slight predominance in females has been observed, whereas systemic infections caused by *A. haemolyticum* show a tendency toward males[3]. No seasonal prevalence has been reported[1].

The typical form of presentation is odynophagia, fever, and rash, often indistinguishable from that caused by group A streptococci[1-5]. Exceptionally, it can cause invasive systemic infections, mainly endocarditis, osteomyelitis, meningitis, and pneumonia. These occur mainly in adults with comorbidities such as diabetes and other immunocompromising conditions, although there are descriptions in healthy hosts[1,6].

Regarding microbiological diagnosis, its slow growth may lead to it being overlooked in cultures, but its detection does not require special processing of the sample. Current bacterial identification methods, such as mass spectrometry, have facilitated their identification[1,3,7].

For treatment, both penicillin and erythromycin are effective. The prognosis in cases of *A. haemolyticum* pharyngitis is good, even in untreated patients[1].

There are no reports of clinical cases of infection by this microorganism in Uruguay.

We present the case of a previously healthy adolescent with the typical clinical manifestations of *A. haemolyticum* infection, intending to raise awareness of this etiology within the scientific community.

Clinical case

A 14-year-old adolescent, previously healthy, and up-to-date vaccinations, presented to the pediatric outpatient clinic with a 72-hour history of odynophagia, without fever. He also reported mild headache and asthenia. Pruritic skin lesions appeared on his limbs. No other respiratory symptoms were present. On physical examination, the patient was alert, responsive, and in good general condition. Hemodynamically stable and afebrile. Skin lesions were observed on the upper limbs over both elbow joints and the lower limbs, involving the dorsum and soles of both feet. The lesions were macular, erythematous, with well-defined borders, and pruritic (Figure 1). No enanthem was observed. The pharynx appeared congested (Figure 2). Painful cervical lymphadenopathy was present, but not palpable in other areas. The rest of the physical examination was unremarkable.

A rapid antigen detection test for *S. pyogenes* was performed, which was negative. Empirical treatment with oral clindamycin was initiated pending the results of the pharyngeal culture.

The throat swab culture yielded *A. haemolyticum* after 48 hours of incubation. The isolate was susceptible to penicillin and erythromycin. Microorganism identification was performed using mass spectrometry (VITEK® MS Maldi-Tof), and antimicrobial susceptibility was determined using a gradient strip (E-test).

At the 24-hour follow-up after starting treatment, the patient showed improvement in the skin lesions, no signs of pharyngitis were observed, and remained with no fever. Treatment was changed to amoxicillin, completing a total of 10 days with good clinical progress.

Discussion

A. haemolyticum was first identified as Corynebacterium haemolyticum in 1946 in pharyngeal cultures from World War II soldiers and Pacific Islanders with pharyngitis, which was clinically indistinguishable from infection caused by group A streptococci[3]. Since 1982, it has been reclassified into the new genus Arcanobacterium, with *A. haemolyticum* as a single species[8].

Figure 1. 14-year-old adolescent, pharyngitis and rash due to *A. haemolyticum*. Macular rash on the foot and forearm.

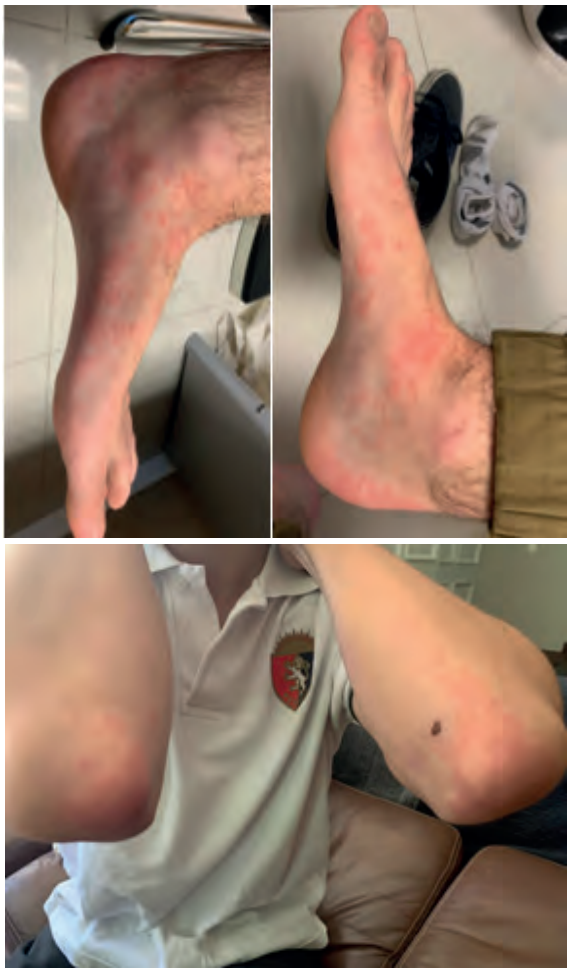
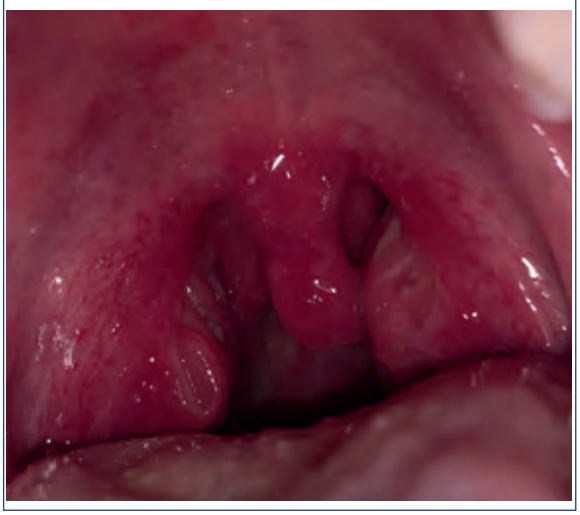


Figure 2. 14-year-old adolescent, pharyngitis and rash due to *A. haemolyticum*. Congestive pharynx.



Recently, it has been in creasingly associated with pharyngitis and rash[3]. Although, so far, there are no reports of cases with this clinical presentation in the pediatric population.

Pharyngitis is the most common finding in *A. haemolyticum* infection, presenting with odynophagia and fever[1]. Pharyngeal erythema is universally present and tonsillar exudate is common and occurs in up to 70% of cases. Lymphadenopathy occurs in 26% to 81% of reported patients, mainly affecting the anterior cervical or submandibular lymph nodes bilaterally[3]. These symptoms, described as typical of the disease by *A. haemolyticum*, are those presented by the patient, without being able to clinically rule out other etiologies.

Generally, in up to 75% of cases, a skin rash appears 1 to 4 days after the onset of odynophagia[3,6]. This rash is toxin-mediated, similar to what happens in infections caused by group A streptococci[1]. It is a scarlatiniform rash that begins in the distal extremities and then spreads centrally to the trunk and neck, most frequently affecting the extensor surfaces. It affects the face, palms, and soles. In 50% of cases, it is associated with pruritus. Urticaria and erythema multiforme have also been described. The rash persists between 2 and 5 days, and eventually, a slight desquamation of the skin on the hands and feet follows[3,6]. As evidenced in the images, the case we report included the rash, within the expected time frame, on extremities and affecting the extensor surfaces, further supporting this etiology.

This disease, typical of *A. haemolyticum*, is clinically indistinguishable from the one caused by group A streptococcus[1]. Findings such as circumoral pallor, Pastia'slines, and strawberry tongue are observed in scarlet fever but do not occur in *A. haemolyticum* infection[1,6]. Our patient did not present these differential signs of *Streptococcus pyogenes* (*S. pyogenes*), nor the typical rash distribution starting around the neck and extending to the trunk and extremities. However, due to its higher frequency, a differential diagnosis with this pathogen was considered, which led to performing a rapid streptococcal antigen detection test as an initial step. With the negative result, this etiology was quickly ruled out. It is worth noting that we found no reports of cross-reactivity in these tests with *A. haemolyticum*.

Sayad E et al, in their systematic review on the burden of *A. haemolyticum* pharyngitis, suggest a diagnostic and management algorithm based on a systematic approach with emphasis on medical history, patient age, absence of a viral prodrome, and a negative rapid *S. pyogenes* test as clues for diagnosis, highlighting the need in these cases for confirmatory culture[9].

Other common causes of pharyngitis and rash in adolescents and young adults are infections by *Mycoplasma pneumoniae*, *Neisseria gonorrhea*, and many other pathogens including viruses such as influenza or Epstein-Barr virus[1]. Viral etiology in this patient should have been considered because of the headache and asthenia as accompanying symptoms. Kawasaki disease, toxic shock syndrome, primary HIV infection, and secondary syphilis are other possible differential diagnoses[10]. In some cases, rash has been observed before the development of pharyngitis, which raises other diagnoses. Carlson et al. reported the clinical case of a 19-year-old patient who initially presented with skin rash, followed by pharyngitis and fever, which initially led to a diagnosis of an allergic reaction[10].

To confirm the diagnosis of *A. haemolyticum* infection, isolation of the microorganism is required from a throat culture, a skin lesion, or a sterile body site in the case of invasive infections[1]. However, this isolation presents certain challenges such as the fact that *A. haemolyticum* can be found in the pharynx and skin of healthy individuals as a commensal which significantly hinders the diagnosis, and identification of the microorganism must be supported by clinical suspicion[11]. Moreover, *A. haemolyticum* isolates from pharyngeal exudates can be mistaken for streptococci and *Corynebacterium diphtheriae*. It may also be isolated concomitantly with other bacteria, such as group A streptococci and other streptococcal species[3]. In addition, *A. haemolyticum* has slow hemolysis, between 48 and 72 hours, whereas streptococci undergo beta-hemolysis rapidly on sheep blood agar, within 24 hours, which often leads to plates being discarded before *A. haemolyticum* hemolysis occurs[6]. Thus, many infections may go undetected due to the slow growth and hemolysis in culture, especially if streptococcal antigen tests or nucleic acid amplification tests are performed without a supporting pharyngeal culture. Therefore, if an infection by this microorganism is suspected, particularly in an adolescent or young adult with pharyngitis and rash, a pharyngeal culture should be performed and it should be considered to inoculate media containing human or rabbit blood or use sheep blood agar for ≥72 hours, in order to identify the small hemolytic colonies of *A. haemolyticum*[3].

Accordingly, the Infectious Diseases Society of America (IDSA) currently recommends confirmatory bacterial testing in any case of pharyngitis, excluding those with an evident viral infection, due to the significant overlap in signs and symptoms between *S. pyoge-*

nes and other infectious organisms such as *A. haemolyticum*[12,13]. In our institution, all pharyngeal samples obtained from patients with clinical diagnosis of pharyngitis and negative rapid antigen detection tests for streptococcal antigens, are submitted for culture.

Gastón et al. reported three clinical cases of previously healthy 20-year-old patients who presented with pharyngitis and rash, with or without fever. Their cultures were negative for *S. pyogenes*, heterophile antibody tests for Epstein-Barr virus were negative, and *A. haemolyticum* was grown in the pharyngeal culture, with good recovery after antibiotic treatment with penicillin or erythromycin[13].

In the patient, *A. haemolyticum* was isolated given the identification of the microorganism using mass spectrometry available at our institution. Matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry, as well as 16S ribosomal RNA (rRNA) amplification techniques, gene sequencing, and denaturing high-performance liquid chromatography (DHPLC), are more specific identification methods that allow for confirming the diagnosis[3].

More rarely, *A. haemolyticum* can cause deep and systemic infections. Isolated cases have been described, including Lemierre's syndrome, brain abscess, meningitis, meningoencephalitis, orbital cellulitis, endocarditis, osteomyelitis, septic arthritis, deep soft tissue infections, empyema, cavitary pneumonia, pyothorax, sinusitis, bacteremia, and sepsis[1,6]. In 2009, Fernandez-Suarez et al. reported the first case of Lemierre's syndrome caused solely by *A. haemolyticum*. It involved a previously healthy 23-year-old man with acute pharyngotonsillitis and subsequently developed Lemierre's syndrome[14]. Most of these serious infections occur in adults and are frequently associated with previous soft tissue infections, post-traumatic wound infections, or underlying conditions such as diabetes, peripheral vasculopathy, neoplasms, immunosuppression, or intravenous drug use[1,6]. However, Gu et al. described a clinical case of a soft tissue infection in an immunocompetent 7-year-old child, highlighting that the ability of this pathogen to cause more severe infections in otherwise healthy hosts should not be underestimated[15]. In the systematic review by Sayad et al., at least 11 complications were reported among 191 previously healthy young patients, including peritonsillar abscesses, Lemierre's syndrome, pneumonia, sepsis, and meningitis[9]. Therefore, while invasive *A. haemolyticum* disease typically occurs in immunocompromised hosts, immunocompetent individuals can also develop severe illness.

Regarding treatment, there are practically no recommendations due to the small number of reported cases and scarse clinical experience[11]. According to the literature, *A. haemolyticum* is susceptible not only to penicillin and erythromycin, but also to other β-lactams, clindamycin, chloramphenicol, azithromycin, vancomycin, ciprofloxacin, tetracyclines, and rifampicin. In contrast, most strains are resistant to sulfonamides and trimethoprim-sulfamethoxazole[1]. Some authors have reported the existence of *in vitro* penicillin-tolerant strains[14-16]. Therefore, erythromycin has been suggested as first-line treatment for pharyngitis caused by this pathogen, considering that although almost all *A. haemolyticum* strains are highly susceptible to erythromycin, it is not bactericidal[1]. In this case, although *A. haemolyticum* was sensitive to clindamycin, treatment was adjusted to an aminopenicillin, with good clinical outcome and no evidence of the previously described tolerance to this class of antimicrobials.

Neither the benefit of antimicrobial therapy for *A. haemolyticum* pharyngitis nor the comparative efficacy of therapeutic agents has been established in prospective randomized clinical trials. No recognized post-infectious complications have been associated with *A. haemolyticum* pharyngitis[17].

In relation to deep infections and sepsis, the few references available suggest treating with high-dose intravenous penicillin as the first choice, with or without gentamicin. Alternatively, penicillin can be used in combination with an aminoglycoside[6]. In any case, the treatment of systemic infections should be adjusted according to the antibiotic susceptibility profile and the site of infection[17].

Long-term sequelae of *A. haemolyticum* infection have rarely been reported. Persistent infection due to delayed recognition of the organism as the causative agent may lead to increased morbidity and mortality, especially in patients with comorbidities[6].

Conclusions

In conclusion, the clinical case presented highlights the importance of considering *A. haemolyticum* as a causative agent of pharyngitis and rash, especially in adolescents and young adults. This microorganism, often overlooked due to its similarity to other pathogens, can cause symptoms that mimic streptococcal pharyngitis. In addition, *A. haemolyticum* has been observed to cause severe and systemic infections in rare cases. Therefore, a high index of suspicion is required for timely diagnosis.

Bibliographic references

1. Ching N. Arcanobacterium haemolyticum. En: Cherry J, Harrison G, Kaplan S, Steinbach W, Hotez P. Feigin and Cherry's textbook of pediatric infectious diseases. 8 ed. Philadelphia: Elsevier, 2019:946-50.
2. Tanz R. Faringitis aguda. En: Kliegman R, Stanton B, St. Geme J, Schor N, eds. Nelson tratado de pediatría. 20 ed. Barcelona: Elsevier, 2015:2113-7.
3. Norton L, Bratcher D. Arcanobacterium haemolyticum. En: Long S, ed. Principles and practice of pediatric infectious diseases. 6 ed. Philadelphia: Elsevier, 2023:784-6.
4. Mackenzie A, Fuite L, Chan F, King J, Allen U, MacDonald N, et al. Incidence and pathogenicity of Arcanobacterium haemolyticum during a 2-year study in Ottawa. Clin Infect Dis 1995; 21(1):177-81. doi: 10.1093/clinids/21.1.177.
5. Karpathios T, Drakonaki S, Zervoudaki A, Coupari G, Fretzayas A, Kremastinos J, et al. Arcanobacterium haemolyticum in children with presumed streptococcal pharyngotonsillitis or scarlet fever. J Pediatr 1992; 121(5 Pt 1):735-7. doi: 10.1016/s0022-3476(05)81903-1.
6. Vu M, Rajnik M. Arcanobacterium haemolyticum Infections. En: Stat Pearls. Treasure Island (FL): StatPearls Publishing, 2024. Disponible en: https://www.ncbi.nlm.nih.gov/books/NBK560927/. [Consulta: 9 enero 2024]
7. Balıkcı A, Topkaya A, Belaş Z. A frequently overlooked bacteria in clinical microbiology laboratories: Arcanobacterium haemolyticum. Mikrobiyol Bul 2011; 45(3):535-40.
8. Collins M, Jones D, Schofield G. Reclassification of 'Corynebacterium haemolyticum' (MacLean, Liebow & Rosenberg) in the genus Arcanobacterium gen.nov. as Arcanobacterium haemolyticum nom.rev., comb.nov. J Gen Microbiol 1982; 128(6):1279-81. doi: 10.1099/00221287-128-6-1279.
9. Sayad E, Zeid C, Hajjar R, Cabrera N, Radi Abou Jaoudeh R, Malek A. The burden of Arcanobacterium haemolyticum pharyngitis: a systematic review and management algorithm. Int J Pediatr Otorhinolaryngol 2021; 146:110759. doi: 10.1016/j. ijporl.2021.110759.
10. Carlson P, Seppänen M, Tarvainen K, Nousiainen T, Aaltonen T, Malinen H. Pharyngitis and exanthema caused by Arcanobacterium haemolyticum. Acta Derm Venereol 2001; 81(2):143-4. doi: 10.1080/00015550152384344.
11. Puerto J, García P, Girón J. Infecciones por Arcanobacterium haemolyticum: un patógeno emergente. An Med Interna (Madrid) 2002; 19(9):473-6.
12. Shulman S, Bisno A, Clegg H, Gerber M, Kaplan E, Lee G, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis 2012; 55(10):1279-82. doi: 10.1093/cid/cis847.
13. Gaston D, Zurowski S. Arcanobacterium haemolyticum pharyngitis and exanthem. Three case reports and literature review. Arch Dermatol 1996; 132(1):61-4.
14. Fernández A, Aguilar J, López A, Díaz J. Lemierre's syndrome and septicaemia caused solely by Arcanobacterium haemolyticum in a young immunocompetent patient. J Med Microbiol 2009; 58(Pt 12):1645-8. doi: 10.1099/jmm.0.007492-0.
15. Gu Y, Millan G, Sebaratnam D. Arcanobacterium haemolyticum- Infection in an Immunocompetent Child. Pediatr Infect Dis J 2024; 43(1):e28-9. doi: 10.1097/INF.0000000000004147.
16. Nyman M, Banck G, Thore M. Penicillin tolerance in Arcanobacterium haemolyticum. J Infect Dis 1990; 161(2):261-5. doi: 10.1093/infdis/161.2.261.
17. Carlson P, Korpela J, Walder M, Nyman M. Antimicrobial susceptibilities and biotypes of Arcanobacterium haemolyti-cum blood isolates. Eur J Clin Microbiol Infect Dis 1999; 18(12):915-7. doi: 10.1007/s100960050432.

Correspondence: Dra. Emilia Alonso
E-mail: emilia.alonso1@gmail.com

Data availability
The dataset supporting the results of this study is NOT available in open-access repositories.

Authors contribution
Emilia Alonso, Eduardo Rompani and Catalina Pírez: responsible for the conception, design, execution, analysis, drafting, critical review, and final approval of the manuscript, assuming responsibility for the content of the article.
Adriana Varela: drafting, critical review, and final approval, assuming responsibility for the content of the article.

Emilia Alonso, ORCID 0000-0002-7297-6884.
Eduardo Rompani, ORCID 0000-0002-0800-5880.
Adriana Varela, ORCID 0000-0001-8505-1154.
Catalina Pírez, ORCID 0000-0002-6165-0678.