International Journal of Research in Medical Sciences
Mosquera OAH et al. Int J Res Med Sci. 2026 Apr;14(4):1704-1708
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20260992

Review Article

Severe manifestations of *Streptococcus pyogenes*: a narrative review

Orestes André Hurtado-Mosquera[1]*, Nathalia Fernández-Gómez[2], Isabella Cardona-Santana[1], Sergio Andrés Romero-Seguro[1]

[1]Department of Medicine, Universidad CES, Medellín, Colombia
[2]Department of Health Sciences, Corporación Universitaria Remington, Medellín, Colombia

Received: 07 February 2026
Accepted: 11 March 2026

***Correspondence:**
Dr. Orestes André Hurtado Mosquera,
E-mail: orestes.hurtadom@gmail.com

ABSTRACT

Streptococcus pyogenes is a pathogen capable of causing a wide spectrum of diseases, ranging from mild infections to severe invasive conditions. This narrative review focused on two of its most serious manifestations: meningitis and streptococcal toxic shock syndrome (STSS). A systematic search was conducted in PubMed, Scopus and ScienceDirect for articles published in recent years in both English and Spanish. Studies addressing severe presentations in the pediatric population were included. *S. pyogenes* meningitis, although a rare disease, carries a high mortality rate (up to 75%) if not treated early. STSS, on the other hand, constitutes a medical emergency with variable mortality rates ranging from 5% to 56%, influenced by factors such as the EMM genotype and the expression of superantigens. Both conditions often present nonspecific symptoms, complicating initial diagnosis. Diagnostic and therapeutic delays can be decisive in unfavorable outcomes. Invasive forms of *S. pyogenes* infection require early suspicion, prompt intervention and aggressive clinical strategies to reduce mortality. Initial underestimation can be fatal; therefore, continuous medical education and active surveillance are essential.

Keywords: Meningitis, Streptococcal infections, Shock, Toxic

INTRODUCTION

Streptococcus pyogenes, also known as Group A Streptococcus (GAS), is a Gram-positive bacterium responsible for a wide range of infectious diseases in humans. These infections range from common, self-limited conditions such as pharyngitis and impetigo to severe, life-threatening invasive diseases. The term Streptococcus was originally introduced by the surgeon Theodor Billroth.[1,2] GAS infections may involve the skin, soft tissues, upper respiratory tract and, in severe cases, sterile sites such as blood, cerebrospinal fluid and deep tissues. In recent years, an increase in invasive GAS infections has been reported worldwide, particularly affecting pediatric populations and individuals at the extremes of age.[6,9] This rise has been associated with the emergence of more virulent strains, changes in host susceptibility and improved surveillance. Among invasive manifestations, meningitis and STSS represent two of the most severe and challenging clinical entities. GAS meningitis, although rare, is associated with high mortality and significant neurological sequelae.[3,8] STSS is an acute medical emergency characterized by rapid progression to shock and multiorgan failure, driven by bacterial toxins and an exaggerated host immune response. Both conditions often present with nonspecific symptoms, which may delay diagnosis and initiation of appropriate therapy.

The aim of this narrative review is to synthesize current evidence on the epidemiology, clinical presentation, pathophysiology and management of severe manifestations caused by *Streptococcus pyogenes*, with particular emphasis on meningitis and STSS in the pediatric population.

A narrative literature review was conducted using the PubMed, Scopus and ScienceDirect databases. The search

strategy included the following terms: "severe manifestations," "severe disease," or "critical illness" combined with "Streptococcus pyogenes" (Title/Abstract) and "children" or "infant." The last search was performed on 2nd February 2, 2026.

Articles published in recent years were considered eligible if they addressed severe or invasive manifestations of Streptococcus pyogenes infection. Publications written in English or Spanish were included. No exclusion criteria were applied regarding study design. Two authors independently screened the articles based on title and abstract. Studies deemed potentially relevant were subsequently reviewed in full text. Discrepancies in selection were resolved through discussion. Data extracted included epidemiological characteristics, clinical presentation, microbiological features, treatment strategies and clinical outcomes related to meningitis and STSS.

MICROBIOLOGICAL CHARACTERISTICS AND VIRULENCE FACTORS

Streptococcus pyogenes (*S. pyogenes*) has a characteristic structure with a peptidoglycan layer surrounding its cytoplasmic membrane. Morphologically, it consists of spherical cocci measuring between 1 and 2 µm in diameter, arranged in short chains. It is a non-motile, non-spore-forming, facultative anaerobic, catalase-negative bacterium capable of producing beta-hemolysis, which results in complete erythrocyte lysis and generates a characteristic yellow coloration on blood agar plates. The bacterial cell wall is composed primarily of chains of N-acetylglucosamine and rhamnose, which make up between 40% and 60% of its structure.[3]

S. pyogenes expresses a variety of structural and extracellular components, proteins and toxins that contribute to its virulence and pathogenicity, including M protein, streptolysin O and S, nicotinamide adenine dinucleotidase (NADase), streptokinase and several toxins classified as superantigens, such as streptococcal pyrogenic exotoxin A and B.[4] Transmission routes for *S. pyogenes* infection occur in approximately 50% of cases through the pharynx, mucous membranes, skin and vagina, however, in up to 50% of invasive disease cases, the portal of entry remains unknown.[5]

Clinical manifestations include pharyngitis, scarlet fever (as a common but not exclusive complication of pharyngitis), skin and soft tissue infections (both superficial and deep), post-infectious complications such as rheumatic fever, acute glomerulonephritis and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). Invasive *S. pyogenes* infections those in which the pathogen is isolated from a normally sterile site (blood, cerebrospinal fluid, synovial fluid, etc.) may lead to bacteremia, osteomyelitis, cellulitis, meningitis, necrotizing fasciitis and streptococcal toxic shock syndrome.[6,7]

Streptococcus pyogenes meningitis

Meningitis caused by *S. pyogenes* is a rare disease and its pathophysiology is still not fully understood. It is known that the virulence factors of this bacterium facilitate its dissemination and invasion within the host, particularly in immunocompromised individuals or those at the extremes of age, such as neonates and older adults.[3] Although *S. pyogenes* is not a leading cause of meningitis, it can occur at any age, with neonates being the most affected group, accounting for 50% of reported cases. In children, group A streptococcal meningitis may be associated with prior infections such as otitis media, sinusitis or mastoiditis, although in many cases a clear portal of entry is not identified.[8]

A study aimed at assessing the epidemiology of invasive *S. pyogenes* disease in the pediatric population across two regions of Spain (Catalonia and Gipuzkoa) over a 12 years period (2005–2016) identified seven cases of meningitis, all reported in Catalonia, with an incidence of 2.5–2.6 cases per 100,000 inhabitants among invasive infections caused by this pathogen. Most meningitis cases were associated with the emm1 type, a genetic subtype of the bacterium based on the emm gene encoding the M protein, known for causing more severe infections and higher lethality rates. The mortality rate associated with these infections reached 75% when antibiotics were not administered within the first 24 hours.[9]

Additionally, approximately 32% of patients develop severe neurological sequelae, including motor deficits, sensory impairment, epilepsy and sensorineural hearing loss. One clinically relevant but uncommon neurological complication is cranial nerve palsy. A case reported in Germany in 2000 described third cranial nerve palsy in an 11 years old girl with *S. pyogenes* meningitis. Furthermore, a para-infectious immune response manifesting as facial nerve palsy has been documented, with complete recovery following corticosteroid therapy.[10,11] In Spain, a multicenter prospective study conducted between 2019 and 2023 analyzed invasive group A streptococcal infections in children under 16 years of age.

The study found that meningitis caused by this microorganism is rare, representing less than 1–2% of invasive group A streptococcal (iGAS) infections. Among the 454 patients included, only 13 developed meningitis, corresponding to 2.3% of cases. An increase in incidence was observed beginning in October 2022.[8] Regarding clinical manifestations, the presentation is similar to bacterial meningitis of other etiologies. It commonly manifests as fever without a focus in infants and as headache and vomiting in preschool-aged children. Physical examination may reveal signs of meningeal irritation and cerebrospinal fluid analysis typically shows findings consistent with bacterial meningitis.[12] In a short case series and systematic review conducted in Beijing between 2010 and 2021, fever, vomiting and seizures were

reported as the most frequent manifestations, occurring in 84.2%, 41.4% and 35.7% of cases, respectively.[13] With respect to treatment, penicillin has classically been considered the drug of choice for GAS infections due to its good meningeal penetration and low resistance rates. Its bactericidal effect is enhanced when combined with clindamycin, given the latter's action on bacterial ribosomes. However, ceftriaxone is recognized as an effective alternative against the most prevalent pathogens causing community-acquired meningitis when GAS has not yet been isolated.[14] A study published by Perera et al which reviewed 25 cases reported in the literature, found that 84% were treated with penicillin monotherapy, while the remaining cases were managed with a third-generation cephalosporin alone or combined with ampicillin, yielding good outcomes. Among the 25 patients, only one death was reported.[15]

Streptococcal toxic shock syndrome

Toxic shock syndrome (TSS) is an acute and severe condition characterized by high fever, hypotension, diffuse rash and multiorgan dysfunction secondary to toxins produced by Staphylococcus aureus or group A streptococcus (most commonly S. pyogenes).[16] It was first described in 1978 following a case of S. aureus infection in children, later, in 1980, an epidemic associated with tampon use was reported. In 1987, a disease with similar features was identified but caused by invasive streptococci, leading to what is now known as streptococcal TSS.[5] Although the incidence of streptococcal TSS has not been fully elucidated, several studies have documented an increase in cases since the 1990s.[17] The incidence varies across regions and published reports.

A cohort study conducted in the United States between 1995 and 1999 described an annual incidence of invasive *S. pyogenes* infections of 3.5 cases per 100,000 inhabitants, with the highest rates occurring at the extremes of age (adults over 65 years and children under 2 years). Within these invasive infections, streptococcal TSS accounted for 6% of cases.[5] In Israel, a study published in 2002 reported an annual incidence of 0.25 cases per 100,000 persons, with a comparatively higher rate of 0.36 cases per 100,000 in children under 5 years of age. In other countries, the annual incidence also varies, ranging from 0.38 per 100,000 children in the United Kingdom to 0.53 per 100,000 in Australia.[18]

Regarding mortality, streptococcal TSS presents a wide range of fatality rates from 4.2% to 56%. In Ontario, Canada, one study reported a mortality rate as high as 81%, suggesting that the true burden may be even higher. In pediatric populations, however, reported mortality tends to range between 5% and 10%.[16,17,19] The main virulence factor of *S. pyogenes* is the M protein, whose characteristics vary depending on its precursor gene (EMM). Approximately 200 serotypes have been identified and some cases involve co-infection with more than one serotype. The emm1 and emm3 genotypes are the ones most commonly associated with streptococcal TSS.[18] Another important determinant in the development of streptococcal TSS is the presence of superantigens. These proteins induce an immune response not mediated through conventional antigen presentation, but rather through direct binding to major histocompatibility complex (MHC) class II molecules on antigen-presenting cells and to the variable region of the T-cell receptor.

Strains of *S. pyogenes may* express up to 11 different superantigens, among which streptococcal pyrogenic exotoxins are the most strongly associated with TSS.[16,20] Streptococcal TSS is thought to represent a cytokine storm triggered by the action of superantigens, resulting in activation of more than 20% of T cells and the release of mediators such as TNF-α and IL-6.

Additionally, M protein can be released into the bloodstream, where it binds to fibrinogen to form a complex that attaches to neutrophil integrins, activating these cells and promoting endothelial adhesion and degranulation, thereby amplifying systemic involvement.[16,21] From a clinical perspective, some authors describe streptococcal TSS as progressing through three phases. The first phase is characterized by fever, myalgias, headache, chills and occasionally nonspecific gastrointestinal symptoms such as nausea, vomiting and diarrhoea. The second phase involves systemic manifestations, including tachycardia, tachypnea, fever, abdominal pain and in some cases early signs of necrotizing fasciitis. The third phase corresponds to shock and clear evidence of multiorgan dysfunction and some patients may develop neurological manifestations such as confusion, agitation or coma.[22] In 2010, the centers for disease control and prevention (CDC) in the United States redefined the diagnostic criteria for streptococcal TSS based on clinical and laboratory findings, as shown in table 1.[18]

Regarding treatment, early initiation of fluid resuscitation and antibiotic therapy is essential. Similar to the management of undifferentiated shock, the therapeutic regimen often includes a third-generation cephalosporin combined with an agent active against staphylococci and streptococci, such as clindamycin or vancomycin. Clindamycin appears to be particularly effective because its antimicrobial action is not influenced by inoculum size, it inhibits protein synthesis independently of penicillin-binding proteins, it suppresses M protein and bacterial toxin production and it has a longer post-antibiotic effect than β-lactams.[16]

Nonetheless, clindamycin should not be used as sole empiric therapy, given that 1–2% of *S. pyogenes* strains exhibit resistance. Another adjunctive therapy is intravenous immunoglobulin (IVIG), due to its potential toxin-neutralizing properties, immunomodulatory effects and its ability to enhance the immune system's bactericidal activity.[18]

Table 1: Diagnostic criteria for streptococcal toxic shock syndrome (STSS).

Clinical criteria	Laboratory criteria
Hypotension: - Systolic blood pressure <5th percentile for age in patients <16 years - Systolic blood pressure <90 mmHg in patients ≥16 years Plus criterion 2. Evidence of multisystem involvement (two or more of the following): - Renal: Serum creatinine >2 times the upper limit of normal - Coagulopathy: Platelet count <100 × 10^6/L or disseminated intravascular coagulation - Hepatic: Bilirubin and/or transaminases >2 times the upper limit of normal - Respiratory: Acute respiratory distress syndrome - Skin: Generalized erythematous macular rash, may be followed by desquamation - Soft tissue necrosis: Necrotizing fasciitis, myositis or gangrene	Isolation of Group A Streptococcus (*Streptococcus pyogenes*)
Probable case: Meets clinical criteria in the absence of another identified etiology and with isolation of Group A Streptococcus from a non-sterile site. Confirmed case: Meets clinical criteria with isolation of Group A Streptococcus from a normally sterile site.	

Probable case: Meets the clinical criteria in the absence of another identified etiology for the clinical presentation and with isolation of Group A Streptococcus from a non-sterile site. Confirmed case: Meets the clinical criteria with isolation of Group A Streptococcus from a normally sterile site.[18]

DISCUSSION

Severe clinical manifestations associated with Streptococcus pyogenes, such as streptococcal toxic shock syndrome and meningitis, represent a significant clinical and public health challenge. Although most GAS infections are mild, a progressive increase in the incidence of invasive and severe forms has been documented in recent decades, with a considerable impact on morbidity and mortality.[13]

Retrospectively, these severe clinical presentations may be related to a combination of factors, including the emergence of more aggressive GAS strains and changes in population susceptibility, potentially involving a genetic predisposition. It is important to consider that, although these conditions are not highly prevalent, they are associated with a poor prognosis, particularly when diagnosis is delayed or initial management is ineffective, which may contribute to increased mortality.[23] Both conditions share an important clinical issue: they are often not suspected in the early stages of presentation. This may be related to their low reporting frequency, the overlap of symptoms with other differential diagnoses such as septic shock or meningitis of other etiologies or the lack of specific clinical markers to identify these entities. Delayed recognition and treatment can be fatal due to the rapid clinical deterioration seen in toxic shock syndrome and streptococcal meningitis. Over the past year, in our clinical experience, we encountered two cases of invasive GAS disease presenting as STSS and meningitis, both of which had a fatal outcome despite clinical suspicion and early initiation of treatment. This underscores the importance of improved clinical vigilance, early suspicion and increased clinician awareness regarding these severe manifestations, as well as the need to implement aggressive therapeutic interventions promptly, including targeted antibiotics and intensive hemodynamic support, to improve survival.

CONCLUSION

The severe forms of STSS and meningitis, although uncommon, represent a significant threat due to their high morbidity, mortality and rapid clinical progression. Current evidence shows an increasing trend in the incidence of these manifestations, possibly related to the emergence of more virulent strains. Early diagnosis is hindered by the nonspecific nature of initial symptoms and their resemblance to other conditions. It is essential to promote a high index of clinical suspicion in compatible scenarios and to optimize early therapeutic management through the combined use of antibiotics and intensive

supportive measures. Epidemiological surveillance and continuous medical education remain fundamental pillars to improve clinical outcomes in these patients.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Al-Akel FC, Chiperi LE, Eszter VK, Bacârea A. Streptococcus salivarius role as a probiotic in children's health and disease prophylaxis: a systematic review. Life (Basel). 2024;14(12):1613.
2. Etymologia: Streptococcus. Emerg Infect Dis. 2016;22(11):1977.
3. De Almeida Torres RSL, Fedalto LE, De Almeida Torres RF, Steer AC, Smeesters PR. Group A Streptococcus meningitis in children. Pediatr Infect Dis J. 2013;32(2):110–4.
4. Santiago AD, Moral SD, Pascual IP. Infecciones por estreptococo. Med Clin (Barc). 2022;13(50):2901–8.
5. Chuang YY, Huang YC, Lin TY. Toxic shock syndrome in children. Paediatr Drugs. 2005;7(1):11–25.
6. Doern CD. Group A Streptococcus (Streptococcus pyogenes): the most interesting pathogen in the world. Clin Microbiol Newsl. 2023;45(5):39–46.
7. Multicenter study on invasive Streptococcus pyogenes infections in children in Argentina. Arch Argent Pediatr. 2016;114(3):199–206.
8. Cobo-Vázquez E, Aguilera-Alonso D, Rello-Saltor V, Gamell A, Mellado-Sola I, Oltra-Benavent M, et al. Central nervous system infection by Group A Streptococcus in children in Spain (2019–2023). Pediatr Infect Dis J. 2024;43(10):368–74.
9. Sánchez-Encinales V, Ludwig G, Tamayo E, García-Arenzana JM, Muñoz-Almagro C, Montes M. Molecular characterization of Streptococcus pyogenes causing invasive disease in pediatric population in Spain: a 12-year study. Pediatr Infect Dis J. 2019;38(12):1168–72.
10. Steppberger K, Adams I, Deutscher J, Müller H, Kiess W. Meningitis in a girl with recurrent otitis media caused by Streptococcus pyogenes. Infection. 2001;29(5):286–8.
11. Kaddoura R, Abdalbari K, Kadom M, Badla BA, Hijleh AA, Hanifa M, et al. Post-meningitic syndrome: pathophysiology and consequences of streptococcal infections on the central nervous system. Int J Mol Sci. 2024;25(20):11053.
12. Ballesteros Moya E, Herrera Castillo L, Escosa García L, Romero González MP, Lázaro Perona F, José Gómez MID. Meningitis bacteriana por Streptococcus pyogenes: revisión de la literatura. Pediatr Aten Primaria. 2013;15(60):173–6.
13. Dou ZZ, Li W, Hu HL, Guo X, Hu B, Chen TM, et al. Group A streptococcal meningitis in children: a short case series and systematic review. Eur J Clin Microbiol Infect Dis. 2024;43(8):1517–31.
14. Meningitis caused by Streptococcus pyogenes: pediatric case report. Arch Argent Pediatr. 2020;118(3):309–13.
15. Perera N, Abulhoul L, Green M, Swann R. Group A streptococcal meningitis: case report and review of the literature. J Infect. 2005;51(2):1–4.
16. Silvestre C, Vyas H. Toxic shock syndrome: diagnosis and management. Paediatr Child Health. 2022;32(6):226–8.
17. Cook A, Janse S, Watson JR, Erdem G. Manifestations of toxic shock syndrome in children, Columbus, Ohio, USA, 2010–2017. Emerg Infect Dis. 2020;26(6):58.
18. Giang V, McMullan B. Treatment of toxic shock in children. Arch Dis Child Educ Pract Ed. 2025;110(2):64–9.
19. Davies HD, Simor AE. Invasive Group A streptococcal infections in Ontario, Canada. N Engl J Med. 1996;335(8):547–54.
20. Lynskey NN, Lawrenson RA, Sriskandan S. New understandings in Streptococcus pyogenes. Curr Opin Infect Dis. 2011;24(3):196–202.
21. Low DE. Toxic shock syndrome. Crit Care Clin. 2013;29(3):651–75.
22. Kempsell-Smith M, Fitzsimons C. Managing the deteriorating child with suspected Group A Streptococcus infection. Nurs Child Young People. 2023;35(6):35–42.
23. Waddington CS, Snelling TL, Carapetis JR. Management of invasive group A streptococcal infections. J Infect. 2014;69(1):63–9.

Cite this article as: Mosquera OAH, Gómez NF, Santana IC, Seguro SAR. Severe manifestations of *Streptococcus pyogenes*: a narrative review. Int J Res Med Sci 2026;14:1704-8.