







# Оригінальні дослідження / Original Researches

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# Analysis of cases of severe streptococcal infection in children and adults in Khmelnytskyi region

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Abstract. Background. Group A beta-hemolytic streptococcus (Streptococcus pyogenes) is a widespread bacterial pathogen that can cause many clinical variants of diseases in humans and be a trigger factor for the development of various autoimmune conditions. The purpose of the study was to show the current state of infection caused by group A beta-hemolytic streptococcus in adults and children using case studies. Materials and methods. The article describes 5 cases of streptococcal infection caused by Str.pyogenes with different clinical symptoms. The streptococcal etiology was confirmed by bacteriological method, the levels of ASLO antibodies were evaluated by biochemical method, clinical and biochemical studies were performed to determine markers of organ dysfunction. Results. The paper presents cases of severe streptococcal infection, which occurred in the form of phlegmon (single or multiple), multiple fasciitis of various localizations, development of destructive pneumonia, which was complicated by pneumothorax and pyopneumothorax, streptococcal septic shock, as well as epidermolysis syndrome ("scalded skin" syndrome). Conclusions. There has been a significant increase in the incidence of diseases caused by group A beta-hemolytic streptococcus. This outbreak is characterized by a severe course of infection with the development of various clinical forms with skin and soft tissue damage, destructive pneumonia, and septicemia. All cases are caused by antibiotic-resistant strains.

**Keywords:** children; adults; streptococcal infection; group A beta-hemolytic streptococcus; laboratory diagnosis; clinical forms

#### Introduction

Group A beta-hemolytic streptococcus (*Streptococcus pyogenes*) is a globally distributed and adapted bacterial pathogen that has developed a whole arsenal of evasion strategies to overcome the mechanisms of immune sanitation of the human body [7]. This pathogen can cause a variety of clinical variants of diseases from mild inflammatory processes in the throat (pharyngitis, sore throat) to severe generalized forms of infections with manifestations of septic shock [19, 21]. The group of streptococcal infections includes scarlet fever, which is a classic streptococcal infection, erysipelas, acute glomerulonephritis, and osteomyelitis. The role of streptococcus has been recognized in the development of rheumatism, infective endocarditis, myocarditis, and autoimmune processes [17].

Pyogenic streptococcus is characterized by the production of certain virulence factors, such as streptolysin-O, superantigens, bacterial wall proteins, including M-protein, fibronectin, and capsular polysaccharide, which is bound to hyaluronic acid [4, 17]. Epidemiologically, group A streptococci are categorized into 220 types, each of which is determined by the sequence of amino acids in the C-terminal region of the M-protein that determines the degree of virulence of the bacteria. Types 1 (18.3 %), 12 (11.1 %), 28 (8.5 %), 3 (6.9 %), and 4 (6.9 %) are responsible for 40 % of cases of streptococcal infection [19]. In the pathogenesis of the infection, an important role is played by the activation of T lymphocytes by streptococci superantigens, which is a trigger for the massive release of proinflammatory cytokines, in particular interferon-gamma, interkeukin 1, tumor

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necrosis factor  $\alpha$  [7]. The overproduction of these cytokines causes severe tissue and organ effects, the development of shock, and depends on the expression of the Spea 1-Spea 3, *emm* 1 genes [13, 20]. One of the features of streptococcal strains is the ability to form biofilms [2]. Many strains of *Str. pyogenes* are coated with a polysaccharide capsule, which is known to contribute to the development of severe infections. The hyaluronic acid capsule of *Streptococcus pyogenes* prevents neutrophil-mediated clearance *in vivo* and is a key factor in the virulence of *Str.pyogenes* [7].

An increase in lung infection with invasive streptococcus after the development of seasonal influenza (pulmonary invasive group A streptococcal (PiGAS) infections), initially diagnosed in children, has also caused complications in adult patients. For example, Shihui Hou and colleagues (2023) noted the development of streptococcal nephritis and myocarditis, which had specific manifestations in the form of cardiorenal syndrome with symptoms of edema, hematuria, proteinuria, elevated levels of antibodies to streptolysin-O (ASLO), decreased levels of complement and corresponding manifestations in kidney biopsy [18]. The frequent development of glomerulonephritis after a streptococcal infection in children is indicated by Kate A. Worthing et al. (2019) [10] and Anjali A. Satoscar et al. (2020) [2]. Nobuo Okahashi and colleagues (2022) indicate that Str.pyogenes infection during seasonal influenza is often associated with pneumonia, septicemia, and the development of necrotizing fasciitis [14]. Zehra Nihan Coşkun and co-authors (2023) point to the frequent development of toxic shock syndrome, which resembles septic shock in clinical picture, frequent detection of Streptococcus pyogenes cultures in the pleural fluid of such patients, and initial antibiotic therapy with vancomycin, ceftriaxone, clindamycin [3, 22]. In the original study by Johannes Forster and colleagues (2024). Str.pyogenes was isolated in 20 % of children with pleural effusion and pleural empyema, and it should be noted that antibiotic regimens included aminopenicillins, macrolides, cefuroxime both in monotherapy and in combination with aminoglycosides when patients were in the Department of Anesthesiology and Intensive Care [8]. ASLO can be considered a marker of

patients' sensitization to streptococcus, the beginning of an increase in levels of which is observed by the end of the first week, reaches a maximum in 3–5 weeks and is maintained for up to 6 months [1].

**The purpose** of the study was to show the current state of streptococcal infection caused by group A beta-hemolytic streptococcus in adults and children using case studies.

## Materials and methods

The clinical picture and laboratory parameters were analyzed in the patients admitted for treatment to the emergency department, the department of anesthesiology of Khmelnytsky Regional Hospital and the department of anesthesiology and intensive care of the Khmelnytsky City Children's Hospital during 2023 and 6 months of 2024, in which the streptococcal etiology of the disease, namely *Str. pyogenes*, was verified. There were 7 pediatric patients and 10 adults. Their distribution by age is shown in Table 1.

Table 1 shows that among children with streptococcal infection, patients aged 6–14 years predominated, while among adults, those aged 30–50. No gender difference was found.

All patients underwent clinical blood and urine tests, an extended blood chemistry test to determine lactate, detect markers of organ dysfunction, bacteriological tests of the skin, mucous membranes, blood, urine, pharynx, gastrointestinal tract, cerebrospinal fluid (if necessary), and an immunochromatographic test to determine serum procalcitonin.

Group A beta-hemolytic streptococcus (*Str.pyogenes*) was isolated from all patients. Among them, it was identified by bacteriological method in 12 cases, and 5 patients had high ASLO values (from 400 to 1200 U/ml with an acceptable value of 150 U/ml). In 52.8 % of cases, *Str.pyogenes* was antibiotic-resistant, retaining only sensitivity to glycopeptides, rifampicin and oxazolidinones. In rare cases, resistance to glycopeptides was also observed.

## **Results**

The clinical picture of streptococcal infection caused by *Str.pyogenes* was characterized by an acute onset in all age groups. Patients reported hyperthermia, sore throat when

Table 1. Age distribution of patients with streptococcal infection							
Age (years old)	Adults	Children	Female	Male			
0–1		1	0	1			
2–5		1	1	0			
6–14		4*	1	3			
15–18		1	1	0			
19–29	1		0	1			
30–40	2		1	1			
41–50	3		1	3			
51–60	1		1	0			
61–70	1		1	0			
71–80	1		1	0			
Total	10	7	8	9			

Table 1. Age distribution of patients with streptococcal infection

Note: \* — probability of difference in the frequency of streptococcal infection in children aged 6–14 and other age groups (p < 0.05).

swallowing, arthralgias and myalgias, and general weakness. At the initial examination, catarrhal phenomena in the form of pharyngitis and tonsillopharyngitis were noted in 85.0 % of the patients. A patchy papular rash resembling a scarlet fever was detected from the first day of the disease in 2 pediatric patients, and from the third day in 3 adult patients. Pleuropneumonia was diagnosed in 7 pediatric patients and 10 adult patients, carditis — in 3 adults and 3 children, nephritis — in 4 adult patients, and 5 children had acute renal failure. Renal replacement therapy was required in 2 adult patients, and 4 pediatric and 4 adult patients were on mechanical ventilation. In 5 (71.4 %) children and 4 (40 %) adults, streptococcal sepsis occurred, according to the criteria of the Sepsis-3 Consensus (2016) [12]. Bullous changes in the skin, peeling of the palms and soles with epithelial desquamation were noted in 5 children and 6 adults. Multiple soft tissue phlegmon requiring surgical treatment was diagnosed in 5 adult patients and 2 children in this sample, multiple fasciitis and epidermolysis — in 2 children, and a widespread form of erysipelas in the other 2 children. The data are presented in Table 2.

In the clinical picture of patients with severe streptococcal infection, destructive pleuropneumonia most often occurred, accompanied by fever and combined with soft tissue necrosis, multiple phlegmon or fasciitis, which required careful noninvasive monitoring (ultrasound, radiography, computed tomography). Fig. 1 shows a destructive pneumonia with pneumothorax that developed on an outpatient basis in an 8-year-old child on the third day after the onset of the disease, and was verified upon admission to the pediatric hospital. The child was on a ventilator.

A widespread form of lower extremity erysipelas in a 6-year-old child with severe fever and a threat of phlegmon is shown in Fig. 2.

Fig. 3, 4 show bullous-necrotic changes in the elbow bends and area of the ankle joint with the development of interfascial phlegmon.

Similar changes were observed in adult patients with the development of phlegmon of both forearms and ulcerative-necrotic lesions at the site of bullous skin changes (Fig. 5), the peeling of the palms and soles was also a characteristic feature of the disease (Fig. 5, 6).

Almost every second patient with severe infection caused by group A beta-hemolytic streptococcus, confirmed by bacteriological methods, had ASLO antibodies below the reference values.

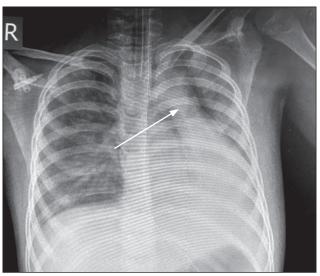


Figure 1. Streptococcal pneumonia with the development of left-sided total pneumothorax (marked with an arrow) in an 8-year-old child who was on mechanical ventilation

Table 2. Clinical symptoms and syndromes that characterized the course of streptococcal infection in the described groups of patients

Clinical manifestations	Children (n = 7)		Adults (n = 10)	
Clinical mannestations	Abs.	%	Abs.	%
Hyperthermia	7	100.0	10	100.0
Sore throat	4	57.1	2	20.0
Rash	6	85.7	3	30.0
Epidermolysis	2	28.6	2	20.0
Desquamation and peeling of skin of palms and soles	5	71.4	6	60.0
Septic shock	5	71.4	4	40.0
Destructive pleuropneumonia	7	100	10	100.0
Carditis	3	42.9	3	30.0
Nephritis	5	71.4	4	30.0
Erysipelas	2	28.6	0	0
Hemodialysis	0	0	2	20.0
Soft tissue phlegmon	2	28.6	5	50.0
Hemoculture/bacillus culture from the pharynx	5	71.4	10	100.0
ASLO↑	4	57.1	4	40.0
Lactate > 2 mmol/l	7	100.0	10	100.0

## **Discussion**

There is a significant increase in the infection of the European population with streptococcus, as well as the rapid formation of its resistance, in particular, to macrolides (30–40 % to erythromycin), causing nosocomial infections by streptococci, as indicated in the review by R. Creti and other scientists [8, 16]. In this clinical study, *Str.pyogenes* was antibiotic-resistant in every second case.

María José González-Abad and Mercedes Alonso Sanz (2020) reported an increase in the risk of severe streptococcal infections caused by pyogenic streptococcus after analyzing the epidemiological situation in Europe in 2011–2018 [11]. A similar trend was also highlighted by Eva Ramírez de Arellano and co-authors (2024) in their study of the clinical, microbiological, and molecular features of invasive infections in pediatric hospitals in Spain [5]. In the presented 5 cases, it was shown that 2 children and 2 adult patients (80 %) developed streptococcal shock with multiorgan failure and severe skin and soft tissue lesions, heart failure of varying degrees, as evidenced by a sharp decrease in the minute blood volume (ejection fraction).

Peter J.B. Davies and colleagues (2023) noted an increase in the number of destructive pneumonias caused by hemolytic streptococcus, in particular, with the development of pleural empyema in pediatric patients admitted to Scottish hospitals in winter [15]. Our data are in line with those of the authors.

The primary development of seasonal influenza infection or metapneumovirus infection was caused by the addition of streptococcal infection (PiGAS), which was not typical for the epidemiological situation, since most often *Str.pneumoniae*, *H.influenzae*, *S.aureus* infection occurs [9, 22]. Giada Maria Di Pietro and co-authors in their 2024 review also point to a high potential for sensitization to this pathogen with the development of glomerulonephritis, as well as specific forms of the disease, such as necrotizing fasciitis and streptococcal toxic shock syndrome [6]. We ob-

served these forms of streptococcal infection in our patients. Prior to this outbreak of streptococcal infection, necrotizing fasciitis and epidermolysis syndrome were not often observed in adults, and extremely rarely in children. Since the latter developed against the background of antibiotic therapy and during early convalescence, as well as the effect of local and systemic glucocorticosteroids, it is believed that this clinical form of infection caused by group A beta-hemolytic streptococcus is an example of an autoimmune complication.



Figure 2. Widespread erysipelas on the thigh and lower leg of a 6-year-old child



Figure 3. Skin changes on the elbow joints in a 12-year-old child with epidermolysis ("scalded skin" syndrome)



Figure 4. Necrotic skin changes on the ankle and elbow joints in a 12-year-old child

## **Conclusions**

- 1. An urgent issue of modern infectology is the significant increase in the population with highly virulent strains of group A beta-hemolytic streptococcus, which is characterized by the formation of antibacterial multidrug resistance, in Europe.
- 2. The characteristic features of these cases are the development of destructive forms of pneumonia with pleurisy, myocarditis, septic shock, as well as soft tissue and skin



Figure 5. Edema, skin necrosis and formation of interfascial phlegmon with characteristic fluctuation and ultrasound picture in a 61-year-old patient



Figure 6. Peeling and desquamation of the epidermis of the soles as a characteristic sign of the disease (day 12 of treatment)

damage in the form of erysipelas, phlegmon, multiple fasciitis, epidermolysis, which was rarely observed before.

3. Not all patients with bacteriologically confirmed streptococcal infection had an increase in ASLO, which requires repeated examinations, as these antibodies may not be synthesized for a long time in a severe condition. Particularly high titers of ASLO were observed in patients with carditis, nephritis, and epidermolysis.

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### Аналіз випадків тяжкої стрептококової інфекції в дітей та дорослих на Хмельниччині

Резюме. Актуальність. Бета-гемолітичний стрептокок групи А (Streptococcus pyogenes) — значно поширений бактеріальний патоген, здатний спричиняти різноманітні клінічні варіанти захворювань у людей та бути тригером розвитку різних авто-імунних станів. Мета дослідження: показати сучасний стан інфекції, викликаної бета-гемолітичним стрептококом групи А, у дорослих осіб та дітей на прикладі випадків із практики. Матеріали та методи. У статті відображено 5 випадків стрептококової інфекції, викликаної Str.pyogenes, із різною клінічною симптоматикою. Стрептококову етіологію підтверджували бактеріологічним методом та визначали рівні антитіл АСЛ-О біохімічним методом, проводили клінічні й біохімічні дослідження з метою оцінки маркерів органної дисфункції. Результати. У роботі представлено випадки тяжкого пере-

бігу стрептококової інфекції у вигляді флегмони (одиничної або множинної), множинних фасциїтів різної локалізації, деструктивної пневмонії, яка ускладнювалася пневмотораксом та піопневмотораксом, стрептококового септичного шоку, а також епідермолізу (синдрому «ошпареної шкіри»). Висновки. Спостерігається значне зростання частоти захворювань, викликаних бета-гемолітичним стрептококом групи А. Для цього спалаху характерним є тяжкий перебіг інфекції з розвитком різноманітних клінічних форм з ураженням шкіри і м'яких тканин, розвитком деструктивної пневмонії, септичного стану. Усі випадки викликані антибіотикорезистентними штамами. Ключові слова: діти; дорослі; стрептококова інфекція; бе-

**Ключові слова:** діти; дорослі; стрептококова інфекція; бета-гемолітичний стрептокок групи А; лабораторна діагностика; клінічні форми