



ORIGINAL ARTICLE

**Evaluation of cytokines produced by  $\beta$ -hemolytic streptococcus in acute pharyngotonsillitis** ☆,☆☆



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**KEYWORDS**

Pharyngitis;  
Cytokines;  
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**Abstract**

*Introduction:* The most common pathogen in bacterial pharyngotonsillitis is group A  $\beta$ -hemolytic streptococcus, although groups B, C, F, and G have also been associated with pharyngotonsillitis. *Objective:* To assess the levels of the cytokines TNF- $\alpha$ , IL-6, IL-4, and IL-10 in bacterial pharyngotonsillitis caused by group A and non-A (groups B, C, F and G)  $\beta$ -hemolytic streptococcus.

*Methods:* The study was conducted at a pediatric emergency care unit. The sample comprised children (5–9 years old) with acute bacterial pharyngotonsillitis diagnosed between December of 2011 and May of 2012. The research involved collection of blood samples from the patients, enzyme-linked immunosorbent assay detection of TNF- $\alpha$ , IL-6, IL-4, and IL-10, and collection of two oropharyngeal swabs for bacterial isolation. Additionally, the medical history of the study participants was also collected.

*Results:* In the studied group (mean age: 5.93 years), higher pharyngotonsillitis incidence was observed in the female gender (64.76%). Higher incidence of tonsillar exudates was observed with groups A and C. No statistically significant differences in cytokine levels were observed among groups. However, the group A and the control group showed a difference in the IL-6 level ( $p = 0.0016$ ).

*Conclusions:* The Groups A and C showed higher cytokine levels than the Groups B and control, suggesting similar immunological patterns.

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**PALAVRAS-CHAVE**

Faringite;  
Citosinas;  
Streptococcus

### Avaliação das citosinas produzidas por estreptococos $\beta$ -hemolíticos em faringotonsilites agudas

**Resumo**

**Introdução:** O patógeno mais comumente associado à faringotonsilite bacteriana é o estreptococo  $\beta$ -hemolítico do grupo A, a despeito dos grupos B, C, F e G terem também sido associados como faringotonsilite.

**Objetivo:** Determinar os níveis das citosinas TNF- $\alpha$ , IL-6, IL-4, e IL-10 na faringotonsilite bacteriana causada pelos estreptococos  $\beta$ -hemolíticos do grupo A e não-A (grupos B, C, F e G).

**Método:** O estudo foi conduzido em uma emergência pediátrica. A amostra estudada compreendeu crianças (entre 5 e 9 anos) com faringotonsilite aguda bacteriana diagnosticada entre dezembro de 2011 e maio de 2012. A pesquisa envolveu a coleta de amostras sanguíneas dos pacientes, a detecção, através do ELISA, de TNF- $\alpha$ , IL-6, IL-4 e IL-10, além da coleta de dois swabs orofaríngeos para isolamento bacteriano. Adicionalmente foi coletada a história médica dos participantes do estudo.

**Resultados:** No grupo estudado (idade média: 5,93 anos), a maior incidência de faringotonsilites foi observada no gênero feminino (64,76%). Foram detectadas maiores incidências de exsudatos tonsilares nos grupos A e C. Não foram observadas diferenças estatisticamente significantes dos níveis de citosinas entre os grupos. Porém os grupos A e o controle mostraram diferença nos níveis de IL-6 ( $p=0.0016$ ).

**Conclusões:** Os grupos A e C mostraram maiores níveis de citosinas que os grupos B e o controle, sugerindo mecanismos imunológicos similares.

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**Introduction**

Acute pharyngotonsillitis (PT) is one of the most common conditions observed by pediatricians, otorhinolaryngologists, and primary care physicians in their daily practice. It is estimated that >50% of cases of PT are of viral origin; among the bacterial cases, the most common pathogen is group A  $\beta$ -hemolytic streptococcus (GAS).<sup>1-3</sup> However,  $\beta$ -hemolytic streptococci groups B, C, F, and G (especially C and G) can also cause self-limiting PT with non-suppurative sequelae, such as rheumatic fever.<sup>4,5</sup>

In the last 50 years, the overall incidence of bacterial PT caused by groups B, C, F, and G has increased. A 2011 study on the prevalence of  $\beta$ -hemolytic streptococci groups C and F in patients with acute pharyngitis demonstrated that these microorganisms cause PT in 6.2% of all cases of acute streptococcal infections.<sup>6-8</sup>

In turn, groups C and G streptococci (GCS and GGS) have been described as pyogenes-like, as these organisms share important virulence factors such as hemolysins, streptolysin O, extracellular enzymes, and M proteins, similar to GAS. They can also cause exudative isolated PT in addition to cellulitis, thus becoming clinically indistinguishable from GAS. Previous studies demonstrated that GCS causes a strong immunological response, as can be observed from the increase in antistreptolysin O (ASO) titer during streptococcal infection of the oropharynx.<sup>9-11</sup> GBS also shows virulence factors similar to the GAS, including hemolysins, encapsulated polysaccharides, and C5a peptidase; hyaluronidase may also appear in some strains.<sup>12</sup>

Considering the abovementioned data on the shared virulence factors and clinically similar PT development, especially among groups A, C and G, this study aimed to assess the levels of TNF- $\alpha$ , IL-6, IL-4, and IL-10 cytokines in patients with PT, in order to distinguish pharyngotonsillitis caused by GAS from non-GAS.

**Methods**

The study was carried out at an emergency unit of the city of Aracaju. The study population included children (5–9 years old) with acute bacterial PT diagnosed between December 2011 and May 2012.

Sample size calculation was performed considering the overall incidence of acute PT, which according to Simões et al. (2002) in a study carried out in Portugal, was 3440.3/105 for the age group of 5–9 years.<sup>6</sup> The population of children in this age group in the city of Aracaju is 40,442 inhabitants, according to the 2010 Census (Brazilian Institute of Geography and Statistics – IBGE, 2012). Applying the incidence reported by the abovementioned study, using the formula for sample size calculation for a finite population – chi-squared – a sample of 50 children was attained.

The control group consisted of 25% of the total sample (12 patients) and was selected among the children accompanied by adults (relatives) who were admitted to the emergency room due to conditions unrelated to respiratory diseases. The accompanying children were declared healthy by their parents.

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