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Study of streptococcal antibody (Anti-Streptolysin O) among citizens in Bitola, North Macedonia, for the period 2020-2024 year

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Abstract
Introduction: Streptococci are common human pathogens, colonizing the gastrointestinal tract, urinary tract, and oral cavity. The majority of pathogenic streptococci are group A, with Streptococcus pyogenes being the most common representative. Currently, there is a lack of quantitative representative data in our country on the prevalence of group A beta-hemolytic streptococci in the overall population, so we conducted this study to determine what percentage of the population is a carrier of group A beta-hemolytic Streptococcus. We conducted a retrospective study over 5 years from January 2020 to December 2024. We aimed to determine the concentration of ASO in all patients in whom the physician assessed the need for this analysis, outpatients and inpatients. Of the 8117 participants; 7559 (93 Persent) had normal ASO values, while 558 (7 Persent) had elevated ASO values. We analyzed the patients with ASO positive tests and found that 254 (46 Persent) were male and 304 (54 Persent) were female. Group A Beta-hemolytic streptococcus is showing a tendency to increase globally, especially in children and older adults, a fact that is worrying. Our country continuously monitors the epidemiological situation at the national and international levels, this is essential for detecting new waves associated with the severe presentation of group A Beta-hemolytic streptococcus.

Keywords: ASO, Group A Beta-hemolytic Streptococcus, Norht Macedonia, children

Introduction

Streptococci are common human pathogens, colonizing the gastrointestinal tract, urinary tract, and oral cavity. The majority of pathogenic streptococci are group A, with Streptococcus pyogenes being the most common representative. Group A beta-hemolytic streptococci usually infect children aged 5–15 years. Group A streptococci cause death in approximately 500,000 patients per year worldwide as a result of the infectious diseases they cause [1]. Streptococcus causes otitis media, impetigo, sinusitis, peritonsillar and retropharyngeal abscesses, scarlet fever, pneumonia, erysipelas, lymphangitis, cellulitis, puerperal sepsis, vaginitis, myositis, perianal abscess, gangrene, etc. The most common streptococcal sequelae are acute rheumatic fever and acute glomerulonephritis [2]. Most strains of group A and many other strains of group C and G Streptococcus bacteria secrete the Streptolysin O antigen test (SLO) [3]. Anti-streptolysin O (ASO) is an antibody produced against streptolysin O. Anti-streptolysin O titers increase during the first week after infection with Streptococcus pyogenes and reach a maximum peak after three to six weeks. ASO plays a key role in detecting recent streptococcal infection [4, 5]. Numerous studies have shown that age, geographic area, frequency of streptococcal infections, and nutritional status of children affect the concentration of ASO in the blood of subjects [6, 7]. Elevated ASO concentrations are most often the result of recent pharyngitis due to group A beta-hemolytic streptococcal infection. ASO concentrations remain low in healthy children at the beginning of life, but an increase in ASO concentrations is most often observed between 5 and 15 years of age, a period when children encounter this pathogen in kindergarten or school [8]. Currently, there is a lack of quantitative representative data in our country on the prevalence of group A beta-hemolytic streptococci in the overall population, so we conducted this study to determine what percentage of the population is a carrier of group A beta-hemolytic Streptococcus

Methods

We conducted a retrospective study over a 5-year period from January 2020 to December 2024. We aimed to determine the concentration of ASO in all patients in whom the physician assessed the need for this analysis, outpatients and inpatients.

Sample characteristics

We measured the concentration of ASO in 8117 patients who were referred by their primary care physicians to the laboratory department of the Clinical Hospital in Bitola. The healthy subjects were 7559 aged 0 to 99 years. Demographic characteristics such as age, gender, place of residence was collected from the subjects. Venous blood samples were taken from each patient and the analyses were performed on the Abbott platform in 2020 - 2022 on Abbott Architect, and from 2022 to 2024 on Abbott Alinitu.

Statistical analysis

Participants were divided into three age groups, as there are differences in reference values according to age. The age group 0-5 years has a reference value < 100 U/ml, the age group 6-18 years has a reference value < 250 U/ml and the

age group 19-99 years has a reference value < 200 U/ml. Descriptive statistics were performed to calculate the number of participants, percentages, mean and standard deviations for each subgroup. ASO was calculated according to gender, age and referral site of the patients. P < 0.05 was considered significant. Statistical analysis was performed using SPSS version 20.

Results

Of the 8117 participants; 7559 (93%) had normal ASO values, while 558 (7%) had elevated ASO values. We analyzed the patients with ASO positive tests and found that 254 (46%) were male and 304 (54%) were female.

The participants were divided into three age groups. In the age group 0-5 years, 270 patients were analyzed, of which 27 had elevated ASO values, while 243 patients had normal ASO values. In the age group 6-18 years, 1025 patients were analyzed, of which 140 patients had elevated ASO values, and 885 had normal values. In the last age group 19-99 years there was the largest number of respondents 6818, 396 had increased values, while 6453 had normal values for ASO.

The prevalence of the carrier state of β-hemolytic Streptococcus group A was 10% in children 0-5 years, 14% in children 6-18 years and 6% in adult patients. These results are presented in Table 1.

Table 1: Epidemiologic characteristics of participants.

	Number (%)
Total ASO (+ and -)	8117 (100%)
ASO (-)	7559 (93%)
ASO (+)	558 (7%)
Gender	
Male ASO (+)	254 (46%)
Female ASO (+)	304 (54%)
Age total	
0-5	270 (3%)
6-18	1025 (13%)
19-99	6818 (84%)
Age group ASO (-)	
0-5	243 (90%)
6-18	885 (86%)
19-99	6453 (94%)
Age group ASO (+)	
0-5	27 (10%)
6-18	140 (14%)
19-99	396 (6%)

Table 2 presents the total number of all respondents participating in the study, the analysis was conducted over the last five years, and the respondents are shown as a total number divided by the year in which the tests were conducted. We note that last year, 2024, we have an increased number of antistreptolysin O tests.

Table 2: Total number of examinated participants by year

Age	**2020 Number**	**2021 Number**	**2022 Number**	**2023 Number**	**2024 Number**
0-5	39	64	67	63	37
6-18	128	165	207	275	250
19-99	1205	1320	1374	1358	1565

When we analyzed the results of patients with increased antistreptolysin O concentrations in the last five years in the three age groups, we note that in 2023 we had the most ASO positive results in children in the age group 0-5 and 6-18 years. In the age group 19-99 years we had the most ASO positive results in 2024, these results are shown in Table 3.

Table 3: Result of positive antistreptolysin O testing in the studied population for 2020 – 2024

Lab findings ASO + results	**Age group 0-5 (n=27)**	**Age group 6-18 (n=140)**	**Age group 19-99 (n=396)**
2020 year	6 (15%)	18 (14%)	78 (6%)
2021 year	3 (5%)	17 (10%)	55 (4%)
2022 year	2 (3%)	9 (4%)	62 (5%)
2023 year	11 (17%)	45 (16%)	92 (7%)
2024 year	6 (16%)	41 (16%)	109 (7%)

We analyzed positive Antistreptolysin O tests in males and females and observed that females were more affected by group A β-hemolytic streptococcus, 300 females had ASO positive results and 254 males. In children and adolescents aged 0-18 years, males were more affected than females, while in adult patients, females were more affected by group A β-hemolytic streptococcus.

Table 4: Number of patients and percentages with positive antistreptolysin O testing divided by gender

Age years	2020		2021		2022		2023		2024	
	Males	Females	Males	Females	Males	Females	Males	Female	Males	Females
0-5	4 (63%)	2 (33%)	3 (100%)	0 (0%)	1 (50%)	1 (50%)	9 (82%)	2 (18%)	4 (67%)	2 (33%)
6-18	10 (56%)	8 (44%)	11 (65%)	6 (35%)	5 (56%)	4 (44%)	29 (64%)	16 (36%)	36 (88%)	5 (12%)
19-99	27 (35%)	51 (65%)	25 (45%)	30 (55%)	15 (24%)	47 (76%)	40 (43%)	52 (57%)	35 (32%)	74 (64%)

We analyzed the patient referrals, whether they were outpatients or inpatients in our hospital and observed that most of them were outpatients. 480 participants were outpatients and 74 were inpatients, hospitalized in our hospital.

Discussion

Group A streptococci are one of the most common infectious agents, the most widespread pathogen affecting humans in the world. The most serious complications of group A β-hemolytic streptococci are acute rheumatic fever and acute glomerulonephritis. Timely diagnosis of group A β-hemolytic streptococcal infection also allows us to treat and monitor patients in a timely manner. Laboratory diagnoses are performed by three different methods: throat swab, rapid antigen detection test or streptococcal serology. For the diagnosis of group, A β-hemolytic streptococcal infection, we applied a method of streptococcal serology including ASO antibodies. The ASO test is one of the most common and inexpensive methods for confirming group A β-hemolytic streptococcal infection. The test plays an important role in developing countries, where throat swabs are not performed in a timely manner [9]. Elevated antistreptolysin O concentrations vary depending on the population studied, geographical location, age group, and seasonal variations [8, 10]. In this study, we found that the percentage of ASO positive tests is 7% in the general population, while in school-aged children it is 14%, which is also confirmed by other studies, where it ranges from 10.9% to 16% [11, 14]. The study was conducted for five consecutive years from January 2020 to December 2024, and a trend of a constant increase in the number of affected patients is observed, and of course, the number of tests can also be observed. Valcarcel reported the largest increase in children aged 0–9 years in early 2023 and in older adults (≥70) in early 2024, and also noted an increase in the severity of the disease in children aged 0–9 years [15]. Since December 2022, several European [16, 18] and non-European [19, 20] countries have documented an increase in group A β-hemolytic streptococcal infections, particularly in the pediatric population, but also in older age groups [21, 22]. The reason for this global increase is still unclear. However, sequencing of isolates globally has decreased in the post-pandemic period. In our study in the pediatric and adolescent population, we observed that males were more commonly affected by group A β-hemolytic streptococcus, which was confirmed by Nadir and colleagues in 2016 when they reported that gender differences were very pronounced, with males more commonly affected by group A β-hemolytic streptococcus. Consistent with our results, a higher proportion of male group A β-hemolytic streptococcus cases have also been previously reported in Norway [23]. Also, Guy and Abo *et al*. suggest a potentially higher risk for males. To date, penicillin is the drug of choice for group A β-hemolytic streptococcal infection and has excellent sensitivity, and therefore this drug is prescribed to patients in order to eradicate this disease and prevent serious complications of the disease that may occur.

Conclusions

Group A β-hemolytic streptococcus is showing a tendency to increase globally, especially in children and older adults, a fact that is worrying. Ongoing research is needed in order to understand the main factors that drive these changes and to effectively identify which public health interventions would help stop the increase. Our country continuously monitors the epidemiological situation at the national and international levels, this is essential for detecting new waves associated with the severe presentation of group A β-hemolytic streptococcal infections. Physicians should be familiar with the recommendations for timely identification of group A β-hemolytic streptococcus to reduce the risk of complications and to reduce further transmission of the disease.

Abreviations

ASO – anti streptolysin test 0

Authors' Contribution

Biljana Ilkovska – Writing draft, analysis, data visualization
Bisera Kotevska – Writing draft, analysis, data visualization

Conflict of Interest

None to declare.

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