## ANALYSIS OF INFLAMMATORY DISEASES OF THE THROAT AND THE ANTIBIOTICS USED IN THEM

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Annotation. Research objective: To determine the etiology of throat diseases in the population of the Republic of Uzbekistan in 2023-2024 and to describe their antibiotic resistance status. Materials and methods: The infections detected in patients with throat infections from the second half of 2023 to the beginning of 2024 at the Bacteriological Laboratory of the Tashkent Medical Academy of the Republic of Uzbekistan, as well as the microorganisms identified in them and their antibiotic sensitivity were analyzed. Bacteriological and statistical methods were used. Analysis and discussion of results: During this 6-month period, 200 patients (25 men, 175 women) complained of inflammatory diseases in the throat. When samples taken from them were laboratory diagnosed, more than 400 different bacteria were detected in all patients (Streptococcus ssp.-60%, Candida ssp.-30%, Staphylococcus aureus-10%). Conclusion: As a result of the analysis, we can see that women are more likely to get sore throats (88%) (average age was 27). The most common cause of inflammation is Streptococcus ssp (60%), and the most effective antibiotics for the bacteria: Sulfamethoxazole, Levofloxacin, Amoxicillin and Ampicillin gave good results.

*Keywords:* upper respiratory tract inflammation, throat inflammation, bacteria, antibiotics, microorganisms, tonsillopharyngitis, acute tonsillitis, acute pharyngitis.

Relevance. It manifests as a symptom or as a primary disease in upper respiratory tract infections. Acute pharyngitis and tonsillitis is the most common reason why people want to visit their primary care physician (8). Acute tonsillitis is diagnosed in 1-2% of all adult visits to hospitals, emergency departments, and outpatient clinics. 5% of acute tonsillitis is caused by bacterial infection: group A hemolytic streptococcus (15). Tonsillitis encompasses a spectrum of infectious and inflammatory processes that can be bacterial or viral(sing). Tonsillitis in adults is a medical problem and a significant social burden (15). Acute tonsillitis is often characterized by a sudden onset of clinical symptoms: namely, enlarged tonsils, hyperemia, enlargement of the cervical lymph nodes, fever, and general malaise (11). Acute (and mainly viral) tonsillitis is a frequent disease, said to account for about one-third of all respiratory tract infections treated in primary care (23). Exact numbers are difficult to obtain, with all the previously mentioned difficulties of definition and unreliable diagnostic criteria. Despite these circumstances, it is estimated that 600 million symptomatic GAS cases are diagnosed worldwide each year. About one among 10 of these patients develop recurrent acute tonsillitis. Nevertheless, it affects hundreds of thousands of children and young adults every year. The prevalence of recurrent episodes is about 12% in patients with tonsillitis, i.e., about 12,000 per 100,000 individuals having had at least one tonsillitis episode before (5). A GAS infection as a cause of a tonsillitis episode is the only known hard risk factor for the development of recurrent acute tonsillitis. Recurrent acute tonsillitis could be a genetic immunosusceptibility disease because it is reported that patients younger than 12 years with recurrent acute tonsillitis show some (otherwise subclinical) antibody deficiency and aberrant T-cell function (5). Acute pharyngitis is also a common cause of throat infections(6). Pharyngitis is inflammation of the pharynx, which is a part of the Upper Respiratory Tract Infection (URI) and is quite often found (13). Acute pharyngitis is a common event accounting for 2–5% of pediatric ambulatory visits, and it is one of the main reasons for prescribing antibiotics in children (9). Although it is not life-threatening, pharyngeal pain and

dysphagia require the use of appropriate antibacterial agents to quickly relieve symptoms. One of the serious problems in the diagnosis of acute tonsillitis is its misdiagnosis, which is often due to a viral infection, and therefore the use of antibiotics for pharyngitis can have disastrous consequences(1). In the differential diagnosis of the disease, we can compare the symptoms and causes of the disease with those caused by: Epstein-Barr virus, Adenovirus, Fucobacterium, Archaea hemolyticum, Corynebacterium diphtheriae, Frankincense tulerensis, Yersinia enterocolitica, and Neisseria gonorrhoeae. Of these, Epstein-Barr virus causes the most common types of tonsillitis: mononucleosis and pseudomembranous tonsillitis(2). Also, effective antibacterial therapy helps to reduce the spread of infection and prevent the process from developing into serious complications such as rheumatic fever(12). Overuse of antibiotics in the treatment of pharyngitis is a significant global problem that contributes to the increase in antibiotic resistance(3). The debate on the optimal treatment and surgical indications for recurrent acute tonsillitis is still ongoing (5). Acute tonsillopharyngitis can result in many complications, the most serious of them is rheumatic fever. Therefore, it is very important to properly diagnose and use antibiotic therapy when necessary (8). In recent years, significant progress has been made in the fight against many infectious diseases in the Republic of Uzbekistan, and some epidemics of infectious diseases have been eliminated. However, the fact that different infectious agents cause different symptoms complicates treatment measures and encourages the development of new drugs. One of the most important aspects of eliminating such problems is correct diagnosis and timely application of treatment measures.

**Research objective:** To determine the etiology of throat diseases in the population of Tashkent city and describe their antibiotic resistance status during 2023-2024.

**Inspection material and methods**: The Bacteriological Laboratory of the Tashkent Medical Academy in Tashkent city analyzed the infections detected in patients with throat infections from the second half of 2023 to the beginning of 2024, as well as the microorganisms identified in them and their antibiotic sensitivity. Bacteriological and statistical methods were used.

Analysis and discussion of results. During this 6-month period, 200 patients (25 men, 175 women) complained of inflammatory diseases of the throat. As a result of the examinations, it was determined that these patients had symptoms consistent with the disease: sore throat, general weakness, fever, cough, loss of appetite. The clinical signs of the disease were almost the same in women and men. Based on the data obtained as a result of the examinations, in this diagram we have determined the level of infection by gender: in men and women





As you can see from the diagram, women are more likely to get throat infections than men. When samples taken from patients were examined at the Bacteriological Laboratory of the Tashkent Medical Academy, about 400 different bacteria were identified. We have analyzed these bacteria in the table and diagrams below.

## Table 1.

## Bacteria isolated from patients with throat infections, comparative analysis, CFU/ml 1g (M±m)

N⁰	Isolated microorganisms	KHQB/ml 1g
1	Staphylococcus aureus	4,125±0,2
2	Candida ssp.	3,75±0,2
3	Staphylococcus aureus	$4 \pm 0,3$

*Note:* \*-; \*\*- *significant difference compared to group 1 (P<0.05, P<0.01).* 

As a result of our investigation (Table 1), it was found that not only one bacteria, but also different bacteria, develop the disease in patients with nasal infections. We distributed the quantitative indicators of the bacteria according to the results of the analysis of each patient. We also calculated the percentage of their disease-causing bacteria in the patients and presented them in the form of a diagram (Fig 2).



Fig. 2. Disease-causing percentages of bacteria

We also found in our examination (diag.2), that in patients Streptococcus ssp. (Streptococcus ssp.-60%, Candida ssp.-30%, Staphylococcus aureus-10%,) caused 1.5 times more disease than other bacteria. Also, cases of monoinfection, diinfection and polyinfection were observed among patients. We calculated the results of the examinations and presented these cases in the form of a diagram.



Fig 3. Occurrence of mono, di, and poly infections in patients.

As can be seen from this diagram 3, patients with dual infection were 1.22 times more likely to be infected than patients with mono and poly infection. In the treatment of diseases caused by these bacteria, antibiotics sensitive to each bacterium were used, and patients were cured within 1-2 weeks, and in some cases up to 1 month.

During our research, we used and studied many foreign literatures, below we present the results of some of these articles for comparison:

This study was a descriptive study on secondary data that aimed to analyze the visits of patients with pharyngitis and tonsillitis at the ENT clinic of Wlingi Hospital in 2019-2021. The subjects of this study were all patients with pharyngitis and tonsillitis who visited the ENT clinic of Wlingi Hospital in 2019-2021. The data were collected in the form of examination records obtained from the medical records of patients with pharyngitis and tonsillitis who underwent examinations at the ENT clinic of Wlingi Hospital in 2019 2021. The collected data analyzed by descriptive statistics method, then processed using Microsoft Office 2016 and Microsoft Excel 2016 and presented as a distribution table with explanations arranged in narrative form and grouped according to the research objectives(13).

Patients with pharyngitis who visited the ENT clinic of Wlingi Hospital in 2019-2021 were dominated by patients with an age range of 45-64 years, followed by patients with an age range of 25-44 years. Furthermore, patients with tonsillitis who visited the ENT clinic of Wlingi Hospital in 2019-2021 were dominated by patients with an age range of 5-14 years, followed by patients with an age range of 15-24 years.

Patients with pharyngitis who visited the ENT clinic of Wlingi Hospital in 2019-2021 were dominated by women, which was 62.6%. Meanwhile, patients with tonsillitis who visited the ENT clinic of Wlingi Hospital in 2019-2021 were dominated by women, which was 50.3%. This figure is slightly different from the number of male patient visits. Acute tonsillitis in the ENT outpatient clinic of Wlingi Hospital was dominated by patients aged 5-24 years. According to Alasmari, tonsillitis can occur at any age but is most commonly found in children aged 5 to 15 years. Research by Abraham in 2019 showed that acute tonsillitis cases at Dar es Salaam National Hospital Tanzania were mainly found in children aged 1-10 years. This study's findings align with other theories and research conducted. Sari mentioned that pharyngitis was not influenced by gender, but a study by Trilana in 2013 showed that. From the research results, patients with pharyngitis who visited the ENT outpatient

clinic at Wlingi Hospital were dominated by females (62.6%). Pontin, in his research, stated that tonsillitis was not influenced by gender, but a study conducted by Priyanka in 2019 showed that tonsillitis cases were more common in males. From the research results, patients with tonsillitis who visited the ENT clinic of Wlingi Hospital were also dominated by females (50.3%), showing a slightly different percentage compared to the males. These two findings differ from the results of several other studies, but from the theory obtained, there is no significant difference between pharyngitis and tonsillitis related to gender. The results of this study confirm a decrease in the number of visits at the ENT outpatient clinic of Wlingi Hospital in 2019-2021, that the most common disease was ear disease. Patients with pharyngitis who visited the ENT outpatient clinic of Wlingi Hospital in 2019-2021 were dominated by patients with an age range of 25-44 years, while tonsillitis who visited the ENT outpatient clinic at Wlingi Hospital in 2019-2021 were dominated by females (13).

A total of 337 practitioners from 19 different special- ties were recruited. 236 (70.0%) practitioners reported seeing cases with features characteristic of streptococcal pharyngitis (pharyngeal erythema, tonsillar erythema, hypertrophy of the tonsils with or without exudates, anterior cervical lymphadenopathy, and pe- techiae on the soft or hard palate). 301 (89.3%) clinicians reported cases with inconclusive clinical features, while 21 (6.2%) reported never having a challenging diagnosis. 244 (72.4%) reported having a diagnostic approach (personal or literature-based) to determine antibiotic applicability. Nearly all respondents (99.1%) wanted a lo- cal protocol for determining antibiotic use in sore throat. A total of 5,329 public visits and 1,813 private health claims were recorded for pharyngitis, tonsillitis, tonsillopharyngitis and 'strep throat' within the age group, period, and jurisdiction of in- terest. Of the 373 visits reviewed for clinical management, 321 (86.1%) had sufficient documentation for scoring. Antibiotics were prescribed in 292 (91%) cases. Antibiotics use was justified in 65 (22.3%) cases (Centor score  $\geq$ 4) and avoidable in 213 (93.8%) of 227 with a Centor score < 4 (3).

Molecular diagnosis was performed for EBV, Adeno and HSV 1 detection with swab samples from tonsil lar membranous exudate of 51 paediatric patients with Exudative tonsillopharyngitis after GAS ruled out (21 men and 30 women, ages between 2 and 16 years) from tonsillar membranous exudate, using the Magnesia® Extrac tion Kit by using the Nucleic Acid Extraction robot. Bosphore® EBVDNA, ADENO and HSV type 1 Quantification Kits were used for EBVDNA, ADENO and HSV type 1 PCR by Montania® 4896 RT PCR platform. The frequency of positive EBV DNA cases in the ton sillar membranous exudate in swap samples were 21.5% (11/51). Monospot test was only one of the positive cases in EBV DNA pos itive. On the side a case of adenovirus, the HSV-1 was detected in two cases.

A meticulous clinical examination would differ entiate between the 2 most common causes; Streptococcus and EBV. Adeno and HSV were determined as less causative agents. Streptococcal tonsillitis can be successfully treated with suitable antibiotics. Acyclovir, ganciclovir, and foscarnet have been shown to inhibit EBV DNA polymerase enzyme. (2)

This was a prospective observational study conducted at an urban primary care health centre in Catalonia. Patients aged 15 or older with acute pharyngitis who attended the centre starting from January 2019 were consecutively invited to participate. Non-infectious causes of pharyngitis (aphthous ulceration, pharmacological causes), oral can didiasis, patients treated with systemic antibiotics in the two previous weeks, immunocompromised individuals, preg nant women, persons institutionalized in a nursing home, in emergency situations, difficulty in attending the visit, and/or patient or guardian/parent incapacitation to sign the consent were excluded from the study. The inclusion of cases was concluded in March 2020 due to the outbreak of the COVID-19 pandemic. Patients were given a symptom diary, used previously in other studies, to be completed before bedtime, and symptoms were assessed on Likert scales with a 7-point rating (0 = no problem/not affected, 1 = very mild problem, 2 = mild problem, 3 = moderate problem, 4 = significant prob lem,

5 = serious problem, 6 = the most serious it can be).7 The following items were recorded in the diary: febrile sen sation, headache, general discomfort, cough, odynophagia, difficulty swallowing (solids or liquids), and difficulty in daily activities. The sum of all these symptoms was calculated. The days with severe symptoms, scoring 5 or more in any of these symptoms, and moderate symptomatology, scoring 3 or more, were counted. A total of 149 patients with acute pharyngitis were recruited before the COVID-19 pandemic, with an average age of 36.7 years (SD 15.5 years), ranging from 15 to 87 years. Of these, 92 presented with pharyngeal exudate (62.2%), 57 with painful lateral cervical lymph nodes (38.3%), 59 with fever (39.6%), 59 with cough (39.6%), and 20 experienced recur rences (13.4%). Eighty-four patients (56.4%) were treated with antibiotics. A total of 138 patients returned their diaries (92.6%) (1).

This retrospective study included 78 pregnant women admitted to our clinic between January 2005 and January 2015 suspected as having AA. Of these, 36 women with confirmed AA underwent surgery (the appendectomy group). Forty-two patients were found not to have AA and did not proceed to surgery (the expectant group). The study controls included 29 pregnant women who presented to our clinic for routine examinations during the same period (the healthy pregnant control group) and 30 nonpregnant women who presented to our polyclinic with breast pain during the same period but had no pathology on examination (4).

A retrospective study was carried out to examine the association between serum 25(OH) vitamin D levels and recurrent GAS tonsillopharyngitis in adults. The following were compared between the groups of subjects with and without GAS tonsillo pharyngitis: age, gender, body mass index (BMI), serum iron, C reactive protein (CRP), diabetes mellitus, and serum levels of 25(OH) vitamin D. Information concerning medical conditions, drug therapy, and the results of laboratory tests were extracted from the medical charts of each subject in both groups. (In general, every patient who visits the Infectious Diseases Unit or Medicine Clinic completes a standard questionnaire at every visit concerning his/her medical condition, anthropometric information, dietary habits, smoking, drug therapy, family history of different diseases, and systemic bacterial infections. Laboratory tests were performed within 4 days from the beginning of the tonsillopharyngitis symptoms and included serum CRP levels, creatinine, serum calcium, and serum iron, and a complete blood count. Serum 25(OH) vitamin D levels were measured in the winter and summer seasons (twice a year) for all patients visiting our units. Serum 25(OH) vitamin D levels were measured using a commercial enzyme immunoassay (EIA) kit.

Data were analyzed using SPSS version 19. Continuous variables are expressed as the mean stan standard deviation. The Chi-square test was used to test differences in categorical variables between the cases and controls, and analysis of variance (ANOVA) or the Student's t-test was used for comparisons of continuous variables. Spearman rank correlation and univariate regression analysis were used to determine the strength of the relationship between the risk factors for recurrent GAS tonsillophar yngitis, namely age, gender, BMI, diabetes mellitus, creatinine, serum CRP, serum 25(OH) vitamin D, serum iron, and serum calcium. A multiple logistic regression analysis was done to determine the association between the different risk factors for recurrent GAS tonsillopharyngitis.

The Medical charts of 173 Adult patients with acute tonsillopharyngitis were reviewed for the years 2007–2009. Forty-two Patients were excluded because of: malignancy (n = 11), Taking immunosuppressant drugs (n = 7), Renal failure with creatinine clearance <35 ml/min (n = 9), Pregnancy (n = 6), Connective tissue disease (n = 4), Low compliance (n = 3), And vitamin D supplementation (n = 2). One Hundred and thirty-one patients with acute tonsillopharyngitis were assessed and a further 77 Were excluded because of non-GAS tonsillopharyngitis or no recurrent GAS tonsillopharyngitis. Finally 54 Patients with recurrent GAS Tonsillopharyngitis were included in the study. Table 1 summarizes the differences between the cases and controls (15).

Previous studies have demonstrated that iron deficiency is prevalent in children with recurrent tonsillitis and in children undergoing adenotonsillectomy. Low serum iron levels have been associated

with abnormalities in the cell-mediated response as well as a decreased ability of phagocytic cells to kill certain types of bacteria. Elverland et al. showed a beneficial effect of tonsillectomy and adenoidectomy on hemoglobin and iron metabolism and found that iron deficiency was common among children with recurrent tonsillitis and upper airway obstruction. In our study, we did not find any correlation between serum iron levels and recurrent tonsillopharyngitis in adults (12).

We conclude that recurrent GAS tonsillopharyngitis in adults could be related to vitamin D levels. Data from epidemiological studies indicate that vitamin D deficiency has become a common finding in recent years and appropriate replacement may offer immune and antimicrobial benefits. Because measurement of vitamin D levels is easily done and vitamin D supplements are readily obtainable and inexpensive, further studies are needed to assess whether this represents a causal association and whether vitamin D replacement therapy can prevent the recurrence of GAS tonsillopharyngitis (15).

It was unclear until recently if a tonsillectomy is effective in patients suffering from severe recurrent acute tonsillitis. The Cochrane review from 2014 based on seven trials (five in children and two in adults; revealed that good information about the effectiveness of tonsillectomy (with/without adenoidectomy) was only available for the first year following surgery in children and for 5–6 months in adults. Children had a small benefit from surgery: children who had surgery had three episodes of sore throat on average compared to 3.6 episodes experienced by the other children, i.e., 0.6 episodes of any type of sore throat in the first year was avoided. In adults, conclusions on the effectivity could not be drawn: the two included trials suggested that the number of days with sore throat may be fewer in the first 6 months following tonsillectomy compared to a conservative management. This was the reason why the UK's National Institute for Health Research commissioned the NATTINA trial. NATTINA is so far the largest multicenter clinical trial (453 participants randomized) to assess the effectiveness of surgical intervention in adults compared to a conservative management. NATTINA represents a new milestone on the importance of tonsillectomy in adults. The primary outcome measure was the total number of sore throat days, reported weekly over 24 months. It was shown that compared with conventional medical management, tonsillectomy is both clinically effective and costeffective. Tonsillectomy reduces sore throat days by almost 53% in over 2 years. Based on the main NATTINA result that tonsillectomy is more beneficial mainly for severe cases of recurrent acute tonsillitis, current clinical guidelines recommend tonsillectomy if the patient experiences at least five to seven sore throat episodes within 1–2 years. For example, the German guideline explicitly requires episodes of acute tonsillitis. In addition to the number of episodes, nearly all guidelines require additional parameters to substantiate the severity and a high probability that the episodes were episodes of bacterial tonsillitis. The NATTINA trial probably will define the new standard to count the number of episodes, i.e., following the UK guideline (5).

From 2017 until 2018, Popovych et al. conducted a study on the effectiveness of BNO 1030 extract in combination with standard therapy in children with acute non-bacterial tonsillitis. BNO 1030 extract (Imupret®) is an herbal aqueous-alcohol extract containing seven plants: marshmallow root (Radix althaeae), chamomile flowers (Flores chamomillae), horsetail herb (Herba equiseti), walnut leaves (Folia jun gladis), yarrow herb (Herba millefolii), oak bark (Cortex quercus), and dandelion herb (Herba taraxaci). Two hundred and thirty-eight children aged 6–18 years were included in a randomized, open-label, multicentred, comparative, non-placebo-controlled study. Standard therapy was acetaminophen as an antipyretic agent in age-specific doses and benzydamine hydrochloride oral spray. The results showed a sig nificant decrease of sore throat (both during swallowing and at rest), improvement of the patients' general condition after 5 days (p < 0.05) and withdrawal of antipyretics (p < 0.005). Patients' symptoms were evaluated using a 4-point scale for symptoms and a 10-point visual- analogue scale. No adverse events were recorded. The authors concluded that BNO 1030 (Imupret®) is a safe and effective product for treatment of acute non-bacterial tonsillitis in children. 6 In 2021, the authors published the associated one-year follow-up

data. Self-assessment of general health was significantly better after day 5. Significant improvement of assessed symptoms (hyperaemia of the posterior wall and swollen, plaque) in the treatment group after 6 months were reported. 21 A significantly lower recurrence rate (p < 0.05) with BNO 1030 treatment was described in the follow-up year. Despite our thorough literature search, it is possible that relevant studies were missed, since CAM and IM comprise a broad spectrum of different therapies which may not have been represented in the search terms used for this review. Furthermore, studies written in languages other than German and English were excluded. A meta-analysis could not be performed due to the small and diverse number of clinical trials (11).

**Conclusion.** The results of the analysis showed that sore throats are mainly manifested as an additional symptom in seasonal infectious diseases. In addition, in a high percentage, the infectious agent itself causes the disease independently. As a result of the analysis, we can see that women (88%) are more likely to suffer from sore throats (average age 27). The most common cause of inflammation is Streptococcus ssp. (60%), and the most effective antibiotics for the bacteria: Sulfamethoxazole, Levofloxacin, Amoxicillin and Ampicillin gave good results. The use of correct treatment methods for patients with this infection helps to cure the disease faster.

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