CONFORMANCE OF MC ISAAC MODIFICATION OF CENTOR SCORE WITH MICROORGANISMS OF TONSIL CORE TISSUE IN CHRONIC TONSILITIS PATIENTS

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Abstract

Background: A viral, bacterial, or fungal infection may cause tonsillitis, which is an inflammation of the palatine tonsils. The McIsaac modified Centor score, which differs from the original Centor score in that it only applied to patients who were at least 15 years old, is a tool for predicting tonsillitis brought on by group A -hemolytic Streptococcus. Because the McIssaac modified Centor score adjusts by age, it may be used on both children and adults. **Objective**:To identify whether patients with chronic tonsillitis are suitable candidates for the modified McIsaac Centor score when tonsil core bacteria are present.. **Method**:a cross sectional research that combines descriptive analysis with analysis. Patients with chronic tonsillitis after tonsillectomy participated in the trial from June 2020 to June 2021 at the ORL-HNS outpatient clinic of RSUDZA. Using the SPSS application, all data were entered, coded, and analyzed using Chi-square statistics and a kappa test with a 95% confidence level. Kappa value > 0,8 - 1 is seen to indicate very high compliance, whereas kappa value 0,2 is thought to indicate very poor conformance. **Results**:The research covered 35 patients in total. There were more women overall (28.6%), those aged 15 to 44 made up the largest age group (41.3%), and T3 tonsils made up the majority (38%). The most prevalent germs were Staphylococcus aureus (59.4%). Levofloxacin, linezolid, gentamicin, and ciprofloxacin had the greatest antibiotic sensitivity tests results for gram positive bacteria, whereas levofloxacin, meropenem, ceftazidime, gentamicin, and amikacin had the highest results for gram negative bacteria. With 100% sensitivity, 79.41% specificity, 12.5% positive predictive value, 100% negative predictive value, and 80% accuracy value, a score of 4 was determined to be the best cut-off point. Based on a Kappa value of 0.181 [CI95% (-0.13) - 0.492] and a p value of 0.062, the McIsaac modified Centor score was 18.1% congruent with the outcomes of the tonsillar core microorganism culture. **Conclusion**: In individuals with chronic tonsillitis, there was very little agreement between the McIsaac modified Centor score and the bacterium in the tonsil core culture.

***Keywords*:** Chronic tonsillitis, tonsil core microorganisms, McIsaac modified Centor score.

INTRODUCTION

Tonsillitis, an upper respiratory infection that causes inflammation of the palatine tonsils, has become a health concern in the otorhinolaryngology sector.[1,2,3] Every year, the prevalence of chronic tonsillitis rises.[4,5] According to estimates from the World Health Organization (WHO), 287,000 children under the age of 15 underwent tonsillectomy with or without adenoidectomy, with 248,000 (86.4%) of those children receiving tonsillo-adenoidectomy and 39,000 (13.6%) receiving tonsillectomy alone. Tonsillitis is most common in school-aged children, although it may affect anybody at any age.[7,8,9,10] In Indonesia, the prevalence of tonsillitis is around 30 cases per 1000 children.[11]

Repeated viral or bacterial infections of the tonsils result in chronic tonsillitis.[10] The failure or poor penetration of antibiotics into the tonsillar core or insufficient antibiotic treatment in acute tonsillitis both contribute to this recurring illness.[12,13] The most frequent etiology for these infections is likely to be Group A hemolytic Streptococcus (GABHS), which is responsible for between 28% and 40% of these infections.[4,16] Serious effects from this bacterial infection might include rheumatic fever and rheumatic heart disease.[16,17] However, anaerobic bacteria, such as *Fusobacterium necrophorum, Streptococcus intermedius, Prevotella melaninogenica, and histicola*, are becoming more prevalent and are to blame for chronic tonsillitis disorders.[18]

According to many studies, the bacteria that cause tonsillitis may also be detected in the tissue that makes up the tonsil's core.[10] Many distinct kinds of microorganisms were detected in the tonsil core as opposed to the tonsil surface in the culture results recovered from the tonsillar surface swabs and tonsillar core tissue, particularly anaerobic bacteria.[14,15,16] The Mc Isaac Modified Centor criteria were the most recent parameters utilized to determine the etiology of tonsillitis. This score is primarily used to identify tonsillitis produced by the GABHS virus and to assist distinguish between tonsillitis caused by bacteria or viruses.[8,17]

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The goal of this study was to examine the description of the microorganisms in the tonsillar core tissue and to assess the suitability of the Mc Isaac Modified Centor criteria so that these criteria can be used as a guide in predicting the microorganisms that cause chronic tonsillitis and help in the selection of appropriate antibiotics, prevent complications, and avoid the use of antibiotics that are not appropriate and could lead to an increase in drug-resistant bacterial strains.[10,18]

METHOD

The ORL-HNS outpatient clinic of RSUD dr. Zainoel Abidin (RSUDZA) Banda Aceh conducted the descriptive analytic study for this research from May 2020 to February 2021, and the Clinical Microbiology Laboratory, an Integrated Clinical Laboratory Installation of RSUD dr. Zainoel Abidin Banda Aceh, conducted the microbiological culture examinations. The study's samples, 35 respondents drawn from all patients with chronic tonsillitis treated at the ORL-HNS RSUDZA outpatient clinic who matched the inclusion criteria, were collected using a total sampling method, which is not based on probability.

The inclusion criteria for this study included chronic tonsillitis patients aged years with recurrent acute infections or subclinical infections lasting more than 3 months and acute exacerbation episodes at least three times annually, tonsillectomy surgery patients who did not receive antibiotic therapy at least 48 hours prior to surgery, and chronic tonsillitis patients with recurrent acute infections or subclinical infections lasting more than 3 months. Patients with chronic tonsillitis who met the study's exclusion criteria, such as those with an acute infection with peritonsillar abscess or suspected tonsil cancer, or those who were immunocompromised, were not allowed to have their tonsils removed.

The isolation of bacterial growth was accomplished using media such as Mac Conkey Agar (MCA) and chocolate agar. After the isolates had been cultured for 24 hours, the bacteria were identified using macroscopic observation, microscopic inspection, and further identification using the VITEK® 2 Compact.Patients having tonsillectomy procedures had samples of their tonsil core tissue extracted using the dissection technique. The tonsil core was then cut with a sterile scalpel and placed in a sterile container containing sterile physiological saline solution (NaCl 0.9%) after the excised tonsillar tissue was dipped in povidone-iodine solution for 30 seconds, rinsed three times with 0.9% NaCl, and dried. The sample in the container is then sent to the Clinical Microbiology Laboratory, a unit of the RSUD dr. Zainoel Abidin Banda Aceh that has an integrated clinical laboratory.In order to evaluate the clinical symptoms of tonsillitis, Mc Isaac's Modified Centor score was calculated based on the history of fever (score 1), tonsillar exudate/tonsil enlargement (score 1), no cough (score 1), enlargement of the anterior cervical glands (score 1), age (3–14 years), age (15–44 years), and age 45 years (score -1).

Chi-square, categorical comparative appropriateness analysis utilizing the Kappa test, and univariate analysis were all employed in the data analysis with a 95% confidence level.

RESULT

The following table 1 displays the characteristics of the 35 participants in this research. The average age of those with chronic tonsillitis was 18 years in the group with positive bacterial growth and 12 years in the group with negative culture, according to the study's responder characteristics. According to the size of the tonsils, it was discovered that the T3 size tonsils had the most responders (24), followed by the T2 tonsils (six), and the T4 size tonsils (five).

Table 1. Characteristic data of patients with chronic tonsillitis based on the growth of microorganisms

Characteristic	Microorganism Culture		P Value
	Positive (n = 30)	Negative (n = 5)	
Age(years) Median (min– max)	18 (9 – 47)	12 (5 – 19)	0,069
Age group n (%)			
3-14	5 (16,7)	3 (60)	
15-44	24 (80)	2 (40)	
≥ 45	1 (3,3)	0	
Sex n (%)			0,658
Man	14 (46,7)	3 (60)	
Woman	16 (53,3)	2 (40)	
Tonsil Size n (%)			-
T1	0	0	
T2	4 (13,3)	2 (40)	
T3	22 (73,3)	2 (40)	
T4	4 (13,3)	1 (20)	
McIsaac Modified Centor Score, median (min – max)	3 (2–4)	2 (2)	0,003*

Based on the size of the tonsils, it was found that the tonsils of T3 were the most with 24 respondents, followed by the T2 tonsils with 6 respondents and the T4 size was the lowest, namely 5 respondents. Based on the total Centor score modified McIsaac, respondents who experienced bacterial growth had an average score of 3 and those who did not have bacterial growth had an average score of 2 which is significant with p value. 0,003 ($\alpha < 0.05$)

Table 2. The results of the tonsillar tissue culture examination

Type of microorganism	n	%
Gram Positive		
Staphylococcus aureus	19	59,4
Streptococcus agalactiae	3	9,4
Enterococcus faecalis	1	3,1
Streptococcus pyogenes	1	3,1
Staphylococcus pseudintermedius	1	3,1
Subtotal	**25**	**78,1**
Gram Negative		
Klebsiella pneumoniae	2	6,3
Enterococcus cloacae	1	3,1
Pseudomonas aeruginosa	4	12,5
Subtotal	**7**	**21,9**
Total	**32**	**100**

Only 30 of the 35 participants in this research had tonsillar core tissue cultures that demonstrated positive development, according to the findings, which are shown in Table 2. There were two specimens out of the 30 that saw the development of many types of bacteria, whereas the other 28 saw the growth of only one kind of bacterium. There were 25 gram-positive bacteria that were responsible for chronic tonsillitis, with 19 (59.4%) of them being Staphylococcus aureus isolates. Pseudomonas aeruginosa isolates made up the majority of the 7 (21.9%) gram-negative bacteria that were discovered.Gram-positive bacteria demonstrated the maximum antibiotic sensitivity to gentamicin, ciprofloxacin, levofloxacin, linezolide, and trimethoprim/sulfamethoxazole, which ranged from 94.74 to 100%, out of the 31 kinds of antibiotics employed to assess the susceptibility of the isolated bacteria. Amoxicillin, ampicillin, cefoxitin, cefepime, ticarcillin, amoxicillin/clavulanic acid, cefotaxime, piperacillin/tazobactam, tetracycline, amikacin, and nitrofurantoin had the lowest antibiotic sensitivity rates, which varied from 5.26 to 36.84%.

Gentamicin, linezolide, and trimethoprim/sulfamethoxazole had the maximum antibiotic sensitivity in Staphylococcus aureus species with 100%, followed by ciprofloxacin, vancomycin, and levofloxacin with 94.74%, tigecycline, 89.74%, clindamycin, azithromycin, erythromycin, and clarithromycin, respectively. – 84.21% each. Antibiotic sensitivity of Streptococcus pyogenes species is still 100% against ampicillin/sulbactam, erythromycin, levofloxacin, ciprofloxacin, gentamicin, tetracycline, and amoxicillin/clavulanic acid.

Levofloxacin, meropenem, ceftazidime, gentamicin, piperacillin/tazobactam, and amikacin all have 100% antibiotic sensitivity rates in gram-negative bacteria such Pseudomonas aeruginosa, Enterobacter cloacae, and Klebsiella pneumonia. The sensitivity, which varied from 50% to 75%, was somewhat low to cefoperazone/sulbactam, polymyxin, tobramycin, cefotaxime, and cefoxitin.The following table shows the Conformity Analysis of McIsaac's Modified Centor Score based on the symptoms experienced by 35 respondents who were calibrated to the outcomes of the microbial development from the tonsillar core culture.

Table 3. Analysis of the suitability of the McIsaac Modification of the Centor score with microorganism culture results

		GABHS CULTURE (*Streptococcus pyogenes*)		Total
		Positive	**Negative**	
McIsaac	**≥ 4**	1 (2,9)	7 (20)	8 (22,9)
	<4	0	27 (77,1)	27 (77,1)
Total		1 (2,9)	34 (97,1)	35 (100)

Kappa 0,181 [IK95% (-0,13) – 0,492];
p-value = 0,062

Table 3 reveals that of the eight respondents with a McIsaac score of less than four, only one reported experiencing the development of group A hemolytic streptococcus (GABHS/Streptococcus pyogenes), whereas the other seven reported experiencing the growth of other bacteria. A match between the McIsaac modified Centor score and the microorganism culture indicating the growth of Group A hemolytic Streptococcus is 18.1%, which means the level of concordance between the examinations is very low. Kappa value analysis: 0,181 [IK95% (-0,13) - 0,492]; p value: 0,062.

The analysis of the diagnostic significance of the McIsaac modified Centor score is shown in the following table.

Table 4. Analysis of the diagnostic significance of the McIsaac modified Centor score

Diagnostic significance	Persentase
Sensitivity	100%

Spesificity	79,41%
Positive predictive value	12,5%
Negative predictive value	100%
Accuracy	80%

The McIsaac modified Centor score has a sensitivity value of 100% and a specificity value of 79.41% for identifying GABHS infection as the root cause of chronic tonsillitis.

DISCUSSION

Tonsillitis was most common in children (46.8%), school-aged teenagers, and a relatively small percentage of those aged 45 or older (3.2%).27 In this research, the age range with the largest frequency was 15–44 years, followed by 3–14 years, and it dropped after age 45. Due to their outdoor activities and increased risk of upper respiratory infections, children often get tonsillitis.[19] Additionally, preservatives, artificial sweeteners, and artificial colours that are irritating to the throat and may cause tonsil or throat infections are often found in the snacks that kids and teenagers eat.

In this research, it was discovered that T3, with 24 respondents, had the largest tonsils, followed by T2 and T4, with 6 and 5 respondents, respectively. This is consistent with the research of Panga et al. They discovered that tonsil enlargement (T3) was more prevalent than T2, T4, and T1 by 30%, 13.3%, and 3.3%, respectively, with a prevalence of 53.3%.20 In contrast to Zautner et al.'s investigation, they discovered that T2 had the highest enlargements (50.0%), followed by T3 and T1 with 40.8% and 9.2%, respectively.21 According to research, clinical symptoms and tonsillar hyperplasia are related to high bacterial concentrations in the tonsillar tissue.[22]

The Gram-positive bacteria Staphylococcus aureus, Streptococcus agalactiae, Enterococcus faecalis, group A -hemolytic Streptococcus (Streptococcus pyogenes), and Staphylococcus pseudintermedius are the most often identified forms of bacteria that cause chronic tonsillitis. Meanwhile, Pseudomonas aeruginosa, Klebsiella pneumonia, and Enterococcus cloacae were the most often identified Gram-negative bacteria.

Staphylococcus aureus was more prevalent, followed by Streptococcus pneumonia, Klebsiella pneumonia, group A -hemolytic Streptococcus, Pseudomonas aeruginosa, Eschericia coli, and Haemophilus influenza, according to research by Panga et al. Additionally, they discovered that bacteria in the tonsil core were less congested than those on the tonsil surface..[20]

However, in a study by Loganathan et al., Group A -hemolytic Streptococcus (32,7%) and Haemophilus influenza (15,8%) were the most frequently isolated bacteria in children, while Staphylococcus aureus was more frequently isolated in adults (45.5%) along with Klebsiella pneumonia (22,7%) and group A -hemolytic Streptococcus (14,2%).[23] The findings of this research and other investigations carried out in other locations may vary owing to the effect of outside influences in each location. Research conducted in various locations will provide various demographic traits.[24]

The research also discovered that there were substantial changes in tonsillitis-causing microorganism types according to age, suggesting that variations in tonsil microorganism types may result from various antibiotics used in the clinical environment. As a result, it's critical to regularly check the tonsils for bacteria using accurate diagnostics, and the bacteriology of the tonsillar core may vary as people age. The research also discovered that there were substantial changes in tonsillitis-causing microorganism types according to age, suggesting that variations in tonsil microorganism types may result from various antibiotics used in the clinical environment. As a result, it's critical to regularly check the tonsils for bacteria using accurate diagnostics, and the bacteriology of the tonsillar core may vary as people age. [18,23]

A total of 31 different antibiotic kinds were utilized to assess the isolated bacteria's susceptibility. The results revealed that different people responded to antibiotics in various ways. Even within the same nation, there are regional differences in the antibiotic resistance of microorganisms. Results on antibiotic sensitivity may vary as a consequence of variations in sample size, location, methodology, and economic conditions.18,25

Because tonsillectomy is typically performed in areas where saprophytic and pathogenic bacteria are present, it is crucial to examine the tonsillar core culture in order to determine bacterial patterns and sensitivity to antibiotics, especially in patients who are having their tonsils removed. This can also serve as a guide for prophylactic antibiotics. Therefore, there is a chance of both local and systemic problems after this operation.[26]

Less than 1% of postoperative morbidity is due to local complications, which typically take the form of an infection of the surgical wound with delayed healing outcomes, increased pain, a need for additional care, and prolonged recovery periods. Systemic complications, such as pneumonia, meningitis, or sepsis, account for the remaining 0.2% of postoperative morbidity.[26] Study in the United States found that the frequency of infections associated with laryngologic procedures including tonsillectomy ranged from 24 - 87% of cases, so that in such cases, prophylactic antibiotics are recommended.[26]

Antibiotics must be administered in this situation in line with the causal pathogen, the findings of the culture, or the pathogen that is most prevalent in a certain location, as well as the appropriate dosage.[26]

The McIsaac modified Centor score and the microorganism culture showing the development of Streptococcus pyogenes had a degree of conformity in this research of 18.1%, suggesting extremely poor compatibility between the tests. McIsaac et al.'s study also discovered that patients with scores of 0 to 2.5%, 1, 5, 11, 22, 27, and 4 to 52.8% had higher growth rates of group A Streptococcus bacteria than those with scores of 1 to 5.1%, 3 to 27.8%, and 4 to 52.8%.[27]

Contrary to previous research, which claims that a higher score increases the likelihood of GABHS infection.

Depending on age, regional incidence, and seasonal fluctuations, the likelihood of contracting GABHS ranges from 25 to 86% for a score of 4 to 2 to 3 percent.28 According to other research, the modified Centor criteria are used to determine the risk of group A streptococcus infection. If the score is 0 then the probability of contracting group a streptococcus is 1-2.5%, if the score is 1 then the probability of contracting group a streptococcus is 5-10%, if the score is 2 then the probability of contracting group a streptococcus is 11-17%, and if the score is 3[29]

The Centor score may be used by doctors to estimate the chance of GABHS, but it cannot be used to provide a precise diagnosis.57,70,74 Negative cultures do not rule out the diagnosis of GABHS since up to 40% of carriers are asymptomatic.[28]

In this investigation, the sensitivity value of the McIsaac modified Centor score (100%) was greater than the specificity value (79.41%). This demonstrates that in more than 20% of participants with a score below 4, the GABHS bacteria cannot be determined as the cause of chronic tonsillitis; more research is required to determine the etiology of chronic tonsillitis. The participants with negative findings (score 4) did not have GABHS infection in 100% of cases, according to the data, which showed that the positive predictive value was 12.5% and the negative predictive value was 100%. According to a research by McIsaac et al., who discovered a high sensitivity for modification scores of almost 83.1%, this is the case.30 According to the research, group A hemolytic Streptococcus growth was only 18.1% consistent with the McIsaac modified Centor score and tonsil core microorganisms in chronic tonsillitis.

Numerous variables contributed to this outcome. First off, the samples utilized for the investigation were taken from chronic tonsillitis patients who do not generally display symptoms like fever, cough, tonsil exudates, or lymphadenopathy. Second, it has been noted that group A haemolytic Streptococcus bacteria, which are often linked to tonsillitis, exhibit inadequate growth on both solid and liquid medium.

For the development of these bacteria, special nutritional agar medium with a large volume of blood, a pH range of 7.4 to 7.6, an ideal temperature of 37°C, and anaerobic conditions are required. Additionally, these bacteria are known to colonize the tonsils sparingly, which makes it even more difficult to identify them.

Finally, according to the research, Group A haemolytic Streptococcus bacterial growth is significantly influenced by seasonal fluctuations, geographic prevalence, and age.70 As a result, more research in the form of microbiological culture is required to ascertain the origin of chronic tonsillitis.

Additionally, tonsillitis with a modified McIsaac Centor score of 4 is not necessarily brought on by Group A hemolytic Streptococcus but may also be brought on by other bacteria. To evaluate the consistency between the McIsaac modified Centor score and the microorganisms in the tonsillar core of chronic tonsillitis patients, more study with a larger sample size is required.

REFERENCES

1. Jin HJ, Dong WL, Ri AR, et al. Bacteriologic Comparison of Tonsil Core in Recurrent Tonsillitis and Tonsillar Hypertrophy. Laryngoscope 2007; 117.

2. Tzelnick S, Hilly O, Vinker S, Bachar G, Mizrachi A. Long-Term Outcomes of Tonsillectomy for Recurrent Tonsillitis in Adults. Laryngoscope 2019; 130:328-331.

3. Bakar MA, McKimm J, Haque SZ, Azim MA, Majumder, Haque M. Chronic Tonsillitis and Biofilms: A Brief Overview of Treatment Modalities. Journal of Inflammation Research 2018; 11:329–337.

4. Furuncuoglu Y, Salgam F, Kutluhan A. Acute Exudative Tonsillitis in Adults: The Use of the Centor Score and Some Laboratory Tests. Turk J Med Sci 2016; 46:1755-1759.

5. Ginting D. Pola Bakteri dari Usapan Permukaan dan Parenkim Tonsil pada Penderita Tonsilitis yang Berulang. Medan. Universitas Sumatera Utara, 2018. Tesis.

6. World Health Organization. Survailance of Risk Factors for Non-Communicable Diseases: The WHO Stepiseapproach Summari. Geneva. 2013.

7. Alotaibi AD. Tonsillitis in Children Diagnosis and Treatment Measures. Saudi J. Med 2017; 2:Iss-8:208-215.

8. Windfuhr JP, Toepfner N, Steffen G, Waldfahrer F, Berner R. Clinical Practice Guideline: Tonsillitis I. Diagnostics and Nonsurgical Management. Eur Arch Otorhinolaryngol 2016; 273:973–987.

9. Gul M, Okur E, Ciragil P, Yildirim I, Aral M, Kilic MA. The Comparison of Tonsillar Surface and Core Cultures in Recurrent Tonsillitis. American Journal of Otolaryngology Head and Neck Medicine and Surgery 2007; 28:173–176.

10. Onal M, Yilmaz T, Bilgic E, Muftuoglu SF, Kuscu O, Gunaydin RO. Apoptosis in Chronic Tonsillitis and Tonsillar Hypertrophy. International Journal of Pediatric Otorhinolaryngology 2015; 79:Issue 2:191–195. Available at: http://dx.doi.org/10.1016/j.ijporl.2014.12.005.

11. Mindarti F, Rahardjo SP, Kodrat L, Sulaiman AB. Hubungan Kadar Anti Streptolisin-O dan Gejala Klinis pada Penderita Tonsilitis Kronis. Jurnal Kedokteran YARSI 2010; 18(2):121-128.

12. Rahman A, Akhtar A, Sharma SC. Current Trends of Surface Versus Core Bacterial Flora among Recurrent Tonsillitis Patients in a North Indian Tertiary Care

Hospital. International Journal of Contemporary Medical Research 2019; 6:Issue 6.

13. Siswantoro B. Pengaruh Tonsilektomi Terhadap Kejadian Bakteremia pasca Operasi. Semarang. Universitas Diponegoro/SMF Kesehatan THT-KL RS Dr.Kariadi, 2003. Laporan penelitian.

14. Dickinson A, Kankaanpa H, Dent B, et al. Tonsillar Surface Swab Bacterial Culture Results Differ from Those of the Tonsillar Core in Recurrent Tonsillitis. Laryngoscope 2019; 1-4.

15. Kasenomm P, Kull M, Mikelsaar M. Association between Tonsillar Core Microflora and Post-tonsillectomy Bacteremia. Microbial Ecology in Health and Disease 2002; 14:122–127.

16. Shishegar M, Ashraf MJ. Posttonsillectomy Bacteremia and Comparison of Tonsillar Surface and Deep Culture. Advances in Preventive Medicine 2014; 5 pages. Available at: http://dx.doi.org/10.1155/2014/161878.

17. Palla AH, Khan RA, Gilani AH, Marra F. Over Prescription of Antibiotics for Adult Pharyngitis is Prevalent in Developing Countries but can be Reduced Using Mcisaac Modification of Centor Scores: A Cross-Sectional Study. BMC Pulmonary Medicine 2012; 12:70. Available at: http://www.biomedcentral.com/1471-2466/12/70.

18. Alasil SM, Omar R, Ismail S, Yusof MY, Dhabaan GN, Abdulla MA. Evidence of Bacterial Biofilms among Infected and Hypertrophied Tonsils in Correlation with the Microbiology, Histopathology, and Clinical Symptoms of Tonsillar Diseases. International Journal of Otolaryngology 2013. Available at: http://dx.doi.org/10.1155/2013/408238

19. Shalihat AO, Novialdi, Irawati L. Hubungan Umur, Jenis Kelamin dan Perlakuan Penatalaksanaan dengan Ukuran Tonsil pada Penderita Tonsilitis Kronis di Bagian THT-KL RSUP DR. M. Djamil Padang Tahun 2013. Jurnal Kesehatan Andalas 2015;4(3):786-94.

20. Panga A, Rani GU, Kumar MV. Chronic Tonsillitis: A Comparative Study of the Causative Organism Cultured Through Throat Swab vs. Core Culture and Biopsy of the Tonsillectomy Specimen. International Journal of Science and Research 2013;5(4):1390-95.

21. Zautner AE, Krause M, Stropahl G, Holtfreter S, Frickmann H, Clauida M, et al. Intracellular Persisting Staphylococcus aureus Is the Major Pathogen in Recurrent Tonsillitis. PLoS ONE 2010;5(3):e9452.

22. Rajesh K, Prabhusaran N, Sahoo GC, Prabhakar K, Jesudoss A. Comparative Study of Surface and Core Microflora of Chronic Tonsillitis. Journal of medical Science and Clinical Research 2016;4(4):10044-49.

23. Loganathan A, Arumainathan UD, Raman R. Comparative study of bacteriology in recurrent tonsillitis among children and adults. Singapore Med J 2006;47(4):271-5.

24. Damayanti E, Iriani Y, Yuwono. Ketepatan Skoring McIsaac untuk mengindentifikasi faringitis Group A Streptococcus pada anak. Sari Pediatri 2014;15(5):301-6.

25. Kebede D, Admas A, Mekonnen D. Prevalence and antibiotics susceptibility profiles of streptococcus pyogenes among pediatric patients with acute pharyngitis at Felege Hiwot Comprehensive Specialized Hospital, Northwest Ethiopia. BMC Microbiology 2021;21:135.

26. Orlowski K, Lisowska G, Misiolek H, Paluch Z, Misiolek M. The Efficacy of Perioperative Antibiotic Therapy in Tonsillectomy Patients. Adv Clin Exp Med 2016;25(3):493–503.

27. McIsaac WJ, White D, Tannenbaum D, Low DE. A clinical score to reduce unnecessary antibiotic use in patients with sore throat. Journal of Canadian Medical Association. 1998;158(1):75-83.

28. Scottish Intercollegiate Guidelines Network. Management of sore throat and indications for tonsillectomy. A national clinical guideline. 2010

29. Pedoman Nasional Pelayanan Kedokteran Tatalaksana Tonsilitis. Perhimpunan Dokter Spesialis Telinga Hidung Tenggorok Bedah Kepala Leher. Indonesia. 2018.

30. Vasudevan J, Mannu A, Ganavi G. McIsaac Modification of Centor Score in Diagnosis of Streptococcal Pharyngitis and Antibiotic Sensitivity Pattern of Beta-hemolytic Streptococci in Chennai, India. Indian Pediatrics, 2019;56:49-52.