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Diagnostic evaluation of viral versus bacterial tonsillopharyngitis using an artificial intelligence mobile application and symptom questionnaire

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Abstract

Objective: In this study, it was aimed to distinguish bacterial/viral tonsillopharyngitis (TP) by scoring the symptom and throat images of pediatric patients with artificial intelligence-based mobile application.

Method: Fifty-one patients who applied to Sakarya University Training and Research Hospital, Department of Pediatrics and Diseases with acute tonsillopharyngitis were included. Samples were taken from patients and mouth/throat pictures were taken so that the tonsils and pharynx were clearly visible. In the microbiology laboratory, identification with culture/MALDI-TOF MS (Biomerieux, France) from the first samples, and nucleic acid isolation from the other for molecular tests were performed. Symptoms such as fatigue, sore throat, muscle pain, cough, sneezing, and runny nose were questioned from each patient on a scale of 1 to 5. By uploading the symptom results and throat pictures to the artificial intelligence application, it was aimed to distinguish bacterial/viral tonsillopharyngitis with the developed scoring system.

Results: Of the 51 samples included in the study, 21 were culture positive and 30 were negative. The artificial intelligence application was defined as 20 out of 21 culture-positive samples, 3 out of 30 culture-negative samples as bacterial tonsillopharyngitis (Sensitivity: 95.2%, specificity: 90%).

Conclusion: This study is one of the first to bring together the artificial intelligence application and microbiology. AI/scoring system may have a role to play in the diagnosis of bacterial vs viral TP, and in doing so may enable more appropriate antibiotic usage targeted to only bacterial TP infections. It is important to distinguish between bacterial and viral tonsillopharyngitis in the COVID-19 pandemic.

Keywords: Artificial Intelligence, Tonsillopharyngitis, Virus, Rational Antibiotic Use

INTRODUCTION

In most of the tonsillopharyngitis cases, it is very difficult to establish the etiological diagnosis by clinical. Although pharyngeal and tonsillar exudates, sensitive lymphadenopathies, skin rashes and conjunctivitis are important in the differential diagnosis, they are not specific findings. Nevertheless, some clinical scoring systems have been developed to predict streptococcal tonsillopharyngitis, especially in line with the clinical studies conducted by McIsaac and Centor (1,2). Each of four clinical features — absence of cough, purulent pharyngeal exudate, anterior cervical lymphadenopathy, and temperature of >38°C — is scored with 1 or 0, depending on whether it is present; 5 scores range from 0 (when none of

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the features are present) to 4 (when all are present) in Centor criteria (3). McIsaac independently derived a prediction system based on a cohort of patients from primary care. In essence, it modifies the Centor system to include an extra variable age. For those aged between 3 years and 14 years, 1 is added to the score, whereas, for those aged ≥45 years, 1 is subtracted from the score; hence, a patient presenting with a sore throat may have a McIsaac score of anything between −1 and 5 (4,5). (Table 1) These clinical scoring systems are especially helpful in preventing unnecessary antibiotic use in primary care.

The clinical use of artificial intelligence systems for detecting and monitoring healthcare-associated infections (HAIs) has become widespread in recent years (6,7). Monitoring with artificial intelligence systems is considered superior because it is faster than conventional surveillance, less people are needed, and it is independent of evaluator errors in traditional monitoring (8,9). Consistent with the idea of “There is no disease, there is a patient” in infections, the results may be uncertain or borderline changes due to the host’s immune status, pathogenic characteristics and the interactivity between the two (10).

Due to the difficulties experienced in the rapid and definite diagnosis of TP etiology, an artificial intelligence system including a symptom / photo questionnaire was developed to assist clinical diagnosis. In our study, it is aimed to investigate the clinical diagnostic accuracy of a medical artificial intelligence system that can be used in the rapid and non-invasive diagnosis of throat infections. In this way, it is thought that it can reduce the use of costly tests used in the diagnosis of TP, give an idea about viral/bacterial TP, and provide ease of use since it can reduce the tonsillopharyngeal swab process, which is especially uncomfortable in children. In the artificial intelligence system developed for this purpose, the complaints of the patients in the childhood age group and the photographs of the throat areas were compared with the traditional throat culture.

METHOD

Study Design

Fifty-one patients who applied to Sakarya University Hospital, Department of Pediatrics with the complaint of acute tonsillopharyngitis between 1-30 December 2019 were included in our study. On 11/11/2019, approval was obtained from the xxx Clinical Research Ethics Committee with the decision number 16214662/050.01.04/179. The inclusion of the patients in the study was on a voluntary basis, and the participants were asked to fill out a voluntary consent form. The inclusion criteria for the study are as follows:

Being in the 0-18 age range,

Volunteering to participate in the study,

Presenting with symptoms of tonsillopharyngitis,

Detection of bacterial TP agent in the patient as GAS and

Not taking any antibiotic treatment.

Samples were taken from the patients with 2 different swabs, and mouth/throat pictures were taken to see the tonsils and pharynx. Throat pictures (51 patients) were taken with the mobile camera of healthcare professionals and recorded with the symptom data of the patients and uploaded to the FluAI application. All symptom information questioned in the questionnaire was obtained from the parents of the children.

In the microbiology laboratory, after the detection of growth on culture,identification was performed with Vitek MS (Biomerieux, France) from the first samples, and total nucleic acid isolation (EZ1-Qiagen, Germany) was performed from the other for molecular tests. Growth of Group A beta hemolytic streptococci in culture was accepted as the diagnostic criterion for bacterial TP. Molecular methods were used for the diagnosis of viral agents.

In addition, symptoms such as fatigue, sore throat, myalgia, cough, sneezing, runny nose were questioned on a scale of 1 to 5 from each patient. Symptom results and throat pictures were uploaded to the artificial intelligence application and targeted. Questionnaire and swab sampling were done by the same person throughout the study to minimize interobserver differences. It was aimed to differentiate bacterial/viral tonsillopharyngitis with the developed scoring system. Scoring results by application were compared with the results of the culture and molecular respiratory panel (Qiastat, Qiagen, Germany). True positive samples were considered as replicating bacterial agents in culture and were defined as bacterial tonsillopharyngitis by the artificial intelligence application scoring system. We compared the accuracy and safety of the FluAI upper respiratory decision support system with gold standard diagnostic methods. Accuracy was evaluated for the suitability of the proposed conditions.

Analysis process

With the first algorithm, the photo taken by the mobile application, it is evaluated whether the throat photo is taken correctly or not. If it is a suitable image for analysis, in the next step, the photo is sent to the analysis engine of FluAI and the images of the infection markers in the photo are analyzed as a result of a computational system. As a result of the analysis of the photo, a symptom check is made to the person, including his complaints about upper respiratory tract infections. At the end of this query, symptom and photo analysis are brought together and decision support is provided to the person.

Model

We used ResNet-50 is a 50-layer deep learning model that has been trained to classify images into 1000 categories. Hence, the ResNet-50 pre-trained model has been used to accelerate the training of deep models for other problems through transfer learning. Fine Tuned Resnet-50 the parameters of the ResNet-50 model are used as initialization of a fine-tuned model for the dataset under consideration. All of the convolutional layers were frozen except for the last ten as the throat images are very different from the ImageNet data. We modified the last three layers of ResNet-50 to adapt it to the target domain.

Figure 1 shows the fine-tuning process. Since the Resnet50 model is trained with the ImageNet dataset, we need to organize its architecture according to our data. We can also speed up training by freezing the first layers of the pretrained Resnet50 model.

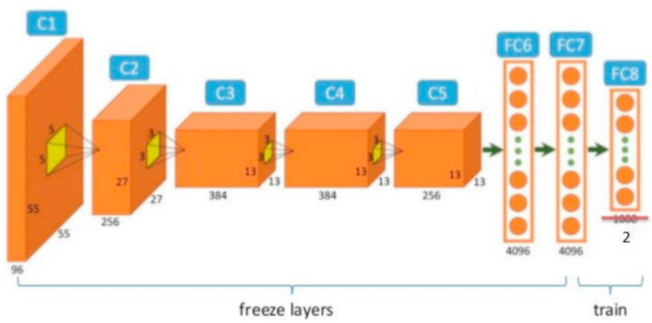

Figure 1. Resnet-50 layers.

ResNet-50 is a convolutional neural network. Convolutional neural networks learn which filters to apply to pictures in the training process. For example, a simple filter can help us distinguish edges or corners. Learned filters become more complex and specialized in our data as layers deepen. Our model distinguishes between 2 classes, so we trained with bacterial and viral TP pictures. In the estimation phase, we estimated the class of the test visuals with our pre-trained model.

Preprocessing of 2D Resnet-50

Pre-processing: The photos we use in the training process can be of many different sizes. The input layer of convolutional neural networks is fixed size, so we have to resize all images in the training and prediction process. During the training process, the size was 224x224. In addition, normalizing the pixel values will positively affect the training process.

Data Augmentation

Data augmentation is the increase of data by exposure to various distortion effects to increase performance, especially in small data sets. In this way, the model is provided to learn about different conditions. With this method, we have more data, and our model is immune to changes in light, angle, and distance.

To avoid the overfitting problem since the number of training throat pictures was limited, various data augmentation strategies were applied including random affine transformation. The affine transformation was composed of rotation (0◦±10◦), horizontal and vertical translations (0%±10%), scaling (0%±20%), shearing in the width dimension (0%±10%), and brightness range (0%±10%).

Heatmap generation

Especially in the field of health, the interpretability of artificial intelligence is very important. To reduce this problem, the method of heat mapping is used in convolutional neural networks. A heat map shows us where the deep learning algorithm focuses the most in the picture when distinguishing between bacterial or viral classes.

To visualize the heatmap, we used a technique called Grad-CAM. The idea behind it is to find the importance of a certain class in our model, we simply take its gradient concerning the final convolutional layer and then weigh it against the output of this layer. We choose the activation_49 layer to create the heatmaps.

RESULTS

Culture results

Of the 51 samples, 21 were culture positive and 30 were negative. The artificial intelligence application contains 20 of the 21 culture-positive samples; it defined 3 of 30 culture-negative samples as bacterial tonsillopharyngitis (Sensitivity: 95.2%, Specificity: %90). (Table 1) When patients whose complaint period exceeds 3 days are excluded from the statistics, the sensitivity of the application increases to 100%.

Table 1: Centor and McIsaac score criteria

Centor score	
Symptom	Score
Body temperature (in the history) >38 °C	1
No cough	1
Cervical lymph node swellings	1
Tonsillar swelling or exudation	1
Total point	Probability of GABHS proof in the swab (%)
0	~2.5
1	~6-7
2	~15
3	~30-35
4	~50-60

Table 1: Centor and McIsaac score criteria

McIsaac score	
Symptom	Score
Body temperature (in the history) >38 °C	1
No cough	1
Cervical lymph node swellings	1
Tonsillar swelling or exudation	1
Age (years) 3-14 15-44 ≥45	1 0 -1
Total point	Probability of GABHS proof in the swab (%)
-1 or 0	1
1	10
2	~17
3	~35
4 or 5	~50

Respiratory panel results

In the details of the study, there is also a distinctive examination as to whether viral tonsillopharyngitis infections are flu or common cold, and when the application and respiratory panel molecular test results are compared, the sensitivity of the application for influenza and cold was found to be 55.6% and 90.5%, and the specificity was 95.2% and 93.3%, respectively.

Application model performance

The experiments were carried out using NVIDIA T4 GPU where the baseline model required 5 minutes (for model training and testing), the ResNet-50 model required 100 seconds (for model testing), and the fine-tuned method required 32 minutes (for training and testing).

Scoring and accuracy

A total of 51 patients were included. For all patients, our model achieved a sensitivity of 0.952, the specificity of 0.9, and accuracy of 0.921. The patients in the first 3 days of their complaints, achieved a sensitivity of 0.1, specificity of 0.916, and accuracy of 0.947 (Figure 2).

Figure 2 is a confusion matrix. “0” values present “Viral pharyngitis”, “1” values present “Bacterial Tonsillopharyngitis”. Colors change with numerical values.

The empirical ROC curve corresponding to the culture method of the artificial intelligence application developed for the diagnosis of tonsillopharyngitis was drawn in Figure 3 with a non-parametric method using SPSS Version 25.0 software (AUC=0.927, 95% confidence interval: 0.84-1.00, p< 0.001). This ROC curve and the corresponding AUC value indicate that AI, as a preliminary diagnostic method, has the predictive ability to distinguish bacterial tonsillopharyngitis from viral.

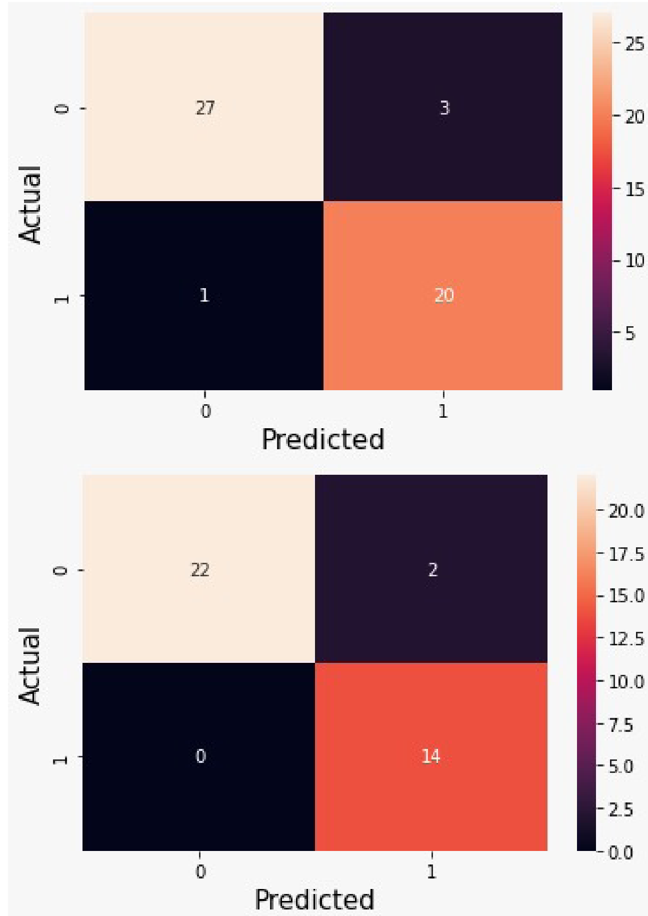

Figure 2. a) All patients. b) First 3 days of complaints.

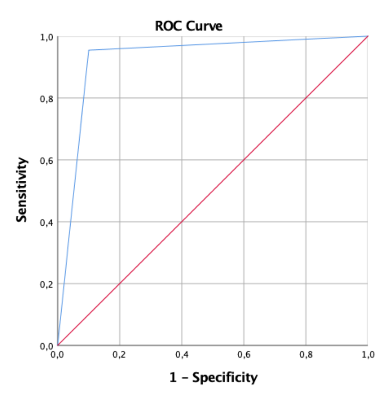

Figure 3: ROC curve analysis for AI and culture method.

The following throat images of patients show original photo and heatmap version, which points the artificial intelligence focuses on during the analysis, thus presenting the decision according to which regions in a more transparent way.

Patients have severe fatigue, severe cough, moderate throat pain, mild headache, and moderate muscle pain. Diagnose was bacterial tonsillopharyngitis. FluAI engine analyzed as “bacterial tonsillopharyngitis” and it shown focused suspected bacterial infection area (Figure 4, 5, 6).

Table 2. Culture and FluAI comparison

	Culture								
	Negative				Positive				Total (n)
	FluAI Negative		FluAI Positive		FluAI Negative		FluAI Positive		
	n	%	n	%	n	%	n	%	51
	27	90	3	10	20	95.23	1	4.77	
Total (n)	30				21				

Figure 4. Patient 1 throat photo, left one is raw, the right one is heatmap edition, after the AI analysis

Figure 5. Patient 2, throat photo, left one is raw, the right one is heatmap edition, after the AI analysis

Figure 6. Patient 3, throat photo, left one is raw, the right one is heatmap edition, after the AI analysis

DISCUSSION

The range of applications of AI and AI-mediated technologies in healthcare is broadly and rapidly increasing. As patients gain more and more ownership of their care, we expect more AI solutions that support the transition from hospital-based service to home care.

There are many studies in the literature as examples of the use of artificial intelligence in clinical diagnosis. A group has recently shown the possibility to develop a low-cost point of care for lymphoma diagnosis based on basic imaging and deep learning (14). New research has shown the added value of machine learning for image processing where classical tools could not identify early signs of diseases (15). This is particularly true for cancer in which diagnosis and treatment are often assisted by AI approaches (16). Also, recent approaches using mathematical modeling are improving surveillance studies. A similar system was developed by Sun et al. (2015) to detect infected patients by classification using vital signs. In this way, respiration rate, heart rate, and facial temperature were used to successfully classify individuals at higher risk for influenza using neural network and fuzzy clustering method (17). Support vector machine by developed Saybani et al (2016) is a much robust classifier and was applied to a tuberculosis cohort. With an accuracy of 100%, sensitivity of 100%, specificity of 100%, Youden’s Index of 1, area under the curve (AUC) of 1, and root mean squared error of 0, the new artificial immune recognition system method was able to successfully classify tuberculosis patients (18). Babalık and Güler (2007) have developed a medical expert system that can be used in the diagnosis of tonsillopharyngitis infections (19). It is possible to expand these examples. In our study, the comparison of the artificial intelligence system developed with the photos of the complaints and throat areas of the patients in the pediatric age group was made, and the sensitivity and specificity of this system were measured according to the culture method.

With our study, we think that this artificial intelligence system, which developed for patients with upper respiratory tract infection, which is one of the biggest responsible for unnecessary antibiotic use and related antibiotic resistance development, has a great potential in raising the awareness of patients about their diseases and conditions from the right source and helping to reduce antibiotic resistance.

Leelasantitham and Kiattisin developed a program for the diagnosis of tonsillitis with an artificial intelligence system and the overall accuracy was found to be about 90% when compared with the doctor’s diagnoses (20). Our study was carried out using NVIDIA T4 GPU technology. A total of 51 patients were included in the study. Of the 51 samples, 21 were culture positive and 30 were negative.

The artificial intelligence application contains 20 of the 21 culture-positive samples; it defined 3 of 30 culture-negative samples as bacterial tonsillopharyngitis (Sensitivity: 95.2%, Specificity: %90). When patients whose complaint period exceeds 3 days are excluded from the statistics, the sensitivity of the application increases to 100%. In the details of the study, there is also a distinctive examination as to whether viral tonsillopharyngitis infections are flu or common cold, and when the application and molecular test results are compared, the sensitivity of the application for influenza and cold was found to be 55.6% and 90.5%, and the specificity was 95.2% and 93.3%, respectively.

The limitations of our study are the small sample size, performing the study in a limited time period and the single-center nature of our study. In addition, due to the limitation of the number of patients in laboratory parameters, a statistically limit value could not be shown.

CONCLUSION

Most bacterial pharyngitis is caused by Group A Streptococci (GAS). Therefore, discrimination between bacterial-viral causes, and rapid diagnosis of GAS are important in terms of guiding treatment in acute tonsillopharyngitis cases (21). The usability of an artificial intelligence application developed in this study to distinguish bacterial / viral agents of tonsillopharyngitis clinically and visually was tested. There are many different artificial intelligence techniques that have the capacity to solve various diseases. More controlled studies are required to measure the practical success of these techniques. Studies so far show that medical artificial intelligence is vital in helping doctors to increase the efficiency of healthcare services. As a result of our study, it was concluded that the FluAI system can be used safely in the diagnosis of tonsillopharyngitis and that it will bring benefits such as early diagnosis and rational use of antibiotics. The comparison of the prediction value of AI versus culture of the swab could be very helpful in the COVID scenario when physicians/pediatricians have less possibility to directly visit patients, potentially limiting the overuse of antibiotic for non-streptococcal infections and thus limiting antibiotic resistance. The potential of artificial intelligence methods in clinical medicine is understood from thousands of publications in a wide variety of fields. The power of these methods in the research and treatment of diseases arouses excitement.

As a result of our study, it was found that FluAI symptom questionnaire and image application have high sensitivity and specificity in differentiation of viral / bacterial TP.

Individuals can understand whether the etiology of tonsillopharyngitis is bacterial or viral in the COVID-19 pandemic, thanks to its highly accurate application, without entering environments with a high risk of infection. In today's world where the pandemic is intense, the ability of individuals to make this distinction without burdening the health system will also contribute to the economy.

Our application can be economically beneficial in that it can reduce the use of high-cost tests required to make this distinction.

It can reduce inappropriate and excessive antibiotic prescription in terms of giving an idea about viral and bacterial infections. It can reduce antibiotic resistance in bacteria, which is an indirectly important problem.

FluAI provides ease of use as it may reduce the tonsillopharyngeal swab process which is uncomfortable especially in children.

However, the widespread use of this technology may cause patients to resort to wrong treatments without consulting the physician.

Conducting such studies with a larger sample for longer periods for future studies will contribute to diagnostic guidelines developed for different diseases.

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Peer-Review

Both externally and internally peer reviewed.

Conflict of Interest

The authors declare that they have no conflict of interests regarding content of this article.

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Ethical Declaration

Ethical permission was obtained from the Sakarya University, Medical Faculty Clinical / Human Research Ethics Committee for this study with date 11/11/2019 and number 16214662/050.01.04/179, and Helsinki Declaration rules were followed to conduct this study.

Authorship Contributions

Concept: MA, YY Design: YY, MA, HT, EPKK Supervising: YY, MA, HT, EPKK, OB, ÖÖ, BE, MK Financing and equipment: YY, MA, HT, OB, ÖÖ, BE, MK Data collection and entry: YY, MA, ÖÖ, BE, MK Analysis and interpretation: YY, MA, HT, EPKK, OB, ÖÖ, BE, MK, Literature search: YY, MA, HT, OB, BE, MK, Writing: YY, MA, HT, EPKK, OB, ÖÖ, BE, MK, Critical review: YY, MA, BE, MK

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