Journal of Kerman University of Medical Sciences
2022; 29(2): 146-151
http://jkmu.kmu.ac.ir/
10.22062/JKMU.2022.91892
Original Article

Evaluation of Viral and Bacterial Causes of Ex udative Pharyngitis in 3 to 15-year-old Children referred to the Clinics Affiliated to Kerman University of Medical Sciences

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ABSTRACT

Background: Exudative pharyngitis is one of the common causes of children referral to medical centers. This problem is caused by various bacterial and viral causes. Antibiotics seem to be taken indiscriminately and irrationally. Investigation of bacterial and viral causes is useful for appropriate treatment. This study aimed to compare the bacterial and viral causes of exudative pharyngitis in children aged 3-15 years who referred to the clinics affiliated to Kerman University of Medical Sciences.

Methods: The study population consisted of children who presented with fever and sore throat and were diagnosed with exudative pharyngitis. Samples were taken from the nasopharynx with sterile swabs and sent to the laboratory to culture group A beta-hemolytic Streptococcus (GAS) and molecular analysis of common viruses. The resulting information was recorded on the data collection form. Data were analyzed by SPSS version 20 using descriptive statistics, and an inference was made.

Results: The mean age of the study group was 7.33 years with a standard deviation of 3.05 and the mean age was 7 years. Most cases (42.6%) referred to the clinics in winter. The most common clinical symptoms were fever (86.9%), sudden onset of the symptoms (77%), sore throat (75.4%), and cough (67.2%), respectively. Seven cases (11.5%) were positive for GAS bacteria. Thirty-two cases (52.5%) were positive for the studied viruses. In housewives, the frequency of positive results in terms of bacteria was significantly lower than that in other occupations. The frequency of virus-positive samples in terms of demographic variables, bacteriological test results in terms of disease symptoms, virology test results in terms of disease symptoms, and comparison of clinical signs and symptoms in the positive group in terms of bacteria and virus were not significant ($P > 0.05$).

Conclusion: Viral causes of exudative pharyngitis are more than bacterial causes. If cultured and laboratory diagnosis is available, it is best to identify the causes of pharyngitis before starting treatment with antibiotics.

Keywords: Children, Pharyngitis, Exudate, Bacterial causes, Viruses

Citation: Hosseininasab A, Sharifi E, Molaei H, Khalooei A, Nazeri P. Evaluation of viral and bacterial causes of ex udative pharyngitis in 3 to 15-year-old children referred to the clinics affiliated to kerman university of medical sciences. Journal of Kerman University of Medical Sciences 2022; 29(1): 146-151. doi: 10.22062/JKMU.2022.91892
Received: 20.01. 2022
Accepted: 13.03. 2022
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Published by Kerman University of Medical Sciences

Introduction

Pharyngitis is sore throat and inflammation of the throat, which is defined by the pharyngeal inflammation of the throat and fever. Exudative pharyngitis is a sore throat with the release of secretions and cellular debris from blood vessels and their deposition on the pharyngeal tissue (1, 2). Exudative pharyngitis is one of the most common diseases in children, which is the third most common disease diagnosed by pediatricians (3), so that it has even been reported as an epidemic and a false epidemic (4, 5).

Bacterial pharyngitis can cause some complications such as peritonsillar abscess, pharyngeal abscess, lymphadenitis, sinusitis, otitis media, mastoiditis, and invasive infections such as toxic shock syndrome (TSS) if not properly diagnosed and treated. Acute rheumatic fever and glomerulonephritis are other complications of the disease, which will vary depending on the cause of the disease, and there are several guidelines for the treatment of pharyngitis (6). Regarding the need for antibiotics for various reasons, many of them are non-bacterial, so antibiotic treatment is not acceptable for all pharyngitis (7, 8).

Staphylococcus is not known as the etiology of pharyngitis with exudate (9).

Exudative pharyngitis has various viral or fungal and bacterial causes,topped by group A beta-hemolytic streptococci, and then, group G and C streptococci (10). Less common causes are arcanobacterium hemolyticum and fusobacterium necrophorum. Also, other organisms such as toxoplasma gondii and candida should be considered (3). The multiplicity of causes of exudative pharyngitis is such that even causes such as corynebacterium pseudo-diphtheria, which pose a challenge compared to the diagnosis of diphtheria, are considered (11). Viruses are the most common cause of acute pharyngitis in children (12). Twenty different viral causes such as adenovirus and coxsackievirus (A and B), influenza (A and B), parainfluenza influenza (types one, two, three), herpes simplex virus 1 and 2, and respiratory syncytial viruses (RSV) are known causes of pediatric pharyngitis (13). It is not easy to differentiate bacterial and viral pharyngitis (10). Clinical and epidemiological findings could be helpful (11).

On the other hand, the only pharyngitis that requires the use of antibiotics is the one that is caused by group A beta-hemolytic streptococcus (9). However, laboratory studies have shown that antibiotic treatment in patients with exudative pharyngitis is higher than the actual level in the group with A beta-hemolytic streptococcus infection (8). Extensive experimental use of antibiotics in patients with exudative pharyngitis leads to increased antibiotic resistance (14). Therefore, considering the key role of clinical and epidemiological findings in diagnosing the cause of exudative pharyngitis, which has not been studied in this region, the study of bacterial and viral exudative pharyngitis in children can be useful in preventing misuse of antibiotics. Therefore, this study was performed to determine the bacterial and viral causes of exudative pharyngitis in children aged 3 to 15 years who referred to the clinics affiliated to Kerman University of Medical Sciences.

Materials and Methods

According to the purpose and application, this is an applied research that was conducted cross-sectionally. The study population was children who referred to Besat Clinic and Afzalipour Hospital affiliated to Kerman University of Medical Sciences, Kerman, Iran. Children with a sore throat who were diagnosed with exudative pharyngitis were included in the study. All eligible patients were enrolled in the study by census sampling method. Inclusion criteria included the diagnosis of exudative pharyngitis in children aged 3 to 15 years whose parents had signed a written consent to participate in the study. All 3 to 15-year-old children with a sore throat who had an exudate in throat examination underwent a complete physical examination and information including fever (above 38°C), sore throat, runny nose, tears, cough, headache, gastrointestinal symptoms (abdominal pain), throat erythema, palatal petechiae, anterior neck adenopathy, painful adenopathy, swollen tonsils, age, and sex were recorded in the collection form.

After clinical diagnosis and obtaining the consent and cooperation of the patients and parents, samples of tonsil and throat secretions of patients were collected. Using a sterile swab, the patient's throat and nasal secretions were sampled and transported in a sterile environment to transmit the virus (by a virology laboratory). The samples were refrigerated until transferred to the virology laboratory.

Virology tests

The virus genome was extracted using genome extraction kits (DNA, RNA), and then, each specific kit was used to identify adenovirus, influenza A and B. To do this, the RNA-assay

extraction kit was used, and according to the instructions written in the kit, viral RNA and DNA were extracted and stored in the freezer at -20°C for molecular testing. Detection was performed using a very sensitive and accurate method based on the TaqMan probe in real-time PCR. For real-time, TaqMan Master Mix (Ampliqon, the Danish company) was used.

For bacterial detection, the samples were first placed in the Cary-Blair transport medium and transferred to a reference laboratory within a maximum of 24 hours. In the laboratory, the samples were cultured and propagated on a blood agar culture (HIMEDIA, India). After 24-48 hours (relative to growth intensity), streptococcal colonies were tested. Gram-positive cocci, catalase-negative, beta-hemolytic were considered. For diagnostic tests, 0.04 unit bacitracin diagnostic disk (Antibody Medicine, Iran) and if needed, PYR test (MAST company, Canada) was used. In the study of the prepared proliferation, the presence of white blood cells of polymorphonuclear type and gram-positive cocci with the arrangement of incised chains was considered. The results of the above-mentioned tests were reported to be positive if there was beta hemolysis and sensitivity to bacitracin with a size of 10 mm.

The data collection checklist included demographic information and laboratory results form. Necessary permissions were obtained from the Ethics Committee of Kerman University of Medical Sciences before the start of the study (Ethical code: IR.KMU.AH.REC.1396.2496). Data were analyzed by SPSS version 20 using descriptive and inferential statistics. In the descriptive statistics section, the mean and standard deviation were used, and in the analysis section, Chi-square test was used.

Results

The mean age of the study group was 7.33 years with a standard deviation of 3.05 and the mean age was 7 years. Most of the subjects (63.9%) were male. More than half of the people were over 3 years old. Most children were cared for at home. In most cases, the father's education and mother's education were above high school education. The income level of the majority (86.9%) was less than 20 million IRR, and in terms of father's accupation, most of the participants' fathers (87.7%) had non-governmental jobs. In terms of mothrs's job, most cases (85.2%) were housewives.

The number of family members in more than half of the subjects (50.8%) was more than 5 and the number of family members under 15 years in most cases (72.1%) was less than 3.

Of 61 children diagnosed with exudative pharyngitis, 12 (19.7%) referred in spring, 4 (6.6%) in summer, 19 (31.1%) in autumn, and 26 (42.6%) referred in winter. The most common clinical symptoms were fever (86.9%), sudden onset (77%), sore throat (75.4%), and cough (67.2%), respectively.

Out of 61 samples, 7 cases (11.5%) were positive for group A beta-hemolytic streptococcus. Thirty-two cases (52.5%) were positive for the studied viruses. Twenty-two cases (36.1%) were negative for viruses and bacteria studied. Out of 32 positive cases in terms of virological tests, 16 cases (50%) of adenovirus, 8 cases (25%) of influenza A, and 8 cases (25%) of influenza B were reported. The frequency of positive bacteriological results was not significant in terms of gender, age group, season, father's education, mother's education, father's job, number of family members, number of people under 15 years, and income level ($P > 0.05$). Mother's job had a significant relationship with group A beta-hemolytic streptococcus infection ($P = 0.007$). In this way, the frequency of positive results in housewives was significantly lower than that in other occupations (Table 1).

Comparison of the frequency of positive samples by virology in terms of demographic variables is shown in Table 1. The frequency of the results was not significant in terms of gender, age group, season, father's education, mother's education, father's job, mother's job, number of family members, number of people under 15 years, and income level ($P > 0.05$). Comparison of the results of bacteriological tests in terms of disease symptoms in the study population showed that only previous use of antibiotics was significant in terms of the test results ($P = 0.037$) (Table 2). Comparison of the results of bacteriological and virological tests in terms of disease symptoms in the study population indicated that none of the clinical symptoms were significant in terms of the test results ($P > 0.05$) (Table 2). Comparison of the frequency of clinical signs and symptoms in the positive group in terms of bacteria and virus indicated that none of the clinical signs were significant in terms of a positive result ($P > 0.05$) (Table 2).

Table 1. Comparison of demographic variables in children with bacterial and viral pharyngitis

Variable	Groups	P-value	Virus		P-value	Bacteria	
			Negative Number (Percentage)	**Positive** Number (Percentage)		**Negative** Number (Percentage)	**Positive** Number (Percentage)
Sex	Male/Female	0.289	12(55.5) 17(6.43)	10(45.5) 22(4.56)	0.505	20(90.9) 34(87.2)	2(9.1) 5(12.8)
Age (year)	Less/more than 7	0.19	13(40.6) 16(55.2)	19(59.4) 13(44.8)	0.173	30(93.8) 24(82.8)	2(6.2) 5(17.2)
Season	Hot (spring-summer)/Cold (autumn-winter)	0.476	7(43.8) 22(48.9)	9(56.2) 23(51.1)	0.403	15(93.8) 39(86.7)	1(2.6) 6(13.3)
Father's education	Under college or more	0.486	120 (50) 17(45.9)	120 (50) 20(54.1)	0.427	22(91.7) 32(86.5)	2(8.3) 5(13.5)
Mothers's education	Under college or more	0.512	9 (50) 20(46.5)	9 (50) 23(53.3)	0.325	17(94.4) 37 (96)	1(5.6) 6 (14)
Fother's job	Retired/unemployed	0.834	25(47.2) 4 (50)	28(52.8) 4 (50)	0.342	48(90.6) 6 (75)	5(9.4) 2 (25)
Mother's job	Housewife/other	0.565	25(48.1) 4(44.4)	27(51.9) 5(55.6)	0.007	49(94.2) 5(55.6)	3(5.8) 4(44.4)
Income (IRR)	Less/more than 20 million	0.298	24(45.3) 5(67.5)	29(54.7) 32(37.5)	0.226	48(9.6) 6 (75)	5(9.4) 2 (25)
Number of family members	Less/more than 5	0.078	18(58.1) 11(36.7)	13(41.9) 19(63.3)	0.226	26(83.9) 28(93.3)	5(16.1) 2 (6.7)
Number of indivuals under 15 years	Less/more than 3	0.069	24(54.5) 5(29.4)	20(45.5) 12(70.6)	0.363	38(86.4) 16(94.9)	6(13.6) 1(5.1)

Table 2. Comparison of clinical signs in children with bacterial and viral pharyngitis

Variable		P-value	Virus	GAS	Total
			Number (Percentage)	Number (Percentage)	Number (Percentage)
Sore throat	Yes/No	0.635	22 (68.8) 10 (31.2)	5 (71.4) 2 (28.6)	46(75.4) 15(24.6)
Headache	Yes/No	0.409	18(56.2) 14 (43.8)	3 (42.9) 4 (57.1)	35(57.4) 26(42.6)
Vomit	Yes/No	0.631	60 (18.8) 26 (81.2)	1 (14.3) 6 (85.7)	13(21.3) 48(78.7)
Cough	Yes/No	0.365	23 (71.9) 9 (28.1)	4 (57.1) 3 (42.9)	41(67.2) 20(32.8)
Hoarseness	Yes/No	0.350	13 (40.6) 19 (59.4)	4 (57.1) 3 (42.9)	23(37.7) 38(62.3)
Abdominal pain	Yes/No	0.365	9 (28.1) 23 (71.9)	3 (42.9) 4 (57.1)	18(29.5) 43(70.5)
Diarrhea	Yes/No	0.650	4 (12.5) 28 (87.5)	1 (14.3) 6 (85.7)	6(9.8) 55(90.2)
Anorexia	Yes/No	0.326	17 (53.1) 15 (46.9)	5 (71.4) 2 (28.6)	32(52.5) 29(47.5)
Fever	Yes/No	0.350	27 (84.4) 5 (15.6)	7 (100) 0 (0)	53(86.9) 8(13.1)
Sudden onset	Yes/No	0.346	22 (68.8) 10 (31.2)	6 (85.7) 1 (14.3)	47(77) 14(23)
Underlying disease	Yes/No	0.554	17 (21.9) 25 (78.1)	1 (14.3) 6 (85.7)	10(16.4) 51(83.6)
Pervious use of antibiotic	Yes/No	0.071	15 (46.9) 17 (53.1)	6 (85.7) 1 (14.3)	29(47.5) 32(52.5)
Symptoms in family members	Yes/No	0.654	9 (28.1) 23 (71.9)	5 (71.4) 2 (28.6)	18(29.6) 43(70.4)

Discussion

This study aimed to investigate the bacterial and viral causes of exudative pharyngitis in children aged 3 to 15 years who referred to Besat Clinic and Afzalipour Hospital affiliated to Kerman University of Medical Sciences.

The seasonal prevalence of the disease in the subjects was as winter, autumn, spring, and summer, respectively. The results of a study by Espadas Macia *et al.* showed that the seasonal prevalence of the disease is 35% in spring, 34% in winter, 28% in autumn, and 3% in summer, respectively (14). However, the severity of the infection has not been emphasized in other studies (15). According to the results of similar studies, the maximum prevalence of the disease is in the cold seasons of the year (16). All studies are consistent in terms of seasonal prevalence, and small differences in the percentage of patients can be due to epidemiological changes in the disease in different seasons and different years. Temperature changes in different years and geographical areas can also be the cause of this problem.

The most common clinical symptoms were fever, sudden onset, sore throat, and cough, respectively. Similar to the findings of this study, fever was the most common symptom in the study of Klug (17). In another study by Espadas Macia *et al*., the most common clinical symptoms were redness of the 99%), sudden prevalence (86%), fever (84%), tonsillar exudate (69%), sensitivity and pain of the anterior lymph nodes of the neck (30%), and gastrointestinal factors (22%), respectively (14). The presence of pus on the tonsils and pharynx and a history of contact with another case of streptococcal infection during the last two weeks provide the most clinical help in diagnosing the disease. However, there are no clinical findings in the history that are sensitive or specific enough to diagnose or rule out streptococcal throat infection (3, 11, 18).

The results of the present study showed that demographic factors have little effect on positive throat culture in children. Only the frequency of positive outcomes in children whose mother was a housewife was significantly lower than that in mothers with other occupations. The presence of the mother at home allows the child to be kept at home, and thus, have less contact with other children.

The frequency of viral samples was not significant in terms of gender, age group, season, father's education, mother's education, father's job, mother's job, number of family members, number of people under 15 years, and income level. These variables were not studied in other studies.

Comparison of the results of bacteriological tests according to history showed that only antibiotics were effective on the test results so that in the case of antibiotics, the result of bacterial culture was more negative. Comparison of the results of virological tests in terms of disease symptoms in the study population showed that none of the disease symptoms were significant in terms of the test results. In a study by Klug, children aged 3 to 15 years with symptoms of respiratory infection also indicated that none of the clinical symptoms were significantly associated with the test results (15).

It seems that the findings of this study on the bacterial and viral causes of pharyngitis indicate a higher frequency of viruses than bacteria. Viruses are generally the most common cause of pharyngitis. Also, because the percentage of clients in winter and autumn was higher than that in other seasons and it coincided with the prevalence of viruses such as influenza and adenovirus in these seasons.

In children who had previously and frequently used antibiotics, the positive culture of positive bacteria was significantly higher. This indicates an inappropriate and ineffective use of previously prescribed antibiotics.

The frequency of virus-positive samples in terms of age group was divided into two categories: Less than or equal to 7 years and more than 7 years. The frequency of positive virus samples was higher (59.4%) in the age group less than 7 years, which is consistent with the study of Sun *et al.* Also, the frequency of positive samples in terms of bacteria studied according to age group was divided into two categories: Less than or equal to 7 years and more than 7 years. The frequency of positive bacterial samples was higher in the age group over 7 years (71.4%), which is consistent with the results of the study of Sun *et al.* in age more than 6 years (71%) (12).

Conclusion

Laboratory examination and antibiotic treatment are very important in patients with exudative pharyngitis. However, the widespread experimental use of antibiotics in patients with exudative pharyngitis has led to increased antibiotic resistance. Therefore, it seems that the findings of this study and similar studies on

bacterial and viral pharyngitis are useful and effective in preventing the misuse of antibiotics. Because the indiscriminate use of antibiotics and resistance to antimicrobial drugs is now a serious issue worldwide.

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