

Incidence and clinical features of viral sore throat among children in rural Haryana, India

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ABSTRACT

Background: Sore throat is one of the commonest symptoms that patients present to a primary care physician. We describe the epidemiology of sore throat and performance of an algorithm to predict viral sore throat in a part of India. **Methods:** Children below 10 years of age were followed in 4 villages of Haryana, India from Aug 2012 to Aug 2014 through weekly domiciliary visits by trained field workers who screened for symptoms of acute respiratory infection (ARI) including sore throat. Nasal and throat swabs were obtained from a random sample of sore throat cases by nurses and sent in appropriate transport media for real-time polymerase chain reaction for detection of viral nucleic acid. Incidence of sore throat and viral sore throat are reported as number of sore throat episodes per 1000 child-years (EPTCY) with 95% confidence-interval (CI). Symptoms, associated with viral sore throat were identified by logistic regression, combined into a clinical score and Receiver Operating Characteristic curve was plotted. **Results:** Over a two-year period, 3765 children were followed up for 5578 child years. 1069 episodes of sore throat were reported, and swabs were collected from 8% of the cases randomly. The incidence of sore throat and viral sore throat was 191.7 (95%CI: 180.5-203.6) and 60.1 (95%CI: 55.1-68.2) EPTCY, respectively. Fever (aOR 5.40, 95%CI: 1.16-25.18) and running nose (aOR 10.16, 95%CI: 1.01-102.42) was significantly associated with viral sore throat. The clinical score (fever, running nose, and headache) had an overall sensitivity of 86.2% (68.3-96.1%), specificity of 62% (47.2-75.3%) and AUC of 0.78 (0.67-0.87) in predicting viral sore throat. **Conclusion:** Viruses contributed to one-third of burden of sore throat and clinical score can be used in primary care settings to aid antibiotic prescription by physicians.

Keywords: ARI, Children, viral sore throat

Introduction

Sore throat among children is one of the most common health condition that primary health care physicians deal with. Viruses are reported to be the most common etiology for sore throat,

common among them are Respiratory Syncytial Virus (RSV), Para-Influenza Virus- (PIV), Human Rhino Virus (HRV), Human Metapneumo virus (hMPV), and Influenza virus.^[1,2] Bacterial sore throats comprise of only 5–15% of sore throat cases, though antibiotic prescription is common in the cases of sore throat.^[3]

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Since majority of the sore throats are viral in origin, unnecessary prescription of antibiotics to prevent the bacteriological complications could lead to side-effects, out-of-pocket

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expenditures, and development of antibiotic resistance in the micro-organisms. Over-prescription of antibiotics and development of antibiotic resistance in micro-organisms is an escalating problem in the country and programs have been formulated recently to curb its rise.^[4] The knowledge about the epidemiology of viral sore throat and symptom complex algorithm for prediction of viral sore throat would help in understanding the burden as well aid policy makers in making policy decisions. The main objective of the current study was to describe the epidemiology of viral sore throat among a cohort of children under 10 years of age in rural north India. Also, we evaluated the performance of a clinical score for predicting viral etiology based on symptoms which were significantly different between viral and non-viral sore throats.

Methods

This study was conducted in the platform established for community-based surveillance of Acute Respiratory Infections (ARI) among children in rural, Haryana. The characteristics of the cohort are published previously in another paper.^[5] Children aged <10 years were followed in 4 villages from Aug 2012 to Aug 2014 through weekly domiciliary visits. A written informed consent was obtained from the either parent of the children for children under 7 years of age and from both parents and children for children aged 7 or more years. Socio-economic status of all households in the study area were assessed based on the possession of various consumer items and based on wealth index used in the National Family Health Survey (NFHS).^[6] The Institutional Ethics Committee approved the study. Ethical approval was obtained from the institute's ethics committee (AIIMS, New Delhi) and is mentioned at the last as a separate section in Page no 6 (Approval no: IEC /NP- 27/2012 & RP-05/2012).

Trained field workers screened all enrolled children weekly for any of the five ARI symptoms (cough, sore throat, nasal congestion, earache/discharge, breathing difficulty). Anyone with throat pain or discomfort in the throat were considered to have sore throat. Detailed clinical history and examination was done for all identified cases. Child was deemed to have sore throat if the mother/care giver reported that the child have "pain in throat" or "difficulty in swallowing". Nasal and throat swabs were obtained from a random sample of 10% of ARI cases and then sent in viral transport media to department of Microbiology for real-time polymerase chain reaction (RT-PCR). RT-PCR was performed for the detection of following viruses: influenza virus, rhinovirus, para-influenza viruses 1-3, human meta-pneumo virus, and respiratory syncytial virus.

Data analysis was done using STATA 13.0 (StataCorp, 2011). Incidence of sore throat was reported as number of sore throat episodes per 1000 child-years with the 95% confidence interval (CI) using normal approximation method for gender and various age groups. The incidence of viral sore throat in the

cohort was estimated by applying the quarterly sample positivity rate (SPR) of viruses among the sore throat cases to the quarterly sore throat rates which were summed and then divided by the overall follow-up years to estimate the overall incidence of viral sore throat [Table 1]. Incidence of sore throat and viral sore throat was calculated within various wealth quintiles of the cohort and reported with 95%CI.

The association of various associated signs and symptoms with viral sore throat were calculated as odds ratios (OR) and reported with 95% CI [Table 2]. In calculating the association, cases were viral sore throat (sore throat cases wherein a virus was isolated) and controls were non-viral sore throat cases (sore throat cases with no virus isolates on testing). Variables with *P* value of less than 0.4 in the bivariate analysis were fitted in the multivariable logistic regression model and their corresponding adjusted odds ratios (aOR) were calculated with 95%CI and the goodness of fit was reported using pseudo-R².

The symptoms were combined to calculate their corresponding sensitivity and specificity. Each symptom was given a score depending on their aOR and the total score was summed. Receiver Operating Characteristic (ROC) curve was plotted for the proposed score for screening viral sore throat and its sensitivity, specificity and Area Under the Curve (AUC) was calculated with 95%CI.

Results

A total 3765 children were followed up for 2 years for an overall 5578 child years. The mean age of the study cohort was 4.07 years (SD - 1.51 years). The overall incidence of sore throat was 191.7 (95%CI: 180.5-203.6) episodes per 1000 child years. Specimen for virus testing were obtained from 79 (8%) episodes of sore throat out of the total 1069 episodes reported. A virus was isolated from 29 (36.7%) specimens. The estimated incidence of viral sore throat was 60.1 (95%CI: 55.1-68.2) episodes per 1000 child years. Viral nucleic acid was detected from specimens of one third (31.3%) of the incident sore throat cases. Among the specimens in which viruses were detected, 68.9% of the specimens were positive for one virus and 31.1% reported co-infection with other viruses. The various viruses detected were as follows; RSV (15.4%), HRV (53.8%), PIV (15.4%), hMPV (11.5%), and influenza (27.6%).

There was no significant difference in incidence of sore throat between boys (184.5 EPTCY; 95%CI: 169.9-200.3) and girls (180.6 EPTCY; 95%CI: 165.4-197.2); however, the incidence of viral sore throat was significantly higher among boys (92.4 EPTCY; 95%CI: 62.4-138.1) [Table 1]. There was an increase in the incidence of sore throat with age and was higher in children above 5 years of age (aOR-2.70, 95%CI: 2.20-3.33), in the contrary to viral sore throat, which decreased with age [Table 1]. Also, the incidence of viral sore throat was lesser in the wealthier quintiles.

Table 1: Incidence of sore throat and viral sore throat according to socio-demographic features

Socio-demographic features	Incidence of sore throat (EPTCY*) (95% CI)	Incidence of viral sore** throat (EPTCY) (95%CI)
Gender		
Girls	180.6 (165.4-197.2)	21.6 (9.6-52.8)
Boys	184.5 (169.9-200.3)	92.4 (62.4-138.1)
Age		
Less than 2 years	91.5 (75.7-110.6)	70.8 (34.8-151.2)
2-5 years	141.6 (125.5-159.7)	64.8 (34.7-118.8)
5-10 years	247.3 (229.6-266.3)	51.6 (28.8-90.1)
Wealth quintile		
1 st quintile (poorest)	211.1 (182.1-244.5)	57.6 (21.6-152.4)
2 nd quintile	189.4 (162.2-221.1)	57.5 (21.6-151.2)
3 rd quintile	177.7 (151.5-208.4)	112.8 (56.4-225.6)
4 th quintile	206.1 (177.7-238.1)	27.6 (7.2-112.8)
5 th quintile (richest)	197.2 (169.8-229.6)	27.4 (7.2-111.6)

*EPTCY - Episodes Per Thousand Child Years, ** - the swabs were tested for the following viruses: HRV, RSV, HMPV, PIV-1, PIV-2, PIV-3, Influenza A and B.

Table 2: Bivariate and multi-variable analysis for symptom association with viral sore throat

Symptom/ sign	Viral sore throat (n=29) %	Non-viral sore throat (n=50) %	OR (95%CI)	p	aOR* (95%CI)
Cough	27 (93.1)	41 (82)	1.1 (0.59-2.10)	0.8	NI**
Earache	1 (3.5)	3 (6)	0.54 (0.09-3.15)	0.5	
Running nose	28 (96.6)	37 (74)	9.84 (1.21-79.73)	0.04	10.16 (1.01-102.42)
Fever	26 (89.7)	24 (48)	9.39 (2.51-35.06)	0.001*	5.40 (1.16-25.18)
Rash	1 (3.5)	3 (6)	0.56 (0.06-5.64)	0.6	NI**
Headache	11 (37.9)	6 (11)	4.48 (1.44-13.95)	0.01*	3.47 (0.70-17.14)
Myalgia /Fatigue	3 (10.3)	2 (4)	2.77 (0.43-17.64)	0.3	0.34 (0.03-3.75)
Vomiting	6 (20.7)	7 (14)	1.60 (0.48-5.33)	0.4	0.74 (0.18-3.01)
Watering of eyes	2 (6.9)	2 (4)	1.78 (0.24-13.34)	0.6	NI**

*Adjusted for factors with p-value less than 0.4 in the bivariate analysis, **NI – not included in multivariable analysis

Among the symptoms, after adjustment [Table 2], the following were significantly associated with viral sore throat: fever (aOR 5.40, 95%CI: 1.16-25.18) and running nose (aOR 10.16, 95%CI: 1.01-102.42).

The clinical score was designed by giving scores to the following variables approximating to their adjusted odds ratios as follows: headache, 3; fever, 5; running nose, 10. Combining the symptoms into a clinical score yielded an overall sensitivity of 86.2% (95%CI: 68.3-96.1%), specificity of 62% (95%CI: 47.2-75.3%), and AUC of 0.78 (95%CI: 0.67-0.87) for a cut-off of 13 [Tables 2 and 3].

Discussion

This is one of the first studies to report incidence of sore throat and viral sore throat in India. The study clearly demonstrates sore throat to be a significant problem among children in the community. The incidence of sore throat in the study was 191.7 (95%CI: 180.5-203.6) episodes per 1000 child years. The reported incidence was lower as compared to other studies reporting the incidence of URTI.^[7-9] URTI is a broad category of diseases, with sore throat as one of its components. Since burden of overall spectrum of URTI was not the primary objective in this study, the reported incidence would have been lower as compared to other studies reporting overall URTI. The incidence of sore throat among children was found to increase

with age in the contrary to viral sore throat [Table 1]. Few studies, conducted worldwide have reported inverse relationship between age and incidence of sore throat among children, with higher rates in children less than five years.^[10] However, majority of these studies focused on children under five years of age, whereas in the current study, children upto the age of 10 years was included and thus could have resulted in the shift. Also, it is reported that bacterial pharyngitis is more common in children above 5 years age group, supporting the decreasing incidence of viral sore throat with age in the current study.^[11] The incidence of viral sore throat was higher among the poorer quintiles (1st, 2nd, and 3rd) in this study corroborating with other studies.^[12] This could have been due to poor housing conditions or over-crowding in the households. However, the study was not powered enough to study the association of socio-economic risk factors with viral sore throat.

The estimated incidence of viral sore throats in the current study was 60.1 (95%CI: 55.1-68.2) episodes per thousand child years [Table 1], which was one-third of the overall sore throat incidence estimated. There are very few community-based studies on epidemiology of viral sore throats. One study conducted among children visiting a family-medicine center in Turkey reported a slightly higher contribution of sore throats by viruses among the sore throat cases visiting the center.^[13] The age-groups included in the study were different, as the

Table 3: Clinical score for diagnosing viral sore throat*

Score	Sensitivity (%) (95%CI)	Specificity (%) (95%CI)	Correctly classified (%)
5	100 (95.4-100.0)	16 (9.1-26.5)	46.8
8	100 (95.4-100.0)	24 (15.1-35.1)	51.8
10	96.6 (82.2-99.9)	26 (14.6-40.3)	51.9
13	86.2 (68.3-96.1)	60 (47.9-70.4)	69.6
15	86.2 (68.3-96.1)	62 (47.2-75.3)	70.9
18	34.5 (23.9-45.7)	92 (82.6-96.4)	71

*Following symptoms were included in the clinical score: Headache (3), Fever (5) and running nose (10)

above-mentioned study included adults and was done in a hospital setting. Similar to the current study, other studies have reported viral etiology among one-third to half of the URTI cases.^[14-16] In this study, the most commonly found virus in the isolate was HRV. Globally, Rhinovirus is reported to be the most common causative organism for URTI.^[17-21] Also, many Indian studies have reported Rhinovirus to be most common etiology for URTI.^[22-24] Certain studies also reported influenza group of viruses to be the common etiology,^[25,26] however, the above studies could not be compared with the current study, as the setting (community vs. hospital), demographic profile of participants (geography, age group, occupation etc.) and methodology were different. In the current study, influenza viruses were also found to be of significant concern, as they contributed a significant proportion. Similar to other studies, parainfluenza group of viruses and HMPV were also detected.^[13] Co-infection with other viruses have been reported in the study. In studies done globally, most of the co-infections were due to adenovirus as they continue to shed from the nasopharyngeal mucosa for a longer duration as compared to other viruses, thereby increasing their probability of concomitant infections.^[22] However, in the current study RSV was the commonly associated co-infection, as the swabs were not tested for adenovirus.

The following symptoms were found to be significantly associated with viral sore throat: running nose, fever, and headache. Though, very few studies have focused on the association of signs and symptoms with viral URI/sore throat, a large number of studies have studied the associations with specific viral infections, affecting the lower respiratory tract and bacterial sore throat.^[26] Sentinel surveillance of febrile respiratory illness patients who sought primary health care in Singapore reported that symptoms such as fever and running nose were more common among those diagnosed with viral as compared to bacterial infections.^[27] Also, a recent systematic review and meta-analysis reported significant association between influenza infection and fever or headache, as well as between RSV infection and cough.^[28] However, similar association of symptom complex with specific viruses could not be estimated in the current study as it was not the study objective.

Rational usage of antibiotics and explicit mentioning on optimal prescription antibiotics for conditions such as common cold and other non-specific upper respiratory tract infections are

given by the national guidelines.^[29] However, studies indicate a higher proportion of antibiotic prescription for such infections, especially in the primary care settings (both public and private).^[30] In low-resource primary care settings, microbiological or rapid diagnosis for bacteriological and viral etiology of sore throat is not an economically feasible option. There are many clinical prediction models for diagnosing bacterial sore throat such as: McIsaac score and Centor score, etc.^[31,32] However, similar algorithms for prediction of viral sore throat is scarce. The current study validated a clinical algorithm with three-symptom complex predicting the probability of viral sore throat. In comparison, study by Mistik *et al.*, included other symptoms in addition such as sneezing, stuffy nose and absence of tonsillar hypertrophy in the scoring for diagnosing viral sore throat.^[13] Also, Mistik *et al.*, documented reduction in antibiotic prescription by combined usage of viral prediction scores along with bacterial prediction scores.^[13] However in our study, scores for bacterial sore throat could not be validated as the swabs were not tested for bacterial culture and it was primarily a study on epidemiology of viral-ARI. In both the studies presence of headache was associated with viral sore throat, however specificity was higher in the current study. The current study reports a good sensitivity and moderate specificity as compared to the study by Mistik *et al.* This could be due to higher proportion of sore throats contributed by viruses in the current study. The clinical scores need further validation for checking their applicability in Indian settings.

This is one of the first community-based studies on epidemiology of viral sore throat and a clinical prediction model for viral sore throat in India. Robust techniques were employed in data collection, handling the specimens and identification of organisms. Another strength was that the association was estimated with laboratory proven infections and not with presumptive viral sore throats. One of the limitations in the study was the small sample size of viral sore throat testing due to high-cost of conducting RT-PCR. Other limitation was both throat and nasal swab were obtained from a given case from which RNA was extracted for PCR testing. However, it is assumed that virus is implicated in sore throat even if shedding is only from nose. We did viral testing only for four viral pathogens. If we had we tested for more viral pathogens, proportion of viral sore throat among all sore throat cases was likely to be higher. Further studies need to be conducted to assess the distribution and burden in other parts of the country to come to a consensus on the epidemiology of viral sore throat.

Conclusion

Viral sore throat contributes to a significant problem in the community. This study adds to the information and knowledge about epidemiology of viral sore throats in India and also emphasizes on symptom attributes of URIs due to viral etiology. Such, clinical scores could be utilized in primary care settings for predicting viral URI, thereby guiding antibiotic prescription. These algorithms will be cost-effective, less time consuming and have a greater impact in aiding primary care physicians for optimal utilization of antibiotics.

What is already known?

Upper respiratory infections are the most common reason for consulting a doctor and are prescribed the maximum percentage of antibiotics.

What this study adds?

Viral sore throat contributes a significant burden in the community. Clinical scores could help in predicting viral sore throat thereby reducing the amount of prescribed antibiotics for sore throat.

Ethical approval

The Institutional Ethics Committee of the AIIMS, New Delhi approved the study, with an institutional reliance by the United States Centers for Disease Control and Prevention (CDC) Institutional Review Board.

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Conflicts of interest

The authors do not have a commercial or other association that might pose a conflict of interest with respect to this study.

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