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Frequency of Pediatric Acute Respiratory Tract Infections in Iran; A Systematic Review

Ahmad Reza Shamshiri [1], Alireza Fahimzad [2], Seyed Ahmad Tabatabaie [2], Farideh Shiva [2], Maryam Kadivar [3], Alireza Khatami [4], Shadab Salehpour [5], Abdollah Karimi [2,*]

[1] Dental Research Center, School of Dentistry, Tehran University of Medical Sciences, Tehran, IR Iran
[2] Pediatric Infections Research Center, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
[3] Department of Pathology, Tehran University of Medical Sciences, Tehran, IR Iran
[4] Mofid Children Hospital, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
[5] Loghman Hospital, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

* *Corresponding author:* Abdollah Karimi, Pediatric Infections Research Center, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran. Tel.: +98-2122226941, Fax: +98-2122226941, E-mail: dr_akarimi@yahoo.com

ABSTRACT

Introduction: Acute respiratory infections (ARIs) continue as the leading cause of mortality in under 5-year-old children worldwide. We decided to review available data about the incidence and prevalence of all diseases included in this category in Iran.
Methods: A systematic review was designed to obtain related data from English and Farsi sources, published or unpublished. An internet search of known data sources and websites of Iranian medical universities was conducted. In addition, we reviewed abstract books of related Persian seminars and prevalence reports of ARI in children from different departments in the Ministry of Health and Medical Education of Iran. After deleting duplicates obtained material was evaluated by two epidemiologists and selected documents underwent quality assessment through data extraction checklists. We have included the most valid studies in this review.
Results: Only 19 out of 98 documents reported frequency of a disease in a defined population, a group of outpatients, or hospitalized patients. Almost all of the studies had some limitations. In addition, there were no similarities in methods or place/time to make a summary on any ARIs' frequency. So, we discussed each study, separately.
Conclusion: Available data about frequency of ARIs in Iran were not beneficial enough to calculate burden of related diseases and make decision analysis for suggested interventions. Valid and large longitudinal population-based studies should be designed in different regions of the country supported by the Ministry and research centers.

Keywords: Respiratory Tract Infections; Prevalence; Incidence

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Implication for health policy/practice/research/medical education:
To produce and implement rational management strategies for pediatric acute respiratory tract infections on local evidence-based guidelines, availability of epidemiologic data to health policy makers is imperative. Several studies have been performed in Iran on selected populations of children with ARI in different regions of the country with diverse results; however, overall statistical figures about the rate and significance of ARI are not available. By this study, we tried to show and emphasis on this gap in basic information in Iran.

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1. Introduction

Acute respiratory tract infections (ARI) are the most common reason for children to visit physicians and the major cause of mortality and morbidity in children < 5 years of age (1). Studies have revealed that ARIs account for 30-60% of visits to health providing centers and 30-40% of admissions to pediatric hospitals thus incurring huge expenses on caretakers and the health care system of a country. In developing countries, 30-50% childhood deaths are caused by ARI, particularly pneumonia (1). Several studies have been performed in Iran on selected populations of children with ARI in different regions of the country with diverse results; however, overall statistical figures about the rate and significance of ARI are not available. As ARIs in children constitute a large burden of diseases need health care, it is imperative availability of exact data about etiology, frequency, clinical presentation, complications, and days missed from school or parental days missed from work to health policy makers to produce and implement rational strategies for the management of these illnesses according to local evidence-based guidelines. Such data would also enable health care providers to recommend specific immunizations against the most common illnesses and to advise against irrational antibiotic usage.

We found two systematic reviews performed to define the role of specific etiologic agents that cause ARI. In first study, authors have estimated the overall incidence and complications of influenza in the Netherlands by gathering required data from Medline. Their estimation for annual incidence of influenza was 5-9. 5% (without seasonal considerations) according to the results of two prospective studies (2). Another systematic review was done to define the prevalence of group A streptococcal infection and asymptomatic carriage in < 18-year-old patients; the authors searched Medline and analyzed 29 papers which fulfilled the inclusion criteria for this meta-analysis. Their results indicated the prevalence of group A streptococcal infection as 37% (95% CI: 32-43%) in this age group; carrier prevalence was 12% (95% CI: 9-14%)(3).

In our literature searching, we did not find any records of a systematic review about ARIs in children from Iran; so the objective of this review was to fill this knowledge gap which was essential in research priority setting and planning of rational health care policies.

2. Methods

In this systematic review, we searched wide range of published and unpublished information sources, consisting of abstract books from local and national pediatrics and infectious diseases congresses; Iranian (SID, Irandoc, Iran Medex, and Magiran) and foreign databases (Scopus, Web of Science, Pubmed, Embase, and EBSCO); theses (either from the Irandoc database or portals of medical science universities); some related research centers; professional medical societies; and the ministry of health (center for disease control and prevention, and vaccine preventable diseases office). All sources in Persian and English were searched by three physicians till mid-2010. In *Table 1* both persian and english keywords for searching are presented. In order to get more sensitive results we did not use "acute" as a keyword. Also, searches were repeated for each keyword in some electronic Persian databases sensitive to those letters with different characters such as "ی" and "ي" or "ک" and "ك". EndNote-X3 software was used to categorize and manage all retrieved data. Using this software, we found and deleted duplicates automatically in the first step. However, dissimilarities between some databases in some fields such as titles and authors' names led to ineffective automatic deletions; so in the second attempt, we tried to find duplicates manually. In cases of multiple publications, we kept the last version or the most complete one.

Table 1. Keywords for Literature Review in Iranian and Foreign Databases

English Keywords[a]	Persian Keywords
Respiratory infection	عفونت تنفسی – عفونتهای تنفسی – عفونت‌های تنفسی
Pneumonia	پنومونی
Influenza, Flu	انفلوانزا – آنفولانزا– انفولانزا
Cold – Common cold	سرماخوردگی
Sinusitis	سینوزیت
Laryngitis	لارنژیت
Pharyngitis	فارنژیت
Tracheitis	تراکئیت
Bronchiolitis	برونشیولیت
Bronchitis	برونشیت
Pertussis	سیاه سرفه
Diphtheria	دیفتری
Otitis media	اوتیت، اتیت، گوش میانی
Croup	لارنگوتراکئیت – خروسک

[a] "Iran" was combined with each keyword in English database searching

Consistency of studies with our objectives was screened by reading titles and abstracts, if needed. Final selected studies were reviewed by two epidemiologists utilizing a checklist of validity criteria (*Table 2)*; however, they were not strict in selecting the studies.

Table 2. Validation Criteria for Selecting Appropriate Studies

	Inclusion Criteria	Exclusion Criteria
Study population and sampling methods	Detailed statement of persons and their age, geographic area and also sampling base (hospital or population)	Presence of selection bias or unclear definition of study population and sampling method
Time (duration)	Statement of time period of data collection	Unclear time period of data collection
Study objective	Any direct or indirect objective that leads to frequency (prevalence or incidence) estimation of ARI[a]	Any study performed on special groups such as patients with immunosuppression or survivors of natural disasters
Study design	Observational (descriptive or analytic) studies and clinical trials (data of non-intervention groups)	Case reports and case series
Sample size	Any sample size	-
Diagnostic method	Diagnosis according to a gold-standard or any confirmed diagnostic method (laboratory tests or clinical criteria)	Diagnosis with unacceptable method or any ambiguity in case definition

Abbreviation: ARI, acute respiratory infection

Data extraction from selected studies was performed by one epidemiologist. In accordance with our study objective, main data extraction was focused on sample size, year of study, duration of observation and follow-up, number and types of events (infections), and summary measure of event frequency and its 95% confidence interval (95% CI). If no 95% CI was found, we calculated it by binomial exact method with STATA software, version 11.0. Two similar studies were not found to perform meta-analysis or pooled data analysis; so, we reported each study results with some comments on its weakness and strength.

3. Results

Results from non-Iranian sources are presented in *Table 3*. SCOPUS and Pubmed were main sources of relevant studies.

Table 3. Number of Retrieved Studies from Non-Iranian Sources

No	Database	All Sudies	Studies Not Repeated	Related Studies
1	Pubmed	728	302	8
2	Springer (+abstracts and posters)	574	81	0
3	Ovid	215	8	0
4	Science Direct	1265	79	2
5	Scopus	1284	282	28
6	Ebsco	177	6	0
7	PQWeb	28	10	0

A retrospective questionnaire-based study was performed from January to December 2001 in Tehran, (4) to determine the effect of paternal smoking on the rate of respiratory tract infections in young children. 595 immune-competent children between the ages of 6 months and 2 years were enrolled. Children with co-morbidities and congenital anomalies, or those exposed to second hand smoke (SHS) from sources other than their fathers were excluded. Outcomes of interest included the prevalence, duration and severity of upper respiratory tract infections (URTI), and/or otitis media in children with or without exposure to SHS from their fathers. Results revealed that 353 children had no exposure to SHS at home (group A); in 153 children, the father was a smoker but did not smoke inside the house (group B1); and in 84 children, the father continued to smoke in the presence of the child (group B2). In this study, URTI was diagnosed by the history of common cold symptoms (cough, rhinorrhea, and/or hoarseness). This study was based on parental recall subject potentially to errors; it was limitation of the study.

A summary of their results is given below:

1. URTI: At least 1 episode of URTI in study participants during the preceding year:

Group A: 81.6% (95% CI = 77.1-85.5%)

Group B1: 84.1% (95% C I= 77.5-89.5%)

Group B2: 95.2% (95% CI=88.3-98.7%)

Overall: 84.2% (95% CI = 81-87%)

2. Average number of URTI episodes in infants between the ages of 6-12 months, according to exposure to SHS:

Group A: 1.8 times since birth. (CI not available)

Group B2: 4 times since birth. (CI not available)

3. Average number of URTI episodes during the preceding year, in children between the ages of 1yr. to 5 yrs.

Group A: 2.7 times since birth. (CI not available)

Group B2: 5.3 times since birth. (CI not available)

No figures were given for children with smoker fathers who did not smoke at home (in the presence of children); therefore, the figures were prone to bias. We could not get hold of raw data enabling us to calculate and report weighted mean for total population.

4. Otitis media: At least 1 episode of acute otitis media (AOM) in study participants during the preceding year:

Group A: 10.7% (95% CI = 7.7-14.5%)

Group B1: 10.1% (95% CI = 5.9-15.9%)
Group B2: 19% (95% CI = 11.3-29.9%)
Overall: 11.8% (95% CI = 9.3-14.6%)

A research group consisting of centers for disease control and prevention, world health organization, and Johns Hopkins Bloomberg school of public health (5) have proposed a new tool for rapid assessment of Haemophilus influenzae type b infection (Hib) in developing countries. Two different methods are applied in this tool to estimate the rate of Hib infection. In the first method, initially the local incidence rate of Hib meningitis is calculated; then, based on previous reported ratio of 1:5 between Hib meningitis and Hib pneumonia, pneumonia rates are calculated. The second method starts with determining under-5 mortality rate and case fatality rate for Hib pneumonia moving to the incidence of Hib meningitis. According to the first method, 2994 case/ year of Hib pneumonia have been calculated for Iran with 180 deaths; the second method puts the figures at 9876 case/year with 593 deaths. Although the authors have addressed the various limitations of the study, they believe that the tool could rapidly assess the Hib infection rate within 7-10 days in a country.

A cohort study was conducted between January 1997 and February 1998 in Mashad-Iran to compare the growth rate and morbidity between infants exclusively breastfed for 6 months and those who were breastfed but started complementary foods at 4 months (100 infants in each group) (6). Findings revealed that among children with the ages of 4 and 6 months, the rate of respiratory infections was higher in infants who were given complementary food compared to exclusively breast-fed babies (35%, 95% CI = 25.7- 45.2%; vs. 23%, 95% CI = 15.2-32.5%). Definition and examples of respiratory infection in this study was not clear.

As part of international study of asthma and allergies in childhood, (ISSAC), a large study was performed in Isfahan-Iran from October 1998 to December 2000 on 11666 schoolgoers aged 6-18 years. The object of this study was to study the relationship between self-reported common cold episodes and symptoms that could be attributed to asthma/ allergy (7). Common cold was defined as a self-limited illness presenting with nasal stuffiness and discharge along with one of the following symptoms: sneezing, cough, and/ or sore throat. Rate of = 4 common cold episode/year was found as follows:

Boys: 19.3% (95% CI = 18.2-20.3%)
Girls: 23.7% (95% CI = 22.6-24.7%)
Overall: 21.6% (95% CI = 20.8-22.4%)

Also, the authors reported the rate of frequent chest infections in their study subjects as follows: (this term was not defined in the paper):

Boys: 2.0% (95% CI = 1.7-2.4%)
Girls: 1.5% (95% CI = 1.2-1.8%)
Overall: 1.8% (95% CI = 1.5-2.0%)

Since this was a retrospective, questionnaire-based study, it was prone to recall errors, and since the study was performed in one city, it might not represent national incidence rate.

In another study in Rasht, North of Iran, frequency of ARI was studied in a cohort of 50 families with once a week follow up for a period of 2 months during winter 2004 (8). Families with intermediate socio-economic level having at least 2 children one of which was < 1 year of age were included in the study. ARIs were categorized into URTI and lower respiratory tract infections (LRTI). Out of 113 children, (median age 3 years) included in this study, 81 patients (72%; 95% CI = 62.4-79.8%) incurred at least 1 episode of ARI, and total number of 94 episodes of ARI were documented in these children during the study period. Infants < 6 months old were least prone to infections. In 75% of cases, children were the first members of the family to get an ARI.

In a placebo-controlled clinical trial conducted in the Altimor, a small town near Mashad, during fall and winter of 2005, the effect of zinc supplements on the frequency and duration of common colds was studied in children aged 7 to 10 years (9). Common cold was defined as having at least 2 of following symptoms: headache, cough, hoarseness, myalgia, nasal discharge, nasal congestion, sore throat, itchy throat, and/or sneezing and fever. Mean episodes of common cold during 5 months follow-up in children administered with zinc supplements were 1.7 ± 0.86 (range 0-6 times) vs. 3.1 ± 0.55 (range 0-8 times) in those who were given placebo. Absence from school was recorded for 0.55 ± 1.09 days in zinc group vs. 1.35 ± 1.79 days in placebo group. Episodes of respiratory tract bacterial infections (acute pharyngitis, acute otitis media, sinusitis, and pneumonia) needing antibiotics were also assessed; frequency was recorded as 20% in intervention group vs. 47% in placebo group. These statistics are useful to get some idea about the frequency of ARIs in primary school children from families with low to intermediate socio-economic status.

Results from literature review from Iranian sources are presented in *Table 4* . The following studies were reviewed: 15 citations from IranDoc, 13 citations from SID, 10 citations from Magiran, and 4 citations from IranMedex.

Table 4. Selected Studies Published in Iranian Sources

No.	Site searched	Dissertation		Project		Paper	
		All results	Related studies	All results	Related studies	All results	Related studies
1	Irandoc	409	24	107	5	334	10
2	Magiran	-	-	-	-	1043	53
3	Sid	-	-	-	-	266	21

A study was done in the Shahid Jamali Health Clinic in Shahr-e-Rey in January 1997 to estimate the prevalence of otitis media in < 5 year olds children (10). All children visiting the clinic (diseased or not) during the study period were included; out of 276 subjects, 18 cases of otitis media were detected (6.5%; 95% CI = 3.9-10.1%). Since this study was done in a single health facility with local referrals, this study cannot serve as a base to calculate the incidence of acute otitis media at the national level.

In winter 1997, a research was performed in the city of Ahwaz on primary school pupils (first grade) age group to determine the prevalence of otitis media with effusion (OME) (11). Two thousand pupils from first graders of 25 schools situated in all 4 districts of the city were enrolled. Children were examined by 1 ENT specialist and 1 final-year ENT resident; 222 cases, (11.1%) of OME were diagnosed (95% CI = 9.8-12.6%; without adjustment for sampling method). OME was diagnosed in 10% of girls and 12.2% of boys. However, since most cases were asymptomatic, we believe that the presence of OME results in underestimation of AOM prevalence.

A Dissertation was written on the basis of a research conducted in Kerman during July and August 1997 (12). Objective of the study was to define the prevalence of OM (otitis media.) in 939 six-year-old children examined at the handicapped children's health clinic. Prevalence of OM reported in this study was as follows:

Girls: 7% (95% CI = 4.9-9.6%)

Boys: 11% (95% CI = 8.2-14.3%)

Overall prevalence: 9% (95% CI = 7.1-10.8%)

As the details of recruitment and methodology were not available for scrutiny, no comments can be made on the validity of the results.

Two studies were done in 6 months from December 2001 till May 2002 in Bu-Ali Sina hospital in Sari and Amir Kola Hospital in Babul on all hospitalized children aged between 1 month and 10 years (13, 14). A total number of 1197 patients were enrolled (41% were girls). Findings revealed that 150 children (12.5%, 95% CI = 10.7-14.5%), were admitted because of LRTI; boys constituted about 2/3 of patients (68.7%). LRTI was defined when at least one of the following symptoms was present: moderate to severe croup, tachypnea, dyspnea, wheezing along with intercostal retraction, and crackles along with difficult breathing; presence of fever was not mandatory for diagnosis. The authors aimed to determine viral causes of LRTI in these patients. Frequency of different viruses was as follows: Para-influenza virus type 3, 27 cases (18%); respiratory syncytial virus (RSV), 18 patients (12%); Influenza A virus, 14 children (9.3%); Para-influenza virus type 2, 12 cases (8%); Para-influenza virus type 1, 11 patients (7.3%); Adenovirus 10 children (6.7%); and Influenza virus type B, 5 cases (3.3%). This was a rigorous study, but as it was done on in-patients, the results cannot be applied in the community in general.

A study was conducted in 2004 on 1672 patients hospitalized in Razi hospital, Kermanshah. Pneumonia was diagnosed in 107 cases (6.4%, 95% CI = 5.27-7.68%) (15). Diagnosis was based on CDC criteria; ratio of boys to girls was almost 3:2 (60.7% vs. 39.3%). The study was a retrospective; this is a limitation for it. Moreover, study subjects all were hospitalized.

Table 5. Four Reports of Bacterial Causes in Acute Respiratory Infections from Shiraz University of Medical Sciences

	No. of Cases From 1997-2000, (%)	2004-2006, (%)	2006-2007, (%)	Total (1997-2000 and 2004-2007), (%)	2009, (%)
Purulent rhinitis	827 (64.6)	1450 (70.9)	743 (73)	3020 (69.5)	614 (74)
Sinusitis	235 (18.3)	217 (10.6)	84 (8.2)	536 (12.3)	40 (4.8)
Acute pharyngitis	95 (7.4)	115 (5.6)	65 (6.4)	275 (6.3)	49 (5.9)
Otitis media	74 (5.7)	151 (7.3)	69 (6.7)	294 (6.7)	46 (5.5)
Purulent conjunctivitis	42 (3.3)	95 (4.6)	52 (5.1)	189 (4.3%)	
Cervical lymphadenitis	7 (0.5)	15 (0.7)	4 (0.4)	26 (0.6)	[a]
Bacterial Causes					
Positive, %	64.6	58.9	56.7		57.1
Staphylococcus aureus	254 (23.5)	289 (39.9)	171 (27.7)	714 (29.5)	157 (32.9)
Strep. Pneumonia	403 (37.3)	112 (15.4)	67 (10.8)	582 (24)	61 (12.7)
M. catarrhalis	173 (16)	174 (24)	250 (40)	596(24.6)	81 (16.9)
H. influenza	82 (7.6)	68 (9.4)	48 (7.8)	198 (8.1)	45 (9.4)
Group A β-hemolytic *Streptococcus*	155 (14.3)	55 (7.6)	61 (9.9)	271 (11.2)	56 (11.7)
Non-group A Streptococcus	12 (1.1)	26 (3.6)	18 (2.9)	56 (2.3)	45 (9.4)

[a] In addition, other diagnoses made in 2009 were: non-purulent rhinitis, 41 cases (4.9%); naso-pharyngitis, 25 patients (3%); 'other' diagnoses including cervical adenitis and scarlet fever, 14 cases.

Table 6. A summary From Selected Studies From Iranian and Non-Iranian Sources

No	Year of Publication	Authors	Disease Studied	Reported Frequency of the Disease
			Studies Selected From Non-Iranian Sources	
1	2003	Shiva *et al.* (4)	URTIs	1-5 year olds: At least 1 episode/year: 84.2% (95% CI: 81.0-87.0%). Mean no. of episodes/year in non-smoking families: 2.7; if exposed to unrestricted SHS: 5.3. Infant 6-12 mo: in non-smoking families: 1.8; if exposed to unrestricted SHS: 4.
			Otitis media	At least 1 episode/year: 11.8% (95% CI: 9.3-14.6%)
2	2004	Fieken *et al.* (5)	Hib Pneumonia	< 5 year olds: No. of episodes/year in Iran: 2994- 9875.
3	2004	Khadivezadeh *et al.* (6)	ARI	4-6 months of age: No. of episodes in 2 months. in babies on complementary foods: 35% (95% CI: 25.7-45.2%). In exclusively breast-fed babies: 23% (95% CI: 15.2-32.5%)
4	2006	Amra *et al.* (7)	Common cold	6-18 year-olds: Rate of ≥ 4 common cold episodes/year: Boys: 19.3% (95% CI: 18.2-20.3%); Girls: 23.7% (95% CI: 22.6-24.7%) Overall: 21.6% (95% CI: 20.8-22.4%)
5	2007	Naghipour *et a.*(8)	ARI	At least 1 episode of ARI was reported 81/113 or 72% (95% CI: 62.4-79.8%). 94 episodes in 81 children
6	2009	Vakili *et al.* (9)	Common cold	Age 7 to 10 years: Mean episodes of common cold during 5 months 3.1 ± 0.55 (range 0-8 times)
			Studies selected from Iranian sources	
7	1997	Rashidi *et al.* (10)	Otitis media	276 children: 6.5% (95% CI = 3.9-10.1%)
8	1998	Asadi *et al.* (12)	Otitis media	In girls: 7% (95% CI = 4.9-9.6%); boys 11% (95% CI = 8.2-14.3%); overall: 9% (95% CI = 7.1-10.8%)
9	2002 and 2003	Saffar *et al.* (13-14)	Acute LRTI	1197 in-patients during 7 months; age 1mo-10 yrs: 12.5% (95% CI = 10.5-14.5%)
10	2004	Saki *et al.* (11)	OME	2000 1st graders in winter: 11.1%(95% CI = 9.8-12.6%)
11	2006	Gheini *et al.* (16)	Pneumonia	1672 in-patients: 6.4%(95% CI = 5.27-7.68%)
12	2008-2009	Sadeghi *et al.* (17, 18)	ARI	1997-2000; 2004 to 2006; and 2006-2007. No. of patients with ARI: 4340. Presentations: Purulent rhinitis: 3020 (69.5%); Sinusitis: 536 (12.3%); pharyngitis/ tonsillitis 275,(6.3%); otitis media 94 (6.7%); purulent conjunctivitis 189 (4.3%); cervical adenitis 26 (0.6%). Most common bacteria in the first period:*S.pneumonia*(37.3%); in second period:*S.aureus*, (39.9%); in the final study:*M.catarrhalis*, (40%). 2009:*S.aureus*; 32.9%;*M.catarrhalis*16.9%;*S.pneumonia*12.7%.
13	2012	Tabatabaei *et al.*	ARI (different presentations)	1209 outpatient children during 1 yr: common cold 54%; acute sinusitis 17.5%; AOM 8.3%; Pharyngitis 5.1%; croup 3.9%; pneumonia 3.9%; bronchitis 2.7%; para-pertussis 2.4%; bronchiolitis 2.1%.

Abbreviations: SHS, second hand smoke; URTI, upper respiratory tract infection; LRTI, lower respiratory tract infection; ARI, acute respiratory infection

A study from Shiraz university of medical sciences looked at the bacterial causes of ARIs, particularly Moraxella catarrhalis, and the patterns of antibiotic resistance during three different periods namely from 1997 to 2000, from 2004 to 2006, and from 2006 to 2007 (16). The authors observed an increase in M. catarrhalis infections during the recent years as during the first period, this pathogen was the third most common bacteria isolated from patients with ARI; in the second span of time, it was the second most common; and in the last period, it was the most common bacterial pathogen. On the other hand, Streptococcus pneumonia, the most frequent isolated bacterium in the first phase, was replaced by Staphylococcus aureus in the second phase. No change was demonstrated in the frequency of Haemophilus influenza. Another study performed in 2009 (17) on 829 cases revealed that S. aureus was more frequent than M. catarrhalis; however the spike in the frequency of M. catarrhalis during 2006 and 2007 was not explained anywhere. These 2 papers were presented in 2 different seminars, but we could not find any published record to access to methodology details. Results of these two studies are presented in *Table 5* .

A study was done in Mofid children hospital from October 2007 for 2 years (18). Pediatric infectious disease specialists visited 1209 children diagnosed with ARI in accordance

with a diagnostic algorithm. About 45% of patients were < 2 years of age. Different presentations of ARI were as follows:

URTI: 82%; Acute LRTI: 14.5%, and no definite diagnosis: 3.5%

URTIs included Common cold: 54%; acute sinusitis 17.5%; AOM 8.3%; Pharyngo-tonsillitis: 5.1%.

LRTIs were comprised of croup, 3.9%; pneumonia, 3.9%; bronchitis, 2.8%; para-pertussis syndrome, 2.4%; and bronchiolitis, 2.1%. This was a well-conducted study but since only patients visiting the hospital clinics were selected for the study, the statistics may not apply to the community at large.

A brief description of selected studies is shown in the *Table 6* .

4. Pertussis

With the advent of regular immunization, the incidence of whooping cough had declined in children; however in the recent years researchers have observed an increase in the prevalence of this highly communicable disease, especially in older children and adolescence. This could be attributed to increasing susceptibility in the older age group due to waning immunity, and to better diagnostic methods (i.e. PCR) due to improvement in health care systems. In 1979, the incidence of whooping cough in Iran was reported as 40/100,000, which dropped to 0.13/100000 in 2004, but increased to 0.44/100000 in 2007 and 0.99/100000 in 2009. Results from 2006 to 2009 and those shown in *Table 7* were obtained directly from the center for disease control and prevention (ministry of health and medical education) (*Table 7* and *Figures 1* and *2*).

Table 7. Frequency of Reported Patients With Confirmed and Probable Pertussis in Iran

Year	Confirmed Pertussis [a]	Probable Pertussis [b]
2004 (19)	---	91
2005	---	---
2006	1	87
2007	29	331
2008	37	902
2009	92	832

[a] Clinical manifestation compatible with pertussis + positive culture for Bordetella pertussis or isolation of B. pertussis from nasopharyngeal secretions by immunofluorescence.

[b] Presence of 1 clinical manifestation compatible with pertussis (persistent cough ≥ 2 weeks or whoop or post-tussive vomiting) + 1 of the following: sub-conjunctival hemorrhage, local pertussis outbreak, lymphocyte count ≥15000/μL.

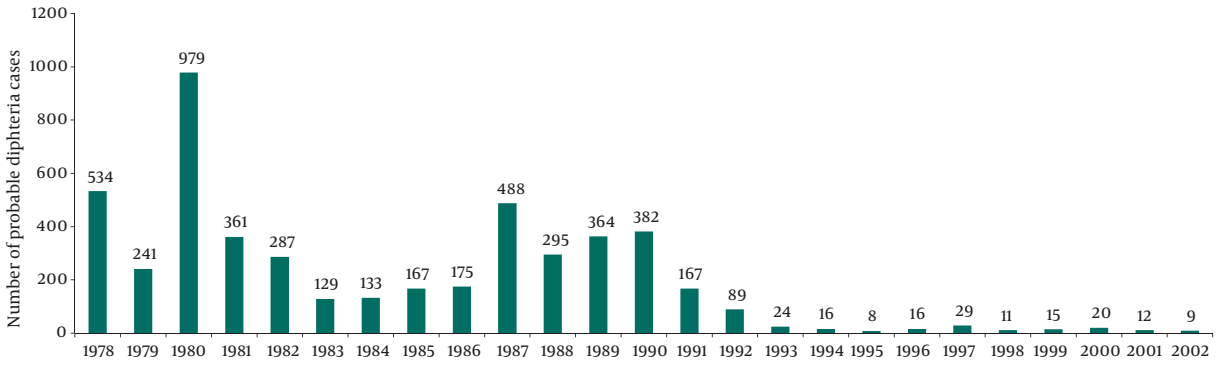

Figure 1. Incidence Rates of Probable Pertussis in Iran From 1991 to 2007 (20)

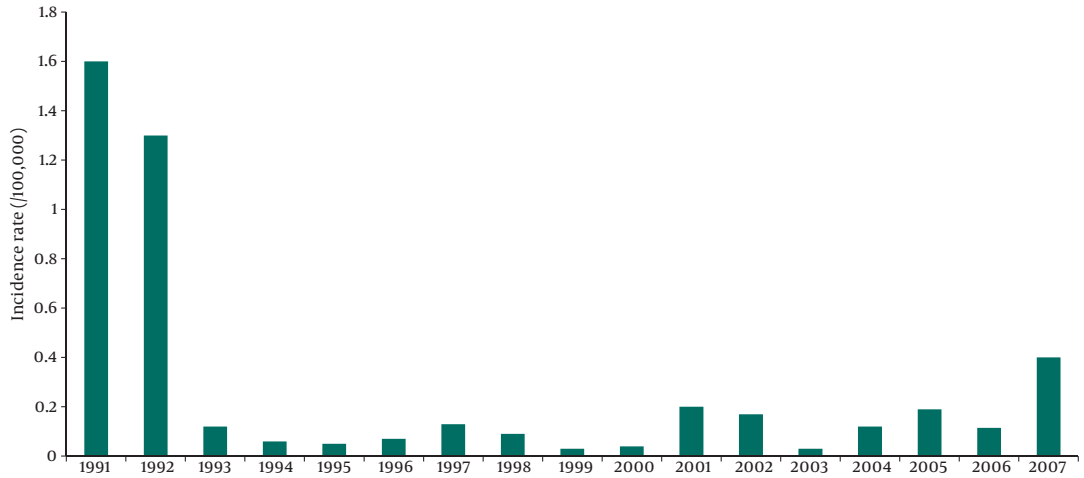

Figure 2. Reported Number of Probable Pertussis in Iran From 1994 To 2002 (21)

A cross-sectional study was done in 2008 in Tehran (district 9) to define the prevalence of pertussis in school children aged 6-14 years with = 2weeks of persistent cough (22). Out of 6601 youngsters, 328 met the inclusion criteria. Nasopharyngeal swabs (Dacron swabs) were collected from the selected cases to isolate B. pertussis by culture and PCR. Cultures positive for B. pertussis were found in four children, while PCR could detect 21 cases of the micro-organism. Incidence of pertussis was thus calculated as 318/100000. Following is a summary of their results (95% CIs were calculated irrespective of sampling method):

Estimated incidence based on culture: 61/100000 (95% CI: 17-155/100000).

Estimated incidence based on PCR: 318/100000 (95% CI: 197-486/100000).

Since this was a cross-sectional study, annual incidence cannot be calculated on these results. However, the study does highlight the significant prevalence of pertussis in school-age youngsters that calls for prompt action from the health authorities of the country.

5. Diphtheria

According to the records available from Iran Ministry of Health, incidence of diphtheria was 0.29 and 0.02 per 100,000 in 1991 and 2001, respectively (See *Figure 3)* (21). More data were recently obtained from the office of preventable diseases in center of disease control and prevention, directly *(Table 8)*.

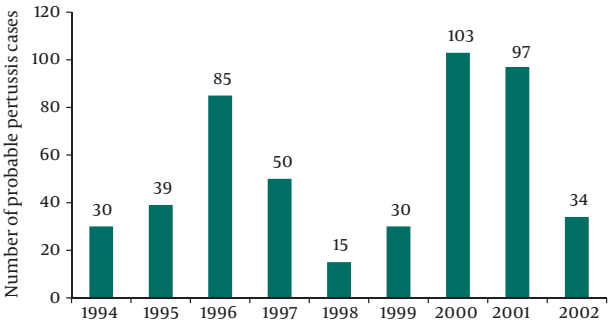

Figure 3. Frequency of Probable Diphtheria in Iran From 1978 to 2002

Table 8. Probable Case Defines as an Illness Characterized byLaryngitis, Pharyngitis, or Tonsillitis, and an Adherent Membrane of the Tonsils, Pharynx and/or Nose

Year	Probable Diphtheria Cases[a]	Confirmed Diphtheria Cases[b]
2004 (19)	---	8
2005	---	---
2006	26	---
2007	39	2
2008	50	0
2009	60	0

[a] Probable case defines as an illness characterized by laryngitis, pharyngitis, or tonsillitis, and an adherent membrane of the tonsils, pharynx and/or nose.
[b] Confirmed case defines as a probable case that is laboratory confirmed or linked epidemiologically to a laboratory confirmed case.

6. Discussion

ARIs are responsible for the majority of childhood deaths in young children under the age of 5 years. It has been estimated that 95% of cases of childhood pneumonia occur in developing countries, amounting to 151 million cases per year, from which 7-13% (i.e. 11 to 20 million) patients need hospitalization (23).

Although the overall incidence of ARI is comparable in different parts of the world, the distribution of different presentations of ARI is different, with more serious infections like pneumonia occurring in underprivileged countries with limited resources, especially in locations with high prevalence of malnourishment and HIV infections (24).

There are numerous studies in Iran to define the etiology of ARI in different population but findings of this meta-analysis reveal a lack of sufficient data estimating the frequency of ARI in Iranian children or the pattern of different forms of ARI. This limitation is not specific to Iran as in another systematic review, the authors found just 28 articles from 1961 to 2000 that possessed enough validity for inclusion in the meta-analysis (25).

Basic epidemiologic information is essential for health policy makers to decide about efficient health related interventions such as adding new vaccines to the national immunization program schedule. As mentioned earlier, such studies were planned and reported elsewhere (2, 3) and used for calculating burden of infectious diseases (26, 27). However to get valid and un-biased estimations about acute respiratory infections in different places in the country, great efforts are needed.

Obtaining an accurate estimation for ARI incidence in children applicable nationwide is an intricate task that needs planning of large-scale studies with trained personnel, equipment, and funding from the ministry of health.

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Authors' Contribution

A.R.Sh., A.F., S.A.T., M.K., A.Kh., Sh.S. and A.K. designed and performed the research; A.R.Sh., A.F., S.A.T., M.K., A.Kh. and Sh.S collected the data, A.R.Sh. summarized and analyzed the data, and wrote the manuscript draft; F.Sh. wrote the final manuscript in English; and all authors proofread the manuscript and agreed upon the data presented.

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