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REVIEW

Prevalence of human respiratory syncytial virus circulating in Iran

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Summary Respiratory syncytial virus (RSV) is a leading cause of acute respiratory infection during early childhood and is associated with a great burden on patients, parents, and society. While no treatment is yet available, results from recent phase 2 clinical trials of cell-entry inhibitors and RSV vaccines are promising. To prepare for introduction of these novel therapeutics, good understanding of its molecular epidemiology and continuous RSV surveillance data are necessary. This paper provides an overview of RSV prevalence and genotype distribution in Iran from 1996 to 2013. This meta-analysis includes 21 published studies. In total, 775 (18.7%) of 4140 respiratory specimens were positive for RSV infection. The male-female ratio of RSV-positive patients was 1.5:1. Significant peaks of RSV infection were detected during the cold season (November—March). RSV infection was mainly observed in patients <2 years of age. Phylogenetic studies showed that genotypes GA1, GA2, GA5, and BA co-circulated in Iran in 2007—2013. This review highlights the necessity of

Abbreviations: RSV, respiratory syncytial virus; Flu, influenza; PIV, parainfluenza; AdV, adenovirus; hBoV, human bocavirus; hMPV, human metapneumovirus.

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introducing standard molecular surveillance programs to inform the epidemiological, clinical, and pathological characteristics of various RSV genotypes. Improved understanding of the molecular epidemiology will be useful for development of novel RSV therapeutics.

Contents

Introduction

Viral respiratory infections pose considerable health difficulties for people of various ages worldwide [1]. Respiratory syncytial virus (RSV) infection is a leading cause of hospitalization in infants less than 1 year old and an important cause of clinical referral among children less than 5 years of age in developed countries [2,3]; it is also considered a significant pathogen in adults [1]. The major viral respiratory pathogens include RSV, influenza (Flu) types A and B, parainfluenza (PIV) types 1—4, adenovirus (AdV), rhinovirus, enterovirus, human bocavirus (hBoV) and human metapneumovirus (hMPV), all of which present with similar clinical features in infected patients [4]. RSV is a pneumovirus belonging to the *Paramyxoviridae* family. This negative-sense single-stranded RNA virus is characterized by large syncytia in single-layer cells [5]. Epidemiological studies have reported that RSV has a seasonal distribution pattern, with peak prevalence between early November and late January in most communities [5]. RSV can be involved in upper and lower respiratory tract infections and progress to bronchiolitis and pneumonia in infants. Recent studies describe the increased risk of wheezing and asthma after RSV bronchiolitis [6].

Increased risk of severe RSV infection has been reported among premature infants; those with bronchopulmonary dysplasia, airway congenital abnormalities, cystic fibrosis, atopy, and Down syndrome; and preterm children with chronic lung disease [1,7]. Considering the critical role of the immune system, particularly neutrophils, in RSV infection, research has focused on its immunopathogenesis in order to characterize the molecular mechanisms of virus replication to design more efficient drugs and vaccines [8—10].

Both classical and molecular diagnosis methods are currently used for RSV detection; however, molecular assays, especially reverse transcription PCR (RT-PCR), offer increased sensitivity, specificity, and rapidity [5]. The RSV genome encodes 11 proteins, including two nonstructural proteins. The nucleotide sequence of the variable regions within the G glycoprotein are mainly used to determine RSV genotype and for epidemiological purposes [11]. Based on its reaction with monoclonal antibodies against glycoprotein G and fusion protein F, RSV has two main genetic subtypes,

A and B. There are 11 genotypes in subtype A (GA1-7, SAA1, ON1, and NA1-2) and 20 in subtype B (GB1-4, BA1-10, SAB1-4, and URU1-2) [12]. Although these subtypes can co-circulate, subtype A tends to be predominant, which might reflect time or geographical factors; virus circulation and evolution can be affected by several other factors including virus infectivity and spontaneous mutations as well as host group immunity [13,14]. Gender-related susceptibility to RSV infection, with male children reportedly more at risk than females, remains controversial [12]; however, comparatively higher percentages of respiratory infections are reported in women, which might be due to increased exposure to airborne infections through frequent contact with children and elderly family members.

Since RSV plays a critical role in respiratory infection epidemics and might be associated with asthma occurrence and development in later life [15], RSV detection is of particular interest. The multi-seasonal climate of Iran as well as its highly populated regions and diverse ethnic populations prompted us to analyze published studies in order to provide valuable information about the prevalence of this virus in this population. Regional data is crucial for predicting the impact of RSV infection on developing asthma and for improving virus diagnosis.

Methods

We reviewed all published studies about RSV in Iran identified by searching PubMed, Medline, national databases (Scientific Information Database [SID], Irandoc, Iranmedex, MagIran), and related references from relevant articles. Search key words included ''RSV'', ''respiratory syncytial virus,'' and ''Iran'' in both English and Persian language. Overlapping, unrelated, and unreliable data were excluded. The following details were extracted from each source: journal name, year of publication, first author, season, number of cases, sample size, age range (if available), city, number of RSV-positive individuals, patient clinical features (if available), methods (direct immunofluorescence assay [IFA], indirect IFA, RT-PCR, real-time PCR, enzyme-linked immunosorbent assay [ELISA], or immunochromatography), sample type (nasopharyngeal swabs, nasopharyngeal aspirate, or throat swabs), hospitalization history (if available), and other respiratory viruses. Ten papers were identified by ''snowballing'' (pursuing references of references and electronic citation tracking), and 17 papers by database browsing. A total of 21 reliable published studies were considered in the current review (Table 1). The data from these 21 cross-sectional studies were both quantitative and qualitative. A total of 4140 respiratory specimens investigated in 21 studies in Iran from 1996 to 2013 were included in our survey. These cases were mainly acute upper and lower respiratory infections. The age distribution of patients ranged from 1 month to 60 years. Data were entered into a Microsoft Excel version 14 spreadsheet and descriptive analyses conducted.

Result

Prevalence of RSV circulating in Iran

The age distribution of the 4140 cases was as follows: in 14 of 21 studies, respiratory specimens were collected from children less than 5 years of age; in 5 out of 21 studies, respiratory samples from children less than 15 years of age were included in the survey; the remaining studies collected samples from patients 5—60 years of age. Thus, the majority of samples were from children less than 5 years of age. Based on data analysis of 21 studies in Iran, 775 of 4140, respiratory specimens were positive for RSV. The average percentage of RSV positivity in all samples was 18.7% during 1996—2013 (Table 1). This pattern was consistent with estimated RSV infection prevalence of reported in epidemiologic studies in other countries. Molecular epidemiology of circulating RSV detected in the Philippines [14] and rural Thailand [16] revealed that 19% of cases hospitalized with severe pneumonia were positive for RSV. In the current study, the percentage of RSV positivity among respiratory samples from neighboring countries such as Pakistan was 17.8% among children hospitalized for severe pneumonia during 2010—2011 [17]. A study conducted in Kenya reported 16.5% of severe pneumonia cases were RSV-associated, consistent with our findings [18]. The percentage of RSV positivity in Iran, however, was higher than in countries such as Cameroon (5.7%) [19] and Kenya (12.5%) [20], but lower than in recent reports from Latvia (33% to 57%) [21] and Turkey (37.9%) [22]. The rate of RSV detection varied over time in studies conducted in Iran, with low and high rates of 5.7% and 45.8% reported in 2007 and between 2009 and 2011, respectively (Table 1). Despite the use of sensitive techniques like RT-PCR, lower detection rates were reported in Arak and Ahwaz during 2008—2009 (Table 1); there are several possible reasons for this observation, including hospitalization history, since all samples in the Arak study were from outpatient cases. The

Table 1 RSV positivity rate from 21 studies of acute respiratory infection in Iran, *n* (%).

Location	Year	Age range	No. of cases	RSV positive rate	Type of sample[d]	Method[e]	Clinical features	Hospitalization	Ref.
Tehran	Oct 1996 —Mar 1998	<14 yr	268	33 (12.3%)	NPS	Cell culture and DIF	Cough, bronchiolitis, fever	Outpatient	[40]
Tehran	Nov—Mar 1998	<5 yr	365	70 (19.2%)	NPA	Cell culture and DIF	Cough, coryza, pneumonia, bronchiolitis	14 (20%)	[41]
Tehran	Jan—May 1999	<5 yr	145	56 (38.6%)	NPA	DIF	Bronchiolitis	36 (37.9%)	[42]
Tehran	Mar—Nov 2001	2 m—14 yr	83	20 (23%)	NPS	IIF	Cough, fever, rhinorrhea, wheezing	20 (100%)	[43]
Mazandaran	Oct 2001—May 2002, Jun to Nov 2003	1 m—5 yr	202	26 (12.9%)	NPS	IIF	Fever recurrent wheezing	26 (100%)	[44]
Tabriz	2002	1 m—5 yr	252	62 (24.6%)	Not stated	DIF	Pneumonia, bronchiolitis, wheezing, cyanosis, conjunctivitis	Not stated	[45]
Rasht	Nov 2003—Mar 2004	2 m —5 yr	261	39 (15%)	NPA, NPS	RT-PCR	cough, fever, tachypnea	122 (46.7%)	[46]
Tehran	2005—2006	5—60 yr	212	34 (16%)	NPS	DIF	Body pain, fever, cough, malaise	Not stated	[47]
Kerman	2006	<2 yr	168	63 (37.5%)	NPS	RT-PCR	Bronchiolitis	Not stated	[48]
Tehran	2007	3 m—15 yr	160	9 (5.7%)	NPS	IMC	Fever, cough, vomiting, diarrhea, sore throat, abdominal pain, conjunctivitis	Not stated	[49]
Tehran	Oct 2007 —Sep 2008	<17 yr	50	7 (14%)	NPA, NPS	RT-PCR and Rt-PCR	Fever, cough, Dyspnea, Rales, Wheezing	Not stated	[50]
7 cities[a]	2007—2008	<5 yr	72	14 (19.4%)	TS	RT-PCR	Wheezing, fever, caught	10 (71.4%)	[27]
Shahre-kord	2007—2008	2 m—5 yr	300	26 (8.6%)	Serum	ELISA	pneumonia, pharyngitis, bronchiolitis, croup	26 (100%)	[51]
Arak	Nov-2008	2 m—10 yr	300	18 (6%)	NPS	RT-PCR	Coryza, cough, sneezing, sore throat, headache, fever, conjunctivitis, abdominal pain, hoarseness	Outpatient	[52]
Tehran	Mar 2008—May 2009	<6 yr	202	34 (16.8%)	TS	RT-PCR	acute respiratory symptoms	34 (100%)	[24]
Ahwaz	Oct 2008 —Apr 2009	<5 yr	100	9 (9%)	NPS	RT-PCR	Bronchiolitis, cough, coryza, fever, chest wall retraction, wheezing, cyanosis	9 (100%)	[53]
13 cities[b]	2009	<5 yr	107	24 (22.4%)	TS	RT-PCR	Wheezing, cough, fever	24 (100%)	[28]

Babol	2008–2010	<4 yr	180	40 (22.2%)	Plasma	ELISA	Stridor, tachypnea, retraction, crackles, wheezing	40 (100%)	[54]
Tehran	Sep 2009–Mar 2010	<5 yr	96	44 (45.8%)	NPA	RT-PCR	Wheezing, acute bronchiolitis, asthma bronchiolitis	41 (43%)	[25]
Tehran	Nov 2009–Mar 2011	<3 yr	132	53 (40.2%)	NPS, NPA	DIF	Fever, cough, coryza, bronchial whizzing	53 (100%)	[55]
NIC[c]	Nov 2007–Apr 2013	<2 yr	485	94 (19.4%)	TS	RT-PCR	Acute respiratory symptoms	85 (90.43%)	[13]

[a] Tehran, Karaj, Ghazvin, Isfahan, Shahreza, Kerman, Bandarabbas.
[b] Tehran, Varamin, Kelardasht, Isfahan, Semirom, Hamedan, Zanjan, Aligudarz, Shahindej, Khoy, Chaldoran, Miandoab, Naghadeh.
[c] National Influenza Center of Iran.
[d] Nasopharyngeal swabs (NPS), Nasopharyngeal aspirate (NPA), Throat swabs (TS).
[e] Direct immunofluorescence (DIF), indirect immunofluorescence (IIF), Reverse transcription polymerase chain reaction (RT-PCR), Real-time polymerase chain reaction (Rt-PCR), Enzyme-linked immunosorbent assay (ELISA), immonochromatography (IMC).

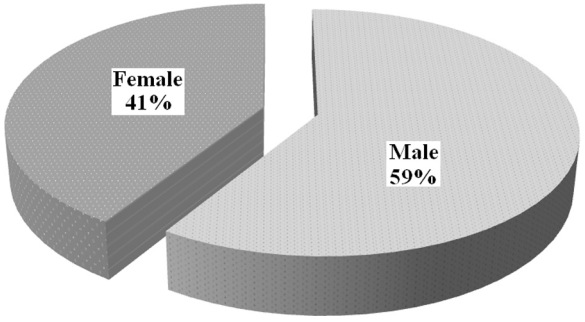

Figure 1 Distribution of respiratory syncytial virus infections in Iran between 1996 and 2013, according to gender.

small sample size in the Ahwaz study also might have influenced the findings. High-quality samples are required for good virus detection; lower sample quality in these cities might also have contributed to the reduced detection rate of RSV. High detection rates have been reported in a number of studies from Tehran (38.6%, 40.2%, and 45.8%) and Kerman (37.5%) (Table 1), which were higher than the 12.6–24.6% reported in other places (Table 1). RSV infections were more frequently observed in hospitalized patients (14 studies). Sixteen studies specified the number of inpatients and outpatients, and more than 63% of RSV-positive cases were hospitalized. Our results using available studies indicate that most RSV-positive outpatients were less than 5 years old. RSV infections were mainly observed before 2 years of age [23]. No lethal RSV infections were reported in Iran from 1996 to 2013.

RSV gender differences

The male-female ratio of RSV-positive patients in our analysis was 1.5:1, indicating a higher occurrence of RSV infections in male patients (Fig. 1). However, higher percentage of men enrolled in the surveys might contribute to this finding, since studies from other countries have not reported significant gender differences [23].

Regional differences in RSV

Our analysis revealed that available data on RSV-related reports evaluated 19 of 31 provinces in the center, northern, northwestern, and southwestern parts of Iran. No data were reported from the western, eastern, northeastern, or southeastern regions of Iran, except for Hormozgan and Kerman provinces, which are located in the south (Fig. 2). The reasons for variable geographic RSV prevalence cannot be concluded from available data, but one possible explanation might include the local climates in these provinces [21]. It is apparent

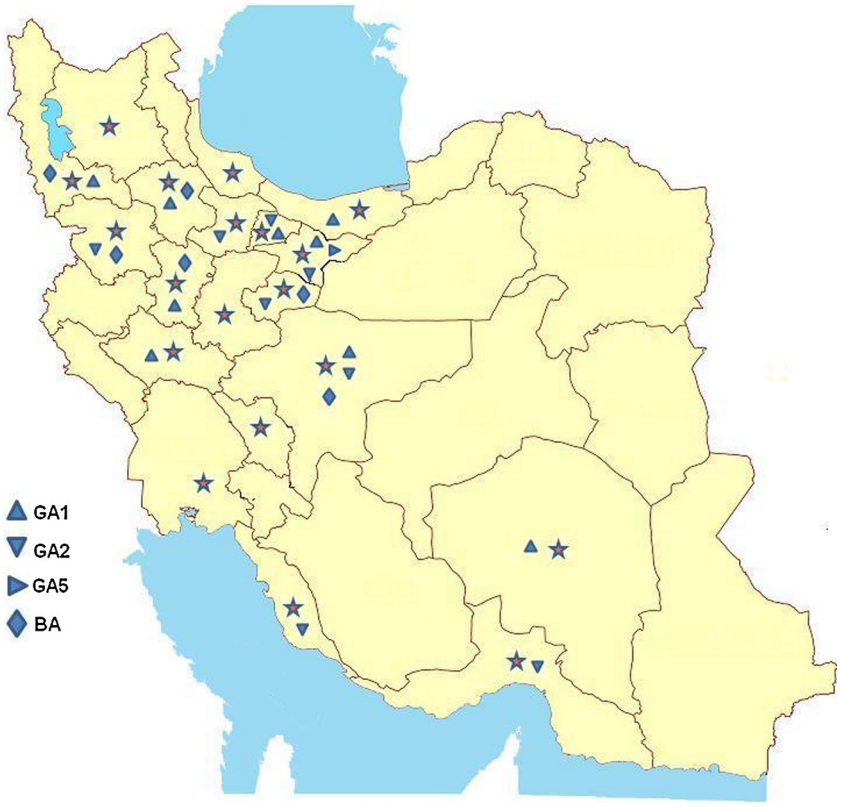

Figure 2 Geographic distribution of respiratory syncytial virus cases between 1996 and 2013 (small stars) and genotype distribution of respiratory syncytial virus cases related to geographical location in Iran, 2009—2013 (small triangles).

that additional data from all provinces in Iran are required to determine the exact prevalence pattern and frequency of RSV genotypes nationwide. Significant peaks of RSV prevalence were detected in the cold seasons (November—March). This finding underlined the seasonal characteristics of RSV infections in Iran, which is consistent with patterns of age and seasonal RSV prevalence reported in other studies [16,18].

RSV co-infection

Co-infection of RSV with other respiratory viruses is common, which may increase the risk of severe acute respiratory infections associated with respiratory distress, such as bronchiolitis, compared to single RSV infections [4]. RSV co-infection was only reported in two studies in our survey, consisting of 9/43(20.9%) [24] and 11/44 (20.5%) cases [25]. According to Malekshahi et al. [24], the rate of RSV co-infection with hMPV, PIV-1, AdV, and Flu was 1/44 (2.32%), 4/44 (9.3%), 3/44 (6.97%), and 1/44 (2.32%), respectively. However, Chavoshzadeh et al. [25] have shown that the RSV co-infection rate with hMPV and rhinoviruses is 5/44 (11.36%) and 4/44 (9.1%), respectively. No relationship between RSV co-infections and increased severity of virus-dependent diseases was found in either study. According to the small number of reports on this topic, the proportion of co-infections requires verification in future studies and evaluations to determine if these findings are incidental or have clinical significance. Mixed infections have been reported in many studies; however, the rates of RSV co-infection with other viruses have varied substantially from 4% to 53% [26]. Hospitalized children had higher rates of co-infections [26], and RSV co-infection with hMPV was reportedly associated with disease severity such that mechanical ventilation was required [17].

In six of 21 studies, other respiratory viruses including AdV, PIV types 1—3, hBoV, Flu type A and B, and hMPV were also detected independently from RSV infections; AdV (14.22%) and PIV type 3 (10.15%) were most commonly observed (Table 2).

Distribution of RSV genotypes

Limited information exists regarding RSV genotypes in Iran. Among the current studies, only three provided information about RSV genotypes using nested RT-PCR and partial G protein sequencing.

Table 2 Detection rates of RSV, adenovirus, influenza virus, parainfluenza virus, boca virus and metapneumovirus in children with acute respiratory infection in 21 studies in Iran between 1996 and 2013.

Viral agent	No. of samples tested	Positivity rat, *n* (%),	No. of studies	Year	Ref.
Respiratory syncytial Virus	4140	775 (18.7%)	21	1996–2013	[13,24,25,27,28,40–55]
Adenovirus	1125	160 (14.22%)	5	2001–2004, 2007–2009	[40,45–47,52]
Parainfluenza virus type 3	404	41 (10.15%)	2	2001–2002, 2009–2010	[45,52]
Human bocavirus	261	21 (8.02%)	1	2003–2004	[46]
Parainfluenza virus type 2	202	13 (6.43%)	1	2001–2002	[52]
Influenza virus type A	1125	59 (5.24%)	5	2001–2004, 2007–2009	[40,45–47,52]
Parainfluenza virus type 1	904	42 (4.65%)	4	2001–2002, 2007–2009	[28,45,47,52,28]
Influenza virus type B	404	8 (1.98%)	2	2001–2002, 2008–2009	[45,52]
Human metapneumovirus	202	1 (0.5%)	1	2008–2009	[45]

We just considered the studies that have detected RSV as well as other respiratory viruses. We have excluded those studies that detected other respiratory viruses except RSV.

The first report, from Faghiloo et al. (2011), reported a prevalence of GA1, GA2, and GA5 during the winter in 2007–2008 [27], and GA1, GA2, and BA during the same season in 2009 [28]. In 2014, the same group identified GA1, GA2, and BA genotypes from 2009 to 2013 [13]. The circulating RSV genotypes in Iran fluctuated in 2007–2013. Accordingly, GA2 was predominant during 2007–2008 and reappeared during 2010–2012. Both GA1 and GA2 circulated in 2011–2013; however, GA1 was predominant. GA5 was only detected in 2008. Genotype BA with a 60-nucleotide duplication in the C-terminal region of the G protein was detected in 2009 and 2013. These findings were consistent with other studies reporting shifts in the predominant genotype between seasons [29]. The interplay of pre-existing immunity in the community and the genetic and antigenic properties of the RSV virus to evade the immune response may explain changes in genotype dominance over time [30]. The predominance of RSV-A viruses has been attributed to increased variability among RSV-A strains [30]. Based on the fact that the dominant strains shift yearly, evasion of immunity induced by previous strains may be a mechanism for re-infection [31].

Geographical differences in RSV genotypes

The geographical distribution of RSV genotypes in Iran also varied: genotype GA2 was predominant in the south; GA1, GA2 and BA in the center; and GA1 in the north (Fig. 2). Monitoring circulating RSV strains in different geographical regions is essential, particularly in the western, eastern, northwestern, and southeastern parts of Iran, where available data is lacking. The continuous circulation of genotype GA2 emphasizes the stability of this subtype; it has become an epidemic in Europe, Asia and Africa [30,32,33]. Genotypes GA2 and BA are also the most common RSV genotypes worldwide [30,32,34]. Recent data from Israel indicated that the majority of RSV-A viruses detected during 2008–2012 was GA2 [32]. These data also suggest that GA2 has been the predominant RSV-A genotype circulating in the Middle East between 2006 and 2012 [32]. However conflicting data exist on whether RSV evolution is temporally or geographically related [30,32].

As indicated in Fig. 2, RSV virus subgroups A (GA1, GA2, and GA5) and B (BA) co-circulate in the same area with various patterns of predominance during epidemic periods. Recent studies demonstrating the predominance of genotype BA at least in subtype B may suggest a selective advantage for this genotype; however, the mechanism has not yet been defined [35]. Genetic changes in the BA genotype have been proposed to confer a neutralization-resistance phenotype that allows these strains to escape previous host immunity and provide an opportunity for increased transmissibility in susceptible populations [35]. An annual shift of dominant strains may explain frequent reinfections due to evasion of immunity induced by previous strains [21]. Several attempts to clarify the relationship between clinical severity of infection and RSV subgroups have postulated that subgroup A is associated with more severe disease [34,36]. Martinello et al. [36] reported that genotype GA3

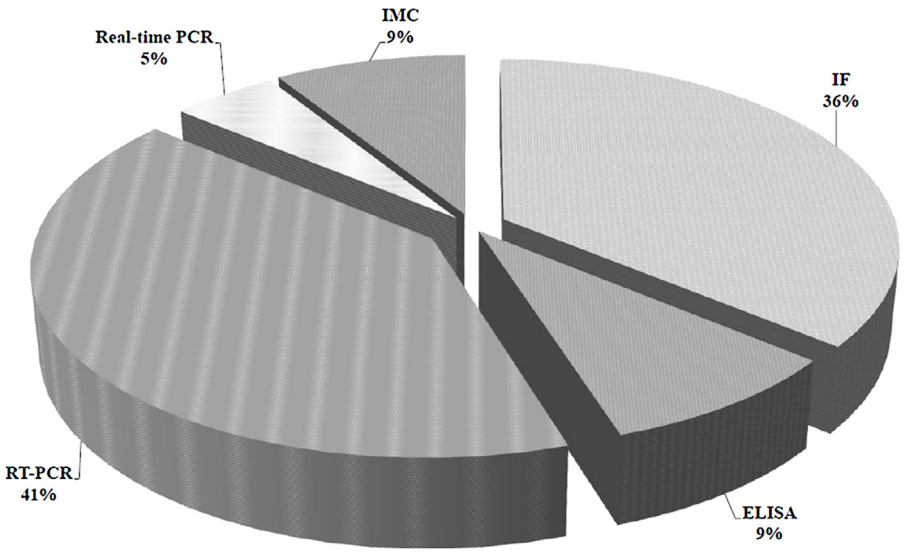

Figure 3 Overview of methods used in studies included in this review. Immunofluorescence (IF), reverse transcription polymerase chain reaction (RT-PCR), enzyme-linked immunosorbent assay (ELISA), immunochromatography (IMC).

might be associated with more severe disease. They claimed that amino acid variations in the third C-terminal hypervariable region of the RSV G gene might be responsible for the severity of RSV infections, such as bronchiolitis [34,36]. However, some reports have concluded that the severity of RSV-related disease was not related to subgroups or genotypes but was instead associated with viral load during primary RSV infection [34]. It is not known to what extent these inconsistencies might be attributed to differences in the definitions of disease severity, RSV subgroup distribution, study design, or study populations [5].

Discussion

RSV is responsible for approximately 3.4 million hospitalizations associated with lower respiratory tract infections and almost 200,000 deaths among children less than 5 years of age [37]. Of these deaths, 99% occur in developing countries [37]. The current review of 21 published studies from various geographical regions in Iran allowed us to estimate the percentage of respiratory tract infections caused by RSV infection as well as the distribution of RSV genotypes in Iran. Our analysis revealed an overall percentage RSV positivity rate of 18.7% during 1996—2013. The sensitivity of the assays used in various studies may be variable [38]. Jansen et al. [39] described a significant efficiency of nasal swabs compared to throat swabs for RSV detection among different sample types. The sample types collected from patients in studies included in our survey included nasopharyngeal swabs (42.8%), nasopharyngeal aspirate (14.3%), both nasopharyngeal swabs and aspirates (9.5%), throat swabs (19%), serum (4.8%), plasma (4.8%); 4.8% of studies did not provide this information (Table 1) [13,24,25,27,28,40—55]. Consequently, proper sampling and standard techniques are highly recommended to avoid underestimating RSV-associated disease burden due to low-quality specimens [31].

Several reasons could explain the controversy regarding RSV infection rates. First, the low sensitivity of conventional virus detection tests such as immunochromatography, ELISA, and immunofluorescence assays, were exploited in several studies (Table 1; Fig. 3). These methods are 12—50% less sensitive than PCR-based methods [3,38]. Second, RSV might have been cleared prior to sampling and delayed sampling may lead to underestimation of the true viral infection rate. Third, viral RNA may have degraded during storage in hospital freezers. Finally, differences in study design, sample types, hospitalization period, and patient age might influence study outcomes. However, these discrepancies might also reflect real regional and temporal differences.

Besides epidemiological characteristics, significant genetic variation in circulating strains may involve different pathogenicity and virulence among patients with RSV infections. Several publications have recently documented that novel variants may have enhanced clinical severity with increased replication in the lower respiratory tract [34,36]. However, our findings do not support these

observations. Emerging RSV variants with a selective advantage due to increased genetic diversity may confer low cross-protection by pre-existing antibodies to RSV strains previously circulating in Iran. Multiple genotypes co-circulated during 2007—2013. The co-circulation of multiple genotypes in some regions of Iran might be associated with the outbreak of RSV among children with fever and respiratory symptoms in the epidemic season (Fig. 2).

Because there are few studies on the molecular epidemiology of RSV in Iran, a larger population-based study is required to further delineate the association of clinical severity of infection with virus genotype in different areas. Better understanding of the molecular epidemiology of RSV will prove instrumental in developing efficient vaccines and antiviral pharmacotherapy [8,9,35]. There were several limitations in our study, including: (1) RSV viral load was not measured by quantitative PCR; viral load may have been associated with co-infection or disease severity. (2) Most studies were conducted in a single hospital or city; however, patterns of RSV genotype frequency and distribution may vary with location. (3) Not all regions in Iran were studied or surveyed for RSV genotypes, and additional RSV genotypes are possible. (4) No data were available on the timing of disease onset. Despite these limitations, our study is the first and complete review on RSV epidemiology in Iran covering research over the last 17 years [13,24,25,27,28,40—55].

Although deaths associated with RSV have been rare in the last two decades [3], and no reported lethal RSV infections were reported in Iran, the RSV mortality rate may not be zero. Clinicians should consider that children suffering from complex chronic conditions [6] and genetic disorders [7] are significantly more prone to death from severe RSV infections. Therefore, more comprehensive population-based studies on pediatric infectious diseases are required to determine the risk factors of severe RSV infections in Iran.

In conclusion, this review highlights the necessity of a standard molecular surveillance program in Iran. Future investigations of different areas of Iran, particularly regions with a paucity of data, are needed in order to determine RSV prevalence and genotype distribution nationwide. Improving RSV surveillance would allow timely understanding of the epidemiological, clinical, and pathological characteristics of novel RSV genotypes. Since high-risk populations are at increased risk of RSV infection and there is no data about passive immunization against RSV in Iran, this information will assist policy makers in determining which regions and sub-populations will most benefit from RSV prophylaxis and treatment.

Authors' contributions

VS and MTY participated in the study design and performed statistical analysis. VS and STY conceived of the study. JY, LB, and TMA wrote the manuscript. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Ethical approval

Not required.

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