



Lower Respiratory Tract Infections among Saudi Children: A Review of Literature

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ABSTRACT

Acute lower respiratory tract infections (ALRTIs) account for a critical health problem that affects approximately (15.4%) of the Saudi population. This study focused on previous studies that included children to investigate the epidemiology of LRTIs and respiratory viruses. The detected populations signified that young children are more vulnerable to get ARTIs than adults, as many viruses including human respiratory syncytial virus (HRSV), influenza viruses, and human parainfluenza viruses (HPIVs) were found to be highly infective to infants and children. Conclusion: The study showed that there is a lack of literature that highlights the prevalence of ALRTIs in children or discusses the management and expected complications of these respiratory infections. It also implied the importance of spreading the knowledge about ALRTIs among parents who have newborns and establishing the proper management-guidelines of the disease to face the increasing morbidity and mortality of ARTIs among children.

Key Words: Lower respiratory tract infections, Epidemiology, Risk factors, Saudi children,

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INTRODUCTION

In accordance with pediatricians, ARTIs are the most prevalent infections of the human host particularly children [1, 2]. Although the upper respiratory tract infections (URIs) are the most dominant, lower respiratory tract infections (LRTIs) are also daily frequented problems to the physicians, the most common diseases of children and infants in developing countries, and are highly correlated with significant morbidity and mortality [3]. ALRTIs are composed primarily of pneumonia [4, 5]; moreover, they comprise croup [6], tracheobronchitis, and bronchiolitis [7].

In history, LRTIs burden differs considerably throughout the world, incommensurately affecting young children and the impoverished. In 1881, pneumococcus (*Diplococcus*

[Streptococcus] pneumoniae) was identified as the common cause of pneumonia. Antipneumococcal sera were discovered and developed for treating pneumonia, but the various strains of pneumococcus needed to make certain that the suitable antisera were detected to apply. Then later in the 1930s, sulfa antibiotics showed more effective results than the antisera therapy in the treatment of pneumonia. In the 1950s, many viruses were identified to be involved in causing ARTIs such as; respiratory syncytial virus (RSV), parainfluenza virus, and rhinoviruses [8].

LRTIs are a critical public health problem. Estimates from the Disease Control Priorities Project (DCPP) has indicated that LRTIs caused 3.7 million deaths worldwide in 2001, standing for 6.7% of all causes of death in different ages [9]. Children younger than 5 years recorded

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1.9 million deaths in 2001, which represents 18.3% of overall child deaths [10]. These infections affecting young children were identified as a predisposing factor for obstructive airway diseases and decrease lung function [11, 12]. Pre-school children may catch 6-10 viral colds per year. Parents usually want to make sure that it is not a serious health problem, sometimes triggered by the natural history of the family or worrying diagnosis of a friend's child [13]. Prior studies indicated that children who have siblings [13, 14], and the ones who attend daycare outdoors are more vulnerable to get respiratory tract infections than those who do not have siblings and do not take part in daycare [14, 15].

Most of the conducted studies in Saudi Arabia considering the ARTI have greatly focused on the national and foreign pilgrims that visit Mecca and Medina within the Hajj seasons [16]. Furthermore, most majority of the pilgrims are elderly and adults, so children were practically excluded from these studies.

Epidemiology

ARTIs represent about a third of overall pediatric conferring to primary health care [17]. Approximately, the deaths resulted from LRTIs were 2.38 million cases in 2016, which in turn made LRTIs the 6th leading cause of death covering all ages [18], and the main cause of mortality among children under 5 years with 704,000 deaths per year and over 6 million disability-adjusted life years (DALYs) [19].

Bronchiolitis and pneumonia are the most common LRTIs among children. Moreover, the frequent symptoms in the infected children are coughs and a remarkable rise in the respiratory rate [20]. In 2010, WHO established that respiratory diseases are the 2nd substantial cause of mortality in children under five years [21] and stated that pneumonia is one of the major three causes of newborn infants' death [22]. Earlier in 2008, about 156 million children were diagnosed with pneumonia (there were 151 million in developing countries alone), and caused 1.4 million deaths, ranking (28-34%) of overall deaths in children under 5 years [23]. WHO also recorded reports in some developing countries (Nigeria, Gambia, Senegal, Chad, Cameroon, Burkina Faso, and Mali) These reports demonstrated that the incidence rate of ARTI among young children is (15-21%) [24]. Recent estimates showed that 1.9 million children lost their lives because of ARTIs in 2000 worldwide, 2/3 of them were in Southeast Asia and Africa [25]. Meanwhile, the annual incidence of pneumonia in developed countries is 33/10000 in children younger than 5 years and 14/5 per 10000 in children aging from 0 to 16 years old [26].

According to estimates in 2013, in Saudi Arabia, more than 5 million (15.4%) of the population was affected by ARTI [27]. There are two main factors affecting the

epidemiology and circulation patterns of respiratory viruses in Saudi Arabia; one of them is the high diversity among the workers as there are about 11.9 million foreign workers from over 100 different countries, the motion of this enormous number of workers between their home country and the Kingdom of Saudi Arabia (KSA) can establish new viral strains [28]. The latter factor is loads of over 10 million Muslims from about 184 disparate countries in the holy locations of Mecca and Medina within the seasons of Hajj and Umrah. This large heterogeneous population of pilgrims and foreign employees include distinctly variable rates of LRTIs in terms of public health concern and considering that the overcrowding atmosphere is ideal for the transmission of the respiratory viruses [29, 30]. In 2003, pneumonia was defined as the main leading cause of hospitalization during the season of Hajj in KSA (accounting about 39%), and ranking the 2nd leading cause of intensive care unit (ICU) admissions (rating about 20%) [31, 32], with a reported death rate of 17% [33].

Many studies were conducted to determine the epidemiology of respiratory viruses in Saudi Arabia. A retrospective study in the KSA included 643 hospitalized children, of which 16% were accounted for bronchiolitis, 34.6% for pneumonia, and the respiratory viruses were detected in 48.1% of them [34]. A total of 135 children younger than 5 years were included in a cross-sectional study to detect the respiratory infections in Southwestern Saudi Arabia, a single virus pathogen was found in 76 children, and a mixed viral and bacterial pathogens were detected in 15 patients [35].

Risk factors

The incidence of the respiratory tract infections in young children depends mainly on the environmental-related risk factors including low birth weight, lack of breastfeeding particularly in the first four months after birth, air pollution, malnutrition, and lack of measles immunization in children younger than one year [36]. There are some risk factors with determined effects such as smoking of any of the parents, zinc deficiency, the experience of mothers as caregivers, and with concomitant illnesses (e.g. asthma or heart diseases), the weather condition, and vitamin A deficiency [23].

Causes

Viral and bacterial pathogens are both responsible for respiratory tract infections. It is known that viral organisms usually cause mild to moderate pneumonia, specifically in children younger than 5 years. Moreover, severe pneumonia is caused by bacterial infections [23, 37]. Viral infections are already known as the most prevalent cause of ARTIs in children under 5 years. WHO reported that viruses are accountable for 30 to 67% of pneumonic infections that occur in children younger than 1 year [22].

In KSA, approximately 5.4 million patients of ARTIs were introduced to the emergency departments in 2013 [27]. This situation was already complicated by the release of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Saudi Arabia in 2012 [38]. MERS-CoV is one of the six Coronaviruses that can infect humans. It belongs to the subfamily Orthocoronavirinae (family Coronaviridae, order Nidovirales) [39]. MERS-CoV was reported to be highly fatal with the rates of 40%-60% [30]. Most of the studies in Saudi Arabia have indicated that the incidence among children is low [40]. The first reported case was a single child in the pediatric department in Jeddah on 28 June 2013 [41]. A review collected from the Saudi Ministry of Health website established that from April 2012 to 2016, only 31 pediatric cases with MERS-CoV were reported, of which (42%) were asymptomatic [42]. A total population of 1250 between 2012 and 2015 within MERS-CoV in KSA were reported, among them 3.3% were children aged under 10 years [43]. Another analysis conducted in Riyadh, with 109 patients from April 2014 to August 2015, 4.2% of the cases were younger than 20 years and confirmed to be infected with MERS-CoV [44].

Fagbo et al. [27] determined the respiratory viruses correlated with ARTIs in King Fahd Medical City, Riyadh; the study included 2235 young children (age ≤ 13), of whom (61.5%) were younger than 1 year and the respiratory viruses were detected in (61.02%) of the whole population, with (55.4%) LRTIs among the cases. These viruses included syncytial virus (RSV) with about (24%), human rhinovirus (hRV) accounted for (19.7%), adenovirus (5.7%), influenza virus (5.3%), and parainfluenzavirus-3 (4.6%). This study also reported that most infected children aged 9–11 months (60.9%) [27].

Influenza viruses belong to the family Orthomyxoviridae, influenza (A) virus is one of the seven members of this family depending on the variations in the nucleoprotein and matrix proteins [45]. The KSA was one of the countries affected by the influenza (A) virus, subtype H1N1 pandemic, with 15,850 infected patients and 124 mortality cases in December 2009 [46]. The studies have revealed that the virus significantly targets young adults and children. A study was conducted in King Khaled University Hospital and reported a total of 109 cases with H1N1, of which (16.5%) were younger than 5 years and (33%) aged from 5 to 14 years old [47]. In Riyadh 2009, 1103 children infected with the influenza-like disease, (34%) were laboratory-confirmed with H1N1, of whom 50 (13.3%) were hospitalized, 5 were presented to the ICU, 4 needed mechanical ventilation, and 2 of them (4%) died [48]. Another study in Southern Saudia included 119 patients infected with H1N1, (41.9%) of them were pediatric cases [49]. A cohort of 174 hospitalized children in Riyadh, Saudi Arabia showed that 34 (19.54%) of them

had influenza (A) virus and 24 children were suffering from LRTI [50]. An observational study reported the infection of 47 patients with H1N1 in Riyadh, of which 3 (6.4%) were < 1 year and 13 (29.5%) aged from 1 to 9 years old. The study also indicated that 30 (63.8%) had pneumonia, 7 (14.5%) needed ICU admission, and 4 (8.5%) needed intubation [51].

HRSV is a member of the genus Orthopneumovirus, family Pneumoviridae, order Mononegavirales, phylum Negarnaviricota, and it is considered as one of the highly contagious pathogens that leads to LRTIs in the man of all ages [29, 45]. Nair et al. [52], conducted a meta-analysis that demonstrated the infection of 33.8 million children, 3.4 million of them were hospitalized and about 199,000 died. The study reported that (99%) of these cases were from developing countries. The virus was detected and isolated from the first time in Saudi Arabia. A total of 127 hospitalized children with LRTI at King Khaled Hospital in Riyadh, the examination was conducted during the autumn-winter season from September 1991 to February 1992 and indicated that 69 (54%) cases were diagnosed with HRSV. Most of the children were younger than 1 year old and bronchiolitis and bronchopneumonia were the most common diagnosis on admission [53]. Retrospective data was analyzed in King Abdul-Aziz Medical City (KAMC), at a tertiary hospital in Riyadh, the study included 4611 children with a median age of 16 months and 1115 of the sample had identified viruses, of the infected sample 1086 (97.4%) had HRSV [54]. A cohort study was included 174 children in Riyadh, the sample aged from 0 to 60 months, this study detected 11 respiratory viruses in 105 (60.34%) of the sample, among which 39 (22.41%) were identified with HRSV infection, and all of the infected children had LRTI [50].

HPIVs are members of the family Paramyxoviridae, order Mononegavirales, the detected types of HPIV in frequent outbreaks are four; HPIV-1, -2, -3, and 4 [29]. The main effects of HPIV infections are acute laryngotracheobronchitis, bronchiolitis, pneumonia, tracheobronchitis, and afebrile wheezing [55]. In KSA, the statistics and information regarding HPIV epidemiology are insufficient [29]. The spread of HPIV was defined in few districts such as; Abha, Al-Qassim, and Riyadh. In Al-Qassim within winter in 2003 and 2004, a population of 282 newborns and young children were hospitalized and diagnosed with ALRTIs and notable bronchiolitis, further tests revealed that HPIV was detected in 9 (3.2%) of the total sample [56]. In Riyadh from April 1993 to March 1996, a total of 1429 children younger than 5 years complained of suspected ARTI, the viral infection could be determined in 522 (37%) of them and the infected children with HPIV type 3 were only 42 (8%) [55]. In the Southwest of Saudia, particularly Abha, a case-control study was conducted on 51 children of ≤ 5 years old, HPIVs was

found in (18%) of the studied participants; HPIV-1 was detected in (4%) of the sample, HPIV-2 in (2%) and HPIV-3 was the most prevalent with the percentage of (14%). Moreover, within the same sample, in (40%) of the population, HRSV was laboratory-confirmed [57].

Influenza viruses are members of the family Orthomyxoviridae. They are categorized into three types counting on their core proteins; type A, B, and C. Influenza B and C mostly infect humans, while influenza A virus undergoes high rates of mutation and the risk of developing LRTIs after influenza viruses infection has been determined [58]. A laboratory-based study was conducted at King Faisal Specialist Hospital and Research Center (KFSH & RC) in Riyadh on 950 children with an age range from 3 weeks to 14 years and 35.9% of them were <1 year old. The study showed that influenza A and B viruses were detected in 61 (23.8%) children [59]. Adenoviruses and influenza were determined to be the 2nd most common cause of LRTI in young children, meanwhile, HRSV and HPIV were the 1st leading pathogens that cause LRTIs in children [60]. Al-Hajjar et al. [59], also defined HRSV as the most prevalent pathogen in 73 (28.5%) of their sample, adenovirus followed by HRSV affecting 70 children with a rate of (27.3%), and finally, enteroviruses and HPIV came at the bottom of the list by infecting 39 (15.2%) and 13 (2.3%) children, respectively. Furthermore, the study indicated that HRSV, influenza viruses, Adenovirus, and HPIV-3 all were associated with pneumonia as a clinical symptom, and both HRSV and influenza viruses infections were accompanied by bronchiolitis and tracheobronchitis, respectively [59].

Human metapneumovirus (hMPV) was found to be the cause of nearly 5%-10% of hospitalized children due to severe pneumonia and bronchiolitis worldwide [29]. A study included 512 patients with a median age of 1 year old to detect their infection with respiratory viruses and found that 424 (83%) of them were already infected; hMPV affected 63 (13.3%) of the patients, whereas, enterovirus and rhinovirus ranked 219 (42.8%) of the total samples [60]. Four types of HPIV were recorded in 72 infected cases with a percentage of (14%), HRSV came with 52 (10.2%), human Bacovirus (HBoV) affected 64 (12.5%), influenza A and B viruses were recorded in 23 (4.5%), and adenovirus was accountable for 86 (16.8%) of the cases [60]. A systematic review was conducted to probe the epidemiology of hMPV infection among children. The incidence rate of the infection in Saudi Arabia was found to be 10.9% within 174 children as a total population [61].

Management and outcomes

In developing countries, ALRTI is known as the main cause of morbidity and mortality (25%-50%) [62]. A huge study in a pediatric hospital in Riyadh followed up the admission of 5917 patients younger than 48 months with

ALRTIs, the researchers found that pneumonia was responsible for (73.3%) of the cases, bronchiolitis for (26.7%) and ALRTI accounted for 13.7% of the total hospital admission [62]. This study implied the critical situation Saudi Arabia faces in front of ALRTIs among children. The hospital indicated that their management guidelines of ALRTI have two major aims; the first is to enhance the target the newborns who seek primary health care as they are at the highest risk of mortality, and the latter is to reduce the financial cost of management by leading the examinations and treatment [63].

CONCLUSION

Most of the foregoing studies considering ARTIs in the KSA had a great focus on Hajj seasons and the pilgrims as the main point of transmission of the respiratory viruses. Paradoxically, a little is known about the pattern of respiratory viruses' infection, complications, and management among children. Our review established that HRSV, rhinovirus, HPIV, and influenza viruses are extensively common among children, especially those younger than 1 year old. Meanwhile, MERS-CoV had the least prevalence among young children. The study also called the attention to acknowledge and educate the parents who have newborns about ARTIs, and to run more clinical researches to determine the application of proper management-guidelines as a prerequisite to come up against the high morbidity of ARTIs and to ensure that the young children have conventional health care.

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