Acute respiratory tract infections among hospitalized Palestinian patients: a retrospective study

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Research article

Keywords: Acute respiratory tract infections, West Bank, Bordetella pertussis, enterovirus, influenza A virus, influenza B virus, respiratory syncytial virus, adenovirus, Streptococcus pneumoniae

Posted Date: May 24th, 2019

DOI: https://doi.org/10.21203/rs.2.9815/v1

Abstract

Background: Respiratory tract infections (RTIs) are a major public health concern. This study aims to investigate the profiles and epidemiological characteristics of acute RTIs and respiratory pathogens in Palestinian hospitalized patients. Methods: Clinical samples from hospitalized patients with symptoms of acute RTIs admitted between January 2011 and December 2016 are referred to Palestinian Central Public Health Laboratory (PHCL) to identify the causative pathogen. Patients' demographic information and the results of the molecular identification were retrieved from the electronic database at the PHCL. The results of the detections were analyzed to explore the distribution of pathogens resulting in hospitalization among patients with RTIs across age, gender, region, year and season. Results: A total of 15413 patients with acute RTIs were hospitalized during the study period. The causal agent was identified only in 28.7% of the patients. Overall, influenza viruses were the most common cause of RTIs among hospitalized Palestinian patients in the West Bank. The elderly population (≥60 years old) had the highest rates. Respiratory syncytial virus (RSV) and Bordetella pertussis (B. pertussis) followed influenza, respectively. Children showed the highest hospitalization rates for these two infections along with adenovirus, enterovirus and Streptococcus pneumoniae. Outbreaks of RTIs occurred mainly during winter (between December and March). Conclusions: Influenza viruses are the major cause acute RTIs among hospitalized patients in the West Bank. Children and elderlies have the highest risk for RTIs. The reoccurrence of B. pertussis in spite of vaccination is alarming and requires further investigation.

Background

Respiratory tract infections (RTIs) are considered to be the most common infectious diseases worldwide and the second leading cause of death among children under five years old [1, 2]. In Palestine, infectious diseases contribute to less than 10% of all deaths; respiratory diseases (ICD10 code: J00 - J99.9) contribute to 70% of those deaths with a mortality rate of 17.0 per 100,000 population during 2016, being the sixth most common cause of death [3].

The etiological agents of respiratory diseases include a wide range of respiratory viruses and bacteria. They appear with a spectrum of symptoms that include fever, cough, malaise and chest pain. Rapid interventions are necessary as these infections could result in either mild illness, or could lead to severe complications, hospitalization and death [4, 5]. Identification of the causative agent of respiratory diseases based on signs and symptoms alone is not reliable. Therefore, understanding the epidemiology of RTIs and identification of the patterns and etiologies are critical for successful treatment and prevention programs [6] . The purpose of the current study was to investigate the profiles and epidemiological characteristics of acute RTIs and respiratory pathogens in hospitalized patients in the West Bank, Palestine.

Methods

A retrospective study was conducted during the period from January 2011 to December 2016. Demographic data and test results were retrieved from the health information system at the Palestinian Central Public Health Laboratory (PHCL). Samples including nasopharyngeal aspirates, nasopharyngeal swabs, oropharyngeal swab, sputum, blood, and bronchoalevlar lavage fluid are routinely collected by qualified medical personnel from hospitalized patients with symptoms of acute RTIs and delivered to the PHCL for testing. Samples were tested by polymerase chain reaction (PCR) to confirm clinical diagnosis. Laboratory testing is available for microorganisms including *Bordetella pertussis (B. pertussis)*, enterovirus, influenza A virus, influenza B virus, respiratory syncytial virus (RSV), adenovirus, and *Streptococcus pneumoniae (S. pneumoniae)*.

Data were analyzed using IBM SPSS statistics version 20.0. Descriptive statistics were done in the form of means, frequencies, percentages and ranges of the variables. Population data for the calculation of rates were obtained from the Palestinian Central Bureau of Statistics (PCBS) 2011-2016. Rates were calculated using Microsoft Office Excel 2010.

Results

A total of 15413 Palestinians patients were hospitalized between 2011 and 2016 with acute RTIs. The mean incidence rate of hospitalization for acute RTIs in the West Bank during this period was 91.4 per 10^5 population with a range between 34 and 149. Table 1 shows the demographic characteristics of the cases. Acute RTIs were equaly common among males and females but the highest incidence rates were seen among children less than 10 years old and elderlies (55 years of age or more). The mean age of cases was 32.8 years. During the six years of the study, hospitalization for acute RTIs increased, but a drop was recorded during 2014. Overall, hospitalization rates were highest in the northern governorates of the West Bank.

During the study period, the causal agent was only identified in 28.7% of the referred cases. The highest detection rate was for RSV followed by influenza A viruses (Table 2). When we compared the hospitalization rate of each organism between males and females, we didn't detect significant differences (Table 2).

Influenza A was the major cause of acute RTIs among hospitalized patients (Table 2). Between 2011 and 2013, hospitalization rate increased from 4.3 to 30.0 per 10^5 population, and between 2015 to 2016 from 26.0 to 39.3 per 10^5 population. A sharp drop between the two periods (during 2014) was noticed (Table 3). Hospitalization rates of influenza A virus increased with age, especially after the age of 60 years (Fig. 1c). The highest number of cases was recorded during cold months; December and January (Table 4). There were no cases of avian flu (H5N1) recorded during the period between 2011 and 2016, but swine flu (H1N1) was relatively common with a total of 1373 confirmed cases. Hospitalization rates of swine flu were highest during 2016 (IR=13.7 per 10^5) and 2013 (IR=13.4 per 10^5) (Tables 2 and 3). The highest rates were seen in northern governorates (Table 5). As for influenza B, hospitalization rates were relatively low, being highest during 2011 (Table 3).

The second major cause of hospitalization for RTIs was RSV (Table 2). The highest hospitalization rates were among children <5 years old (Fig. 1e). The rates were highest during 2016 and 2014, respectively (Table 3). Further, the central governorates recorded three-fold higher rates as compared to northern and southern ones (Table 5). Like influenza A, most cases occurred during December and January (Table 4).

Regarding pertussis cases, they were mainly children and the highest rates were seen among those between 5-9 years old (Fig. 1a). During 2012, hospitalization rate was almost five times higher compared than the other years. Since 2013, a gradual increase in hospitalization rates was observed (Table 3). About half the number of cases occurred during spring (March-June) (Table 4) and the central region showed the highest rate while the lowest rates were observed in the south (Table 5).

Discussion

During the last few decades, a shifting in the burden of diseases from communicable to non-communicable diseases has been noticed in many developing countries. Nevertheless, infectious diseases continued being a major cause of morbidity and mortality among Palestinians, especially children under 5 years old [3]. In developing countries, *B. pertussis*, enteroviruses, influenza viruses, RSV, adenoviruses, and *S. pneumoniae* are considered to be the main causes of RTIs resulting in 4-5 million annual deaths among children only [7]. This study investigated the most common causes of acute RTIs among hospitalized patients in the West Bank. The data obtained through this study are population-based and therefore useful for predicting pathogen patterns and disease burden, in addition to planning for vaccine research and control strategies.

During the study period, 15413 cases of severe acute RTI cases were hospitalized at the Palestinian hospitals in the West Bank. Hospitalization rates were high during the study period and increased from 2011 to 2016. The majority of RTI cases were caused by influenza, followed by RSV. Similar patterns were reported worldwide [5]. Data from the surrounding countries are limited and were incomparable to our study. For instance, a study conducted in Amman, the capital of Jordan, reported RSV to be the most common viral cause of respiratory tract infections among children [8]. On the other hand, in Beirut, Lebanon, human rhinovirus, RSV, human bocavirus, human metapneumovirus and human adenovirus were respectively reported as the most common causes of RTIs among hospitalized children [9], while in the Egyptian Delta, influenza was the major viral cause of RTIs while RSV was reported as the major cause among children [10].

Our findings show that the largest proportion of hospitalized patients was children less than ten years old, but the highest hospitalization rates were among the older population. This is simply explained by the fact that the Palestinian population is a young population with one quarter the population being less than ten years old [11].

Although the highest number of cases was associated with influenza A; most cases of RSV, adenoviruses, *B. pertussis* and enteroviruses occurred in children less than ten years old. These organisms were previously reported to be most common among children [12, 13, 14, 15]. Further, RSV had the highest incidence among children less than 5 years old. Similar findings were reported in neighboring areas [8, 10, 16, 17, 18]. RSV is the leading cause of RTIs among children worldwide [5]. Susceptibility to RSV infection decreases with age as a result of maturation of the immune system [19].

B. pertussis is a vaccine preventable disease that used to be considered as a universal infection among children less than 5 years old. The infection was reported to kill one in ten infected children in the United States during the 1920s. Whole-cell pertussis vaccine was available since 1940s, and during the nineties it was replaced by acellular vaccines. Studies have shown that immunity against pertussis is not life-long [20]. In Palestine, vaccination against *B. pertussis* is a part of the Expanded Program on Immunization and is given in combination with vaccines against tetanus, diphtheria and Hib at the ages of 2, 4 and 6 months, in addition to a booster dose at 18 months. Our study shows that *B. pertussis* is still considered a major cause of morbidity in the West Bank. Outbreaks of the disease have been reported worldwide regardless of the high vaccine coverage [20, 21]. Studies showed that the waning immunity results in a peak in the incidence of pertussis among school-age children, and the infection spreads from these subjects to infants or not-fully vaccinated young children [21]. In addition, changes in the circulating strains of the bacterium should be considered [20, 21]. Our findings showed similar patterns. The severity of infection among infants is the highest [20]. In this study we only included hospitalized patients, reflecting severe cases of the disease, and excluding mild, non-hospitalized cases who are probably older (adolescents and young adults).

In contrast to RSV and pertussis, influenza cases occurred mostly in elderly population, a pattern of influenza that has been previously demonstrated [22, 23]. Similar findings were reported in the Egyptian Delta, where influenza was the major cause of acute RTIs and was most common among individuals 65 years old or more [10]. Furthermore, in our study, a distinctive pattern of influenza A virus was seen through the study years; a drop in the rate of hospitalized cases of influenza A during 2014 followed by a gradual increase in 2015 and 2016. This could be related to the varying severity of the circulating strains from one year to another [1]. In addition, our findings showed a relatively high number of H1N1 cases. The Eastern Mediterranean Region (EMR) was affected by the worldwide increase of pandemic spread of H1N1 [24]. On the other hand, no cases of avian flu (H5N1) were found in our study. In fact, since the start of the H5N1 epidemic in the region, no human cases of H5N1 have been recorded in Palestine [24].

S. pneumoniae is a major cause of morbidity and mortality. The introduction of pneumococcal conjugate vaccines (PCVs) has reduced invasive disease, yet the burden remains high, mainly due to the emergence of other serotypes not included in the vaccines [25]. Invasive pneumococcal diseases caused by *S. pneumoniae* can be difficult to confirm microbiologically. Our study showed that during the period between 2011-2016, only a very small number of samples (n=18) were tested for *S. pneumonia*. The use of antibiotics without a prescription is a common practice in our community; as a result, physicians can rarely obtain viable samples for testing, which could explain the low number of referred samples. In addition, our study showed that only 17% of these samples tested positive. Although PCR contributed significantly to the diagnosis of infections as it is faster and more sensitive in comparison to standard culture (which is slow and yields false negative as a result of antibiotic treatment prior to sampling), among hospitalized patients, the long time between onset of symptoms and disease progression contribute to poor sensitivity of detection of *S. pneumoniae* in nasopharyngeal swabs by PCR among hospitalized patients [26, 27, 28, 29, 30].

The highest incidence of RTIs was recorded during the cold season (December-March) throughout the study years. Several studies reported annual epidemics of respiratory diseases during the winter season in temperate climates such as Palestine [31, 32, 33, 34, 35]. Outbreaks of influenza during the raining season were reported worldwide [1, 36]. Explanation of the seasonality of infections has been hard. One of the hypothesized explanations states that these seasonal

outbreaks are a result of overcrowding indoors with the lack of proper ventilation during cold seasons. In addition, low temperature and dry conditions were found to be favorable conditions for pathogen transmission in animal studies, which is consistent with indoor state [37, 38]. The hospitalization rates from other organisms were very low during the study period. Therefore we were unable to review patterns and trends accurately.

In summary, RTIs are still a public health concern, especially among children and elderly populations. Influenza viruses are the major cause of respiratory diseases among Palestinians. RSV is the most common cause of pediatric RTIs while influenza is the major cause among the elderly population. In addition, *B. pertussis* is still a common cause of RTIs among children regardless of the vaccination policies.

This study is the first to describe RTIs in Palestine and is one of the largest studies in the neighboring countries. The study included all MOH hospitals in the West Bank, which is the main healthcare provider in Palestine. In addition, the study covered a period of six years; which was suitable to capture changes in the trends of the disease. Regardless, one of the limitations of this study was including only hospitalized patients in MOH hospitals without considering outpatients and patients in other hospitals, inclusion of these cases could have provided more comprehensive and representative view on the patterns of RTIs. Furthermore, some common respiratory tract infections were not examined here as they are not part of the diagnostic tests such as human rhinovirus, human bocavirus and human coronavirus. Moreover, clinical characteristics of the cases and disease outcomes were not considered in our study. Coinfection with two or more pathogens is another missing entity in this study.

Conclusions

We compared the spectrum, seasonality, and age distribution of common causes of RTIs among Palestinians in the West Bank. Our data showed that viral agents caused the majority of respiratory diseases. Further surveillance and follow up on the epidemiology of these diseases is recommended. In most cases of RTIs, the causal agent was undetermined; accurate and rapid diagnosis of the etiological agents are important to select the most effective treatment and avoid complications of the disease that could result in prolonged hospitalization and even death. Furthermore, interventions and policies that promote judicious antibiotic use should be implemented. Lastly, epidemiologic investigation for pertussis should be launched to identify factors and interventions to control these outbreaks of cases and vaccination campaigns against seasonal flu should target elderly population.

Abbreviations

B. pertussis:Bordetella pertussis

EMR: Eastern Mediterranean Region

IR: Incidence rate

MOH: Ministry of Health

PCR:Polymerase chain reaction

PHCL: Palestinian Central Public Health Laboratory

PCBS: Palestinian Central Bureau of Statistics

S. pneumoniae: Streptococcus pneumoniae

RSV:Respiratory syncytial virus

RTI:Respiratory tract infection

Declarations

Ethics approval and consent to participate

This study was undertaken using data from the Palestinian Central Public Health Laboratory (PHCL) with the approval of the Ministry of Health (MOH). The data were previously anonymized and no private information was collected as part of this study. Therefore, no approval from an ethics committee or informed consent from patients was required for this study.

Consent for publication

Not applicable.

Availability of data and material

The data that support the findings of this study are available from The Palestinian Ministry of Health but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of The Palestinian Ministry of Health.

Competing interests

The authors declare that they have no competing interests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

RAS and ON conceived and designed the study. WN, RN, DN, MA, and BA: implementation, contribution to design, analysis and interpretation of data. RAS and ON contributed essential resources. NS and RAS analyzed the data and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

Acknowledgements

None.

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Tables

Table 1: Frequency and incidence rates of hospitalized patients with RTIs in the West Bank (2011-2016).

Variable	Category	Frequency N=15413	Incidence Ratea
		N (%)	(per 105)
Gender	Male	7974 (52)	567.1
	Female	7349 (48)	539.7
Age (years)	0-4	2557 (18.3)	674.3
	5-9	1870 (13.3)	549.4
	10-14	469 (3.3)	144.7
	15-19	475 (3.4)	150.9
	20-24	650 (4.6)	228.1
	25-29	910 (6.5)	395.5
	30-34	1042 (7.4)	567.0
	35-39	775 (5.5)	482.7
	40-44	749 (5.3)	539.6
	45-49	729 (5.2)	437.7
	50-54	775 (5.5)	830.7
	55-59	672 (4.8)	1012.3
	60-64	612 (4.4)	1357.0
	>=65	1725 (12.3)	1920.4
Regionb	North	6535 (42.4)	601.4
	Center	3713 (24.1)	467.1
	South	5165 (33.5)	582.7
Year	2011	880 (5.7)	34.1
	2012	2150 (13.9)	80.1
	2013	3110 (20.2)	112.9
	2014	1402 (9.1)	50.2
	2015	3511 (22.8)	122.7
	2016	4360 (28.3)	148.5

a IR: Incidence rate (hospitalized patients per 105 population). Population was calculated as the average overall population in the West Bank between 2011-2016 according to PCBS data.

b Region: North: Nablus, Tubas, Jenin, Tulkarem, Salfit and Qalqiliya Governorates. Center: Ramallah and Al-Bireh, Jerusalem and Jericho and Al-Aghwar Governorates. South: Hebron and Bethlehem Governorates.

Table 2: Frequency and incidence rates of respiratory tract infection-related hospitalization stratified by gender.

Organism	Suspected (n=15413)	Confirmed (n=4422)		Male		Female	
	N (%)	N	IR **a**	N	IR **a**	N	IR **a**
B. pertussis	1403 (9.1)	324	11.7	160	11.4	153	11.2
Influenza A	11593 (75.2)	3555	128.4	1695	120.5	1848	135.7
Influenza A (H1N1)	5379 (34.9)	1373	49.6	667	47.4	702	51.6
Influenza A (H1)	32 (0.2)	8	0.3	1	0.1	7	0.5
Influenza A (H3)	578 (3.8)	238	8.6	103	7.3	135	9.9
Influenza B	699 (4.5)	61	2.2	29	2.1	32	2.3
RSV	1271 (8.2)	449	16.2	233	16.6	213	15.6
Enterovirus	139 (0.9)	9	0.3	4	0.3	5	0.4
Adenovirus	290 (1.9)	21	0.8	10	0.7	11	0.8
S. pneumoniae	18 (0.1)	3	0.1	3	0.2	0	0

a IR: Incidence rate (hospitalized patients per 105 population). Population was calculated as the average population in the West Bank between 2011-2016 according to PCBS data.

Table 3: Table 4: Frequency and incidence rates of respiratory tract infection-related hospitalization stratified by year.

Organism	Year (IR **a** per 105)					
	2011	2012	2013	2014	2015	2016
B. pertussis	1.4	5.9	0.6	0.8	1.5	1.7
Influenza A	4.3	23.3	30.0	3.5	26.0	39.3
Influenza B	1.1	0.1	0.4	0.4	0.2	0.1
RSV	0.2	1.7	2.2	3.8	3.0	4.9
Enterovirus	0.0	0.0	0.0	0.0	0.1	0.1
Adenovirus	0.0	0.0	0.0	0.1	0.2	0.4
S. pneumoniae	0.0	0.0	0.0	0.0	0.0	0.1

a IR: Incidence rate (hospitalized patients per 105 population). Population was calculated as the average annual population in the West Bank between 2011-2016 according to PCBS data.

Table 4: Frequency and incidence rates of respiratory tract infection-related hospitalization stratified by the month of occurrences.

Organism	Month (N)											
	Jan	Feb	March	Apr	May	June	July	Aug	Sep	Oct	Nov	Dec
B. pertussis	20	19	35	39	39	41	29	20	14	25	24	19
Influenza A	1203	581	482	187	71	12	5	5	12	19	112	866
Influenza B	18	7	14	9	8	2	0	0	0	0	1	2
RSV	142	63	71	50	10	4	3	3	3	1	15	84
Enterovirus	0	0	0	0	0	0	3	1	2	1	1	1
Adenovirus	2	4	5	2	1	1	0	0	1	1	1	3
S. pneumoniae	0	0	0	0	0	0	0	0	0	0	2	1
All RTIs	3974	2464	2444	1349	727	239	167	189	228	333	773	2526

Table 5: Frequency and incidence rates of respiratory tract infection-related hospitalization stratified by region.

Organism	North a		Center a		South a	
	N	IRb	N	IRb	N	IRb
B. pertussis	136	12.5	120	15.1	68	7.7
Influenza A	1695	156.0	592	74.5	1268	143.1
Influenza A (H1N1)	624	57.4	228	28.7	521	58.8
Influenza A (H1)	1	0.1	0	0.0	7	0.8
Influenza A (H3)	149	13.7	43	5.4	46	5.2
Influenza B	22	2.0	14	1.8	25	2.8
RSV	113	10.4	264	33.2	72	8.1
Enterovirus	6	0.6	2	0.3	1	0.1
Adenovirus	0	0.0	3	0.4	18	2.0
S. pneumonia	0	0.0	2	0.3	1	0.1

a Region: North: Nablus, Tubas, Jenin, Tulkarem, Salfit and Qalqiliya Governorates. Center: Ramallah and Al-Bireh, Jerusalem and Jericho and Al-Aghwar Governorates. South: Hebron and Bethlehem Governorates.

b IR: Incidence rate (hospitalized patients per 105 population). Population was calculated as the average overall population in the regions of the West Bank between 2011-2016 according to PCBS data.

Figures

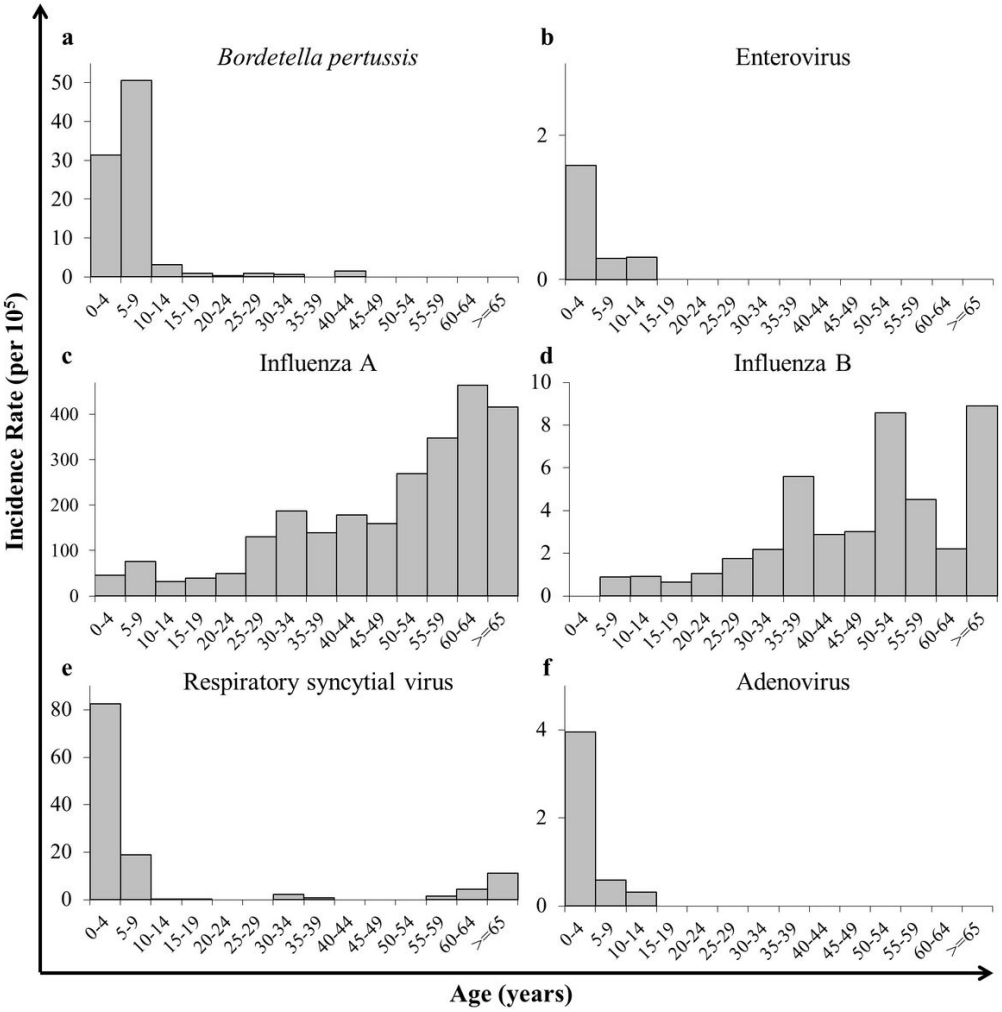

Figure 1

Incidence rates of major causes of respiratory tract infection-related hospitalization (2011-2016) stratified by age, West Bank. (a) B. pertussis; (b) Enterovirus; (c) Influenza A; (d) Influenza B; (e) RSV; and (f) Adenovirus.