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RESEARCH ARTICLE

DETECTION OF INFLUENZA VIRUSES AMONG HOSPITALIZED CASES SUFFERING FROM SEVERE ACUTE RESPIRATORY ILLNESS (SARI) IN SANA'A CITY, YEMEN

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ABSTRACT

Objective: Influenza is a major cause of morbidity and mortality around the world. So national influenza surveillance have been important for understanding the epidemiology of influenza over time. The aims of this study were to determine the prevalence rate of influenza viruses among hospitalized patients with severe acute respiratory illness (SARI), identify circulating types and subtypes of influenza viruses among them, and determine the risk factors associated with SARI.

Methods: A total of 320 hospitalized patients suffering from SARI at Al Joumhouri University hospital in Sana'a city were enrolled; and their age was ranged from < 1 year to ≥ 56 years. Both nasopharyngeal and oro-pharyngeal swabs were collected from each patient and tested by using rRT-PCR technique for the detection of influenza A, influenza B and subtypes of influenza A viruses (A/H1N1 (2009) and A/H3N2).

Results: The crude prevalent rate of influenza viruses among SARI patients was 10.9%; the female rate was 12.4%, and the male rate was 9.9%.. The rate of Flu A in the total SARI cases was 5.9% and for Flu B was 5%. In addition 3.8% of SARI patients were suffering from influenza A/H3N2, 2.2% from influenza A/H1N1(2009) infections; and the mortality rate for influenza infections was 17.1%. Also, a high mortality rate was occurred in influenza infections in age groups 36-45 years and 6-15 years. Also, there was a significant association between flu infection; and 46-55 years group (OR=2.8), Winter time (OR=17.5), cardiac diseases (OR=9.1), and diabetic mellitus (OR=3.7).

Conclusion: In conclusion: both influenza A and B were represented as a causative agents of SARI, and *Influenza* A/H3N2 was present subtype followed by A/H1N1(2009). The frequency of influenza viruses ascertain among SARI patients in Yemen highlights the need for health authorities to develop strategies to reduce morbidity among at-risk population in the course of vaccine recommendation.

Keywords: Influenza Viruses, Sana'a City, Severe Acute Respiratory Illness (SARI), Yemen.

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INTRODUCTION

Severe acute respiratory infections (SARI) are among the leading cause of hospitalization and deaths worldwide[1]. It is estimated that about 4.2 million of deaths worldwide are attributed to SARI annually[2]. SARI may be caused by various pathogens, while bacterial infections play a critical role in causing life-threatening pneumonia[1,3,4], viral infections are associated with significant proportion that range from mild to severe infections[5,6]. Following the A/H1N1/2009 influenza pandemic that was associated with a high morbidity and an increased risk of mortality among particular groups[7], a number of countries have strengthened observation for the surveillance of severe diseases and deaths in order to rapidly detect new viruses and to provide information in assessing the impact on the population and having operational preparedness plans. So far, only few Arabic countries including Yemen are collecting data on hospitalization associated to acute respiratory illness[8,9]. Influenza virus infection is a major cause of SARI and results in significant global morbidity and mortality every

year[10,11,12]. However, the majority of available information on influenza disease problem originates from developed countries. In recent years, influenza sentinel surveillance has been established in several Arabic countries including Yemen[9] and influenza virus infection has been reported to be associated with mild and severe illness including death on the Arabic countries[9].

Table 1: Distribution of SARI cases by sex and age groups.

Age (Yr)	Male (n=191)		Female(n=129)		Total (n=320)	
	No	%	No	%	No	%
< 1	68	35.6	48	37.2	116	36.3
1 - 5	27	14.1	12	9.3	39	12.2
6-15	7	3.7	11	8.5	18	5.6
16-25	18	9.4	8	6.2	26	8.1
26-35	9	4.7	8	6.2	17	5.3
36-45	7	3.7	6	4.7	13	4.1
46-55	17	8.9	13	10.1	30	9.4
≥ 56	38	19.9	23	17.8	61	19.1
	21.2 ± 25years		27.5 ± 29 years		23.7 ± 27 years	

Nonetheless, estimates of the burden of influenza associated hospitalization are severely limited in Arabic countries. In Yemen, data are still scarce regarding the epidemiology of SARI and influenza. During the last influenza pandemic in 2009, an excess of mortality was observed among inhabitant of the capital city of Sana'a city[8].

Table 2: The prevalent rate of influenza types and A subtypes among 320 SARI cases

Influenza types	No	%
Flu A	19	5.9
Flu B	16	5
Subtype A		
Flu A/H3N2	12	3.8
Flu A/H1N1(2009)	7	2.2

The aims of this study were to determine the prevalence rate of influenza viruses among hospitalized patients with severe acute respiratory illness (SARI), identify circulating types and subtypes of influenza viruses among them, and to determine the risk factors associated with influenza infections.

SUBJECTS AND METHODS

This study was conducted on 320 hospitalized patients suffering from SARI patients at Al Joumhouri University hospital (the reference hospital for SARI program for the whole country) in Sana'a city during the period from November 2014 to September 2016. The clinical samples analyses were done at National Center of Public Health laboratories Sana'a (NCPHL). All patients admitted to the hospital with respiratory disease were identified. The SARI cases were defined as a patients suffering from; Sudden onset of fever >38°C, cough or sore throat, and abnormal breathing sounds, tachypnea, sputum production, Hemoptysis, chest pain and shortness of breath (dyspnea)[9].

Patient data were collected using questionnaire including personal data, clinical symptoms, signs, and history of preexisting chronic diseases. Both respiratory specimens nasopharyngeal (NP) and oro-pharyngeal (OP) swabs were collected from each hospitalized SARI patients and placed into a single viral transport media (VTM). Then the samples were transported to the NCPHL rapidly using ice box for processing.

Table 3: The prevalent rate of influenza viruses among different age and sex groups in SARI cases.

Characters	Influenza viruses positive		*OR*	*CI*	*P*
	No.	%			
Sex					
Male n=191	19	9.9	0.8	0.4-1.7	0.48
Female n=129	16	12.4	1.3	0.6-2.7	0.48
Age groups					
< 1 n=116	7	6	0.14	0.1-0.3	<0.001
1 -5 n=39	3	7.7	3.3	0.6-14	0.07
6 - 15 n=18	3	16.7	1.7	0.4-6.7	0.42
16 - 25 n=26	1	3.8	0.3	0.01-2.2	0.2
26 - 35 n=17	4	23.5	2.7	0.7-9.7	0.08
36 -45 n=13	2	15.4	1.5	0.0-7.7	0.59
46 –55 n=30	7	23.3	2.8	1.1-7.8	0.02
≥ 56 n=61	8	13.1	1.3	0.5-3.2	0.5
Crude rate	35	10.9			

OR: Odds ratio >1 at risk. *CI*: Confidence interval, *p*: Probability value < 0.05(significant)

The influenza viruses then tested by rRT-PCR technique for the detection of influenza A, influenza B and subtypes of influenza A viruses (A/H1N1(2009) and A/H3N2).

RESULTS

A total of 320 SARI hospitalized patients (191 males and 129 females) their mean ±SD age=23.7±27 years were enrolled in this study. The most frequent age groups were infants (36.3%), age group≥56 years (19.1%) and children 1-5 years (12.2%); while other age groups were less frequent. The prevalence rate of influenza virus among SARI was 10.9%; influenza B (5.0%) and influenza A (5.9%), 12 (3.8%) were flu A/H3N2 and 7 (2.2%) were belonged to Flu A/H1N1 (2009). A slightly higher prevalence rate of Flu virus was in female (12.4%), than in male (9.9%). Table 3 shows the prevalence rate of influenza viruses A and B according to the age groups, a high prevalence rate of Flu virus was in age groups 26-35 years and 46-55 years (23.3%), followed by age group 36-45 years (15.4%) and 6-15 years (16.7%). When the association between chronic diseases and risk of contracting Flu virus were studied, there was high significant association with cardiac diseases (OR=9.1, CI=3.25-25.4, p<0.001), diabetics mellitus (OR=3.7, CI=1.2-11.3, p=0.007). Also, high rates of flu occurred in renal diseases and asthma patients, but these results were not statistical significant. When the association between seasons and risk of contracting Flu virus were studied, there was a high significant association with Winter time in which OR=9.1, CI=3.25-25.4, and p<0.001 (Table 4). Table 5 illustrates the output of SARI cases confirmed with influenza in comparison with SARI

cases caused by other agents. The proportions of cure, ICU admission, isolation and death among SARI cases positive for influenza were higher than SARI cases negative for influenza infections. The mortality rate among SARI cases confirmed for influenza was 17.1%, higher than that among other SARI cases (6.7 %).

Table 4: The association of influenza with chronic medical conditions among SARI cases in Sana'a city.

Chronic medical conditions	Influenza viruses positive		*OR*	*CI*	*P*
	No	%			
Cardiac disease n=22	10	45.5	9.1	3.25- 25.4	<0.001
Asthma n=20	3	15	1.4	0.3-5.8	0.54
Renal disease n=7	2	28.6	3.4	0.44- 20.9	0.13
Diabetics mellitus n=21	6	28.6	3.7	1.2-11.3	0.007
Seasons					
Winter n=140	32	22.9	17.5	5.2-58	<0.001
Spring n=136	2	1.5	0.06	0.01-0.29	<0.001
Summer n= 24	0	0	0.0	undefined	0.07
Autumn n=20	1	5	0.41	0.05-3.1	0.37

OR: Odds ratio >1 at risk. *CI*: Confidence interval, *p*: Probability value < 0.05(significant)

DISCUSSION

This study confirms that influenza was prevalent throughout Sana'a city and considers as one of the causes of SARI cases. The current study findings strengthen the data focused on the epidemic of influenza as a global contributor to respiratory disease burden and it is important to include Yemen in global influenza prevention activities. The crude rate of influenza among SARI cases in the current study was 10.9% (Table 2), nearly in agreement with report from Kenya by Caselton *et al.*,[13] who found that 11.5% of SARI cases were positive for influenza. Influenza A commonly spreads among humans and animals, and has a wide range of symptom, starting from mild or asymptomatic respiratory illness to severe pneumonia or even death. While influenza B produces lower community-wide infection than Influenza A[9]. In the current study prevalent rate of influenza types among SARI patients was roughly equal (influenza A =5.9%, and influenza B=5%) (Table 2). It was also shown that the common influenza A subtypes was A/H3N2 (3.8%) followed by Influenza A/H1N1 (2009) (2.2%). These findings were in disagreement with the study conducted by Ramadhany *et al.*,[14] in Indonesia which shown that Influenza A was most prevalent among SARI patients than influenza B, and the most common influenza A subtype was A/H3N2 strain. Also the current findings were in contrast to surveillance study done in Egypt during 2009-2011 by Labib *et al.*,[15] which shown that 6% were pandemic H1N1, 4% Flu-B and 2% were Flu-A/H3N2.

Influenza rate among females SARI patients in current study was 12.4% slightly higher than that on male patients 9.9% (Table 3). This result was similar to finding reported by ICDDR,[16] in Bangladesh in which higher rate occurred on females than on males. Influenza is a serious public health problem affecting all age groups, in the current result a high prevalent rate of flu virus was occurred in age groups 26-35 years old (23.5%) and 46-55 years old (23.3%), while prevalent rate among children less than 1 year and 1- 5 years were low (6% and 7.7% respectively) (Table 3).

Table 5: The output of SARI cases confirmed with influenza in comparison with SARI cases caused by other agents

Outcome	SARI confirmed with influenza (n=35)		Other SARI cases (n=285)		Total (n=320)	
	No	%	No	%	No	%
Cure	29	82.9	266	93.3	295	92.2
ICU	5	14.2	4	1.4	6	1.9
Isolation	1	2.9	0	0	1	0.31
Death	6	17.1	19	6.7	25	7.8
Total n=320	35	10.9	285	89.1	320	100

These results were dissimilar with that reported by Thompson *et al.*,[17] in the United State which demonstrated that, significant numbers of influenza associated hospitalizations occurred among person aged 50 years through 64 years and children younger than 5 years. In this study the total 35 hospitalized influenza cases had associated underlying medical conditions (Table 4). The most common associated risk factors were cardiac disease (45.5%), followed by diabetic's mellitus (28.6%), chronic renal disease (28.6%), and then respiratory disease including asthma (15%). These associated risk factors of influenza infection were similar to that reported by WHO[18] from USA in which among adults hospitalized with laboratory-confirmed influenza, the most commonly identified associated risk factors were cardiovascular disease, asthma or chronic lung disease, and metabolic disorders. Mortality reflects the severity of influenza infections because many severe illnesses do not result in death. When the outcome of flu in the current study was considered comparing with SARI; the mortality rate among SARI patients confirmed with influenza was 17.1% higher than that among non-flu SARI patients (6.7%) (Table 5). In contrast to study done by Thompson *et al.*,[17] in USA in which they found lower influenza-associated mortality rate. The high mortality rate in Yemen might be attributed to, malnutrition, low immunity, low rate or absent of vaccination against influenza in Yemen. Also this high mortality rate might be due to high rate of underlying medical conditions among Yemeni patients, in which the flu can worsen chronic health problems e.g. people with chronic bronchitis or asthma may experience shortness of breath while they have the flu, and influenza may cause worsening of coronary heart disease or congestive heart failure which might lead to death[19]. Preventing of influenza illness and complications are a public health concerns. However rates of vaccination against seasonal influenza viruses vary worldwide, which probably reflect the availability of vaccines in developed countries when compared to in developing countries, for example in the United States, the estimated number of persons reporting receipt of one or

more seasonal influenza vaccinations was 95% people during August 2011 through May 2012[20], but in current study the rate of vaccination among 320 SARI patients was extremely low (0.6%) and that was different from the recommendation by Rothberg *et al.*,[21] in which annual vaccination is the foundation stone of prevention of flu, particularly for risk groups.

CONCLUSION

The present study has provided useful information about circulation of Influenza viruses among SARI patients in Sana'a city with equal rate of Influenza A and influenza B; and occurrence of Influenza A/ H3N2, influenza A/H1N1 2009. A higher mortality rate was occurred among SARI cases positive of influenza than that occurred among other SARI patients. The risk factor of SARI cases associated with influenza were cardiac disease, diabetics mellitus, and Winter time.

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CONFLICT OF INTEREST

No conflict of interest associated with this work.

AUTHOR'S CONTRIBUTION

This research work is part of M.Sc. thesis. The candidate is the first author (DAA) who conducted the works and the experiments and wrote up the thesis. The corresponding author (HAA) supervised the clinical and laboratory work, revised and edited the thesis draft and the manuscript. AHA and BMJ were co-advisors of the work and helped in revised and edited the thesis draft and the manuscript and in the laboratory works**.**

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