Adult Cases of H1N1 Influenza Admitted from 2015 to 2016

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Background: The clinical characteristics, risk factors and outcomes of H1N1 influenza cases in Bahrain have not been reported.

Objective: To evaluate personal and clinical characteristics, risk factors, and outcomes in adults with confirmed H1N1 infection.

Setting: Salmaniya Medical Complex, Bahrain.

Design: A Retrospective Observational Study.

Method: All H1N1-confirmed-patients admitted between 1 September 2015 and 31 March 2016 were reviewed. Personal and clinical characteristics, risk factors, and outcomes were documented. The analyses were performed using STATA software, version 12 and P-value of <.05 was considered significant.

Result: Twenty-six confirmed H1N1 cases were admitted and reviewed. Eight (30.7%) were admitted to the intensive care unit and 5 (19.2%) died. None of the patients received flu vaccine. The age range was 24 to 83 years.

The presence of comorbid conditions and smoking were common among the study population; however, it was not statistically significant. A significant association was discovered between mortality and the need for vasopressors (all patients requiring vasopressors died compared to only one among other patients, P-value<.005).

Conclusion: In our study of the flu season of 2015-2016, 5 patients died. We recommend vaccination, especially for high risk groups. The study is limited by the small study-population size and one missing file.

H1N1 virus was identified by the Centers for Disease Control and Prevention (CDC) in two cases suffering from febrile respiratory illness in South California on 17 April 2009[1].

In June 2009, the World Health Organization (WHO) declared phase 6 global influenza pandemic causing significant morbidity and mortality[2]. During the flu season, from September 2015 to March 2016, 519 cases were confirmed H1N1 in all age groups with a reported incidence of 39.5 per 100,000.

The aim of this study is to evaluate the personal factors, clinical features and clinical outcomes of confirmed cases of H1N1 in adults admitted between 2015-2016.

METHOD

All confirmed cases of H1N1 from September 2015 to March 2016 were included in the study.

Patients' personal and clinical characteristics were documented. Data included gender, age, nationality, dates of admission and discharge, presenting symptoms, history of flu vaccination, associated comorbid conditions, oxygen saturation upon admission, findings on chest X-ray, and the outcome. The following laboratory investigations were requested: complete blood count and platelets, creatinine, lactate, C-reactive protein, urine and blood cultures and deep tracheal aspirate

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(DTA) culture. Patient course during hospital admission was documented including treatment with oseltamivir (Tamiflu), antibiotics, admission to Intensive Care Unit (ICU), the requirement of ventilation, vasopressors and renal replacement therapy.

Frequencies, percentages and comparisons between groups were made using Fisher's exact test. Because of the small sample size and unbalanced dataset, univariable and multivariable analyses were performed with exact logistic regression. All variables with P-value ≤.10 in the univariable analyses were included in the multivariable analysis to identify independent factors associated with mortality. Odds ratios (OR) and 95% confidence intervals (95% CI) were also estimated.

The analyses were performed using STATA software, version 12 and P-value of <.05 was considered significant.

RESULT

Twenty-six adult patients with laboratory-confirmed Influenza A (H1N1-2009) were reviewed between September 2015 to March 2016.

Patient age ranged from 24 to 83 years, a median of 53.5 years and interquartile range of 42 and 36 years. Eleven (42.3%) patients were in the age group of 40 to 60 years; three patients died from this age group. Nine (34.6%) patients were >60 years and six (23.1%) patients were <40 years. Nineteen (73.1%) patients were males; the male-to-female ratio was 2.7:1.

Twenty-two (84.6%) patients were Bahrainis. All reported mortalities were in the Bahraini group. Eight (30.8%) patients required admission to ICU. Twenty-one (80.8%) patients were discharged; five (19.2%) patients died from the study group during their hospital stay, see table 1.

The most common symptom was cough in 24 (92.3%) patients, followed by fever, 20 (76.9%) and dyspnea, 15 (57.7%), see figure 1. The most common comorbid conditions were cardiovascular disease, 10/25 (40%), and diabetes, 8/25 (32%). Six of twenty-three (26%) patients were smokers, see figure 2. Other less frequent comorbidities were COPD, malignancy, renal disease, obesity and Wegner's granulomatosis, seen once each.
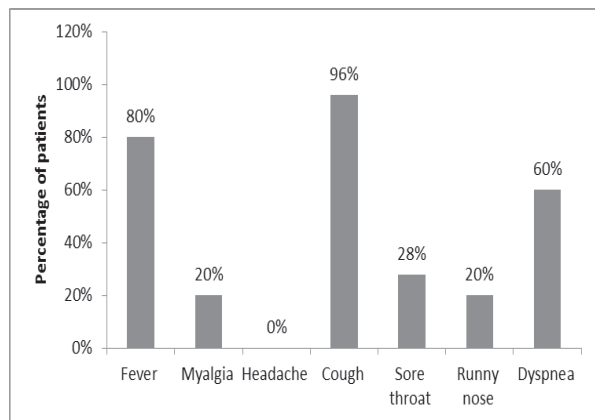

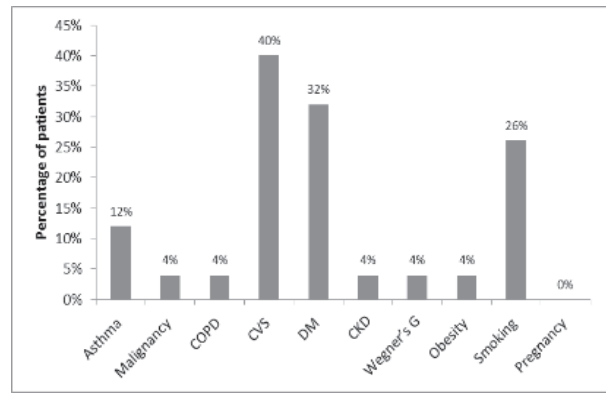**Figure 1: Clinical Presentation of Patients**

Figure 2: Comorbid Conditions

None of the patients received flu vaccine in the year preceding admission, see table 1.

Twenty (76.9%) of 26 patients had abnormal chest X-ray. Oxygen saturation was below 90% in 5/26 (19.2%) patients, and between 90%-94% in 6/26 (23%) patients. Nine (34%) of 26 patients required assisted ventilation. Creatinine level was elevated in 17/26 (65.4%) patients; however, only 3/26 (11.5%) needed renal replacement therapy, see table 1. The most common hematological abnormality was lymphocytopenia 12/26 (46.2%) followed by neutrophilia 7/26 (26.9%), see figure 3.
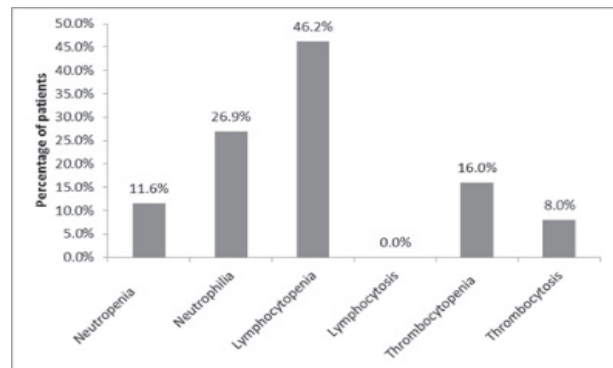

Figure 3: Hematological Abnormalities

None of the patients had septicemia, two (8%) of 26 had urinary tract infection, and four (15%) tested positive for deep tracheal aspirate (DTA) culture, see figure 4.
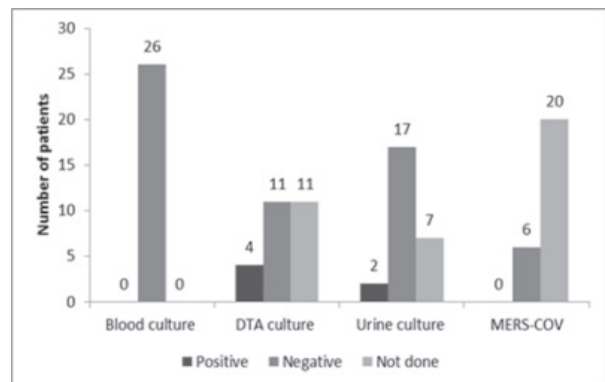

Figure 4: Types and Frequency of Cultures

Table 1: Patients' Characteristics, Investigations, Management and Outcome

| | | All Patients | Outcome | | P-value |
| | | | Discharge | Death | |
		Number & Percentage	Number & Percentage	Number & Percentage	
Age					
	< 40 years	6 (23.1%)	6 (100%)	0 (0)	
	40 -60 years	11 (42.3%)	8 (72.7%)	3 (27.3%)	0.571
	> 60 years	9 (34.6%)	7 (77.8%)	2 (22.2%)	
Gender					
	Males	19 (73.1%)	5 (71.4%)	2 (28.6%)	0.588
	Females	7 (26.9%)	16 (84.2%)	3 (15.8%)	
Nationality					
	Bahraini	22 (84.6%)	17 (77.3%)	5 (22.7%)	0.555
	Non-Bahraini	4 (15.4%)	4 (100%)	0 (0)	
Comorbid conditions					
*Cardio vascular disease **(25)**	Yes	10 (40.0%)	6 (60.0%)	4 (40.0%)	0.064
	No	15 (60.0%)	14 (93.3%)	1 (6.7%)	
Diabetes **(25)**	Yes	8 (32.0%)	5 (62.5%)	3 (37.5%)	0.167
	No	17 (68.0%)	15 (88.2%)	2 (11.8%)	
*Smoking **(23)**	Yes	6 (26.1%)	3 (50.0%)	3 (50.0%)	0.089
	No	17 (73.9%)	15 (88.2%)	2 (11.8%)	
Results					
Chest x-ray					
	Normal	6 (23.1%)	15 (75.0%)	5 (25.0%)	0.298
	Abnormal	20 (76.9%)	6 (100.0%)	0 (0)	
Oxygen saturation* (23)					
	≥ 95%	12 (52.2%)	11(91.7%)	1 (8.3%)	
	90-94%	6 (26.1%)	5 (83.3%)	1 (16.7%)	0.062
	< 90%	5 (21.7%)	2 (40.0%)	3 (60.0%)	
Creatinine****					
	Normal	9 (34.6%)	8 (88.9%)	1 (11.1%)	0.42
	High	17 (65.4%)	13 (76.5%)	4 (23.5%)	
Management					
Treated with Tamiflu* (25)					
	No	1 (4.0%)	0 (0)	1 (100%)	0.2
	Yes	24 (96.0%)	20 (83.3%)	4 (16.7%)	
Initiation of Tamiflu* (24)					
	Within 3 days of admission	23 (95.8%)	19 (82.6%)	4 (17.4%)	0.999
	>3 days after admission	1 (4.2%)	1 (100.0%)	0 (0)	
Tamiflu dose					
	Standard dose of 75 mg BD	15 (57.7%)	14 (93.3%)	1 (6.7%)	0.128
	Higher dose of 150 mg BD (as a full course or as part of the course)	11 (42.3%)	7 (63.6%)	4 (36.4%)	
Treated with antibiotics					
	No	2 (7.7%)	2 (100.0%)	0 (0)	0.646
	Yes	24 (92.3%)	19 (79.2%)	5 (20.8%)	
Admitted to ICU* (25)					
	No	17 (68.0%)	16 (94.1%)	1 (5.9%)	0.081
	Yes	8 (32.0%)	5 (62.5%)	3 (37.5%)	
Assisted ventilation					
	No	17 (65.4%)	16 (94.1%)	1 (5.9%)	0.034
	Yes	9 (34.6%)	5 (55.6%)	4 (44.4%)	
Vasopressor					
	No	22 (84.6%)	21 (95.5%)	1 (4.5%)	<0.005
	Yes	4 (15.4%)	0 (0)	4 (100%)	
Renal replacement					
	No	23 (88.5%)	20 (87.0%)	3 (13.0%)	0.085
	Yes	3 (11.5%)	1 (33.3%)	2 (66.3%)	
***data was not recorded ****categorization was done based on Ministry of Health laboratory reference range**					

Table 2: Univariable Exact Logistic Regression Analyses for Factors Associated with Deaths

Variable	Unadjusted Odds Ratio (SE)	95% CI	Unadjusted P-value
Age			
< 60 years	1.00	(0.09 , 14.58)	0.99
≥ 60 years	1.32		
Gender			
Female	1.00	(0.04 , 7.34)	0.82
Male	0.48		
Nationality			
Bahraini	1.00	(0 , 7.00)	0.80
Non-Bahraini	0.72*		
Dyspnea			
No	1.00	(0.69 , ∞)	0.11
Yes	5.84*		
History of chronic dx**			
No	1.00	(0.69 , ∞)	0.11
Yes	5.84*		
Smoking			
No	1.00	(0.53 , 115.54)	0.18
Yes	6.67		
Chest x-ray			
Normal	1.00	(0.27 , ∞)	0.47
Abnormal	2.38*		
Oxygen saturation			
≥ 90%	1.00	(0.73 , 206.50)	0.10
< 90%	10.17		
Creatinine			
Normal creatinine	1.00	(0.19 , 136.14)	0.84
High creatinine	2.39		
Tamiflu			
No	1.00	(0 , 9.75)	0.40
Yes	0.25*		
Initiation of Tamiflu			
Within 3 days	1.00	(0 , 195.00)	0.99
>3days	5.00*		
Tamiflu dose			
Standard dose of 75 mg BD	1.00		
Higher dose of 150 mg BD (as a full course or as part of the course)	7.36	(0.58, 421.34)	0.16
ICU admission			
No	1.00	(0.55 , 534.38)	0.16
Yes	8.59		
ventilation			
No	1.00	(0.87 , 668.3)	0.07
Yes	11.36		
Vasopressor used			
No	1.00	(4.93 , ∞)	0.0007
Yes	50.79		
Renal replacement			
No	1.00	(0.47 , 823.98)	0.17
Yes	11.33		

*median unbiased estimate
** CVS, CKD, DM, malignancy, Wegner's granulomatosis, asthma or COPD

Oseltamivir was initiated in 24/25 (96%) patients with a mortality rate of 16.7%. Oseltamivir was not used in one (4%) patient who had a delayed diagnosis; the patient died, P-value = 0.200.

Oseltamivir was initiated within three days of admission in 23/24 (95.8%) patients and delayed in 1/24 (4.1%) patient, P-value=.999.

Twenty-four (92.3%) patients received antibiotics with the antiviral. Two (7.69%) patients did not receive antibiotics.

Four (15.4%) patients required vasopressors, none of them survived. Among the other 22 (84.6%) patients who did not need vasopressors, one (3.8%) patient died, P-value <.005.

Multivariable exact logistic regression analysis which included factors having P-value ≤ .10 in the univariable analyses showed that the only factor that is significantly associated with mortality was the need for vasopressors which was associated with 20.51 odds ratio of death (OR=21.51, 95% CI=1.77, ∞; P=.01), see table 3.

Patients who needed vasopressors as part of their management were significantly more likely to die as all four (15.4%) of 26 patients who required vasopressors died compared to 1/26 (3.8%) death among those who did not require vasopressors, P-value<.005. Furthermore, patients who required assisted ventilation were significantly more likely to die; 4/26 (15.4%) out of the nine patients who required assisted ventilation group died compared to 1/26 (3.8%) death in the group that did not require assisted ventilation, P-value=0.034, see table 1. This was further supported by the univariable exact logistic regression analyses which showed that patients who needed vasopressors as part of their management had 50.79 (95% CI: 4.93, ∞; P=.0007) times the odds of death compared to those who did not require vasopressors and those who required assisted ventilation had 11.36 (95% CI: 0.87, 668.3; P=.07) times the odds of death compared to those who did not require assisted ventilation, see table 2.

Table 3: Multivariable Exact Logistic Regression Analysis

Variable	Adjusted Odds (Ratio (SE)	CI 95%	Unadjusted P-value
Oxygen Saturation			
90% ≤	1.00	(∞ , 0.04)	0.80
90% >	*1.5		
Ventilation			
No	1.00	(∞ , 0.01)	0.99
Yes	*0.5		
Vasopressor			
No	1.00	(∞ , 1.77)	0.01
yes	*21.51		
median unbiased estimate*			

DISCUSSION

Five Bahraini patients died compared to no deaths among the non-Bahraini. This difference in mortality could be attributed to the difference in prevalence of comorbidities in Bahraini patients. None of the patients had received influenza vaccine before admission, despite it being available and easily accessible from the local health centers. We found cardiovascular disease, diabetes and smoking to be independently associated with a higher likelihood of severe illness.

We found a smaller proportion of patients with history of COPD and asthma among the severely ill group, which is similar to other studies[3]. A possible explanation would be that patients in this category get early attention to respiratory symptoms and early intervention, which improves the overall outcome.

Antibiotics were prescribed for all patients except two. Due to initial presentation which had a differential diagnosis of both H1N1 influenza and pneumonia, the two patients were treated with both antibiotics and antivirals.

There was a higher mortality rate in patients who required vasopressors (100%) compared to only 4.5% mortality rate among patients who did not require treatment with vasopressors, P-value<0.005. There was also a higher mortality rate in patients who required renal replacement therapy (66.7%) compared to mortality rate among patients who did not require the treatment (13.5%).

Binsaeed et al studied 117 laboratory-confirmed H1N1 patients and found a mean age of 19.6 years. Similar to our results, male patients predominated; only 31 patients were admitted, with a mortality rate of 6.45%[4]. The most common symptom in our study was cough followed by fever, whereas the most common symptom in other studies was fever[4,5].

The mortality rate in our study was relatively high. A study by Khan et al in the United Arab Emirates reported a mortality rate of 0.9% among 2,806[6].

A study by Soub et al in Qatar reviewed 40 confirmed cases admitted to ICU[7]. They found that 82.5% of the patients had at least one risk factor − diabetes, hypertension and obesity being the most common. The overall mortality rate was approximately 25% compared to approximately 37.5% in our ICU admissions.

A study by Webb et al in Australia found that 14.3% of the 722 patients with confirmed H1N1 infection admitted to ICU over a 3-month period died[8].

A study by Jain et al in the United States reported 272 patients hospitalized and tested positive for H1N1; the mortality rate was 7%[9].

Our study had two major limitations. Some of the data were not recorded for one patient. Another major limitation was the small sample size, and accordingly, the study power has been limited and major conclusion was not possible. However, it is correlated with Bahrain's small populations.

CONCLUSION

In this study, none of the patients had received the flu vaccine, and the mortality rate was approximately 19%. ICU admissions were approximately 32%. The major comorbidities were cardiovascular disease, diabetes and smoking. We highly recommend activating the influenza vaccination programs, with specific attention towards the high-risk groups.

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