A Mass Gathering Experience at the 2009 Pilgrimage in Makkah, Saudi Arabia, During the 2009 Novel Influenza A (H1N1) Pandemic

Sherif R. Omar¹, Raouf M. Afifi²

 ¹ Department of Tropical Health, High Institute of Public Health, University of Alexandria, Egypt / Preventive Medicine Department, Armed Forces Hospitals, Taif, Kingdom of Saudi Arabia
 ² Preventive Medicine Department, Armed Forces Hospitals, Taif, Kingdom of Saudi Arabia / International Management Health Services, Indianapolis, State of Indiana, United States of America sherif omar67@yahoo.com

Abstract: Background: Saudi Arabia hosted 2.5 million pilgrims in 2009 amidst H_1N_1 pandemic. The Armed Forces Hospital in Mina caters for pilgrims during Hajj, annually. In the hospital, rigorous infection control precautions were taken to mitigate the transmission of the pandemic among the care seekers and the hospital's health workers. Objective: To study the distribution of confirmed H_1N_1 infection among suspected H_1N_1 patients admitted to the hospital. Methods: Patients who met disease severity criteria were admitted to the H_1N_1 isolation ward, nasopharyngeal and throat swabs for H_1N_1 virus assay, using real-time polymerase chain reaction (RT-PCR) technique taken. Results: Out of 39 admissions, females significantly predominated [74.4% vs. 25.6%, $X^2(1)$ 9.26, *p* 0.002]. Eleven (29.7%, n=37) patients tested H_1N_1 -polymerase chain reaction (PCR) positive. No health worker reported suspected H_1N_1 symptoms during the mission. Patients significantly differed in the rate of positive- and negative H_1N_1 -PCR-test [29.7%, 70.3%, $X^2(1)$ 6.81, *p* 0.014]. Test positivity did not differ by nationality (Saudi vs. non-Saudi). Conclusion: Dealing with a pandemic in a mass gathering situation is a unique experience. This work provides that although the burden of H_1N_1 infection may well be enhanced by Hajj mass gathering, applying systematized infection control measures in a well-defined hospital setting could help mitigate the transmission of H_1N_1 within the facility environment.

[Sherif R. Omar and Raouf M. Afifi. A Mass Gathering Experience at the 2009 Pilgrimage in Makkah, Saudi Arabia, During the 2009 Novel Influenza A (H1N1) Pandemic. J Am Sci 2013;9(4):563-571]. (ISSN: 1545-1003). http://www.jofamericanscience.org. 60

Keywords: Hajj, pandemic H₁N₁, Saudi Arabia.

1. Introduction:

The twenty first century saw its first pandemic when the World Health Organization (WHO) declared the emergence of novel influenza A (H1N1) viral infection in late April 2009.[1] On June 11, 2009, the pandemic alert level was raised to phase-6, until the end of 2009 when infection had been reported in almost the whole world.[2] Early in the outbreak, observers started to identify some differences of note in the epidemiologic characteristics and clinical presentation between the novel 2009 influenza A (H1N1) and known seasonal influenza infections. Unlike most strains of influenza, H1N1 did not disproportionately infect adults older than 60 years, an unusual characteristic feature of the H1N1 pandemic.[3] Even for persons previously very healthy, a small percentage of patients would develop viral pneumonia or acute respiratory distress syndrome, typically occurring 3-6 days after initial onset of flu symptoms.[4] Other differences of note, e.g., risk-outcome profile, between the new pandemic and seasonal influenza were still not understood. For example, while people with certain underlying medical conditions are known to be at increased risk for seasonal influenza complications, new risk factors, such as morbid obesity, have been suggested to be associated with the novel pandemic influenza severity. Nonetheless, the majority of infected individuals worldwide experienced uncomplicated influenza like illness, with full recovery even without medical treatment.[5] At the time, serious preparatory steps in facing expected regional and local spread of the novel influenza A (H1N1) were taken by almost every world's country. However the virus continued to spread globally, and clinics in some areas were overwhelmed by people infected.[6]

In Saudi Arabia, the situation was more challenging. Every year, millions of Muslims from all over the world, and domestically converge in certain holy spots in Saudi Arabia, take part in the annual Hajj (pilgrimage). Such gathering raises the Saudi Arabian health officials' fears that it could provide a breeding ground for infectious diseases transmission, including novel influenza A (H1N1) virus. Hajj preparations regularly starts anywhere after the middle of the 11th month of the Hijrat (H) Islamic calendar (a lunar-calendar), and ends before the middle of the 12th month of the year. That year

(1430H), Hajj corresponded to mid-November 2009 until before mid-December 2009. In practice, most Muslims only tend to stay on average between 1-3 weeks, depending on the arrival destination, affordability, etc. Some other factors added to the Saudi's concerns: a) the Saudi Arabian authority had to assume receiving the same huge annual influx of pilgrims that the greater the number of pilgrims the greater magnitude of the problem, b) the pandemic coincided with the southern hemisphere's regular influenza season (late November 2009), impacting the 2009's pandemic, c) there was not much certainty whether an influenza H1N1 vaccine would be produced time enough before November 2009, and even if released on time, the produced amounts may barely satisfy the overwhelming majority of people worldwide, d) resource-limited countries with large numbers of incoming pilgrims could then be vulnerable, given their limited ability to purchase the vaccine and their capacity to respond to a possible wave of H1N1 introduced via returning pilgrims,[7] e) although Saudi Arabia would not mean to turn away anyone who wanted to come to Hajj, certain risk groups, e.g., children younger than 12, people older than 65, pregnant women, chronically sick individuals, all were urged not to make the pilgrimage. Internationally, the situation was frustrating, too, and there was a strong belief that without a vaccine against the 2009 H1N1 virus, available control measures including both pharmaceutical interventions (the use of antiviral agents) and non-pharmaceutical interventions, e.g., isolation, quarantine, school closures, etc., would not be satisfactory to combat the epidemic. It was then determined quickly that the 2009 H1N1 virus was resistant to the adamantane antiviral agents but susceptible to neuraminidase inhibitors (oseltamivir® and zanamivir[®]),[8] which could be used for treatment and chemoprophylaxis.[9] At the individual country level, many took more or less additional precautions but mostly integral with the world-wide measures taken by the world health organization (WHO), which was orchestrating the scene.[10] After all, a strategic preparedness plan in Saudi Arabia to gear up efforts facing the coming pandemic was promptly started, aiming to deploy most effective and efficient measures available to prevent, contain, and mitigate the spread of influenza A (H1N1) during the upcoming (2009) Hajj. As a result, the Saudi Arabian Ministry of Health convened a preparedness consultation group in June, 2009 with consultants from global public health agencies in order to envisage the preparedness plan for the pandemic influenza during the 2009 Hajj.[11] Several recommendations to be put into practice before, during, and after Hajj were contemplated. Data from

the 2008 Hajj season were studied by the Saudi Arabian Ministry of Health to predict the numbers and epidemiological profile of the 2009-Hajj populations, and then to provide the required resources. Subsequently, almost 2.5 million pilgrims were expected to gather in Makkah in the 2009 Hajj.

In spite of the "reassuring" reports, and beside the availability of the earliest influenza A (H1N1) vaccine batches by mid-September, 2009,[12] and the fact that pilgrims were been urged as usual to receive the vaccine prior to traveling to Saudi Arabia,[13] the Saudi Arabian authority opted to keep utmost attention. Adequate amounts of antiviral agents offered free of charge to any pilgrims in need, regardless of their national origin, were also secured by the Saudi Arabian government.[14] In line with the dynamic efforts the Saudi Arabian health authority has been doing to provide an H1N1 riskfree Hajj, the armed forces hospital in Mina shared with these efforts to minimize the pandemic burden within the hospital's jurisdiction. Therefore, time enough before Hajj mission, the hospital was set up, customized, and equipped, e.g., assigning influenza H1N1 isolation ward, rearrange in-and out patienttraffic, to meet highest infection control standards. With the start up of the hospital's operations, measures to hinder the spread of infection between the incoming patients and hospital staff, as well as to mitigate possible complications of the infection, particularly among high risk groups were swiftly introduced. This work, thereby, aimed to describe the armed forces hospital in Mina's experience handling an expected influx of H1N1 admissions, analyzing associated risk factors and outcomes, given the infection prevention and control precautions enforced.

2. Methods:

The study was conducted between the 4th- until the 13th- day of the 12th month of 1430H (coincided November 12- December 2, 2009) at the inpatient setting of Armed forces Hospital in Mina, Makkah, KSA. The hospital (50 beds) provides basic emergency, ambulatory and inpatient services and only operates during the annual Hajj ceremony. It was working beside 14 other Ministry of Health hospitals (with total of 2782 beds) set up in Makkah area to serve incoming pilgrims free of charge. The study was designed to describe and analyze suspected and confirmed novel 2009 influenza A (H1N1) virus infection status among the 1430H- pilgrim populations and healthcare workers seeking medical care at the Armed Forces Hospital in Mina, Makkah. Only admitted influenza like illness patients were studied. Criteria of a "suspected influenza A (H1N1) infection" included either fever 238°C plus either

cough, sore throat, rhinorrhea, and/or nasal congestion, [15] or fever \geq 38°C plus any two of the following: muscle pain, malaise, headache, diarrhea, and/or vomiting.[16] Suspected influenza A (H1N1) patients would further need admission because they were presenting with one or more of the following symptoms: a) dyspnea or difficult breathing, b) oxygen saturation (O_2 sat.) at room air (RA) <90%, or O_2 saturation <93% on O_2 (by mask), c) respiratory rate (RR) >30 cycles per minute (cpm), d) systolic blood pressure (SBP) <90mmHg and/or diastolic BP<60mmHg, e) heart rate (HR)>120 beats per minute (bpm), (c, d, and e, adults only). f) Severe dehydration (loss of >10% of body weight), g) central nervous signs, such as altered level of consciousness (e.g., confusion or severe agitation), and seizures, h) recurrent fever after initial improvement, i) persistent fever for more than three days not responding to antipyretics, j) and abnormal chest radiography. [17] Patients with suspected influenza A (H1N1) could also be admitted to armed forces hospital in Mina due to the presence of any other systemic comorbidity that requires inpatient care. All thirty nine patients with suspected influenza A (H1N1) who fulfilled admission criteria to armed forces hospital in Mina were studied. No patients would be excluded because of any variations in the demographic features (e.g., age, sex, ethnicity, and race) or underlying health status. In this work, the term "influenza like illness" may be frequently used interchangeably with the term "suspected H1N1" in describing the clinical illness spectrum that embraces criteria for admission to the study. The former is literally defined as a "documented fever >38°C or a history of fever when the temperature was not known, and cough or sore throat, or both".[18] In our efforts to furnish an effective infection control-compatible environment time enough prior to the Hajj mission, all members of the armed forces hospital in Mina expedition were requested to receive H1N1 vaccine on time (i.e. at least ten days before the mission. Our infection control plan's primary aim was to mitigate the transmission of influenza like illness and suspected H1N1 virus-infection to unaffected patients, hospital staff, and clients. The plan included the following precautions: a) admit triaged influenza like illness patients to influenza like illness-isolation ward based on history taking and temperature measurement, b) reinforce hand hygiene and cough etiquette precautions, as appropriate, c) institute intensified standard and droplet precautions for the care of infected residents, including the use of personal protective equipment (PPE), [19] d) restrict residents, nurses, other health workers, housekeeping, catering staff movement through the H1N1 isolation ward; considering excluding any ill staff member from

work, e) close monitoring of all suspected H1N1 patients, including clinical evaluation, vital signs, O₂ saturation. All throughout our mission, we were in continuous liaison with the local public health authority, in terms of new case notification, daily case-progress reporting, and receiving H1N1 laboratory result notification. Empirical treatment with oseltamivir®, [20] together with other needed supportive measures was offered, often pending laboratory results. Two specimens, oropharyngeal, and nasopharyngeal swabs, combined, were taken from each patient to collect upper respiratory tract material, detect the presence of influenza A (H1N1) virus in the patient's upper respiratory tract mucosa.[21] The virus isolation samples were taken by assigned preventive medicine staff upon admission, applying recommended infection control measures, including using personal protective equipment (PPE).[19] The "Vircell Viral Transport Medium (VTM), REF: MTV001, LOT number 09MTV013" kit from "Microbiologists" was used for specimen collection. The kit consists of: a) the "Eurotub® sterile collection swab, REF: 300201, LOT number 9-11-081, MDD: 2013-02" from "DELTALAB," 0819 Rubi, Spain (in the form of a sterile synthetic polyester tip on a plastic stick shaft), b) Viral transport medium, 2ml of Hank's balanced salt solution (HBSS), containing 20mM HEPES huffer [4-(2-Hydroxyethyl)piperazine-1ethanesulfonic acid, N-(2-Hydroxyethyl) piperazine-N'-(2-ethanesulfonic acid)], 0.5% gelatin and 100µg/ml gentamicin sulphate. The assay procedure was performed following the manufacturer's instructions (sample collection with swab; swab put into viral transport medium tube, end of swab stick cut standing out of the tube, taking care not to touch the tube rim, tube closed tightly, patient data filled out, tube immediately placed in a refrigerator at 2-8°C for transport to the laboratory via refrigerated delivery at 2-8°C).[21] Samples were often stored at 2-8°C overnight until delivered to laboratory. A realtime polymerase chain reaction (RT-PCR) assay[22] for confirming novel influenza A (H1N1) infection among the study group was set up on a real time polymerase chain reaction cycler, using primers and a probe set advocated in similar influenza H1N1 virus detection studies[23] that target the hemagglutinin gene of the 2009 novel A (H1N1). Equal priority was given to all armed forces hospital in Mina patients, and swab results were reported within 12 hours. The rationale was that novel influenza A (H1N1) virus would test positive for influenza A (and negative for H1 and H3) by real time polymerase chain reaction (RT-PCR). If reactivity of the test for influenza A was strong (e.g. Ct < 30) it would be as more suggestive of a novel influenza A (H1N1) virus. Most

patients, especially the uncomplicated, tended to request immediate discharge once they felt better, opting to attend to "time-bound" Hajj duties that were to them top priority. In which case, they were discharged on oseltamivir, plus any other required ambulatory medications and both verbal and multilinguistic written instructions. A summarized discharge report was given upon discharge, for further follow up by patients attending physicians delegated with Hajj tours. Demographic data of interest for the study population included age, sex, and nationality. (Clinical and hospital stay data analysis was out of the scope of this work; so would not be analyzed). The underlying immune status to novel 2009 influenza A (H1N1) could not be uniformly, and reliably, collected for all participants because of poor access to patients' medical record data, equally, especially the international's. Some risk-outcome relationships would be assessed in order to describe the impact of some independent variables (all were nominal), namely age, sex, and nationality/and or country of original stay for international pilgrims, upon the probability of developing a positive real time polymerase chain reaction for influenza A (H1N1) virus test (reflecting a confirmed infection status). For instance, in case there was a desire to test the probability of a positive or negative novel influenza A (H1N1)-PCR test against sex, a chi-square test (or Fisher's exact test, as appropriate) would be performed. In which case, odds ratio (OR) and its 95% confidence interval (CI) would be used, (Mantel Haenszel summary OR (ORMH) was used, as appropriate, to provide a uniform risk assessment in case the ORs for resultant two age strata were unequal). All study data and individual variables were coded, entered into a Microsoft program with adequate backup until analyzed. The SPSS version-15 software was used to run the selected statistical tests. Our tolerable level for error was 5%, results with p-value <0.05 would be considered significant.

3. Results:

Thirty-nine pilgrims with suspected H1N1 were admitted to the H1N1 isolation ward in the armed forces hospital in Mina, Makkah during the 2009 Hajj, from the 10^{th} - until the 14th day of the 12^{th} month of the Hijrat year 1430H, making up to eight patients per day and 73% daily bed occupancy rate. No armed forces hospital in Mina health workers were either admitted with the study pilgrim cohort or complained of influenza like illness during - or after-the study duration. The majority of patient admissions (29/39 = 74.4%) were females, compared to 10/39 = 25.6% male pilgrims (Table 1), (female: male ratio = 2.9:1), yielding a significant female

predominance among the study population $[X^2(1) = 9.26, p = 0.002]$ (Table 1 footnote). Non-Saudis accounted for 25/39 (64.1%), against 14/39 = 35.9% Saudis (Table 2). Nationality-wise, too controlling for sex, an equal Saudi/ non-Saudi male patient distribution (5/39 = 12.8% each) but a higher, yet non-significant, Saudi/ non-Saudi female patient distribution (20/39 = 51.1% vs. 9/39 = 23%) was obtained. The study population's mean age was $31.8y\pm21.5$ (range 1y-70y). The frequency of testing H1N1- polymerase chain reaction positive was significantly lower than that of testing H1N1-PCR negative among our population [29.7%, 70.3%, respectively, (Table 1), n = 37; $X^2(1) = 6.81, p =$ 0.014] (Table 1 footnote).

Laboratory result was further analyzed, controlling for age. No significant difference in the age means was found between the two H1N1-polymerase chain reaction test groups (U = 103, p 0.183; suspected H1N1 with negative test ranked 20.5y, those with a positive test ranked 15.4). Controlling for sex, prior H1N1 immunization status (Table 1), and nationality (Table 2), too, no significant relationships with these respects were found [OR= 0.218, CI 0.044, 1, 075, (Table 1), OR= 0.42, CI 0.042, 4. 08 (Table 1), OR = 0.44, CI 0.102, 1.92, (Table 2), respectively]. Also, no significant relationship between H1N1-- polymerase chain reaction test outcomes and the nationality (Saudi-vs.non-Saudi) was found [OR = 0.44, CI 0.102, 1.92, (Table 2)]. Notably, all patients were discharged after clinical improvement of influenza like illness symptoms and all survived the attack.

4. Discussion

Thirty-nine suspected H1N1 individuals were admitted to the H1N1 isolation ward in armed forces hospital in Mina during Hajj time between the 10th until the 14th- of the 12th month of the Hijrat year 1430H, making up to 8 patients per day and 73% daily bed occupancy. The majority of the study population (74.4%) was significantly for female admissions. Similar finding has also been reported by Carcione et al., [18] while in another H1N1 research. [24] a male-influenza like illness admission predominance was reported. No explanation was given for this difference. The trend that female patients tend to seek medical advice more frequently than males due to influenza like illness during Hajj may well be explained by the notion that male pilgrims are more tolerant to the often tough Hajj duties, even in the presence of occasional complaints or improper health status. Further, given the "hypothesis" that women may generally mount higher immune responses to viral infections [25] that helps heightened virus clearance, admitted women

may have been the sickest among all influenza like illness care seekers when their physical tolerance to influenza virus, including pandemic H1N1, has been overcomed. [26] Even with such female

 Table 1: Distribution of Admitted Influenza Like Illness Pilgrims by Sex, H1N1-PCR Result, and H1N1

 Immunization Status

	Ν	%		
Sex*	39	100		
Male	10/39	25.60		
Female	29/39	74.40		
H1N1 RT-PCR (**)	37/39	(95.0)		
+ ve	11/37	29.70		
- <i>ve</i>	26/37	70.30		
H1N1 Immunization Vaccinated	05/39	12.80		
Non-vaccinated	34/39	87.20		
H1N1-PCR by Sex PCR - ve [4/37(10.8%) male, 22/37(59.5%) female] PCR+ve [5/37(13.5%) male, 6/37 (16.2%) female]	26/37 11/37	70.3 29.7	OR 0.218	95% CI 0.44, 1.075
H1N1-PCR by Immunization PCR - ve [5(13.5%) vaccinated, 21(56.75%) unvaccinated] PCR+ve [0(0%) vaccinated, 11(29.75%) unvaccinated]		70.3% 29.7%	0.42	0.043, 4.087

(*) Chi-square goodness of fit test for sex: $[X^2(1) = 9.26, p = 0.002]$.

(**) Chi-square goodness of fit test for H1N1-PCR-test result: [X2(1) = 6.81, p = 0.014].

Table 2: Distribution of Admitted Influenza Like Illness Pilgrims by H1N1-PCR Result by Nationality

14/39 25/39	35.9 64.1		
25/39	64.1		
2 = 12 0			
37/39	(95.0)	OR	95% CI
11/37	29.70		
26/37	70.30	0.44	0.102, 1.92
	11/37	26/37 70.30	11/37 29.70 26/37 70.30 0.44

*Saudi 14(36%), India 8(20%), Egypt 7(18%), Pakistan 5(13%), Yemen 2(5%), Bengal 2(5%), Palestine 1(3%).

predominance in our study, sex did not impact the presence of a confirmed H1N1 infection among our population. Non-Saudis constituted the majority of our study group (64.1% non-Saudis vs. 35.9 Saudis %). This statistic is more or less proportionate to the total estimate of the number of 2009 pilgrims: according to the "Saudi Arabian Central Department of Statistics", the total number of pilgrims from 2009 Hajj reached 2,454,325; 1,707,814 (69.6%) from outside of Kingdom of Saudi Arabia, and 746,511 (30.4%) from within the Kingdom of Saudi Arabia.[27] So, international pilgrims almost always outnumber domestic pilgrims (a large portion of whom, too, is expatriates working in Saudi Arabia). The rationale is that every year, Muslims from more than 100 countries look forward to traveling to holy Makkah to perform lifetime Hajj. The Saudi Arabian government then forecasts a number of pilgrims' pool to accommodate, and that is broken down into a

number of "Hajj quotas" allotted to subscribing countries in accordance with each country's Muslim population and demand for Hajj. Given the number of pilgrims in 2009 (see above), the 2009 Hajj quota, e.g., for India was 110,000,[28] (4.5%) and for Pakistan was 159,647 (6.5%).[29] On the other hand, 20% of our admitted patients were Indianans, 13% Pakistani, 18% Egyptians, and 36% Saudis. Since the declaration of the first confirmed H1N1 case in Saudi Arabia on June 3, 2009 until the end of the year, the number of laboratory -confirmed H1N1 cases in Saudi Arabia was 15,850, with 124 deaths.[30] The armed forces hospital in Mina records showed that 1,173 pilgrims have visited the emergency and outpatient clinics during 10 days of the hospital's mission, out of which 39 (3.3%) patients were admitted. Nationally, no information on the general numbers of influenza like illness visits have been available since pandemic H1N1 phase has been

declared, and cease-counting ceased.[6] The same trend was seen elsewhere; public health work was mostly directed to report only laboratory -confirmed H1N1 cases. In parallel, studies were focused on describing laboratory confirmed H1N1 experiences in different areas of the world. As a result, the rate of suspected- and hence laboratory-confirmed- H1N1 admissions in reference to the total number of influenza like illness cases could not be tracked down, locally or internationally. Consequently, no reliable comparison with this respect could be conducted between the study populations, e.g., the general influenza like illness pilgrim populations. In literature, H1N1 Hospitalization rate peaks up to almost 15% among confirmed H1N1 cases.[18] The lower admission rate among our population (3.3%) may well be explained by the difference in the reference populations in the two studies. On September 27, 2009, more than 340,000 laboratory confirmed A (H1N1) cases, worldwide and over 4,100 deaths have been reported to the WHO, also excluding the many milder illness cases that have occurred in different community settings but were not reported to their local, and hence international, public health authorities.[31]

From the epidemiological standpoint, most people with flu symptoms generally do not need a test for pandemic H1N1 influenza specifically. because the test results usually do not affect the recommended course of treatment. However, the CDC [32] recommended testing only for people who were hospitalized with suspected influenza, as well as other risk groups (e.g., pregnant women, immunocompromised patients, etc). In our study, 29.7% of influenza like illness patients were confirmed H1N1. In Carcione *et al.*, study[18] comparing pandemic influenza and seasonal influenza, no significant difference between confirmed H1N1 patients and those proved to have had seasonal influenza was found (14.9%, 12.5%, respectively, p 0.22). Given the fact that influenza infections substantially share similar symptoms,[33] despite the difference between Carcione et al., finding and ours in the proportion of the causative influenza virus types in hospitalized influenza like illness patients, the two studies could come up with the same conclusion that H1N1 and influenza seasonal infections may spread contemporaneously in the same demographic and seasonal settings.

Age did not influence H1N1-PCR test outcome. In contrast, those aged less than 40 were the majority among the first 100 confirmed H1N1 cases in Saudi Arabia, compared to other ages.[30] The short duration of the Hajj mission during which the study was carried out could be behind this inconsistency. Sex, too, had no impact upon H1N1 polymerase

chain reaction test outcome. In the same study,[30] AlMazroa et al., did not find a significant impact of sex of their patients upon H1N1 laboratory result [55 female, 45% male; $X^2(1) = 1$, p 0.317; the chi-square test for this statistic was calculated by this study's investigators]. No study subject who reported receiving H1N1 vaccine ≥10days prior to arriving to Makkah (5/37 = 13.5%) had confirmed H1N1 infection. As of November 19, 2009, over 65 million doses of vaccine had been administered in over 16 countries. The vaccine proved effective, producing a strong immune response that protects against infection.[34] Whereas the 2009 trivalent seasonal influenza vaccine neither increases nor decreases the risk of infection with H1N1, the vaccines rushed to combat the new strain were effective against H1N1,[35,36] although they were manufactured similarly. Thereby, testing H1N1-PCR negative may have been either due to successful immunization, where an H1N1 vaccine taken on the right time prior to coming to Hajj produced protective antibody response,[32] or the likelihood that testing H1N1-PCR negative may well be associated with other types of influenza viruses, e.g., A (H3N2), or influenza B. According to the WHO.[33] too, as of November 15,2009, transmission both of influenza A (H1N1) and A (H2N3) with a variable intensity in different world's areas, including Western Asia, was running, another evidence that the three influenza types do circulate simultaneously. Further, the cocirculation of seasonal influenza A (H3N2) and 2009 H1N1 viruses inspired comparing the spread of these viruses, e.g., among 284 persons in 99 Hong Kong households.[37] It was found that the transmission dynamics (secondary attack rate, incubation period, and duration of viral shedding) were similar both for seasonal influenza-A and 2009 H1N1 viruses, suggesting that the spread of the 2009 H1N1 virus was similar to that of seasonal influenza A viruses. By testing nasal and throat swabs from all household members and paired acute and convalescent serum samples from a subgroup of household contacts, the Hong Kong-study investigators identified a wide range of influenza like illness symptoms, including asymptomatic infection and mild illness, which confirmed findings in other studies. The frequency of confirmed H1N1 infection cases in our study did not vary by nationality or ethnic descent. The ultimate outcome was clinical improvement of all our admitted influenza like illness patients (regardless the causative influenza virus infection). From the resource and logistics viewpoint, there was not an intolerable pressure on the armed forces hospital in Mina admitting suspected H1N1 cases throughout the mission. From our previous experience with H1N1 surveillance since the start of the pandemic, an

estimate for the volume and type of resources, e.g., number of beds in isolation ward and the set up needed to satisfy the demand for suspected H1N1 admissions, all could be forecasted. On the broader 2009 Hajj scene, The Saudi Arabian government announced that four pilgrims died of swine flu, three of whom, a woman from Morocco and two men from Sudan and India, were in their 70s; the fourth was a 17-year-old girl from Nigeria. None of the four victims had been vaccinated against pandemic H1N1 virus. Further, all victims had underlying health problems, including cancer and chronic respiratory illness.[38] In our experience, the hallmark of success of the infection prevention and control measures we applied during this mission, is fortunately that none of the hospital's healthcare workers developed influenza-like illness. On the other hand, a study done on 184 healthcare workers during the 2009 Hajj season showed that respiratory symptoms could happen among them, but none came positive for influenza A (H1N1) taking in consideration that only 22% were vaccinated against that strain. The explanation they gave is that influenza A (H1N1) was infrequent among 2009 pilgrims.[39].

Conclusions:

The time of this study, pandemic influenza A (H1N1) was still a significant threat to Saudi Arabia. particularly with the Hajj mass gathering encountered. Undertaking stringent infection prevention and control precautions could both prevent H1N1 virus transmission to the armed forces hospital in Mina health-workers and provide ground rule for favorable health outcomes in the study population, in terms of clinical improvement and survivability of all. As data from the pandemic would be analyzed, a number of factors should be considered by clinicians and epidemiologists in order to better understand the role of determining factors upon H1N1 disease outcomes. These factors include demographic, behavioral and risk-associated differences in exposure and severity of pandemic H1N1, as well as the role of healthcare setting and timeliness in enforcing comprehensive surveillance and infection prevention measures on 2009-H1N1 virus infection. Further studies to identify the burden of pandemic H1N1, as well as with future emerging infectious disease epidemics, probably using mathematical modeling approach, when case counting has been abandoned due to declaration of disease pandemic, are needed. Such studies help forecast the resources and timeframe required to meet the demand for an overflow of hospital admission of the sickest pandemic-disease cases.

Corresponding author:

Dr. Sherif R. Omar,

Associate Professor of Topical Health, Tropical Health Department, High Institute of Public Health, 165 Horreya Ave., Alexandria, Egypt /

Consultant, Preventive Medicine Department, Armed Forces Hospitals, Taif Region, P.O. Box 1347- Taif, 21944, Kingdom of Saudi Arabia, E-mail: <u>sherif omar67@yahoo.com</u>

Cell phone: +20122 7307303 / +96650 3522035

References:

[1] World Health Organization (WHO). Global alert and response (GAR). Swine flu illness in the United States and Mexico – update 2. Available from:

www.who.int/csr/don/2009_04_26/en/index.html.

- [2] World Health Organization (WHO). World now at the start of 2009 influenza pandemic. 11 June 2009. Available from: http://www.who.int/mediacentre/news/statements/ 2009/h1n1_pandemic_phase6_20090611/en/index .html.
- [3] Centers for Disease Control and Prevention (CDC). Update: swine influenza A (H1N1) infections-California and Texas, April 2009. MMWR 2009;58(16):435-7. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/m m5816a7.html.
- [4] Writing Committee of the WHO Consultation on Clinical Aspects of Pandemic (H1N1) 2009 Influenza. Clinical Aspects of Pandemic 2009 Influenza A (H1N1) Virus Infection. N Engl J Med 2010; 362:1708–19.
- [5] World Health Organization (WHO). Clinical features of severe cases of pandemic influenza. 16 October 2009. Available from: http://www.who.int/csr/disease/swineflu/notes/h1 n1 clinical features 20091016/en/index.html.
- [6] European Center for Disease Prevention and Control (ECDC) working group on influenza A(H1N1): Preliminary analysis of influenza A(H1N1) individual and aggregated case reports from EU and EFTA countries. Euro Surveill 2009;14:19238.
- [7] Khan K., Memish ZA, Chabbra A, Liauw J, Hu W, Janes DA, et al. Global public health implications of a mass gathering in Mecca, Saudi Arabia during the midst of an influenza pandemic. J Travel Med 2010; 17(2): 75-81.
- [8] Anderson RM. How well are we managing the influenza A/H1N1 pandemic in the UK? BMJ 2009;339:b2897.
- [9] Lee VJ, Yap J, Cook AR, *et al.* Oseltamivir ring prophylaxis for containment of 2009 H1N1

influenza outbreaks. N Engl J Med 2010;362: 2166-74.

[10] World Health organization (WHO). Guidelines for pharmacological management of pandemic influenza A(H1N1) 2009 and other influenza viruses. Geneva: WHO, Feb. 2010. Available from: http://www.who.int/csr/resources/publications/swi

neflu/h1n1_guidelines_pharmaceutical_mngt.pdf.

[11] Centers for Disease control and Prevention (CDC). Health Requirements and Recommendations for Travel to Saudi Arabia during the 2009 Hajj: Information for U.S. Travelers. Available from:

http://wwwnc.cdc.gov/travel/content/id/2434.aspx

- [12] Wu J, Xu F, Lu M, Miao L, Gao T, Ji W, et al. Safety and Effectiveness of a 2009 H1N1 Vaccine in Beijing. N Engl J Med 2010; 363:2416-2423.
- [13] Hanan H, Balkhy HH, Memish, AA, Bafaqeer, S, Almuneef, MA. Influenza a Common Viral Infection among Hajj Pilgrims: Time for Routine Surveillance and Vaccination. Journal of Travel Medicine 2004;11(2):82–86.
- [14] Ebrahim SH, Memish ZA, Timothy M, Uyeki TM, Khoja TAM, *et al.* Policy Forum. Public Health. Pandemic H1N1 and the 2009 Hajj. Science 326(5955):938-940. 13 Nov. 2009. DOI: 10.1126/science.1183210. Available from: http://www.sciencemag.org/content/326/5955/938 .short.
- [15] Tang JWT, Tambyah PA, Lai FYL, et al. Differing symptom patterns in early pandemic vs. seasonal influenza infections. Arch Intern Med 2010;May 24;170(10):861-7.
- [16] Di Giambenedetto S, Verme LZD, Sali M, et al. Clinical presentation, microbiological features and correlates of disease severity of 2009 pandemic influenza A (H1N1) infection. Euro J Clin Microbiol Infect Dis 2010. Available from: http://www.springerlink.com/content/b1717r5241 560414/.
- [17] Harper SA, Bradley JS, Englund JA, *et al.* Seasonal influenza in adults and children diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis 2009;48: 1003-32.
- [18] Carcione D, Giele C, Dowse GK, Mak DB, Goggin L, Kwan K, et al. Comparison of pandemic (H1N1) 2009 and seasonal influenza, Western Australia, 2009. Emerg Infect Dis 2010;16(9):1388-95. 2010. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20735922.
- [19] Centers for Disease Control and Prevention (CDC). Interim Guidance on Infection Control

Measures for 2009 H1N1 Influenza in Healthcare Settings, Including Protection of Healthcare Personnel. Available from:

http://www.cdc.gov/h1n1flu/guidelines_infection _control.htm. July 15, 2010.

- [20] Centers for Disease Control and Prevention (CDC). Recommendations for early empiric antiviral treatment in persons with suspected influenza who are at increased risk of developing severe disease. Health Alert Network (HAN) info service message. Oct 19, 2009. Available from: http://www.cdc.gov/h1n1flu/HAN/101909.htm.
- [21] Centers for Disease Control and Prevention (CDC). Interim Guidance on Specimen Collection, Processing, and Testing for Patients with Suspected Novel Influenza A (H1N1) Virus Infection. Available from: http://www.cdc.gov/h1n1flu/specimencollection.h tm May 13, 2009.
- [22] National Standard Method: RT-PCR for the Detection of influenza A Viruses, VSOP 42i2. Standards Unit, Department of Evaluation, Standards and Training Center for Infections, Health Protection Agency (HPA, Colindale, London, U.K.); issue no.2, 13.5.200, p.1-13, 2009. Available from: www.evaluationsstandards.org.uk.
- [23] Lim M, Chong C, Tee W, Lim W, Chee J. Influenza A/H1N1 (2009) infection in pregnancy, an Asian perspective. BJOG 2010;117:551–556.
- [24] Cao, B, Li X-W, Mao, Y, Wang, J, Lu, H-Z, Chen, Y-S, *et al.* Clinical Features of the Initial Cases of 2009 Pandemic Influenza A (H1N1) Virus Infection in China. NEJM 361(26):2507-2517, December 24, 2009.
- [25] Klein SL, Huber S. Sex differences in susceptibility to viral infection. In "Sex Hormones and Immunity to Infection." Edited by: Klein SL, Roberts CW. Berlin: Springer-Verlag; 2010. Available from: http://www.bsdjournal.com/content/pdf/2042-6410-1-5.pdf.
- [26] Fish, EN: The X-files in immunity: sex-based differences predispose immune responses. Nat Rev Immunol 2008;8:737-744.
- [27] Cross Roads Arabia. How many attended the Hajj? "Hajj Media Reports and Conflicting Figures" Available from: http://xrdarabia.org/2007/12/23/how-manyattended-thehajj/?utm_source=INK&utm_medium=copy&utm campaign=share"
- [28] "Haj Committee of India". (Constituted under the Act of Parliament No.35 of 2002) Announcement for Hajj 1429 (H) – 2008. Available from:

http://www.hajcommittee.com/index.php?value=a nou.

- [29] Government of Pakistan Ministry of Religious Affairs. Subject: Policy and Plan for Hajj –2009. Salient features of Hajj Policy and Plan for Hajj – 2009, as approved by the Cabinet in its meeting on 17-06-2009. Available from: http://www.hajjinfo.org/policy2009.htm.
- [30] AlMazroa MA, Memish ZA, AlWadey AL. Pandemic influenza A (H1N1) in Saudi Arabia: description of the first one hundred cases. Ann Saudi Med. 2010 Jan-Feb; 30(1): 11–14. DOI: 10.4103/0256-4947.59366. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC28 50176/#CIT12.
- [31] World Health Organization (WHO). Global Alert and Response. Pandemic (H1N1) 2009. Available from: http://www.who.int/csr/disease/swineflu/en/index. html.
- [32] Centers for Disease Control and Prevention (CDC). Influenza Diagnostic Testing During the 2009–2010 Flu Season. CDC, H1N1 Flu. 2009-09-29. Available from: http://www.cdc.gov/h1n1flu/diagnostic testing p

ublic_qa.htm. Retrieved 2009-11-23.

 [33] World Health Organization (WHO). Global alert and response (GAR). Pandemic (H1N1) 2009 update 75. Weekly update. 20 November 2009. Available from:

http://www.who.int/csr/don/2009_11_20a/en/.

[34] Greenberg ME, Lai MH, Hartel GF, Wichems CH, Gittleson C, Bennet J, et al. "Response after One Dose of a Monovalent Influenza A (H1N1) 2009 Vaccine – Preliminary Report". N Engl J

3/20/2013

Med 2009;361(25): NEJMoa0907413. DOI: 10.1056/NEJMoa0907413. PMID 19745216. Available from:

http://content.nejm.org/cgi/content/abstract/NEJM oa0907413v1.

- [35] Centers for Disease Control and Prevention (CDC) (November 2009). "Effectiveness of 2008–09 trivalent influenza vaccine against 2009 pandemic influenza A (H1N1) – United States, May–June 2009". MMWR 58 (44):1241–5. PMID 19910912. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/m m5844a5.htm.
- [36] Hancock K, Veguilla V, Lu X, et al. "Cross-reactive antibody responses to the 2009 pandemic H1N1 influenza virus". N Engl J Med 2009;361(20): 1945–52.
 POI-10 1056(NE Macc0006453 PMID 10745214

DOI:10.1056/NEJMoa0906453. PMID 19745214.

- [37] Cowling BJ, Chan KH, Fang VJ, *et al.* Comparative epidemiology of pandemic and seasonal influenza A in households. N Engl J Med 2010;362:2175-2184.
- [38] ProMed Newsgroup. Further report on recent H1N1 deaths in Saudi Arabia at Hajj. (109): Saudi Arabia, Hajj pilgrims 20091120.3997. Available from: http://www.tmb.ie/exodus/news.asp?title=Furtherreport-on-recent-H1N1-deaths-in-Saudia-Arabia-

at-Hajj&id=175532.

[39] Memish ZA, Assiri AM, Alshehri M, Hussain R, and Alomar I. The prevalence of respiratory viruses among healthcare workers serving pilgrims in Makkah during the 2009 influenza A (H1N1) pandemic. Trav Med Inf Dis 2012;10: 18-24.