Original Article

H1N1 Influenza epidemic in children in Baghdad… a hospital based study

Hayder M. Al-Musawi*	**MBChB, DCH, FABP**
Hasanein H. Ghali**	**MBChB, FICMS, DCH**
Nadia A. Nasir***	**MBChB, FABCM**
Wisam A. Hussein*	**MBChB, FIBMS**
Muhi K. Al-Janabi**	**MBChB, FICMS, DCH, MRCPCH**

Summary:

Background: A confirmed case of influenza A (H1N1) virus infection is defined as a person with an influenza-like illness with laboratory confirmed influenza A (H1N1) virus infection by real-time RT-PCR or viral culture.

Objectives: To identify demographic and clinical predictors, and outcome of proved cases of H1N1 influenza epidemic in children.

Patients and methods: This study was conducted in Children Welfare Teaching Hospital/ Medical City/ Baghdad on 67 hospitalized patients aged 1 month to 18 years with signs and symptoms suggestive of influenza during the period of outbreak of pandemic influenza A (H1N1) from 1st of October 2009 to 1st of January 2010. Demographic aspect, clinical coarse, laboratory investigations, treatment and outcome were reported. For each patient 2 nasal, 2 throat swabs and single blood sample were collected, and sent to Central Health Laboratory. All suspected patients received Oseltamivir for 5 days. The data were analyzed statistically by Chi-square ($\chi 2$) test and Fisher's Exact Test.

Results: The median age for the studied patients was 7.7 years with a range of 1 month -18 years. 39 patients out of 67 (58.2%) were PCR positive. 34 out of 39 (87.1%) were <6-18 year old while 5 out of 39 (12.9%) were >3-6 years old. No case was reported in age group 1 month-3 years. Twenty eight patients out of 67 (41.8%) were PCR negative. 17/28 (60.7%) were <6-18 years old. 5 out of 28 (17.9%) were >3-6 years old. 6 out of 28 (21.4%) were 1 month -3 years old. Female: male ratio in PCR positive patients was 1.05:1 while it was 1.54:1 in PCR negative patients. Most of the children came from urban area in both PCR positive and negative results. Cough and fever had a higher frequency in both PCR positive and negative patients while headache was more in epidemic influenza. All PCR positive and 26 out of 28 (92.8%) of PCR negative patients improved while 2 out of 28 (7.2%) of PCR negative patients died.

Conclusions: Children at school age were more prone to acquire epidemic influenza. Both genders were equally affected. Frequency was more in urban area .Cough and fever was the most frequent presentation. Headache was a more common presentation in H1N1 influenza than in seasonal influenza.

Key words: Influenza, Epidemic, Children, Baghdad.

Fac Med Baghdad
2014Vol.56, No.4
Received: May,2014
Accepted June.2014

Introduction:

A confirmed case of novel influenza A (H1N1) virus infection is defined as a person with an influenza-like illness with laboratory confirmed novel influenza A (H1N1) virus infection by real-time RT-PCR or viral culture.(1)A probable case of novel influenza A (H1N1) virus infection is defined as a person with influenza-like-illness who is positive for influenza A, that is unsubtypeable by real-time RT- PCR OR an individual with clinically compatible illness or who died of an unexplained acute respiratory illness who is considered to be epidemiologically linked to a probable or confirmed case(1). A suspected case of novel influenza A (H1N1) virus infection is defined as an individual with acute respiratory illness and fever and one of the following: cough, sore throat, shortness of breath or chest pain with onset: Within 7 days of close contact with person who is probable or confirmed case, Within 7 days of travel to a country where there has been one or more confirmed case and Reside in community where there is one or more confirmed case (1) . Influenza viruses are members of the family Orthomyxoviridae and are divided into three types: A, B, and C. The majority of the human cases of influenza are caused by types A and B in annual winter epidemics. Influenza A viruses are further divided into subtypes based on the hemagglutinin and neuraminidasegenes, and the WHO nomenclature for classification of influenza strains is as follows: type (A, B, or C)/ geographic origin/year of isolation/ subtype (hemagglutinin and neuraminidase), for example A/ Sydney/97 (H3N2). There are 16 hemagglutinin subtypes

** Children Welfare Teaching hospital, Medical city, Baghdad*
***Dept. of pediatrics, College of Medicine, University of Baghdad*
Email:Muhi-janabi@yahoo.com
****Dept. of Community Medicine, College of Medicine, University of Baghdad.*

and nine neuraminidase subtypes; hemagglutinin 1, 2, and 3 and neuraminidase 1 and 2 typically circulate in humans. (2) Modes or routes of transmission of infectious agents have been classified as contact, droplet, airborne. (3, 4)

The incubation period for influenza is from 1-4 days. The period of communicability continues for up to 7 days after the onset of illness. (4)Viral shedding may be longer in infants, and prolonged in young children and immunodeficient patients. (5)It is possible that prolonged shedding could occur with pandemic influenza because the immune system had no prior experience with related strains. (6)The influenza virus is readily inactivated by hospital germicides, household cleaning products, soap, hand wash or hand hygiene products. (7)Young children and those with certain underlying medical conditions are at increased risk for hospitalization or severe or complicated influenza infection.(8)These include children who have chronic pulmonary disease, congenital heart disease, hemoglobinopathies, metabolic conditions, chronic renal disease, immunosuppression, conditions requiring long-term aspirin therapy (e.g. Kawasaki disease).The major cause of hospitalization in infants with influenza is an undifferentiated febrile illness, which requires an evaluation for sepsis because of the acute onset of fever and absence of localizing signs. (9) The classic features of uncomplicated influenza virus infection include the abrupt onset of fever, headache, myalgia, and malaise. These symptoms are accompanied by manifestations of respiratory tract illness, such as cough, sore throat, and rhinitis.(10) All of the classic features may not be present in children with influenza virus infection. In part, this is because young children cannot vocalize such symptoms as myalgias and headache. (11) In cases of uncomplicated influenza, few localizing physical findings are evident, and in some children, fever and malaise may be the only recognized manifestations. Findings on examination may include: (12)Fever (≥ 38ºC is most frequent),tachypnea, conjunctival erythema, nasal injection, edema, and discharge, oropharyngeal abnormalities other than slight to moderate hyperemia are uncommon, even with complaints of sore throat influenza in otherwise healthy children is generally an acute, self-limited, and uncomplicated disease. However, in certain "high-risk" groups of children, the infection may be complicated and severe. (13)The most common complications of influenza in children are otitis media, followed by lower respiratory tract involvement. (9, 14, 15, 16)Other complications, including CNS involvement, myositis and rhabdomyolysis are less frequent. (17, 18).

Diagnosing H1N1by Rapid Flu Test. (19) Specific H1N1 Swine Flu tests that can definitely diagnose the pandemic H1N1 virus include: Real time (RT-PCR) and a viral culture. These tests can only be performed by certain specialized laboratories and takes several days to receive results. For the 2009-10 flu season, the Center of Disease Control is only performing these tests on people who are hospitalized.(20)Antiviral treatment for confirmed or suspected either hospitalized or at high risk ill case of swine influenza virus infection may include either oseltamivir or zanamavir. Recommendations for use of antivirals may change as data on antiviral susceptibilities become available. (20)Antiviral chemoprophylaxis is generally not recommended. Antiviral chemoprophylaxis (pre-exposure or post-exposure) can be considered for close contacts of a confirmed or highly suspected case of swine influenza virus infection. (21)As with any disease, prevention is better than cure and a few conservative measures can greatly reduce your risk of swine flu infection. Proper hygiene and common sense are of the greatest benefit in dealing with any viral outbreak. (22)Aim of the study to identify some demographic, epidemiologic and clinical predictors to H1N1 influenza in admitted children with influenza like illness.

Patients and methods:

This study was conducted in CWTH/ Medical City/ Baghdad on 67 patients aged 1 month to 18 years with signs and symptoms suggestive of influenza admitted to the consultation clinic and ward especially prepared to receive the patients with suspected epidemic influenza during the period from 1st of October 2009 to 1st of January 2010.Full history and thorough clinical examination were done for all patients and special inquiry sheet was filled for them including age, sex , residence (urban or rural) and complaint including cough ,fever (corrected axillary temp. equal or more than 38 degree Celsius) ,malaise ,headache ,body ache , shortness of breath and chills .For each patient 2 nasal ,2 throat swabs and single blood sample were collected, the swabs were collected properly by a trained person, placed into special transport medium ,each tube was labeled (name ,date of collection and source :nose or throat) and sent to Central Health Laboratory for PCR while blood samples were sent for ELISA test in the same laboratory. All suspected patients received Oseltamivir for 5 days, ≤ 15 kg: 2 mg/kg/dose (maximum dose: 30 mg) twice daily, >15 kg to 23 kg: 45 mg/dose twice daily, >23 kg to 40 kg: 60 mg/dose twice daily, >40 kg: 75 mg/dose twice daily, and children >12 years and adults: 75 mg/dose twice daily .The data were analyzed statistically by Chi-square ($\chi 2$) test and Fisher's Exact Test.P value of less than 0.05 was considered as statistically significant and of less than 0.01 was highly significant.

Results:

Sixty seven patients were included in this study, median age for them was 7.7 year (1 month -18 year) ,39 patients out of 67 (58.2%) were PCR positive , 3439/ were between 6 and 18 years old while 539/ were 3-6 years old , no cases were reported in age group 1 month-3< years old as shown in table 1.Twenty eight patients out of 67 (41.8%) were PCR negative , 1728/ were 6-18> years old , 528/ were 3-6 years old ,628/ were 1 month -3 years old as shown in table 1.P value for

age distribution of PCR positive and negative patients is 0.0063.According to gender distribution , female:male ratio in PCR positive patients were 1.05:1 while it was 1.54:1 in PCR negative patients as shown in table 2.P value for gender distribution of PCR positive and negative patients is 0.4674. Thirty five out of 39 of PCR positive patients came from urban area while 439/ were from rural area as shown in table 3.In PCR negative patients 2228/ came from urban area while 628/ were from rural area as shown in table 3.P value for residence distribution of PCR positive and negative patients is 0.2993. According to the signs and symptoms , cough and fever had a higher frequency in both PCR positive and negative patients as shown in table 4.Cough presented in 3339/,fever in 2839/ of PCR positive patients while 2728/ and 1428/ respectively in PCR negative patients. P values of cough and fever are 0.2247 and 0.0796 respectively.

Headache was the third frequent symptom in PCR positive patients which presented in 27 39/ while 1028/ in PCR negative patients as shown in table 4. P value for headache frequency in PCR positive and negative patients was 0.0121.In PCR positive patients the consequences of other signs and symptoms in decreasing frequency were sore throat 1539/,malaise and SOB 1439/ and body ache 1135/ while in PCR negative patients the consequences were malaise 1228/, headache 1028/, sore throat and SOB 928/ and body ache 328/ as shown in table 4. P values for sore throat, malaise, SOB and body ache are 0.6173, 0.8105, 0.7992 and 0.1276 respectively as shown in table 4.Chills was not recorded in both PCR positive and negative patients as shown in table 4.All PCR positive and 26 28/ of PCR negative patients improved while 2 28/ of PCR negative patients died as shown in tab le 5.

Table 1: The association between influenza & age groups in children with influenza.

Age groups	PCR positive n(%)	PCR negative n(%)	Total n(%)
1 month - 3 year	0	6(8.9%)	6(8.9%)
3- 6 year	5(7.4%)	5(7.4%)	10(14.8%)
6-18 year	34(50.8%)	17(25.5%)	51(76.3%)
Total n(%)	39(58.2%)	28(41.8%)	67(100%)

$\chi 2 = 10.134$, P value = 0.0063

Table 2: The association between influenza and gender in children with influenza.

Gender	PCR positive n(%)	PCR negative n(%)	Total n(%)
Female	20(29.9%)	17(25.4%)	37(55.3%)
Male	19(28.3%)	11(16.4%)	30(44.7%)
Total n(%)	39(58.2%)	28(41.8%)	67(100%)

P value = 0.4674

Table 3: The association between influenza and residence in children with influenza.

Residence	PCR positive n(%)	PCR negative n(%)	Total n(%)
Urban	35(52.2%)	22(32.8%)	57(85%)
Rural	4(6%)	6(9%)	10(15%)
Total n(%)	39(58.2%)	28(41.8%)	67(100%)

P value = 0.2993

Table 4: Association between epidemic influenza and some clinical characteristics.

Clinical features		PCR positive n(%)	PCR negative n(%)	Total n(%)	P value
Cough	Positive	33(49.2%)	40.2%))27	89.4%))60	0.2247
	Negative	6(8.9%)	1(1.7%)	7(10.6%)	
Fever	Positive	28(41.7%)	14(20.8%)	42(62.5%)	0.0796
	Negative	11(16.7%)	14(20.8%)	25(37.5%)	
Headache	Positive	27(40.2%)	10(14.9%)	37(55.1%)	0.0121
	Negative	12(17.9%)	18(28%)	30(45.9%)	
SOB	Positive	14(20.8%)	9(13.4%)	23(34.2%)	0.7992
	Negative	25(37.5%)	19(28.3%)	44(65.8%)	

Table 5: The outcome of children admitted with influenza.

Outcome	PCR positive n(%)	PCR negative n(%)	Total n(%)
Improved	39(58.2%)	26(38.8%)	65(97%)
Died	0	2(3%)	2(3%)
Total n(%)	39(58.2%)	28(41.8%)	67(100%)

Discussion:

This study was done during the epidemic of H1N1 influenza in winter months in Iraq as a part of pandemic in the period from 1st of October 2009 to 1st of January 2010. H1N1 influenza was reported more frequently in children aged 6-18 year old and this was also reported with Juan et al(23) and Pedroni et al(24) and this may be attributed to more frequent exposure to index cases in school aged children. The age group with the lowest frequency of epidemic influenza was from 1 month - 3 year , this agreed with Juan et al(23) and Pedroni et al(24) and this may be due to decrease exposure to index cases and limited number of children attending nurseries and kindergartens. Regarding age distribution there was a highly significant association between advancing age and having H1N1 influenza in children. The gender distribution was 51.2% females, 48.8%males (female to male ratio was 1.05:1) in PCR positive patients .This is in agreement with Juan et al(23) and Romina et al (25) , this can be explained by the fact that both sex were nearly equally exposed in school and community during the epidemic while in

PCR negative patients female to male ratio of 1.54 :1 and there is no significant difference recorded. Thirty five out of thirty nine (89.7%) cases were from urban , 439/ (10.3%) cases from rural areas in PCR positive patients and 22/ 28 (78.5%) urban , 6/ 28 (21.5%) rural in PCR negative patients. Overcrowding in urban may be an important risk factor for frequent exposure than in rural area moreover the study was conducted in urban area. In this study, cough was the most frequent symptom followed by the fever in both PCR positive and negative patients, this is in agreement with Bin Cao et al (26) and Ralf et al (27) while in Juan et al (22) and Romina et al (25) . Fever was the most frequent symptoms followed by the cough. Both of symptoms show no statistical difference between seasonal and epidemic influenza. In children with H1N1 influenza, headache was more frequently recorded than in those with seasonal influenza and this difference was statistically significant. Regarding other signs and symptoms (sore throat, malaise, SOB and body ache) were more frequently recorded in H1N1 than in seasonal influenza but the difference was not significant.Chills was not recorded in any studied child in both types of influenza also in Bin Cao et al(26) study chills was the least frequent sign and symptom. Regarding the outcome 65 children improved and 2 died, both of them presented after 1 week of the illness with fever ,cough and SOB ,the 1st one developed respiratory failure and admitted to RCU and died on the 5th day of admission while the other died on the 2nd day of admission and both of them PCR negative and the cause of death was pneumonia leading to respiratory failure Juan et al(23) had recorded no death from epidemic influenza in Santiago, Chile while in Romina et al(25) study the mortality rate of H1N1 2009 were 10 times more than mortality rate of seasonal influenza in previous year in Argentina .

Conclusion:

Epidemic influenza was more frequent in school aged children.Both genders were nearly equally affected,H1N1 was more frequent in urban area. Cough and fever were the most frequent symptoms in both type of influenza. Headache was recorded more frequently in H1N1 influenza than in seasonal influenza. No fatality among admitted children diagnosed with H1N1 influenza was recorded.

Author Contributions:

Muhi K. Al-Janabi: Study conception, Study design, and critical revision

Nadia A. Nasir : Acquisition of data analysis and interpretation of data

HayderMahdi Al-Mosawi : Data collection, drafting manuscript

Hasanein Habib Ghali: Data collection

Wisam Ali Hussein: Data collection

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