Research Article

Clinical profile of H1N1, H3N2, and flu B influenza in a sample of Iraqi patients: a retrospective study

Haider Noori Dawood[1], Sinan Ghazi Mahdi[2], Ayad Kareem Hwayyiz[3]

ABSTRACT

INTRODUCTION: Influenza infection is an acute viral respiratory disease that can result in severe complications, which may lead to about 650,000 deaths per year.

OBJECTIVE: To describe the epidemiological characteristics, outcomes of influenza type A (H1N1, H3N2) and type B.

METHODS: A retrospective study of 554 patients with H1N1, H3N2, and Flu type B influenza, between the 1\1\ 2019 and 28\12\ 2019. From the medical records in Centre for Disease Prevention and Control (CDC). The diagnosis made by polymerase chain reaction (PCR). Demographic and clinical information include the address of patients (Governorates), occupational history, history of contact with birds, the date of infection happened (months of the year), also the outcome of patients (admitted to hospital and discharged well, admitted to hospital& death, outpatient treatment).

RESULTS: 554 patients involved in the study classified into 5 groups: H1N1 347 patients (62.64%), Flu B 135 patients (24.37%), H3N2 59 patients (10.65%), H1N1 & Flu B 9 patients (1.62%), and H3N2 & Flu B 4 patients (0.72%).The highest age group in those under 5 and ≥ 60 Years in all viral groups except H3N2 & Flu B. male 53.4% is higher than female 46.6%. Self-employed 23.5% and student/child 26.2% are higher occupation rate. Only 2.5 % has history of contact to birds. The highest incidence in Baghdad 37.7%. The highest incidence in December 65.3%. The outcome death is 5.6%.

CONCLUSION: In 2019 season HiN1 was the highest incidence, male is slightly higher than female. Age extremities are higher groups. Baghdad has more incidence than other government. In December more than other months.

Key words: Influenza, H1N1, H3N2, Flu B.

INTRODUCTION

Seasonal or epidemic outbreak of the influenza viruses is a most common cause of the respiratory infections in humans, recently there are different strains have been identified.[1] Influenza is caused by one of four viruses; influenza A, B, C and D.[2] Influenza A and B are responsible for the vast majority of the deaths.[3]

Influenza virus type A is a member of Orthomyxoviridae family, which is an enveloped virus with the negative-sense, has single-stranded RNA genome that is organized in eight gene segments, encode at least eleven proteins. Genetic and antigenic diversity of the two surface glycoproteins are the haemagglutinin (HA) and neuraminidase (NA), used to classify the type A influenza viruses into many subtypes; 18 HA and 11 NA subtypes which are known to date.[4,5] The natural reservoirs of the Influenza A viruses known as aquatic wild birds (order Charadriiformes or Anseriformes), viruses can spill over to the susceptible host as terrestrial birds and the mammals includes humans.[6] Complex interactions between the viral, host, and environmental factors which determine transmissibility and susceptibility of Influenza A viruses.[7]

Continuous evolution of Influenza virus type A is not the risk confined to particular species. The human outbreaks by a zoonotic and pandemic influenza virus at animal human

1 MBCHB. FIBM, FIBM (Resp.), Consultant internist & pulmonologist, Al-Imamein Al- Kadhimein Medical City, Al-Kharkh Health Directorate, Baghdad, Iraq.
2 MBCHB. FICMS Community Medicine, Schistosomiasis and STH Section/ CDC- Baghdad\Iraq.
3 MBCHB. High Diploma Field Epidemiology\Baghdad Field Epidemiology Training Program \ CDC Atlanta_USA Baghdad, Iraq.
Corresponding Author: **Haider Noori Dawood**, Al-Imamein Al- Kadhimein Medical City, Al-Kharkh Health Directorate, Baghdad, Iraq. **E mail:** haider_noori2001@yahoo.com.

borders occurring worldwide with the regular seasonal flu outbreaks and human influenza viruses introduced to the swine by reverse zoonosis.[8] Large pools of influenza viruses are covering all known subtypes in the wild birds especially ducks and geese, which function as a reservoir for influenza viruses in the birds and mammals.[9]

The first H1N1 influenza pandemic happened in 2009 in the USA. The Centers for Disease Control and Prevention (CDC) estimates the global death in 2009 was more than 284,000.[10] Then the infection with this virus has been spread and reported in 191 countries.[11]

H1N1 influenza can cause severe illness that requiring admissions. The major cause of death are viral bronchopneumonia and ARDS. High suspicion index, prompt treatment with oseltamivir and mechanical ventilation had role in reducing mortality.[12] Diagnosis requires clinical, and epidemiological data as any other virus can cause influenza-like illness. It can be confirmed by laboratory data. Hence, the treatment should not be delayed at any cost. Those with comorbid illnesses get more severe and fatal illness. Rapid deterioration can occur in any patient in a few hours' time. The incubation period for the H1N1 virus is approximately 2 - 7 days, the infection usually affects young and middle age.[13] Infected patient's present symptoms such as sudden onset of fever, chills, sore throat, headaches, malaise, dry cough, and sometimes gastrointestinal symptoms such as diarrhoea, nausea, and vomiting.[14]

Detection of the influenza virus may reduce unnecessary laboratory tests for other aetiologies and the inappropriate use of antibiotic, also improve effectiveness of the infection prevention and control measures, in addition to increase the use of appropriate antiviral drugs.[15]

There are three circulating subtypes type A/H1N1, A/H3N2 and type B, which are well known as influenza viruses that can infect humans causing massive and rapidly global epidemics.[16]

The objectives of this study is to describe the epidemiological characteristics, outcome of influenza type A (H1N1, H3N2) and type B, in CDC office / Ministry of Health in Baghdad in 2019.

METHODS

Setting and study design: A retrospective study of 554 adults and paediatric proved to have infection with H1N1, H3N2, and Flu type B influenza was undertaken between the first of January 2019 and twenty-eight of December 2019. From the medical records in Centre for Disease Prevention and Control (CDC) office / Ministry of Health in Baghdad in which all the registered infectious diseases send to this centre.

Inclusion criteria: All patients who has positive results for H1N1, H3N2, and Flu type B influenza by PCR test.

Exclusion criteria: Patients with incomplete data in his medical record, and those with negative test for H1N1, H3N2, and Flu type B influenza were excluded from the study.

Definitions of the outcomes: The diagnosis of H1N1, H3N2, and Flu type B infection were made locally by polymerase chain reaction (PCR) in a respiratory sample; sputum or nasopharyngeal swab where a flexible, fine-shafted polyester swab is inserted into the nostril and back to the nasopharynx and left in place for a few seconds. It is then slowly withdrawn with a rotating motion. A second swab should be used for the second nostril. The tip of the swab is put into a vial containing 2–3 ml of virus transport medium and the shaft cut.

Data collected locally by review of medical records of all microbiologically confirmed cases in the participating centre. Demographic and clinical information which include the province of residence, occupational history, history of contact with birds, month of infection, in addition to the outcome of patients distributed as admission to hospital and discharged well, admission to hospital with death, and treatment as an outpatient. The patient were classified into five groups according to the type of virus infected: H1N1, Flu B, H3N2, and combined in-

Table 1| The mean age of patients confirmed with Flu B\ H1N1\ H3N2\ Combined Influenza Infection.

	N	Mean age (y)	Std. Deviation
Flu B	135	22.9	19.3
H1N1	347	37.3	23.8
H1N1 & Flu B	9	32.7	26.8
H3N2	59	44.2	24.2
H3N2 & Flu B	4	25.8	9.7
Total	554	34.4	23.8

fections H1N1 & Flu B, H3N2 & Flu B.

Statistical Analysis: Surveillance data were transferred from excel sheet to the statistical package for social sciences version 24 for analysis. Discrete variables presented as numbers and percentages and continuous variables presented as means with their standard deviation.

RESULTS

In this study 1157 patients with clinical features of influenza were tested during the study period, 554 of them tested positive for the following viral infections: H1N1 in 347 patients (62.64%), Flu B in 135 patients (24.37%), H3N2 in 59 patients (10.65%), H1N1 & Flu B in 9 patients (1.62%), and H3N2 & Flu B in 4 patients (0.72) as shown in table 1 and figure 1.

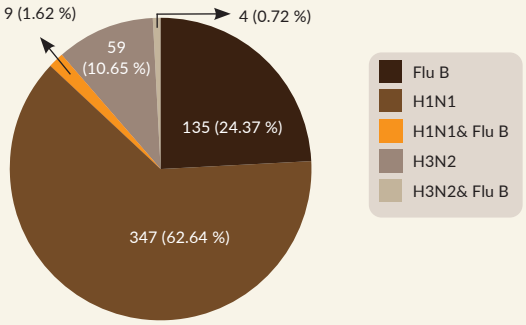

Figure 1| Pie chart showing the differential incidence of specific virus type

Table 2 shows some demographic features of patients infected with influenza viruses. The highest mean of age was reported with H3N2

Table 2 | Demographic features of Patients according to the type of viruses

Features		Flu B		H1N1		H1N1 & Flu B		H3N2		H3N2 & Flu B		All Types	
		N	%	N	%	N	%	N	%	N	%	N	%
	Mean±SD	22.9±19.3		37.3±23.8		32.7±26.8		44.2±24.2		25.8±9.7		34.4±23.8	
Age Group	Under 5	29	21.5	46	13.3	2	22.2	5	8.5	0	0.0	82	14.8
	5-9 Year	15	11.1	25	7.2	1	11.1	1	1.7	0	0.0	42	7.6
	10-19 Years	20	14.8	23	6.6	0	0.0	6	10.2	2	50.0	51	9.2
	20-29 Years	26	19.3	40	11.5	1	11.1	8	13.6	1	25.0	76	13.7
	30-39 Years	18	13.3	41	11.8	1	11.1	8	13.6	1	25.0	69	12.5
	40-49 Years	6	4.4	53	15.3	2	22.2	8	13.6	0	0.0	69	12.5
	50-59 Years	11	8.1	49	14.1	0	0.0	7	11.9	0	0.0	67	12.1
	≥ 60 Years	10	7.4	70	20.2	2	22.2	16	27.1	0	0.0	98	17.7
Sex	Male	60	44.4	199	57.3	4	44.4	31	52.5	2	50.0	296	53.4
	Female	75	55.6	148	42.7	5	55.6	28	47.5	2	50.0	258	46.6
Occupation	Employed	7	5.2	16	4.6	0	0.0	2	3.4	0	0.0	25	4.5
	Health profession	3	2.2	1	0.3	0	0.0	0	0.0	0	0.0	4	0.7
	Housewife	24	17.8	73	21.0	4	44.4	20	33.9	2	50.0	123	22.2
	Military	0	0.0	7	2.0	0	0.0	0	0.0	0	0.0	7	1.3
	Non specified	34	25.2	58	16.7	0	0.0	7	11.9	0	0.0	99	17.9
	Retired	1	0.7	19	5.5	0	0.0	1	1.7	0	0.0	21	3.8
	Self employed	16	11.9	90	25.9	2	22.2	21	35.6	1	25.0	130	23.5
	Student/child	50	37.0	83	23.9	3	33.3	8	13.6	1	25.0	145	26.2
Contact to birds	Yes	2	1.5	10	2.9	0	0.0	1	1.7	1	25.0	14	2.5
	No	133	98.5	337	97.1	9	100.0	58	98.3	3	75.0	540	97.5

Table 3 | Types of the viruses distributed in provinces.

Provinces	Flu B		H1N1		H1N1& Flu B		H3N2		H3N2 & Flu B		All Patients	
	N	%	N	%	N	%	N	%	N	%	N	%
Anbar	2	1.5	5	1.4	1	11.1	2	3.4	0	0.0	10	1.8
Babylon	7	5.2	12	3.5	0	0.0	1	1.7	0	0.0	20	3.6
Baghdad-Karkh	55	40.7	73	21.0	0	0.0	3	5.1	0	0.0	131	23.6
Baghdad-Resafa	25	18.5	50	14.4	1	11.1	2	3.4	0	0.0	78	14.1
Basrah	2	1.5	10	2.9	0	0.0	3	5.1	0	0.0	15	2.7
Dahuk	7	5.2	13	3.7	2	22.2	2	3.4	0	0.0	24	4.3
Diwaniya	2	1.5	3	0.9	0	0.0	1	1.7	0	0.0	6	1.1
Diyala	9	6.7	15	4.3	1	11.1	1	1.7	0	0.0	26	4.7
Erbil	0	0.0	10	2.9	0	0.0	3	5.1	0	0.0	13	2.3
Kerbala	0	0.0	14	4.0	0	0.0	5	8.5	0	0.0	19	3.4
Kirkuk	1	0.7	3	0.9	0	0.0	0	0.0	0	0.0	4	0.7
Missan	1	0.7	17	4.9	0	0.0	1	1.7	0	0.0	19	3.4
Muthanna	2	1.5	35	10.1	0	0.0	1	1.7	0	0.0	38	6.9
Najaf	10	7.4	16	4.6	1	11.1	4	6.8	0	0.0	31	5.6
Ninewa	1	0.7	24	6.9	0	0.0	1	1.7	0	0.0	26	4.7
Salah Al-Din	8	5.9	21	6.1	2	22.2	0	0.0	1	25.0	32	5.8
Sulaymaniyah	1	0.7	5	1.4	0	0.0	4	6.8	3	75.0	13	2.3
Thi-Qar	0	0.0	3	0.9	0	0.0	2	3.4	0	0.0	5	0.9
Wassit	2	1.5	18	5.2	1	11.1	23	39.0	0	0.0	44	7.9

influenza virus (44.2±24.2 years), while the lowest mean was reported with influenza B (22.9±19.3 years). H1N1and H3N2 are more common in males, while Influenza B alone or in combination with others are more common in females. Male gender is higher 53.4% than female 46.6%. The highest incidence (26.2%) was reported in student/child, while the least incidence was in health profession (0.7%). For history of contact with bird only 2.5%, as shown in table 2.

For governorates distribution of patients according to the type of viruses

The highest record of Flu B was in Baghdad Karkh (40.7%) and Resafa (18.5%), for H1N1 was in Baghdad Karkh (21.0%) and Resafa 14.4%), for H1N1 & Flu B was in Dahuk and

Table 4 | Distribution of patients in months of the year according to the type of viruses

Month	Flu B		H1N1		H1N1 & Flu B		H3N2		H3N2 & Flu B		All Patients	
	N	%	N	%	N	%	N	%	N	%	N	%
January	0	0.0	12	3.5	0	0.0	15	25.4	0	0.0	27	4.9
February	0	0.0	2	0.6	0	0.0	21	35.6	0	0.0	23	4.2
March	0	0.0	1	0.3	0	0.0	6	10.2	0	0.0	7	1.3
April	0	0.0	0	0.0	0	0.0	5	8.5	0	0.0	5	0.9
May	0	0.0	1	0.3	0	0.0	1	1.7	0	0.0	2	0.4
June	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	1	0.2
July	0	0.0	0	0.0	0	0.0	1	1.7	0	0.0	1	0.2
August	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	1	0.2
September	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
October	0	0.0	18	5.2	0	0.0	2	3.4	0	0.0	20	3.6
November	1	0.7	104	30.0	0	0.0	0	0.0	0	0.0	105	19.0
December	134	99.3	207	59.7	9	100	8	13.6	4	100	362	65.3

Table 5 | The outcome of patients according to the type of viruses

Outcome	Flu B		H1N1		H1N1 & Flu B		H3N2		H3N2 & Flu B		All Types	
	N	%	N	%	N	%	N	%	N	%	N	%
Death	5	3.7	24	6.9	0	0.0	2	3.4	0	0.0	31	5.6
Discharged well	90	66.7	264	76.1	8	88.9	55	93.2	4	100.0	421	76.0
Out Patient Treatment	40	29.6	59	17.0	1	11.1	2	3.4	0	0.0	102	18.4

Salah Al-Din (22.2%), for H3N2 the highest incidence was in Wassit (39%), and for H3N2 & Flu B the highest incidence was in Sulaymaniyah (75%). For all over types of influenza the highest incidence was in Baghdad (37.7%), while the least incidence was in Thi-Qar (0.9%), See table 3.

The highest incidence of Flu B, H1N1, and H1N1 & Flu B are reported in December (99.3 %), (59.7 %) and (100 %) respectively. While infection with H3N2 is more reported in February (35.6 %). For others see table 4.

Table 5 shows that 421 patents (76%) were treated in hospitals and discharged well. While 102 patients (18.4 %) were treated as an outpatient. The over all mortality of all those tested positive for influenza virus is 5.6 % (31 out of 554). H1N1 has reported the highest mortality 24 out of 347 patients (6.9 %). While the mortality is 0 % in combination of more than one virus.

DISCUSSION

In this study, 554 patients proved to have positive test for different types of viruses: H1N1 347 (62.64 %), Flu B 135 (24.37 %), H3N2 59 (10.65 %), H1N1 & Flu B 9 (1.62 %), H3N2 & Flu B 4 (0.72 %). The National Influenza Centres (NICs), and other national influenza laboratories from 122 countries, and areas reported data to the Flu Net for a period from 3 February 2020 to 16 February 2020. The WHO laboratories tested 201954 specimens during that period; 58268 were positive for the influenza viruses, of which 36 580 (62.8%) were influenza A and 21 688 (37.2%) were influenza B. For sub types of influenza A viruses, 7897 (66.5%) were influenza A (H1N1), and 3978 (33.5%) influenza A (H3N2).[17] Only 10 patients out of 447 with influenza were co-infected with two strains of influenza, 7 persons have influenza B and influenza A(H1N1), and 3 have influenza B and influenza A(H3N2).[18] These results were in approximate to ours, but H3N2 was higher than ours, This may be due to tendency of people from some countries to have indoor domestic animals such as dogs where H3N2 virus has been isolated.[19] The predictive accuracy for influenza in any setting may depend on the circulating influenza strains and other respiratory pathogens locally.[20] The diagnosis in this study depend on polymerase chain reaction (PCR), which is the recommended method by WHO.[21]

For the age group in this study, the highest incidence of overall influenza viruses were in those under 5 years and ≥ 60 years, and for flu B the highest incidence was also in those under 5 years (21.5%); this could be explained at least partially by the immune status of these age groups. Similarly, Xi-Ling study[22] also showed a high incidence in those less than 5 years and Beaute[23] has reported that the proportion of cases aged 0–14 years was higher. We found that H3N2 and H1N1 subtypes have a higher incidence in patients 60 years and above, 27.1 % and 20.2 % respectively. These results were also seen by Xi-Ling,[22] and Soheil[24] in their studies.

We found that male is slightly higher than female, 53.4 % versus 46.6 % in overall influenza infection, this agrees with the results of the United States of America (USA) where the incidence of infection with seasonal influenza viruses is higher in males (60% in the USA) than in females.[25] This may be explained by many factors, the male tend to be more active than female, therefore having higher risk of exposure to the environmental pathogens including influenza by close contact with the infected

people or touching of contaminated surface.[26] The sex steroid hormones have been long identified to modulate host immunity where androgens may lower and oestrogens may enhance several aspects of immunity.[27] Experiments on mice showed that males exhibited lower humoral and cell-mediated immune responses than females after viral infection.[28] Many studies have revealed that haemagglutinin inhibition titers consistently higher in women than the men after seasonal influenza vaccination, which suggesting better protection against influenza in women.[29] in addition, smoking rate is higher and vaccination rate is lower in men.[30] On subtypes level, we found that H1N1 is higher in male than in female, 57.3 versus 42.7, in agreement with that shown by Basavaraj[31] in his study. We also found that the proportion of female involvement with flu B is higher than in male, 55.6 versus 44.4 %. Kam[32] has reported that flu B is found in 52.6 %, especially in age groups between 20 to 74 years. This may be due to pregnancy related immune-suppression, immune responses can be suppressed during the menstrual cycle and pregnancy.[33] Regarding H2N2, we found that it is more common in male than in female, 52.5 % versus 47.5%. Similarly, Monique[34] has found that about 52.5 % of H3N2 is in male.

In our study, student/child has higher incidence (26.2%) of overall influenza infection, a study[35] showed children of 3 years of age were highly infected with influenza A and B viruses that might cause a high mortality rate. For subtypes, the highest incidence of H1N1 is reported in self-employed in 25.9%. Self-employed persons may work at many places and may expose to different levels of educated people and different hygiene levels. The highest flu B is in housewife 33.9%, this may be due to the care of their children who are highly infected with influenza viruses.[36] In this study, health profession has a low rate of flu infection though they are a risk group; this may be due to getting vaccine against influenza annually. In our series, only 2.5% of flu infected persons has a positive history of exposure to birds. Flu viruses spread mainly by droplets when the people with flu cough, sneeze or talk. These droplets can land in the mouths or noses of people then may inhale into the lungs. Less often, a person might get flu by touching a surface or object that contaminated with the flu virus.[37] Humans can be also infected with the influenza viruses that are circulating in animals, as avian influenza virus subtypes A (H5N1) and Ab (H9N2), and the swine influenza virus subtypes A (H1N1) and (H3N2).[38]

We reported that Baghdad is the highest governorate involved with flu infection; in Baghdad-Karkh it is 23.6% and in Baghdad-Resafa is 14.1%, this could be explained by the highest population density in Baghdad facilitating the transmission of Influenza virus. Baghdad is also the highest city involved with flu B and H1N1. These results are in agreement with that of Aufi study.[39] For H3N2, the highest rate was in Wasit 39.0%. Aufi in his study[39] has reported that the rate of infection with H3N2 is highest in Baghdad followed by Wasit.

We have seen that overall flu infection was highest in November and December, the coldest months of the year. Naeme[40] has showed that the peak incidence of flu occurred in December. Patients with Flu B, H1N1 manly recorded in December, in Nadira study [41] Influenza A (H1N1) activity in Iraq starts to increase in winter mainly in January. Also Nasser [42] has showed that December, January and February are the months mostly abundant with infection with H1N1. H3N2 in this study were mainly tested positive in January and February, 25.4% and 35.6% respectively. Aufi[39] reported H3N2 mainly in December and January. We also reported flu B mainly in December, while Aufi[39] has reported it mainly in January.

Of all tested positive with influenza viruses, 81.6% are treated at hospitals, 18.4% treated as an outpatient, and 5.6 % have died. The results of US influenza (type A H1N1, H3N2 and Flu B) associated deaths have been increased from 1976-1977 through 1998-1999.[42] In our study the highest incidence of death was with H1N1 (6.5%), followed by flu B (3.7%) and H3N2 (3.4%). In USA study influenza H3N2 viruses associated with highest mortality rates, followed by influenza B, and H1N1 viruses.[43] the difference in mortality rates may base on

statistical modelling of the national mortality, viral surveillance data, and annual estimation of influenza deaths.

Our study has many limitations as a retrospective study we were complied with only the available records. Many confounders like history of smoking, vaccination, and comorbidities were not included in the database.

CONCLUSION

In this study different influenza types have some similarities and differences in epidemiological characteristics and the outcome. H1N1 has highest incidence than H3N2 and Flu B. Age extremities groups are higher than other groups. Gender is differ according to type of virus but overall male is slightly higher than female. Most cases occurred in winter months. Baghdad has higher incidence than other governments. Most cases treated at hospital and discharged well.

REFERENCES

1. Sekar A, Begum N, and Margret A. An in silico study of lignans as 55 selective estrogen receptor modulators to treat viral infections. *International Research Journal of Biological Sciences*, 2019: 8(3): 19-25.
2. Hause BM, Ducatez M, Collin EA, Ran Z, Liu R, Sheng Z, et al. Isolation of a novel swine influenza virus from Oklahoma in 2011 which is distantly related to human influenza C viruses. *PLoS Pathog* 2013;9(2)e1003176.
3. Cox NJ, Subbarao K. Global epidemiology of influenza: past and present. *Annual Review of Medicine*, 2000; 51:407–421.
4. Tong S, Zhu X, Li Y, Shi M, Zhang J, Bourgeois M, et al. New World bats harbor diverse influenza A viruses. *PLoS Pathog*. 2013;9(10):e1003657.
5. Li Q, Sun X, Li Z, Liu Y, Vavricka CJ, Qi J, et al. Structural and functional characterization of neuraminidase-like molecule N10 derived from bat influenza A virus. *Proc Natl Acad Sci USA*. 2012;109(46):18897-902.
6. Webster RG, Govorkova EA. Continuing challenges in influenza. *Ann N Y Acad Sci* 2014;1323:115-39.
7. Cauldwell AV, Long JS, Moncorge O, Barclay WS. Viral determinants of influenza A virus host range. *J Gen Virol* 2014;95:1193-210.
8. Sung J. Taeyong K, Young S. Challenges of influenza A viruses in humans and animals and current animal vaccines as an effective control measure. *Clin Exp Vaccine Res* 2018;7:1-15.
9. Olsen B, Munster VJ, Wallensten A, Waldenström J, Osterhaus A D M E, Fouchier R AM. Global patterns of influenza A virus in wild birds. *Science* (2006); 312:384–388
10. Sullivan SJ, Jacobson RM, Dowdle WR, Poland GA. 2009 H1N1 influenza. *Mayo Clinic proceedings* 2010;85:64-76
11. Lee H-Y, Oh M-N, Park Y-S, Chu C, Son T-J. Public Health Crisis Preparedness and Response in Korea. *Osong Public Health Res Perspect* 2013;4:278-84.
12. Jacob K, Shiji K, Suma S, et al. Incidence and Outcome of H1N1 Cases in a Tertiary Care Hospital in South India: A Retrospective Observational Study. *International Journal of Scientific Study*. 2016;4:39–43.
13. Bhatt KN, Jethw SC, Bhadiyadar D, Patel D, Joshi K. Study of clinical profile in patients with H1N1 influenza in Surat district, June 2009– March 2010. *J Assoc Physicians India* 2012; 60: 15-9.
14. Ghebrehewet S, MacPherson P, Ho A. Influenza. *BMJ* 2016 Dec 7;355:i6258. doi: 10.1136/bmj.i6258.
15. Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza a. *Clinical Infectious Diseases*, 2019, 68.6: e1-e47.
16. Hillaire ML, van Eijk M, Vogelzang-van Trierum SE, Nieuwkoop NJ, van Riel D, Fouchier RA, et al. Assessment of the antiviral properties of recombinant surfactant protein D against influenza B virus in vitro. *Virus Res*. 2015 Jan 2;195:43-6. doi: 10.1016/j.virusres.2014.08.019. Epub 2014 Sep 6. PMID: 25200748.
17. WHO. Influenza update – 362. 02 March 2020 - Update number 362, based on data up to 16 February 2020. Available from: https://www.who.int/influenza/surveillance_monitoring/updates/2020_03_02_update_GIP_surveillance/en/
18. Timothy R., Beverly M., Cynthia K., et al. Relative Timing of Influenza Disease by Age Group. *Vaccine*. 2014 Nov 12; 32(48): 6451–6456.
19. Bunpapong N, Nonthabenjawan N, Chaiwong S, Tangwangvivat R, Boonyapisitsopa S, Jairak W, et al. Genetic characterization of canine influenza A virus (H3N2) in Thailand. *Virus Genes* 2014;48:56–63.
20. Jonathan Y, Chi Hsien T, Alex R, et al. Differing clinical characteristics between influenza strains among young healthy adults in the tropics. *BMC Infectious Diseases* 2012:12:12
21. World Health Organization (WHO). WHO information for molecular diagnosis of influenza virus in humans - update. Geneva: WHO; 2012. Available from: https://www.who.int/influenza/gisrs_laboratory/molecular_diagnosis_influenza_virus_humans_update_201211.pdf?ua=1
22. Xi-Ling W, Lin Y, Kwok-Hung Ch, et al. Age and Sex Differences in Rates of Influenza-Associated Hospitalizations in Hong Kong. *Am J Epidemiol*. 2015;182(4):335–344.
23. Beauté J, Zucs P, Korsun N, et al. Age-specific differences in influenza virus type and subtype distribution in the 2012/2013 season in 12 European countries. *Epidemiol. Infect.* (2015); 143: 2950–2958.
24. Soheil E, Arefeh B, Mahmoud Sadeghi-H, et al. Outcomes of Patients with Definitive Diagnosis of Influenza A (H1N1) Virus Infection Admitted to Affiliated Hospitals of Babol University of Medical Sciences, 2015 – 2016. *Acta facultatis medicae Naissensis* 2019; 36(4):356-364.
25. Szilagyi PG, Fairbrother G, Griffin MR, Hornung RW, Donau-

er S, Morrow A, et al. Influenza vaccine effectiveness among children 6 to 59 months of age during 2 influenza seasons: a case-cohort study. *Archives of Pediatrics & Adolescent Medicine*, 2008: 162:943–951.

26. Bridges CB Kuehnert MJ Hall CB. Transmission of influenza: implications for control in health care settings. *Clin Infect Dis*. 2003;378:1094–1101.

27. Klein SL. Hormones and mating system affect sex and species differences in immune function among vertebrates. *Behav Processes*. 2000;51(1-3):149–166.

28. Schuurs AH Verheul HA. Effects of gender and sex steroids on the immune response. *J Steroid Biochem*. 1990;352:157–172.

29. Keitel WA Atmar RL Cate TR et al. Safety of high doses of influenza vaccine and effect on antibody responses in elderly persons. *Arch Intern Med*. 2006;16610:1121–1127.

30. Wong CM Yang L Chan KPet al. Cigarette smoking as a risk factor for influenza-associated mortality: evidence from an elderly cohort. *Influenza Other Respir Viruses*. 2013;74:531–539.

31. Basavaraju J, Nagaraja Ch, Veeranna G, et al. Clinical Profile of Suspected and Confirmed H1N1 Influenza Infection in Patients Admitted at a Tertiary Care Teaching Hospital. *J Cardiothorac Med*. 2015;3(4):367370.

32. Kam Ch, Georgina M, Catherine H. Influenza infections in Australia 2009–2015: is there a combined effect of age and sex on susceptibility to virus subtypes? *BMC Infectious Diseases* (2019);19:42.

33. Giefing-Kröll C, Berger P, Lepperdinger G, Grubeck-Loebenstein B. How sex and age affect immune responses, susceptibility to infections, and response to vaccination. *Aging Cell*. 2015; 14(3):309–21.

34. Monique M, David B, Michael W, et al. Influenza A(H3N2) Variant Virus Outbreak at Three Fairs - Maryland, 2017. *MMWR*, 2018: 67(42);1169–1173.

35. Centers for Diseases Control and Prevention (CDC). Influenza Vaccination Information for Health Care Workers. 2018. Available at: https://www.cdc.gov/flu/professionals/index.htm.

36. Centers for Diseases Control and Prevention (CDC). How Flu Spreads. August 27, 2018. Avialble at: https://www.cdc.gov/flu/about/disease/spread.htm.

37. Sara M, Erik N, Joshua J. The effects of employment on influenza rates. *Economics & Human Biology*. 2019; 34: 286-295.

38. Word Health Organization. Influenza virus infections in humans October 2018. Available from: https://www.who.int/influenza/human_animal_interface/virology_laboratories_and_vaccines/influenza_virus_infections_humans_Oct_18.pdf.

39. Aufi I M, Fadhil H Y, Ali A W, et al. Epidemiology Of Seasonal Influenza Outbreak Among Iraqi Population:2018. *Iraqi Journal of Agricultural Sciences* –2020:51(1):454-461.

40. Naeme J, Abdolvahab M, Alijan T, Masoud B. Clinical and Epidemiological Profile of Pandemic Influenza A H1N1, H3N2, and Type B in the South east of Caspian Sea, Iran. *Jundishapur J Microbiol*. 2017 March;10 (3):e35616.

41. Nadira S, Sabah M, Mohammad J, et al. Molecular Detection of Pandemic Influenza A(H1N1) Virus in SARI Patient in South Iraq Governorates using Real-Time PCR. *Iraqi Journal of Biotechnology*, 2016; 15: 9-20.

42. Nasser FG, Mohamed NS, Al-Jassani MJ, AufimI, M, Ahmed MA, Ali K, Dafi I H, Najim A T, Mohamed N and Ghlaim I (2015). Detection of pandemic influenza A H1N1 virus in central Iraq using Real-time PCR. CurrRes. *Microbiol. Biotechnol* ;3:694-700.

43. Thompson WW, Shay DK, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. *JAMA*. 2003;289(2):179–186.

Abbreviations list: Acute respiratory distress syndrome (**ARDS**), Disease Control and Prevention (**CDC**), Haemagglutinin (**HA**), National Influenza Centers (**NICs**), Neuraminidase (**NA**), Polymerase chain reaction (**PCR**), Ribonucleic acid (**RNA**), Standard deviation (**SD**), United States of America (**USA**), World Health Organization (**WHO**).

Conflict of interest: Authors have nothing to declare.

Funding: Authors received no funds to complete this study a part from self funding.