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Journal of Clinical Virology 58 (2013) 568–570

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Short communication

Age-specific and sex-specific morbidity and mortality from avian influenza A(H7N9)

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ARTICLE INFO

Article history:
Received 25 June 2013
Received in revised form 30 August 2013
Accepted 3 September 2013

Keywords:
Age-specific
Avian influenza
A(H7N9)
A(H5N1)
Emerging diseases
Zoonoses

ABSTRACT

We used data on age and sex for 136 laboratory confirmed human A(H7N9) cases reported as of 11 August 2013 to compare age-specific and sex-specific patterns of morbidity and mortality from the avian influenza A(H7N9) virus with those of the avian influenza A(H5N1) virus. Human A(H7N9) cases exhibit high degrees of age and sex bias: mortality is heavily biased toward males >50 years, no deaths have been reported among individuals <25 years old, and relatively few cases documented among children or adolescents. The proportion of fatal cases (PFC) for human A(H7N9) cases as of 11 August 2013 was 32%, compared to a cumulative PFC for A(H5N1) of 83% in Indonesia and 36% in Egypt. Approximately 75% of cases of all A(H7N9) cases occurred among individuals >45 years old. Morbidity and mortality from A(H7N9) are lowest among individuals between 10 and 29 years, the age group which exhibits the highest cumulative morbidity and case fatality rates from A(H5N1). Although individuals <20 years old comprise nearly 50% of all human A(H5N1) cases, only 7% of all reported A(H7N9) cases and no deaths have been reported among individuals in this age group. Only 4% of A(H7N9) cases occurred among children < 5 years old, and only one case from the 10 to 20 year age group. Age- and sex-related differences in morbidity and mortality from emerging zoonotic diseases can provide insights into ecological, economic, and cultural factors that may contribute to the emergence and proliferation of novel zoonotic diseases in human populations.

1. Background

A novel multiple-reassortant avian influenza A (H7N9) emerged into human populations in China during 2013. The first human cases were first detected in China during March 2013, with at least one case retroactively identified as having occurred during February 2013. A total of 136 laboratory-confirmed human infections and 44 fatalities associated with this outbreak were reported as of 11 August 2013, with the most recent case showing signs of disease reported on 3 August 2013.

Phylogenetic analyses have determined that the A(H7N9) virus was derived from at least four progenitor viruses: the six internal genes from at least two different H9N2 chicken viruses, the haemagglutinin from domestic duck virus, and the neuraminidase from a virus of domestic duck or wild bird origin [1,2]. To date, the A(H7N9) virus has been identified from environmental samples and several different poultry species (chickens, ducks, pigeons, quail) collected in live bird markets, but not from any free-living wild bird species. Human and avian A(H7N9) viruses exhibit high degrees of sequence similarity, even though the virus has already diversified into several different lineages [2].

The A(H7N9) outbreak appears to have been brought under control through a concerted response effort by veterinary and medical health authorities in China that included intensive surveillance for new human cases; retrospective testing of potential earlier cases; surveillance and testing of birds in poultry markets; and closing and disinfection of live poultry markets.

2. Objectives

We identified and analyzed the age and sex of reported human A(H7N9) cases in order to compare the human morbidity and

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http://dx.doi.org/10.1016/j.jcv.2013.09.004

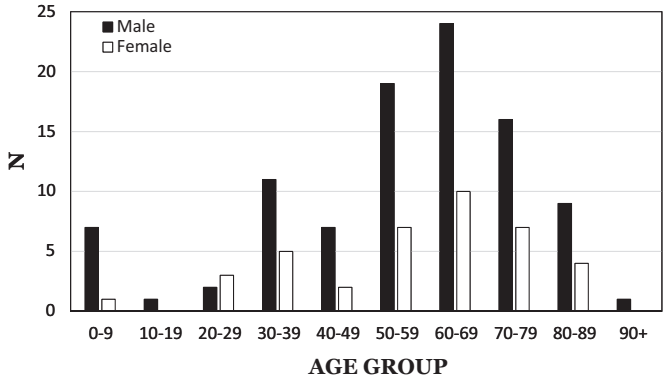

Fig. 1. The age and sex distribution of influenza A(H7N9) virus cases, including fatal and non-fatal outcomes worldwide, during 2013 ($n = 136$).

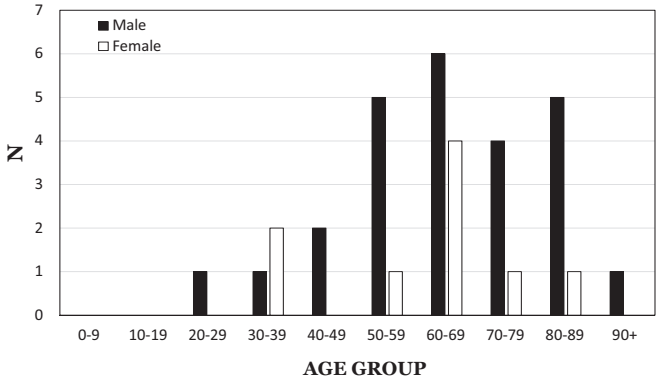

Fig. 2. The age and sex distribution of influenza A(H7N9) virus fatal outcomes during 2013 ($n = 34$, no data available for 10 cases).

All cases			
Age	Total	Male	Female
0–9	8	7	1
10–19	1	1	0
20–29	5	2	3
30–39	16	11	5
40–49	9	7	2
50–59	26	19	7
60–69	34	24	10
70–79	23	16	7
80–89	13	9	4
90+	1	1	0
	136	97	39

Fatalities			
	Total	Male	Female
0–9	0	0	0
10–19	0	0	0
20–29	1	1	0
30–39	3	1	2
40–49	2	2	0
50–59	6	5	1
60–69	10	6	4
70–79	5	4	1
80–89	6	5	1
90+	1	1	0
	34	25	9

mortality patterns of A(H7N9) influenza with those of A(H5N1) influenza, to identify risk factors for human morbidity and mortality, and provide possible insights into environmental and behavioral exposure and infection mechanisms.

3. Study design

We collected data on the age, sex, dates of hospitalization and/or death, area of origin, and occupation for 136 laboratory-confirmed A(H7N9) cases from reports published by the China Centers for Disease Control (CCDC), World Health Organization (WHO), Xinhua, and private sector news media outlets based in mainland China as of 11 August 2013. This total includes two cases not identified in the official CCDC case count ($n = 134$): one asymptomatic case confirmed from a 4-year-old boy in Beijing [3], and one symptomatic case in Taiwan involving a 53-year-old man recently returned from travel to mainland China [4].

4. Results

The age and sex distribution of A(H7N9) cases and fatalities are shown in Figs. 1 and 2. The observed patterns of age and sex bias among A(H7N9) cases are notable in a number of respects:

- PFC for reported infections is 32% ($n = 44/136$).
- 75% of cases of all cases occurred among individuals >45 years ($n = 103/136$);
- 71% of all cases were male (97 of 136);
- male:female ratio among cases ≥60 years was 2.4–1 (50♂, 21♀);
- 74% of all fatalities of known sex were male ($n = 25/44$);
- 7% of cases, none of which were fatal, were individuals <20 years old (9/136);
- 4% of cases were in children 0–4 years old (5/136);
- One case was documented among individuals between 10–20 years old.

5. Discussion

The epidemiological characteristics of the recent outbreak of A(H7N9) in China appear to differ from those due to any other zoonotic influenza, seasonal influenza or pandemic influenza. Most patients initially developed influenza-like illness that progressed to acute respiratory distress syndrome (ARDS) resulting in hospitalization and/or death [5]. There are evident high degrees of age and sex bias among A(H7N9) cases: mortality is heavily biased toward males >50 years; no deaths have been reported among individuals <25 years old; and relatively few cases reported among children and adolescents. While PFC for A(H7N9) infections (32%) is much lower than that for A(H5N1) in China (66%) and Indonesia (83%) [6], it is of comparable magnitude to that for A(H5N1) in Egypt and Turkey (33–36%).

Age and sex differences in morbidity and mortality of A(H7N9) cases in China were evident during the initial phase of the outbreak, with the risk of serious illness more than 5 times higher for persons ≥65 years old than for younger individuals [7]. Analyses conducted during April 2013 determined that [8,9]:

- <3% cases involved individuals 0–4 years old (2/82);
- >70% of documented cases were male;
- male:female ratio among cases ≥60 years was approximately 3.3:1 (30♂:9♀);
- the PFC for all cases, males, and females was 22% (10/45♂; 4/18♀);
- PFC in males ≥60 years was 20% (6/30), with no fatalities among females ≥60 years (0/9).

Our data for the 136 cases documented as of 11 August 2013 show that the age- and sex-specific patterns of morbidity and mortality documented early in the A(H7N9) outbreak have remained largely unchanged: males comprise 71% of all cases (97 of 136), and 74% of all fatalities of known sex ($n = 25/44$). The male:female ratio among cases ≥60 years remains heavily biased toward males, with a ratio of 2.4–1 (50♂, 21♀).

Previous analyses by Cowling and colleagues documented marked differences between the age and sex-specific mortality of human A(H7N9) and those of A(H5N1) avian influenza cases in China, with a higher degree of infection risk for males only among cases from urban areas [7,10]. Our analysis shows that the age-specific and sex-specific patterns of morbidity and mortality from A(H7N9) exhibit even greater disparities with those of A(H5N1) from countries other than China. Although individuals less than 20 years old comprise nearly 50% of human A(H5N1) cases worldwide [11], only 8% of A(H7N9) cases with data available, and no deaths, were reported from this age group. The 20–29 age group, which includes only 4% of A(H7N9) cases, comprises 22.4% of all A(H5N1) cases reported since 2003 [12]. Only one case of A(H7N9) has been documented among individuals 10–19 years of age, the age group with the highest cumulative PFC (74%) from A(H5N1). Age and sex-specific patterns of morbidity and mortality from A(H7N9) exhibit the greatest disparities with A(H5N1) cases in Egypt, where infection and death rates are highest among females, and relatively few cases occur among individuals >40 years old [13,14]:

- <3% of fatalities among individuals >45 years of age ($n = 5/170$ as of 3 February 2013) [15],
- Female deaths outnumber males by a factor of approximately 3–1 (41♀; 14♂) [16].

Interestingly, as of 11 August 2013, there are marked parallels in the observed patterns of human morbidity and mortality from influenza A(H7N9) and those of the novel Middle East respiratory syndrome coronavirus (MERS-CoV). The majority of reported MERS-CoV patients have exhibited respiratory symptoms, and most MERS-CoV cases are hospitalized with severe ARDS, as was the case for nearly all reported influenza H7N9 cases [17]. The median age of MERS-CoV patients is 55 years (range: 2–94), versus a median for H7N9 of 60 years (range 2–91). The MERS-CoV had a male: female case ratio in those older than 60-years of 2.3–1, while that of H7N9 was 2.4–1. Only 4 of 95 (4.2%) MERS-CoV cases were individuals aged <24 years [17,18]. More than 50% of all A(H7N9) cases had underlying conditions, and most fatal cases MERS-CoV also have pre-existing medical conditions [18–20]. While existing chronic disease conditions are recognized as a significant risk factor for human infections by A(H7N9) and MERS-CoV, this has not been the case for the A(H5N1) virus in China or eslewhere [21]. However, the cumulative PFC for MERS-CoV (47%) is more similar to that of H5N1 (59%) than that of H7N9 (22%).

The underlying causes of age and sex-related differences in morbidity and mortality which govern the demographic impacts of emerging zoonotic diseases in human populations are often unknown or uncertain, and can be associated with physiological factors that increase susceptibility, or behavioral and cultural factors that mediate rates of exposure to infected animals or fomites. We hope that this analysis will stimulate further interest in identifying and evaluating environmental, ecological, economic and cultural factors that may contribute to the emergence and proliferation of novel zoonotic pathogens within and among human populations worldwide.

Funding

None.

Competing interests

None declared.

Ethical approval

Not required.

References

[1] Shi JZ, Deng GH, Liu PH, Zhou JP, Guan LZ, Li WH, et al. Isolation and characterization of H7N9 viruses from live poultry markets – implication of the source of current H7N9 infection in humans. China Sci Bull 2013, http://dx.doi.org/10.1007/s11434-013-5873-4.
[2] Liu D, Shi W, Shi Y, Wang D, Xiao H, Li W, et al. Origin and diversity of novel avian influenza A H7N9 viruses causing human infection: phylogenetic, structural, and coalescent analyses. Lancet 2013;381(9881):1926–32.
[3] World Health Organization. China – WHO Joint Mission on Human Infection with Avian Influenza A(H7N9) Virus 18–24 April 2013 Mission Report. Geneva: World Health Organization; 2013. http://www.who.int/influenza/human_animal_interface/influenza_h7n9/ChinaH7N9JointMissionReport2013u.pdf
[4] Chang SY, Lin PH, Tsai JC, Hung CC, Chang SC. The first case of H7N9 influenza in Taiwan. Lancet 2013 May 11;381(9878):1621, http://dx.doi.org/10.1016/S0140-6736(13)60943-5 [Epub 29 April 2013].
[5] World Health Organization. Overview of the emergence and characteristics of the avian influenza A(H7N9) virus 31 May 2013; 2013. http://www.who.int/influenza/human_animal_interface/influenza_h7n9/WHO_H7N9_review_31May13.pdf
[6] Ke Y, Wang Y, Zhang W, Huang L, Chen Z. Deaths Associated with Avian Influenza A(H7N9) Virus in China. Ann Intern Med 2013, http://dx.doi.org/10.7326/0003-4819-159-2-201307160-00669 [Epub 4 June 2013].
[7] Cowling BJ, Freeman G, Wong JY, Wu P, Liao Q, Lau EH, et al. Preliminary inferences on the age-specific seriousness of human disease caused by avian influenza A(H7N9) infections in China, March to April 2013. Eurosurveillance 2013;18(19). Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20475, pii: 20475.
[8] Arima Y, Zu R, Murhekar M, Vong S, Shimada T. World Health Organization Regional Office for the Western Pacific Event Management Team. Human infections with avian influenza A(H7N9) virus in China: preliminary assessments of the age and sex distribution. Western Pacific Surveil Resp J 2013;4(2):1–3. http://www.wpro.who.int/wpsar/volumes/04/2/2013_PE_EMT_Arima/en/index.html
[9] Li Q, Zhou L, Zhou M, Chen Z, Li F, Wu H, et al. Preliminary report: epidemiology of the avian influenza A (H7N9) outbreak in China. N Engl J Med 2013;(April). http://www.nejm.org/doi/full/10.1056/NEJMoa1304617 [Epub ahead of print].
[10] Cowling BJ, Jin L, Lau EHY, Liao Q, Wu P, Jiang H. Comparative epidemiology of human infections with avian influenza A H7N9 and H5N1 viruses in China: a population-based study of laboratory-confirmed cases. Lancet 2013;(June) [Epub ahead of print].
[11] Oner AF, Dogan N, Gasimov V, Adisasmito W, Coker R, Chan PKS, et al. H5N1 Avian Influenza in Children. Clin Infect Dis 2012;55(1):26–32.
[12] World Health Organization – Western Pacific Regional Office. Avian Influenza A (H5N1) Weekly Update Number 384; May 2013. http://www.wpro.who.int/emerging_diseases/AIWeekly384.24May2013.pdf
[13] Dudley JP. Age-specific infection and death rates for human A(H5N1) avian influenza in Egypt. Eurosurveillance 2009;14(18):19198. http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19198
[14] Kayali G, Webby RJ, Ducatez MF, El Shesheny RA, Kandeil AM, Govorkova EA, et al. The Epidemiological and Molecular Aspects of Influenza H5N1 Viruses at the Human-Animal Interface in Egypt. PLoS ONE 2011;6(3):e17730, http://dx.doi.org/10.1371/journal.pone.0017730.
[15] World Health Organization. Update on human cases of influenza at the human–animal interface, 2012. Weekly Epidemiological Record 2013;88(13):137–44. http://www.who.int/wer/2013/wer8813.pdf
[16] World Health Organization – Eastern Mediterranean Regional Office. New Case of Avian Influenza A(H5N1) in Egypt. Weekly Epidemiological Monitor 2013;6(05). http://applications.emro.who.int/dsaf/epi/2013/Epi_Monitor_2013_6_5.pdf [03 February 2013].
[17] Gao R, Cao B, Hu Y, Feng Z, Wang D, Hu W, et al. Human infection with a novel avian-origin influenza A (H7N9) virus. N Engl J Med 2013;368(20):1888–97. http://www.nejm.org/doi/full/10.1056/NEJMoa1304459
[18] Centers for Disease Control and Prevention. Update: severe respiratory illness associated with middle east respiratory syndrome coronavirus (MERS-CoV) — Worldwide, 2012–2013. Morb Mort Wkly Rep 2013;62(early release):1–4. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm62e0607a1.htm
[19] European Centers for Disease Control and Prevention. Rapid Risk Assessment: Severe Respiratory Disease Associated with Middle East respiratory Syndrome Coronavirus (MERS-CoV); 2013, May. http://www.ecdc.europa.eu/en/publications/publications/risk-assessment-middle-east-respiratory-syndrome-coronavirus-mers-cov-17-may-2013.pdf
[20] Kingdom of Saudi Arabia – Ministry of Health. Three New Cases of Coronavirus Recorded in Al-Ahsa and the Eastern Region and One Case Passed Away in Hafr Al-Batin.http://www.moh.gov.sa/en/HealthAwareness/Corona/PressReleases/Pages/MediaStatement-2013-06-12-001.aspx
[21] Ai J, Huang Y, Xu K, Ren D, Qi X, Ji H, et al. Case–control study of risk factors for human infection with influenza A(H7N9) virus in Jiangsu Province, China, 2013. Eurosurveillance 2013;18(26). http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20510, pii: 20510.