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Seasonality of avian influenza A(H7N9) activity and risk of human A(H7N9) infections from live poultry markets

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Dear editor

We read with interest the letter by Yang et al. reporting a human case of influenza A(H7N9) infection during summer in the first epidemic wave in China, 2013.[1] Since then, human H7N9 infections were sporadically identified during summer.[2] Winter 2014/15 saw a third epidemic wave of human infections with A(H7N9) avian influenza viruses (AIVs) in China, following Spring 2013 and Winter-spring 2013/2014. As visiting LPMs which were contaminated by A(H7N9) was identified as a major risk factor for human infections,[3] understanding AIV activity in poultry will further describe human infection risk at different times. While AIV subtype such as H5, exhibited clear seasonality in China,[4] the seasonality of A(H7N9) virus activity in poultry has not been previously characterized.

Retail and wholesale markets are two major types of LPMs in China. The retail LPMs typically process significantly less numbers of poultry when compared to the wholesale

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Conflict of interest

BJC has received research funding from MedImmune Inc and Sanofi Pasteur and consults for Crucell NV.

Authors' contribution

Jie Wu, Jinyan Lin and Changwen Ke designed the study. Lirong Zou, Hongbin Zhang, Yinchao Song and Guofeng Huang collected and collated the data. Eric HY Lau and Hongbin Zhang analyzed the data. Jie Wu, Eric HY Lau, Hui-Ling Yen, Qinbin Xing and Haojie Zhong interpreted the data. Jie Wu, Eric HY Lau, Min Kang and Hui-Ling Yen drafted the manuscript. Benjamin J Cowling and Qinbin Xing edited the manuscript. All authors reviewed and revised the manuscript.

markets, favor mixing of different poultry species and may support extended holding time for unsold poultry. It is possible that the different settings at retail or wholesale LPMs may lead to different AIV dynamics and risks for human A(H7N9) infections. To monitor AIV activity, environmental surveillance at the LPMs has been implemented by the Guangdong Provincial Center for Disease Control and Prevention since 2005. In response to the A(H7N9) epidemic in humans, enhanced environmental surveillance at multiple human-poultry interfaces including retail and wholesale LPMs and poultry farms has been progressively implemented since April 2013. We characterized the seasonality of circulating AIV subtypes H7 and H9 and investigated the link between AIV activity at the human-poultry interface with the incidence of human A(H7N9) infections in Guangdong province from 2013–2015.

From January 2011 to April 2015, 26,935 environmental swab samples were collected monthly from 345 retail LPMs, 24 wholesale LPMs, and 15 poultry farms distributed in 21 cities in Guangdong province as described.[5] The median monthly number of samples collected were 99 (range: 25–2,932), 40 (range: 9–403) and 42 (range: 8–141) for retail, wholesale LPMs and farms respectively. Samples collected for the purpose of investigation of human H7N9 cases were excluded in this study. During 2011–2014 with complete annual data, the highest influenza A positive rates were detected at the retail LPMs, ranging from 29.4 – 41.9%, followed by 0.0 – 24.9% at the wholesale LPMs, and 0.3 – 4.4% at the poultry farms (Table 1). All specimens positive for influenza A virus M gene were further subtyped (H9 or H7) using gene specific primers and probes designed by China CDC.[6] Overall, we observed that the detection rate for influenza A virus of H9 subtype at the retail LPMs were comparable from 2011 to 2014, ranging from 13.3–20.1% (Table 1). Consistent with the surveillance data reported previously, no influenza A virus of H7 subtype was detected in the LPMs in Guangdong prior to April 2013,[7] with increased detection rates noted in winter 2013–2014 and 2014–2015 (Figure 1A).

We explored the seasonality of influenza A virus subtypes H7 and H9 using the positive rates detected at the retail and wholesale LPMs from August 2013 – April 2015, by fitting linear regression models with trigonometric terms. Data from April-July in 2013 were excluded as the presence of H7 during this period most likely reflected the introduction of H7 into the poultry in Guangdong, rather than seasonality. Based on two years of data, we estimated that H7 positive rates peaked in March, with an indication that H7 activities are in phase in retail LPMs (estimated peak at 3.1 month) and wholesale LPMs (estimated peak at 3.0 month). There was no obvious seasonality for H9 virus at the wholesale LPMs, but at retail LPMs there was peak activities around November (estimated peak at 10.9 month). Overall, the results support seasonality for the H7N9 virus in poultry markets, which peaked around March in Guangdong since the virus has been established locally in 2013.

To assess the impact of the presence of H7N9 at the poultry-human interface on human infection, we fitted negative binomial regression models to link the monthly number of H7N9 human cases to H7 positive rates at the retail and wholesale LPMs. We restricted the analysis to April 2013 to April 2015 when H7 was detected. H7 was not detected at the poultry farms in the whole study period. Human H7N9 infections were significantly associated with H7 detection rates at the retail LPMs (relative risk (RR)=1.60, 95% CI,

1.38–1.86) but not associated with that at the wholesale LPMs (RR= 1.16, 95% CI, 0.96–1.41) (Figure 1A). A sensitivity analysis excluding 6 H7N9 cases with occupational exposure obtained similar results. Similar analysis on monthly H9 positive rates found negative association in retail LPMs (RR=0.88, 95% CI, 0.80–0.96) and no significant association (RR=1.04, 95% CI, 0.97–1.12) with wholesale LPMs (Figure 1B). Of note, there was a moderate negative association (spearman correlation $\rho = -0.50$) between H7 and H9 detection rates in retail LPMs, but a moderate positive association ($\rho = 0.64$) in wholesale LPMs. Overall, the data suggests that the retail but not the wholesale LPMs are strongly associated with human H7N9 infection risk.

We found that A(H7N9) virus activity peaked around March in both retail and wholesale LPMs, which is considerably later than the usual peak of A(H5N1) virus in December – January in China.[4] While poultry exposure confers significant risk for human infections of avian influenza, contact with own backyard poultry is associated with increased risk for infection of A(H5N1) but not for A(H7N9).[3] Our results highlight the A(H7N9) activity over winter extending to spring, and the noticeable differential human infection risk to the H7N9 detection rate in retail and wholesale LPMs. The peak timing of A(H7N9) activity was different from other AIVs such as A(H5N1)[4, 8] and human seasonal influenza.[9] Hence, vigilance in control measures and surveillance in LPMs should be maintained over spring. Given the synchrony of H7 detection in retail and wholesale LPMs but low detection in farms, concerted control measures should be implemented in both LPM settings. Long-term control strategy should also identify the key sites for viral amplification.

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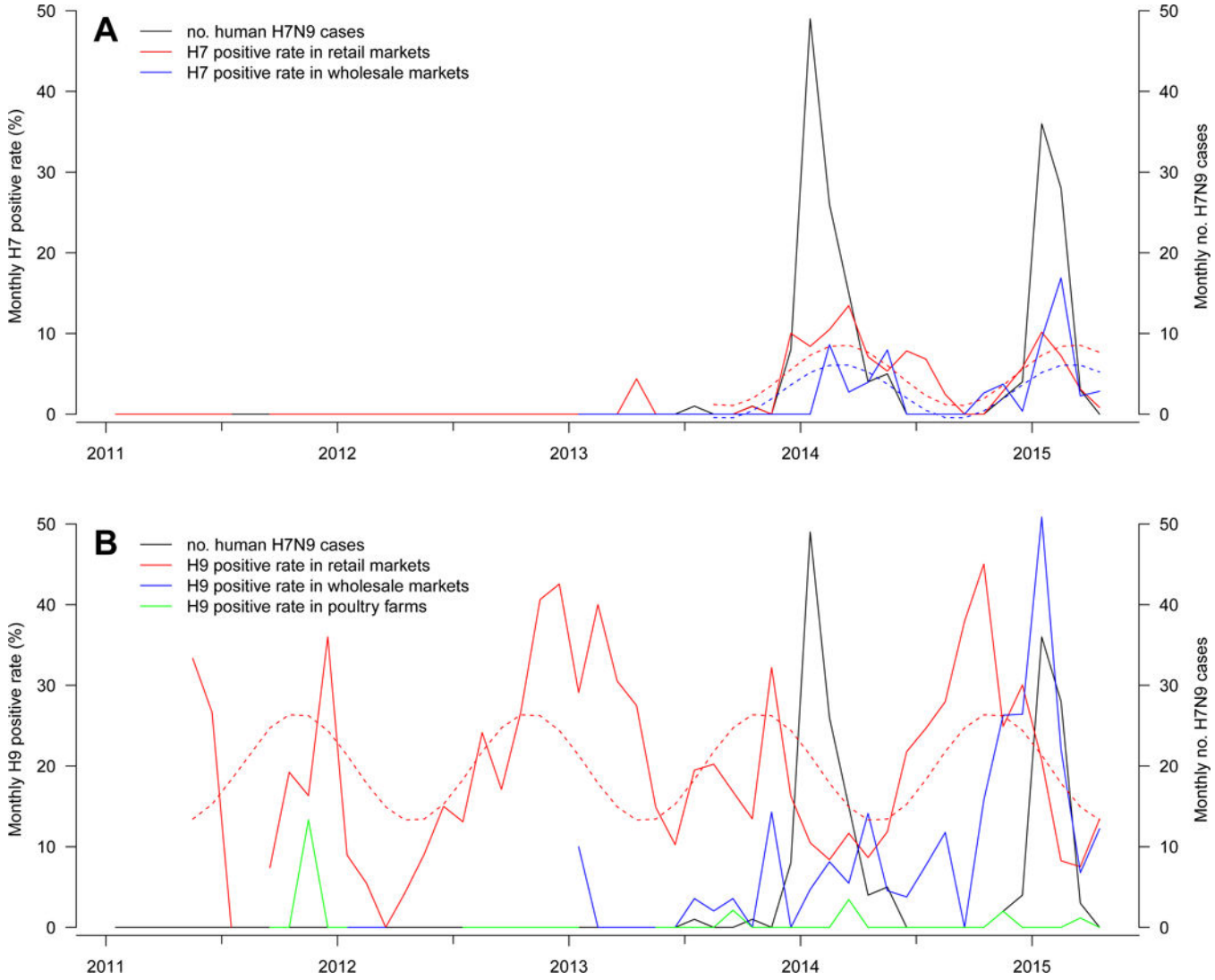

Figure 1.

Monthly positive rates at the retail, wholesale LPMs and poultry farms for (a) subtype H7 and (b) subtype H9, and monthly number of human H7N9 infections in Guangdong, January 2011 – April 2015.

Dotted lines show the fitted trends using sinusoidal function. Influenza A H7 subtype was not detected at poultry farms.

Table 1

Detection of influenza A viruses at the poultry-human interface, January 2011 – April 2015

	Retail LPMs[a]				Wholesale LPMs[b]				Poultry farms[c]			
	Flu A	**H9**	**H7**	**No. swab**	**Flu A**	**H9**	**H7**	**No. swab**	**Flu A**	**H9**	**H7**	**No. swab**
Jan–Dec, 2011	41.9%	13.3%	ND	444	0.0%	0.0%	ND	80	4.4%	4.4%	ND	138
Jan–Dec, 2012	29.4%	16.0%	ND	930	2.0%	0.0%	ND	148	0.9%	0.5%	ND	217
Jan–Dec, 2013	38.3%	20.1%	3.4%	2,008	5.7%	2.1%	0.0%	385	0.3%	0.3%	0.0%	396
Jan–Dec, 2014	32.7%	16.2%	7.8%	8,631	24.9%	15.4%	3.2%	1,661	0.7%	0.5%	0.0%	598
Jan–Apr, 2015[d]	22.0%	11.9%	5.4%	9,880	31.5%	20.7%	6.2%	1,050	0.3%	0.3%	0.0%	369

LPM: live poultry market; ND, not determined.

[a] Swabs were collected monthly at the retail LPMs from January 2011 – April 2015

[b] Swabs were collected once every three months in 2011, once every other month in 2012, and monthly from January 2013 – April 2015 at the wholesale LPMs

[c] Swabs were collected once every three months or once every other month from January 2011 to April 2013, and monthly from April 2013 – April 2015

[d] Detection rates of influenza A and H7 in retail and wholesale LPMs are expected to be higher in this period, comparing to other time of the year