

Detection of 2019 novel coronavirus (2019-nCoV) in patients with influenza-like illness (ILI)

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Abstract

2019 novel coronavirus (2019-nCoV) is firstly found in Wuhan and has caused over 14,000 infections all over the world. We retrospectively investigated the presence of 2019-nCoV among influenza-like illness patients in Wuhan. Nine cases in January 2020 were 2019-nCoV positive, suggesting the virus has established community transmission in Wuhan, the origin and center of this epidemic.

Authors Wen-Hua Kong, Yao Li, and Ming-Wei Peng contributed equally to this work.

Introduction

In late December 2019, clusters of patients with pneumonia of unknown etiology that were epidemiologically linked to a seafood and wet animal wholesale market were reported in Wuhan, Hubei Province, China¹. The causative pathogen of the pneumonia clusters was soon identified as a novel coronavirus which shared 79.5% sequence identity to the severe acute respiratory syndrome coronavirus (SARS-CoV)^{1,2} and was named 2019 novel coronavirus (2019-nCoV). Since then, the virus has spread into all the provinces of China and 23 other countries³. As of February 1, 2020, more than 14,000 cases of 2019-nCoV infection have been confirmed in China and 4109 cases of them were reported in Wuhan.

As the China CDC declared, the community transmission of 2019-nCoV has established in the city of Wuhan and nearby regions⁴. However, the clinical outcome of 2019-nCoV not only includes viral pneumonia like SARS-CoV, but also covers mild illness and even asymptomatic infection^{5,6}. The existing medical resources cannot support the nucleic acid test of a large number of mild cases⁴ and reliable serological assay is still not commercially available. The whole picture of 2019-nCoV epidemic in Wuhan remains unclear.

The Study

In order to better understand the current epidemic in Wuhan, particularly the status of mild illness cases, we retrospectively investigated the presence of 2019-nCoV among local influenza-like illness (ILI) patients who visited hospital between October 6, 2019 and January 21, 2020. Sustained surveillance for ILI cases and their etiology has been implemented in Wuhan since 2005, based on the National Influenza Surveillance Network of China⁷. According to the latest National Influenza Surveillance Plan, a patient is identified as ILI-case if s/he has the sudden onset of a fever $>38^{\circ}\text{C}$ and cough or sore throat⁸. In the two national influenza sentinel hospitals, the Children's Hospital of Wuhan and Wuhan No. 1 Hospital, the number of ILI cases and total outpatient number are collected weekly. Clinical samples of ILI patients are also collected, if the patient had a fever for less than 3 days and has not been treated with antiviral drugs. After verbal informed consent was obtained from parents or caretakers, throat swabs were collected from ILI patients in 3.5 ml viral transport medium and were delivered to Wuhan Center for Disease Prevention and Control for laboratory diagnosis of influenza virus. Each sentinel hospital is required to collect 20 ILI samples every calendar week.

A total of 640 throat swabs were collected from ILI patients in the 16-week period between October 6, 2019 and January 21, 2020 (2019W40 to 2020W03). We performed 2019-nCoV ORF1ab/N qPCR assay (BioGerm, Shanghai, China) on the nucleic acids extracted from these specimens. The nucleic acids have been used in the detection and subtyping of influenza virus⁸. They were initially extracted from 200µl of throat swabs using a PANA9600E automated nucleic acid extraction system (Tianlong, Xi'an, China) and were stored at -70°C. All assays have been established in our laboratory and procedures were performed following the manufacturers' instructions.

The time period in concern coincided with the winter peak of influenza and other respiratory illnesses. The ILI case numbers in all age groups have increased dramatically since early December and reached the peak by the New Year (Fig. 1). Particularly, the 5–14 years group presented an increment over 24-folds (2019W40-W47: 75 cases/week; 2019W52: 1916 cases). The percentage of ILI patients in all outpatients experienced a similar rise: the average percentage was 1.07% during 2019W40 to W47, and soared up to 9.44% in 2020W01.

The ILI patients involved in this study comprised 315 males and 325 females, ranging from 9 months to 87 years (median age 8 years, mean age 22.7 years). The 2019-nCoV RNA was detected in 9 patient specimens (Table1, Supplementary Table 1). All of them were collected in January 2020 (2020W1–2020W3), when the seasonal influenza (mainly A/H3 and B/Victoria) remained to be active, yet no co-infection has been detected.

The basic demographic information and illness timeline of nine 2019-nCoV infected patients is listed in Table 2. Their gender ratio was 1.25 (5 males vs. 4 females) and all of them were adults (age range: 35–71 years). These demographic features are consistent with other available reports about 2019-nCoV patients^{6,9}. The onset date of the earliest case was January 4, 2020, one week after the outbreak was first reported by hospital⁹. Although the weekly sample size was rather small, it seems that 2019-nCoV infection was gradually expanding among ILI cases during January. In the last week of observation, the positive rate of 2019-nCoV has exceeded that of influenza virus among the group over 25 years (Table 1). Interestingly, nine 2019-nCoV patients came from 6 different districts of Wuhan metropolitan and surrounding areas, which provided additional evidence for the community transmission in Wuhan.

Conclusions

Our work provides context for understanding the early stage of the novel coronavirus epidemic. Recent epidemiological studies estimated that the basic reproductive number of 2019-nCoV was 2.2 to 2.68, and the epidemic doubling time was 6.4 to 7.4 days^{9,10}. The occurrence and expansion of 2019-nCoV among ILI patients in Wuhan are consistent with those assessments. Given the fact that community-acquired 2019-nCoV infection cases have been reported outside Hubei¹¹, we suggest strengthening pathogen surveillance of ILI cases in major Chinese cities and other regions in the world.

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Author Contributions

W.-H. K. and M.-Q. L. analyzed the data and prepared the manuscript, Y. L., M.-W. P., and M.-Q. L. conducted the experiments, D.-G. K. and X.-B. Y. collected the specimens and epidemic information, L. W. critically revised the manuscript.

References

1Zhu, N. *et al.* A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med*, doi:10.1056/NEJMoa2001017 (2020).

2Zhou, P. *et al.* Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. *bioRxiv*, 2020.2001.2022.914952, doi:10.1101/2020.01.22.914952 (2020).

3World Health Organization. Novel Coronavirus (2019-nCoV) Situation Report - 12.

4Chinese Center for Disease Control and Prevention. Epidemic update and risk assessment of 2019 Novel Coronavirus.

5National Health Commission of the People's Republic of China. *The diagnosis and treatment plan of the novel coronavirus–infected pneumonia (3rd edition)*, <http://www.chinacdc.cn/jkzt/crb/zl/szkb_11803/jszl_11815/202001/t20200123_211391.html> (2020).

6Chan, J. F. *et al.* A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet*, doi:10.1016/S0140–6736(20)30154–9 (2020).

7Yang, P. *et al.* Review of an influenza surveillance system, Beijing, People's Republic of China. *Emerg Infect Dis* 15, 1603–1608, doi:10.3201/eid1510.081040 (2009).

8National Health Commission of the People's Republic of China. *National Influenza Surveillance Plan*, <http://ivdc.chinacdc.cn/cnic/zyzx/jcfa/201709/t20170927_153830.htm> (2017).

9Li, Q. *et al.* Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med*, doi:10.1056/NEJMoa2001316 (2020).

10Joseph T Wu, Kathy Leung & Gabriel M Leung. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet*, doi:10.1016/S0140–6736(20)30260–9 (2020).

11Pei, P. *Shenzhen confirms community transmission coronavirus cases*, <<http://www.chinadaily.com.cn/a/202002/02/WS5e36c08ba310128217274349.html>> (2020).

Main Tables

Table 1. Virological test results of ILI surveillance samples collected between October 6, 2019 and January 21, 2020 (2019W40 to 2020W03) in Wuhan, China.

ILI surveillance week	2019 novel coronavirus		Influenza virus		
	no. / total no. (%)		no. / total no. (%)		
	All age groups	≥ 25 yr	All age groups	0-24 yr	≥ 25 yr
2019W40	0/40	0/15	0/40	0/25	0/15
2019W41	0/40	0/18	0/40	0/22	0/18
2019W42	0/40	0/17	0/40	0/23	0/17
2019W43	0/40	0/15	0/40	0/25	0/15
2019W44	0/40	0/14	0/40	0/26	0/14
2019W45	0/40	0/18	0/40	0/22	0/18
2019W46	0/40	0/18	0/40	0/22	0/18
2019W47	0/40	0/17	6/40 (15.0)	6/23 (26.1)	0/17
2019W48	0/40	0/17	11/40 (27.5)	11/23 (47.8)	0/17
2019W49	0/40	0/20	11/40 (27.5)	10/20 (50.0)	1/20 (5.0)
2019W50	0/40	NA	17/40 (42.5)	17/40 (42.5)	NA
2019W51	0/40	NA	27/40 (67.5)	27/40 (67.5)	NA
2019W52	0/40	0/1	19/40 (47.5)	19/39 (48.7)	0/1
2020W01	1/40 (2.5)	1/17 (5.9)	18/40 (45.0)	14/23 (60.9)	4/17 (23.5)
2020W02	3/40 (7.5)	3/18 (16.7)	19/40 (47.5)	14/22 (63.6)	5/18 (27.8)
2020W03	5/40 (12.5)	5/20 (25.0)	15/40 (30.0)	14/20 (70.0)	1/20 (5.0)

Table 2. The demographic information and illness timeline of nine 2019-nCoV infected ILI patients in Wuhan.

Sample ID	Gender	Age	Date of onset	Date visiting hospital	Influenza virus	2019-nCoV ORF1ab/N gene
200077	F	46	2020-1-4	2020-1-7	-	+/+
200101	M	36	2020-1-10	2020-1-13	-	+/+
200110	F	35	2020-1-12	2020-1-13	-	+/+
200115	F	48	2020-1-10	2020-1-13	-	+/+
200144	M	53	2020-1-20	2020-1-21	-	+/+
200145	M	59	2020-1-20	2020-1-21	-	+/+
200149	M	71	2020-1-20	2020-1-21	-	+/+
200153	M	53	2020-1-20	2020-1-21	-	+/+
200158	F	45	2020-1-20	2020-1-21	-	+/+

Supplementary Table

Supplementary Table 1. Demographic information of tested ILI-patients collected in Wuhan between October 6, 2019 and January 21, 2020 (2019W40 to 2020W03).

	Tested ILI-patients		
	Total	Influenza virus positive	2019-nCoV
n	640 (100%)	142 (22.19%)	9 (1.41%)
Sex			
Female	325 (50.78%)	69 (21.23%)	4 (1.23%)
Male	315 (49.22%)	73 (23.17%)	5 (1.59%)
Age, years			
Mean (SD)	22.7 (24.6)	10.0 (11.9)	49.6 (11.2)
Range	1-87	1-71	35-71
<5	199	31	0
5-9	136	76	0
10-17	51	21	0
18-29	51	6	0
30-39	43	3	2
40-49	25	0	3
50-60	44	2	3
>60	90	3	1
Days from illness onset to visiting hospital			
0	82	32	0
1	305	78	6
2	181	27	0
3	72	5	3

Figures

Figure 1

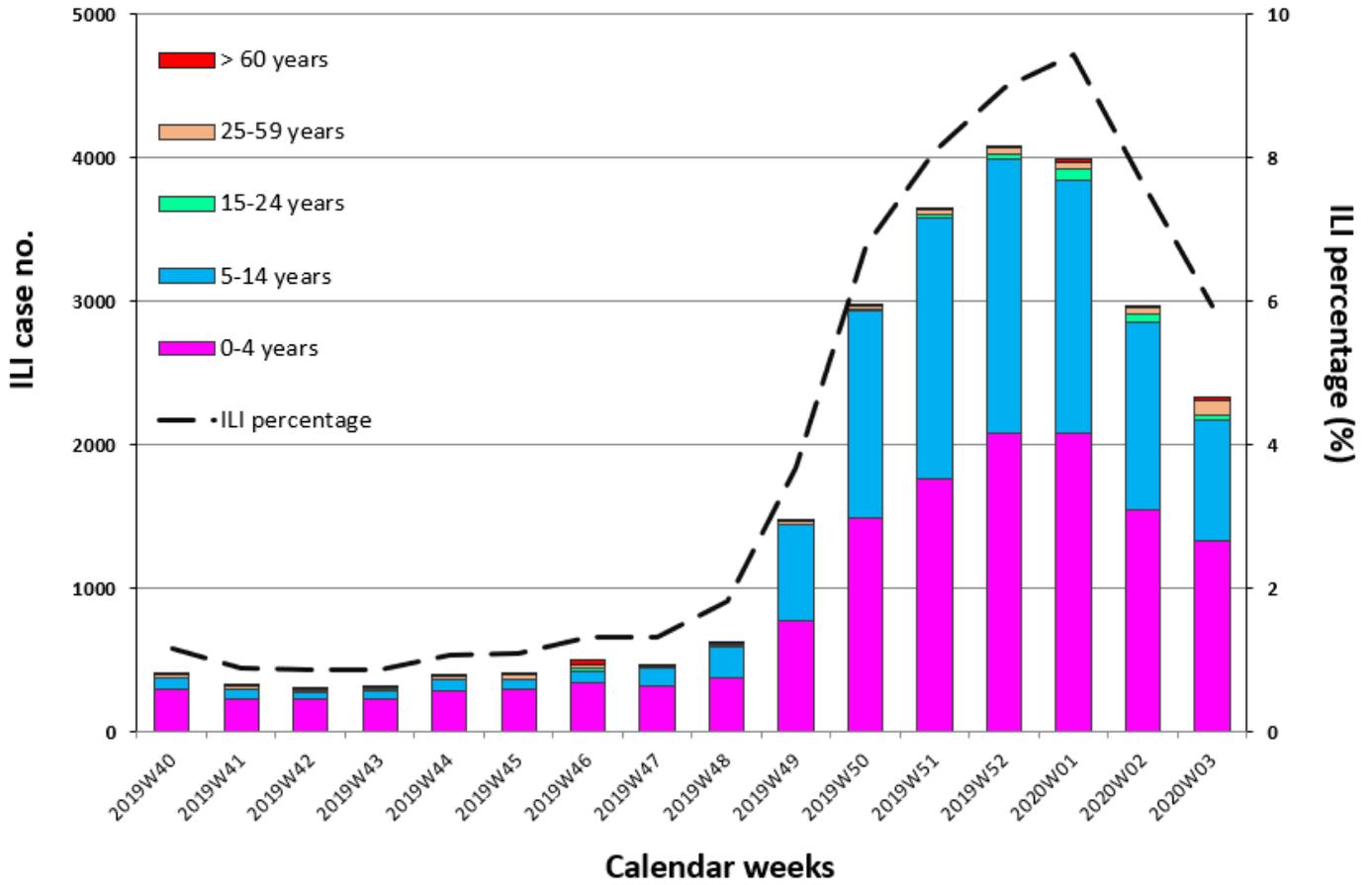


Figure 1

Case number of the influenza-like illness (ILI) and its percentage in all the outpatient. Data were collected from two sentinel hospitals in Wuhan between October 6, 2019 and January 21, 2020 (2019W40 to 2020W03). The vertical columns scaled on the left axis report the weekly ILI case no. and the color blocks on columns represent the age groups of ILI patients. The dash line shows the ILI percentage in outpatient and is scaled on the right y-axis.