Epidemic of the 2019 severe acute respiratory syndrome coronavirus 2 outside of Wuhan, China

Xuan Song
Liaocheng Cardiac Hospital Affiliated to Shandong First Medical University

Xinyan Liu
Liaocheng Cardiac Hospital Affiliated to Shandong First Medical University

Chunting Wang (deyy2020@126.com)
Shandong Provincial Hospital https://orcid.org/0000-0002-4575-3650

Research article

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Abstract

Background

The 2019 severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) responsible for coronavirus disease 2019 (COVID-19) appeared in Wuhan, Hubei in December 2019. Beside from Hubei Province, no large-scale epidemiological data are available. The purpose of the study is to investigate the epidemiology of the patients diagnosed with COVID-19 in Shandong province, China.

Methods

Data were obtained from the Epidemic Daily Report Network. Confirmed patients and suspected cases in Shandong were included in the analysis. Data including age, sex, address, time of disease onset, time of diagnosis, and sources of transmission were collected.

Results

By February 13 th , 2020, 518 patients in Shandong province were formally confirmed with COVID-19 with an additional 78 suspected. Most of the confirmed patients were young or middle-aged (mean: 42.6 years), and the male-to-female ratio was 1.26:1. Among the 596 patients, 29.2% had a history of traveling in Hubei within 14 days. There were 99 cluster outbreaks and 5.23 cases were transmitted by one cluster outbreak. Among the confirmed patients, 17 patients (3.3%) had critical pneumonia, 36 (6.9%) had severe pneumonia and no deaths reported.

Conclusions

Considering the collective confirmed and suspected cases of SARS-Cov-2 in Shandong by February 13 th , 2020, males and the young and middle-aged populations were more frequently affected by the virus, which was most commonly transmitted through cluster outbreaks. Since the initial case of SARS-Cov-2 was identified, the onset-diagnosis delay was reduced with time.

Background

The 2019 severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), which is responsible for coronavirus disease 2019 (COVID-19), appeared in Wuhan, China, and then spread rapidly starting in December 2019. On February 19, 2020, there were 73,332 cumulative cases of SARS-Cov-2 diagnosed across the world (including 25 countries on five continents) with 1873 deaths [1]. Among them, China was the epicenter of the spread, with 72,528 confirmed cases and 1870 deaths [1]. The World Health Organization declared the SARS-Cov-2 an international public health emergency [2].

Whole-genome sequencing demonstrated that the infection agent at the disease origin was caused by a clade within the subgenus sarbecovirus, Orthocoronavirinae subfamily [3], and was later named SARS-Cov-2 by the World Health Organization [1]. Different from the Middle East Respiratory Syndrome (MERS)-

CoV but similar to SARS-CoV, SARS-Cov-2 is the seventh member of the family of coronaviruses that has infected humans [3, 4]. Additionally, SARS-Cov-2 was confirmed in the bronchoalveolar lavage fluid of patients with confirmed diagnoses [3].

The exact origin and source of the virus are still unclear, but previous investigations suggested the virus may be associated with the illegal sale of wild animals in the Huanan Seafood Wholesale Market [5]. Huang et al. [6, 7] reported that a majority of the initial SARS-Cov-2 patient population had a history of visiting this market. Currently, it is confirmed the SARS-Cov-2 is transmitted by human-to-human contact [3, 6, 8–11]. Chen et al. [5] reported SARS-Cov-2 infection clustered within groups of individuals in close contact, and with a higher frequency of men with comorbidities. The symptoms of COVID-19 are similar with those of SARS-CoV and MERS-CoV [12], including fever, non-productive cough, dyspnea, myalgia, fatigue, normal or decreased leukocytes, and imaging suggestive of pneumonia [6]. Severe cases developed shock, acute respiratory distress syndrome (ARDS), acute cardiomyopathy, and acute renal injury leading to death [5, 6]. No effective targeted drugs or vaccines are available to date, but several clinical studies are currently ongoing. Nevertheless, important mobilization and preparation efforts were undertaken in Chinese hospitals [13]. To accelerate triage in emergency rooms and guide appropriate preventive methods, a scoring system was designed [13–15].

To date, most studies about SARS-Cov-2 and COVID-19 are case reports or case series [5, 6, 10, 16–20]. Large-scale epidemiological studies are only available for the Hubei Province, the origin of the epidemic [6]. Therefore, this study aimed to investigate the epidemiology (including the population distribution, temporal trend, and transmission methods of the disease) of patients confirmed with SARS-Cov-2 in Shandong province (China), which has a population of over 100 million. The results could provide new evidence regarding the mode of transmission and natural history of SARS-Cov-2 infection in areas outside of Hubei Province.

Methods

The study protocol was in accordance with the ethics standards and gained approval from Shandong Critical Care Quality Control Administration Ethics Committee. Due to the nature of this epidemiological data study it was exempt from obtaining informed consent by the Ethics Committee.

Data sources

Data were obtained from the Epidemic Daily Report Network. Confirmed patients and suspected cases in Shandong were included in the analysis. The Guidelines of SARS-Cov-2 diagnosis and treatment issued by The National Health Commission of the People's Republic of China has provided guidelines on the diagnosis and treatment of SARS-Cov-2, which included epidemiological characteristics and clinical manifestations (Table 1) [21]. Patients with any one epidemiological characteristic AND any two clinical manifestations were considered as suspected cases. Alternatively, patients without evident epidemiological characteristics, but with all three clinical manifestations, were also considered suspected cases. Furthermore, suspected cases with at least one of the following pathogenetic results were defined

as confirmed patients: 1) positive real-time polymerase chain reaction (RT-PCR) for SARS-Cov-2 and 2) viral gene sequencing showed high homology with SARS-Cov-2.

Table 1
Epidemiological and Clinical Characteristics of SARS-Cov-2 [1]

Epidemiology	Clinical Manifestations
History of living in Wuhan or surrounding areas within 14 days before disease onset, or history of traveling or living in communities with diagnosed SARS-Cov-2 patients	Fever and/or respiratory symptoms
History of contact with cases of SARS-Cov-2 confirmed by nucleic acid testing within 14 days before disease onset	Imaging characteristics of SARS-Cov-2
History of contact with individuals with fever or respiratory symptoms and were from Wuhan, surrounding areas, or communities with patients diagnosed with SARS-Cov-2 within 14 days before disease onset	White blood cell count was normal or decreased in the early phase of disease with reduced lymphocytes count
Cluster cases	

Laboratory testing

Nasopharyngeal swabs were used to collect samples from all the patients. The samples were subjected to RT-PCR for SARS-Cov-2 in the clinical laboratory with testing qualifications and approved by the provincial health administrative department.

Data collection and definitions

Data including age, sex, address, time of disease onset, time of diagnosis, sources of transmission (Hubei, other areas than Hubei, and local), history of traveling in other provinces within the past 14 days (Hubei or other areas than Hubei), clustered cases or not (referred to two or more cases within a relatively small unit), and clinical classification.

The patients were classified as: 1) Mild: mild clinical manifestations and imaging indicated no signs of pneumonia. 2) Regular: fever, respiratory symptoms, and imaging indicated signs of pneumonia; 3) Severe: patients with pulmonary imaging showing lesion progression > 50% within 24–48 h or those presenting with at least one of the following symptoms: a) shortness of breath and respiratory rate (RR) of ≥ 30 times/min and b) finger oxygen saturation ≤ 93% in the resting state; and c) arterial partial pressure of oxygen (PaO_2)/concentration of oxygen inhalation (FiO_2) was ≤ 300 mmHg (1 mmHg = 0.133 kPa) (for high altitude areas (altitude > 1000 m), the PaO_2/FiO_2 was adjusted according to the following equation: (PaO_2/FiO_2 × [atmospheric pressure (mmHg) / 760]). 4) Critical: patients exhibiting as least one of the following conditions: a) respiratory failure requiring mechanical ventilation; b) shock; and c) failure of other organs and required monitoring and treatment in the ICU [22].

Statistical analysis

All statistical analyses were carried using SPSS 16.0 (IBM, Armonk, NY, USA). Only descriptive statistics were used. The continuous data were presented as means ± standard deviation and as medians (range). The categorical data were presented as numbers and percentages.

Results

Distribution of the patients

According the Epidemic Daily Report Network, 596 patients in Shandong province were either confirmed or suspect cases with SARS-Cov-2 by February 13th, 2020. Among them, 518 patients in Shandong province were formally confirmed with SARS-Cov-2. These patients were distributed in 106 counties (municipalities or districts) in 15 prefecture-level cities. In addition, there were 78 suspected cases in 11 prefecture-level cities in Shandong.

Population distribution of SARS-Cov-2

Among the 518 confirmed patients, there were 289 males (55.8%) and 229 females (44.2%). The average age of this patient population was 42.6 years (range: 9 months to 90 years), and 40 patients (7.7%) were younger than 20 years. Among the 78 suspected cases, there were 36 (46.2%) males and 42 (53.8%) females. Their average age was 40.2 years (range: 1 to 76 years), and eight (10.3%) were younger than 20 years.

The highest frequency of confirmed patients and suspected cases were found in the 30–39 age group (Table 2). Most of the confirmed patients were young or middle-aged individuals, and only 5.4% (32/596) patients were ≥ 70 years of age. The percentage of males was higher in confirmed patients (male-to-female ratio of 1.26:1) compared to suspected cases (male-to-female ratio was 0.85:1). Figure 1 shows the distribution of the confirmed patients according to age groups. The highest frequency in males was in the 30–34 age group, while the highest frequency in females was in the 60–64 age group.

Table 2
Age distribution of the cases of SARS-Cov-2 in Shandong province

Age (years)	Confirmed patients (N = 518)	Suspected cases (N = 78)	Total (N = 596)
0–9	26 (5.0%)	5 (6.4%)	31 (5.2%)
10–19	14 (2.7%)	3 (3.8%)	17 (2.9%)
20–29	54 (10.4%)	11 (14.1%)	65 (10.9%)
30–39	143 (27.6%)	25 (32.1%)	168 (28.4%)
40–49	106 (20.5%)	8 (10.3%)	114 (19.1%)
50–59	91 (17.6%)	9 (11.5%)	100 (16.8%)
60–69	55 (10.6%)	14 (17.9%)	69 (11.6%)
70–79	19 (3.7%)	3 (3.8%)	22 (3.7%)
80–89	9 (1.7%)	0	9 (1.5%)
90–99	1 (0.2%)	0	1 (0.2%)

Temporal distribution of SARS-Cov-2

The first case of SARS-Cov-2 in Shandong province occurred on January 14th, 2020 and was confirmed on January 21st, 2020. The number of confirmed patients with SARS-Cov-2 increased with time, and the number of the confirmed cases was higher after January 28th, 2020, which was mainly due to the patients confirmed from previously performed laboratory screening. Nevertheless, the diagnoses were associated with stricter screening and could not reflect the actual status of the infection. Figure 2 shows the delays between symptom onset and diagnosis. The delays were longer in the early period of the epidemic with high frequencies of patients with delays > 7 days.

Epidemic characteristics of SARS-Cov-2

Initially, patients were primarily characterized by histories of traveling in Hubei and other areas, but in the later period, the patients were mainly local individuals with close contacts to virus carriers (Fig. 3). Among the total patient population of 596, 174 (29.2%) had a history of traveling in Hubei province within 14 days and 63 (10.6%) had a history of traveling in other provinces within 14 days. The percentage of cases increased in the local individuals with close contacts to virus carriers. Within the total population, 48.5 (289/596) were confirmed and 3.7% (22/596) were suspected cases of SARS-Cov-2 with close contacts to virus carriers of local individuals, accounting for 52.2% of all cases (311/596).

Cluster outbreaks

There were 99 cluster outbreaks in Shandong provinces, among which 74 (74.7%) were familial clusters, seven were work clusters (7.0%), 14 (14.1%) were mass exposure, two (2.0%) were doctors or nurses, one (1.0%) was in the same village as patients with SARS-Cov-2, one (1.0%) traveled in the same vehicle as a patient with SARS-Cov-2. On average, 5.23 cases were transmitted by one cluster outbreak, while the highest number of patients infected in a single cluster outbreak was 36.

Clinical severity

The clinical manifestations of the confirmed patients and suspected cases were primarily comparative to regular pneumonia. Among the confirmed patients, 3.3% (17/518) and 6.9% (36/518) of patients had critical or severe pneumonia, respectively (Table 3). There was no death case by February 13th, 2020. The proportion of patients with severe pneumonia increased with time, as well as with the changes of disease courses and delayed diagnosis.

Table 3
Clinical severity of the cases

Clinical severity	Confirmed patients (N = 518)	Suspected cases (N = 78)	Total (N = 596)
Mild	77 (14.9%)	15 (19.2%)	92 (15.4%)
Regular	388 (74.9%)	63 (80.8%)	451 (75.7%)
Severe	36 (7.0%)	0	36 (6.0%)
Critical	17 (3.2%)	0	17 (2.9%)

Discussion

The results of this study show that by February 13th, 2020, in Shandong, there were 518 patients confirmed with SARS-Cov-2 and 78 suspected cases (10th in China). Among them, there was no death case. Most patients were middle-aged or young, and the proportion of males was higher than that of females. Additionally, male patients were younger than females. The mode of transmission seems to favor cluster transmission. The onset-diagnosis was reduced as time progressed, probably due to the implemented public health prevention and control measures.

Compared with a previous study by Wang et al. [16], the confirmed patients in the present study were younger (43 vs. 56 years), but similar to patients from Zhejiang Province (41 years) [4]. The percentage of male patients was higher in confirmed patients (similar between the two studies, at 56% and 54%), and the male-to-female ratio was 1.26:1. In contrast, the male-to-female ratio was 0.85:1 in suspected cases. The sex distribution was different between the confirmed patients and suspected patients, which could be associated with the fact that males have more outdoor activities than females, and thus the risk of exposure was higher, while more females received examinations because of having been in close contacts with carriers.

As time progressed, the cause of the disease changed from a history of traveling in Hubei and other high-prevalence areas [3, 6, 8, 9, 16, 19] to local individuals who were in close contact with the virus carriers. In addition, in accordance with the human-to-human transmission mode of SARS-Cov-2 [3, 6, 8–11], the virus was mainly transmitted among individuals living, working, or traveling together, and there were 99 cluster outbreaks in Shandong province. Li et al. reported in Zhejiang that no patient was ever exposed to the Huanan Seafood Market, and all were due to human-to-human transmission, indicating protective measures should be taken to prevent direct human contact transmission [4].

The delay between onset and diagnosis dimension with time, which may be due to enhanced awareness and knowledge of the disease, as well as to the strict preventive measures and reporting policies that were implemented in China to face the epidemic [13–15].

Similarly to SARS-CoV, fever and cough were the dominant symptoms, accompanied by chest imaging suggestive of pneumonia [5, 6], but the gastrointestinal symptoms were rare, which is different from SARS-CoV, MERS-CoV, and influenza [23–25]. Of note, the absence of fever is much higher with SARS-Cov-2 than with SARS-CoV and MERS-CoV,[26] suggesting many cases may have been missed since public health surveillance relied heavily on fever detection [27]. In the present study, a small percentage of patients with confirmed infection were in a critical state, but no deaths were reported. The 62 patients from Zhejiang reported in February 2020 were showing relatively mild symptoms [4]. This is lower than the official death toll of 2.01% in China [1, 22]. Nevertheless, since the first case of SARS-Cov-2 was reported relatively late compared with Hubei, the appropriate detection, prevention, and control methods were already implemented [13, 14], which probably led to a reduction in disease severity and mortality due to early diagnosis and management.

Limitations

There were several limitations to this study. For instance, the asymptomatic cases or cases with mild symptoms that stayed in their homes may not have been accounted for and included in this study. Additionally, we only analyzed the data of the patients from Shandong province, which cannot accurately reflect the data in China, especially in Hubei province. The data were from an electronic database, making it possible for patients seen in outpatient settings or community clinics were not included. There was no comparator group, and only descriptive statistics were completed. Finally, we only analyzed the data by February 13th, 2020.

Conclusion

Considering the collective confirmed and suspected cases of SARS-Cov-2 in Shandong by February 13th, 2020, males and the young and middle-aged populations were more frequently affected by the virus, which was most commonly transmitted through cluster outbreaks. Since the initial case of SARS-Cov-2 was identified, the onset-diagnosis delay was reduced with time, which coincides with the implementation of guidelines for prevention, diagnosis, and treatment of infected patients.

List Of Abbreviations

Acute Respiratory Distress Syndrome, ARDS

Arterial Partial Pressure of Oxygen, PaO_2

Coronavirus disease 2019, COVID-19

Concentration of Oxygen Inhalation, FiO_2

Middle East Respiratory Syndrome coronavirus, MERS-CoV

Real-Time Polymerase Chain Reaction, RT-PCR

Respiratory Rate, RR

Severe Acute Respiratory Syndrome Coronavirus, SARS-Cov

Severe Acute Respiratory Syndrome Coronavirus 2, SARS-Cov-2

Declarations

Ethics Approval and Consent to Participate: The study protocol was in accordance with the ethics standards and gained approval from Shandong Critical Care Quality Control Administration Ethics Committee. Due to the nature of this epidemiological data study it was exempt from obtaining informed consent by the Ethics Committee.

Consent for Publication: Not applicable.

Availability of data and materials: All data generated or analyzed during this study are included in this published article. The datasets generated during and/or analyzed during the current study are available in the Epidemic Daily Report repository. No administrative permissions were required to access raw data from the epidemic daily reporting network.

Competing Interests: The authors declare that they have no competing interests in this section.

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Authors' Contributions: CW had conception, CW and XS participated in design, XS and XL carried out the studies, participated in collecting data and performed the statistical analysis. XS drafted the manuscript. All authors read and approved the final manuscript.

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References

1. World Health Organization. Coronavirus disease 2019 (COVID-19). Situation reporty - 29. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200218-sitrep-29-covid-19.pdf. Accessed 19 Feb 2020.
2. McCullough PA, Soman SS. Contrast-induced nephropathy. Crit Care Clin. 2005;21:261-80.
3. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020.
4. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ. 2020;368:m606.
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507-13.
6. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506.
7. Salata C, Calistri A, Parolin C, Palu G. Coronaviruses: a paradigm of new emerging zoonotic diseases. Pathogens and disease. 2020.
8. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020.
9. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, 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. 2020;395:514-23.
10. Phan LT, Nguyen TV, Luong QC, Nguyen TV, Nguyen HT, Le HQ, et al. Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam. N Engl J Med. 2020.
11. Yu P, Zhu J, Zhang Z, Han Y, Huang L. A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. The Journal of infectious diseases. 2020.
12. Liu J, Zheng X, Tong Q, Li W, Wang B, Sutter K, et al. Overlapping and discrete aspects of the pathology and pathogenesis of the emerging human pathogenic coronaviruses SARS-CoV, MERS-CoV, and 2019-nCoV. Journal of medical virology. 2020.
13. Liao X, Wang B, Kang Y. Novel coronavirus infection during the 2019-2020 epidemic: preparing intensive care units-the experience in Sichuan Province, China. Intensive care medicine. 2020.
14. Jin H, Lu L, Liu J, Cui M. Novel coronavirus pneumonia emergency in Zhuhai: impact and challenges. The Journal of hospital infection. 2020.
15. Cabrini L, Landoni G, Zangrillo A. Minimise nosocomial spread of 2019-nCoV when treating acute respiratory failure. Lancet. 2020.

16. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med. 2020.
17. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. N Engl J Med. 2020.
18. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First Case of 2019 Novel Coronavirus in the United States. N Engl J Med. 2020.
19. Lin X, Gong Z, Xiao Z, Xiong J, Fan B, Liu J. Novel Coronavirus Pneumonia Outbreak in 2019: Computed Tomographic Findings in Two Cases. Korean journal of radiology. 2020.
20. Pan Y, Guan H, Zhou S, Wang Y, Li Q, Zhu T, et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. Eur Radiol. 2020.
21. National Health Commission of the People's Republic of China. The notice of launching guideline on diagnosis and treatment of the novel coronavirus pneumonia (NCP). 5th Edition. http://www.nhc.gov.cn/xcs/zhengcwj/202002/3b09b894ac9b4204a79db5b8912d4440.shtml. Accessed 19 Feb 2020. [
22. Gruberg L, Mehran, R., Dangas, G., Mintz, G.S., Waksman, R., Kent, K.M., Pichard, A.D., Satler, L.F., Wu, H., Leon, M.B. Acute renal failure requiring dialysis after percutaneous coronary interventions. Catheterization and Cardiovascular Interventions. 2001;52:409-16.
23. Assiri A, McGeer A, Perl TM, Price CS, Al Rabeeah AA, Cummings DA, et al. Hospital outbreak of Middle East respiratory syndrome coronavirus. N Engl J Med. 2013;369:407-16.
24. Minodier L, Charrel RN, Ceccaldi PE, van der Werf S, Blanchon T, Hanslik T, et al. Prevalence of gastrointestinal symptoms in patients with influenza, clinical significance, and pathophysiology of human influenza viruses in faecal samples: what do we know? Virology journal. 2015;12:215.
25. Leung WK, To KF, Chan PK, Chan HL, Wu AK, Lee N, et al. Enteric involvement of severe acute respiratory syndrome-associated coronavirus infection. Gastroenterology. 2003;125:1011-7.
26. Zumla A, Hui DS, Perlman S. Middle East respiratory syndrome. Lancet. 2015;386:995-1007.
27. Koneth I, Weishaupt, D., Bachli, E.B. Persistent nephrogram after administration of an isoosmolar contrast medium. Nephrology, Dialysis, Trasnplantation. 2004;19:1654-5.

Figures

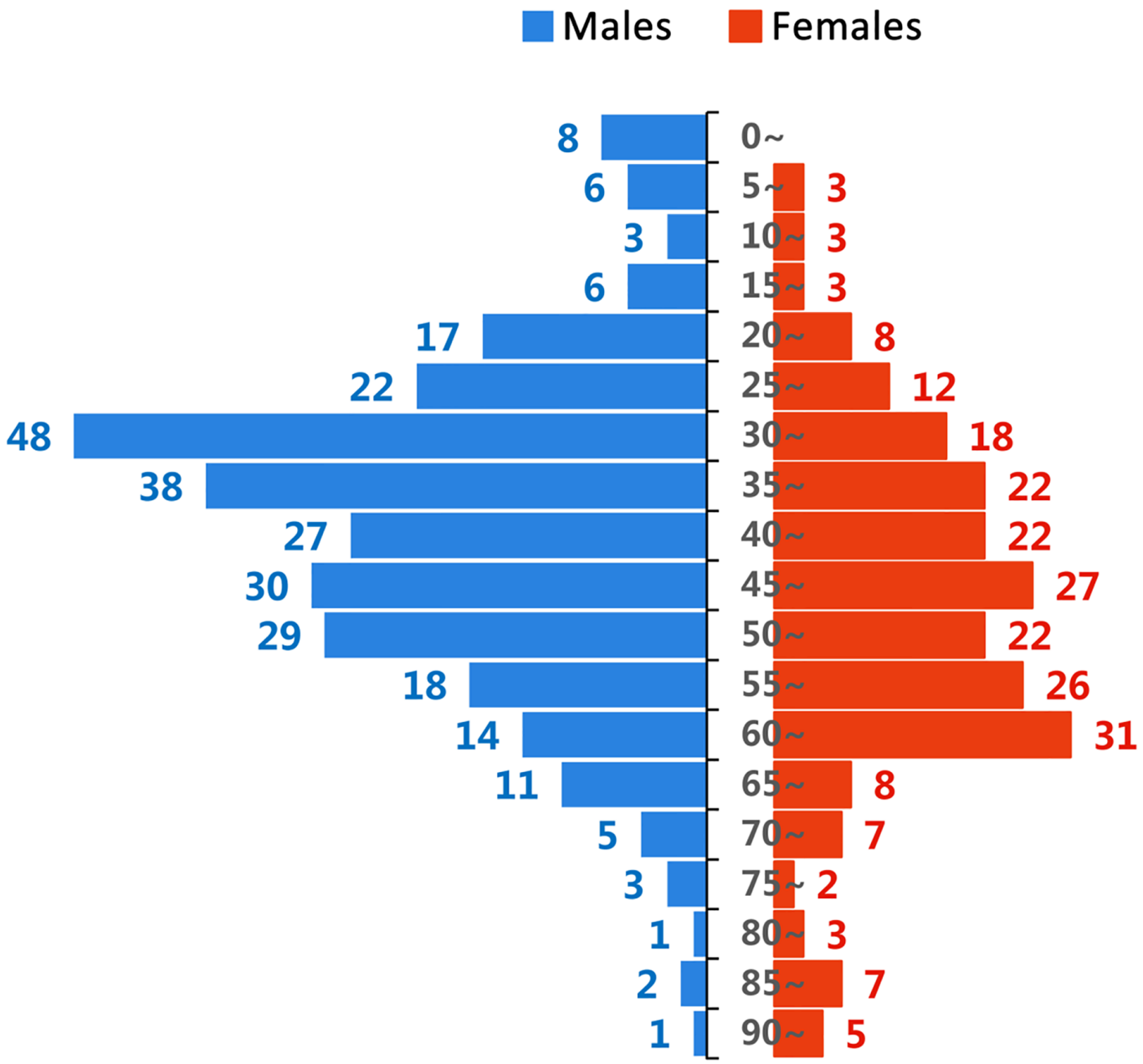

Figure 1

Age distribution of patients confirmed with SARS-Cov-2 according to sex.

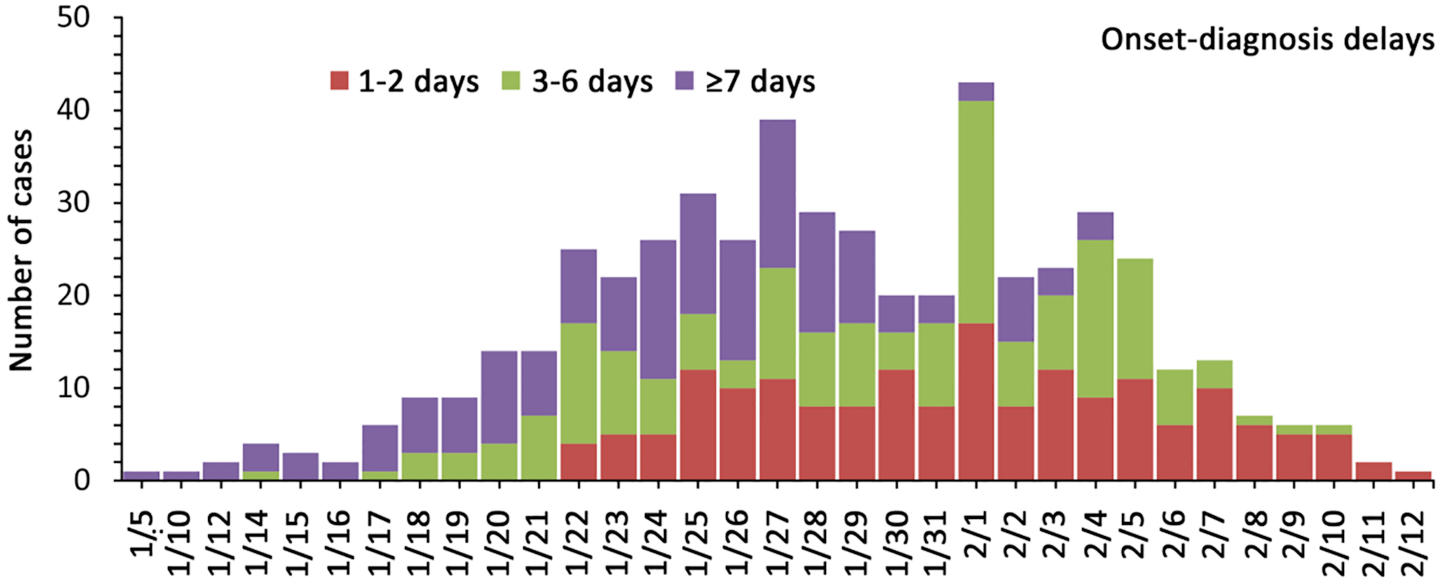

Figure 2

Time between onset and diagnosis of patients confirmed with SARS-Cov-2 in Shandong province.

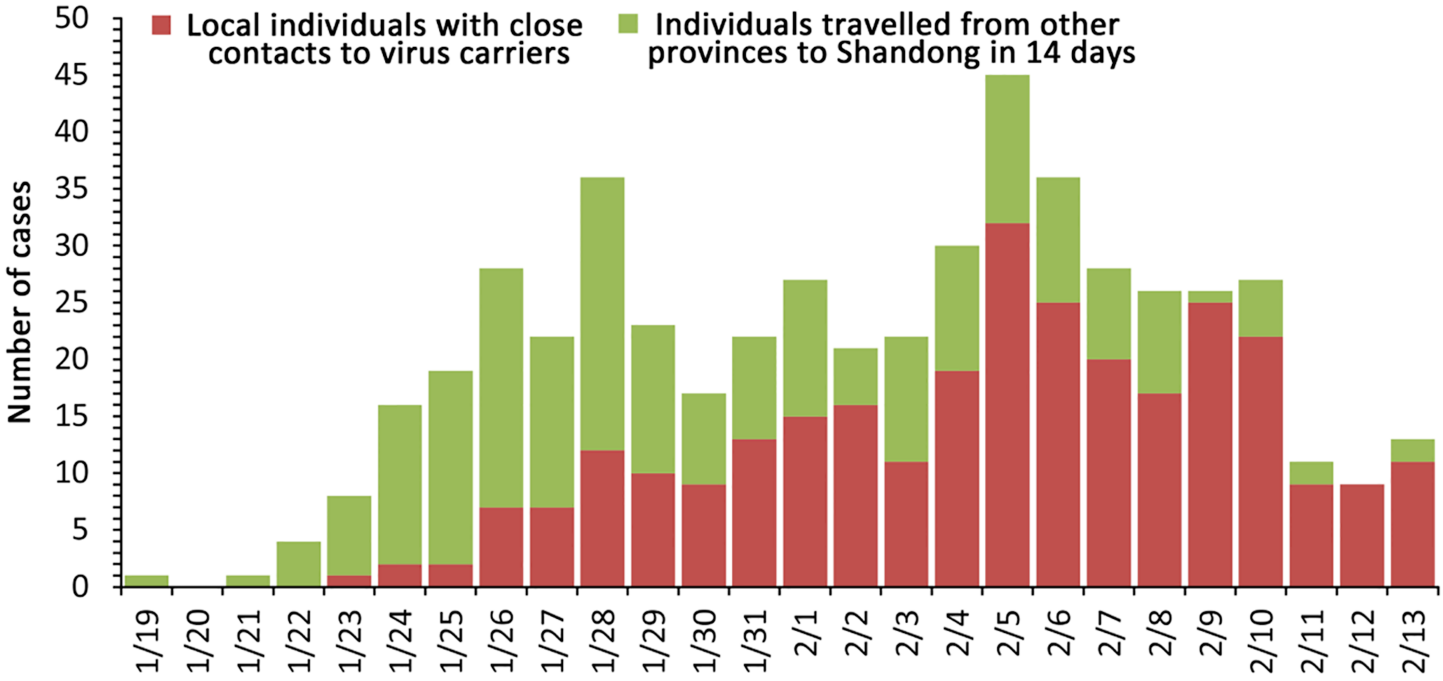

Figure 3

Distribution of the sources of patients confirmed with SARS-Cov-2 in Shandong province.