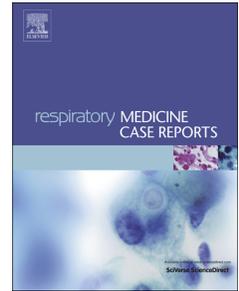


Journal Pre-proof

How the first cases of COVID-19 in 10 countries become infected? a case series

Leila Sadeghmoghadam, Majid Daneshfar, Farshad Sharifi, Vida Alizad



PII: S2213-0071(20)30433-0

DOI: <https://doi.org/10.1016/j.rmcr.2020.101219>

Reference: RMCR 101219

To appear in: *Respiratory Medicine Case Reports*

Received Date: 5 August 2020

Revised Date: 8 September 2020

Accepted Date: 9 September 2020

Please cite this article as: Sadeghmoghadam L, Daneshfar M, Sharifi F, Alizad V, How the first cases of COVID-19 in 10 countries become infected? a case series, *Respiratory Medicine Case Reports*, <https://doi.org/10.1016/j.rmcr.2020.101219>.

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The first cases of COVID-19 in 10 countries: How were they infected?

Leila Sadeghmoghadam ¹, Majid Daneshfar ², Farshad Sharifi ³, Vida Alizad ^{4,*}

1. Department of Nursing, School of Nursing, Social Development and health Promotion Research Center, Gonabad University of Medical Sciences, Gonabad, Iran.
2. Department of Medical-Surgical Nursing, School of Nursing, Gonabad University of Medical Sciences, Gonabad, Iran.
3. Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran
4. Movement Neuroscience Program, Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, QLD Australia and Iranian Research Centre on Ageing, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.

Corresponding author: Vida Alizad, **Email:** vidaalizad5182@gmail.com

The first cases of COVID-19 in 10 countries: How were they infected?

Abstract

Recently, a new respiratory infectious disease called COVID-19 has emerged and created a global emergency. It was initially linked to the animal-to-human transmission. However, it is now thought that COVID-19 is spreading through human-to-human transmission mainly via droplets. As there is no definite antiviral therapy for the treatment of cases with COVID-19 the best option for slowing down the pandemic and reducing mortality rates is protecting us against the virus. To achieve this goal obtaining information about how first cases infected with COVID-19 is crucial. Hence, this study aims to review the studies published in peer-reviewed journals to report the first confirmed cases with COVID-19. Herein, we review the origin, symptoms, diagnostic tests, and progress of the disease and possible actions of authorities which would be effective in similar pandemics in the future. This study reviewed 13 cases (5 females and 8 males; 25-61 years old) from 10 countries. All cases have recovered from COVID-19. The results of this review suggested that timely reports of the confirmed cases, notifying World Health Organization and providing information to the general population about the methods of spreading the virus would have decreased the number of infected cases and mortality rates. In addition, the travel history of the first confirmed cases in various countries suggested that prompt actions in restricting travels and closing borders could be an efficient strategy in preventing the transmission of the disease outside of the affected sites. Efforts should be taken by health authorities for preparing the world for future epidemic/pandemic in terms of developing advanced screening strategies in the borders and diagnostic strategies for early identification of infected cases.

Keywords: First cases, COVID-19, 2019-nCoV, Infection, Coronavirus

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24 **Introduction**

25 Several patients with a primary diagnosis of pneumonia appeared in the central province of
26 Hubei in China with unknown causes in December 2019. The newly emerged infectious disease
27 was officially called later COVID-19 leading to an epidemic in China (1, 2). COVID-19
28 epidemic has rapidly crossed the borders through human to human transmission and disrupted
29 public health systems, global economics and subsequently touched every sector and quality of
30 lives of people across the world, developing a pandemic as declared by the World Health
31 Organization on 11 March 2020 (3).

32 The underlying cause of COVID-19 has not been fully understood. It is thought that the original
33 cause of COVID-19 was linked to bats similar to the previous SARS-Cov and MERS-Cov
34 epidemics. It has also been suggested that snakes can act as intermediate hosts to transfer
35 COVID-19 from bats to humans (1). Given the high incidence and prevalence of the disease,
36 growing human-animal interface, genetic diversity and recombination events across the genomes
37 (3), the outbreak of COVID-19 is likely undertaken by super shaping phenomenon as previously
38 suggested as the main cause for spreading SARS-CoV and MERS-CoV (4). COVID-19 is
39

40 considered as a multi-organ failure disease in which can involve kidney, respiratory system and
41 other organs (5-7).

42 As of Tuesday 24 May 2020, The US has the highest number of infected cases (1547973)
43 followed by Brazil (310087), UK (254199), Spain (234824), Italy (228658) and Germany
44 (177850). The US has the highest number of death (92923) followed by Kingdom (36390), Spain
45 28628, Brazil (20047), Italy (15632) and Germany (8216). While the exact underlying
46 mechanism for spreading the virus is still not clearly understood, it is known that the countries
47 with proximity to China and strong travel and migration history with China have had a higher
48 number of cases infected with the COVID-19. Looking at the first COVID-19, we see a link
49 between direct or indirect travel history to China.

50 Given a large number of infected people and mortality rates caused by the COVID-19 crisis,
51 many countries have adopted restrictive measures to minimize the number of cases and death,
52 yet the numbers are still increasing in some countries. The increasing number of cases and death
53 along with the strict restrictive measures together affects people's mental health and well-being.
54 Therefore, it is critical to identify possible modes of transmission to be equipped with efficient
55 precaution recommendations and infection prevention guidelines to minimize infection
56 transmission and related consequences on the quality of lives of people in future similar
57 situations. Hence, the present paper reviews all peer-reviewed studies that reported the first cases
58 of COVID-19 disease diagnosed in 11 countries between 05 January 2020 and 09 February 2020.
59 Such an analysis provides a better understanding of the spreading mechanism of the virus and
60 provides information for preparedness, early identification of cases and secondary prevention in
61 future potential epidemics or pandemics, and contributes to improvement in the quality of lives
62 of people across the world. The cases were divided into two categories of cases with and without
63 travel history to Wuhan.

64

65 **Reported cases with travel history**

66 *Cases with travel history to Wuhan, China*

67 COVID-19 disease was confirmed for the first time in Yan'an in China. A 60-year-old man from
68 Yan'an, China with a history of travel to Wuhan was the first case in the world who spread the
69 COVID-19 virus. The patient visited the emergency department with a chief complaint of 5-day
70 fatigue without any respiratory symptoms. On identifying his 5-day unexplained fatigue a patchy
71 high-density shadow in both lungs was found in his chest CT scan with a negative result for the
72 oropharyngeal swab for COVID-19 on the real-time Reverse Transcription-Polymerase Chain
73 Reaction (RT-PCR) assay. Laboratory tests revealed a slight decrease in lymphocyte count and
74 an increase in blood levels for erythrocyte sedimentation rate, C-reactive protein, and high-
75 sensitivity C-reactive protein. The white blood cell count and D-dimer were normal. He was
76 admitted to the department of respiratory and critical care medicine and received treatment. Five
77 days after receiving treatments a chest CT scan showed that the dorsal part of the right upper
78 lobe and lower lobe of both lungs developed patchy consolidation with a ground-glass-like

79 shadow around them and grid shadows along with bronchial inflation. The second oropharyngeal
80 swab for 2019-nCov nucleic acid test was positive 6 days after the onset of the symptoms when
81 the diagnosis of 2019-nCoV pneumonia was confirmed. The patient did not develop any other
82 clinical symptoms during hospitalization. Details of treatment and duration of the hospitalization
83 were not reported by the authors (4).

84 Nepal was one of the countries bordered with China that reported its first case of 2019-nCoV.
85 The first infected patient with COVID-19 virus in Nepal was a 32-year man who was a
86 university student in Wuhan, without any underlying conditions and no history of exposure to
87 Wuhan wet market. In his return to Nepal only 10 days after he originally felt sick in China, he
88 was visited at an outpatient department of a tropical and infectious disease hospital with a chief
89 complaint of cough. The patient's throat swabs were tested positive for COVID-19 on real time
90 RT-PCR and the upper lobe of his left lung showed an infiltrate in the chest radiogram. The
91 patient was admitted to the hospital and isolated with 37.2°C temperature and throat congestion
92 and without any other relevant signs or symptoms. Six hours after a protocol of broad-spectrum
93 antibiotics and supportive therapies were provided for him, he had mild difficulties with
94 breathing and decreased oxygen saturation. On the second day of his admission, he presented
95 38.9°C fever followed by more severe breathing difficulties in the supine position along with
96 crepitations in the lower part of the right lung. On the third day of his admission, he did not show
97 fever and his clinical symptoms were improved. His lab tests returned normal and he was
98 discharged from the hospital the next day with a self-quarantine instruction at home. All
99 laboratory tests for influenza virus type A and B, dengue viruses, Brucella and scrub typhus were
100 negative at the discharge. His real-time RT-PCR throat swab was negative for COVID-19 on two
101 follow up assessments. The patient was categorised as a mild COVID-19 and was recovered in 4
102 days (8).

103
104 In Taiwan, the first case had different clinical features and developed typical symptoms related
105 to COVID-19. A 55-year-old woman who worked in Wuhan, China without any underlying
106 condition and exposure to Huanan Seafood Wholesale Market and sick people developed a sore
107 throat, dry cough, fatigue, and low-grade subjective fever. The symptoms were released after she
108 used over-counter medication. After 9 days she returned to Taiwan and immediately presented to
109 quarantine due to the history of developing symptoms. She had low- grade fever of 38.0°C and
110 88-90% oxygen saturation under ambient air in the quarantine. The next day the real-time RT-
111 PCR throat swab resulted in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
112 and she was admitted to hospital while she had stable vital signs except for the sore throat,
113 intermittent dry cough and exertional dyspnea. The supplement oxygen therapy was administered
114 by nasal cannula (3Litre/minute). The lab investigation showed lymphopenia and elevated C-
115 reactive protein, alanine aminotransferase, aspartate aminotransferase, and lactate
116 dehydrogenase. The results of a chest X-ray showed bilateral perihilar infiltration and ill-defined
117 patchy opacities. On the first days of hospitalization, the patient received antitussive agent, saline

118 infusion and empiric antibiotic with ceftriaxone (2 gm everyday intravenously and 2 gm loading)
119 followed by oral amoxicillin/clavulanate 875/125 mg every 12 h on the 8th day of admission to
120 hospital. One week later her real-time RT-PCR of sputum specimens yielded negative results and
121 remained negative 6 days later and serial X-ray and chest CT scan revealed tenacious COVID-19
122 pneumonia and sequelae. The patient discharged on the 28th day of the illness after 17 days of
123 hospitalization when the results of the tests returned negative for SARS-CoV-2 (9).

124 Another case was a 25-year-old Vietnamese woman who traveled to Wuhan and stayed there for
125 2 months with two Vietnamese friends. They confirmed that they did not have any exposure to
126 the wet market and contact with sick people. They all returned to Vietnam together on the same
127 date and flight. On the 6th day after they returned to Vietnam, the patient displayed fever,
128 fatigue, coughing, sneezing, and mild chest pain. She visited a local hospital where she was
129 suspected of severe COVID-19 and referred to a relevant hospital. Her two colleagues also
130 displayed similar symptoms and were admitted to a different hospital and tested positive for
131 COVID-19. A nasopharyngeal swab specimen revealed negative results for all relevant
132 pathogens and her nasopharyngeal specimen test was positive for SARS-CoV-2 after 6 days. The
133 clinical symptoms including high fever, chest pain and dry cough remained for 2 days and were
134 managed on day 3 of her admission to hospital followed by an improvement in cough and chest
135 pain on day 5. The patient discharged on day 9 (10).

136 The case report published to report the first cases in South Korea employed a different approach
137 in the report and highlighted three cases among the first 24 cases. The first South Korean patient
138 was a 35 years old woman who developed pneumonia in three days after onset of her symptoms
139 with no pneumonia clinical features, and with a travel history to Wuhan. The reason behind the
140 early identification of pneumonia was only scanning her lungs with a high-resolution computed
141 tomography scan. The patient developed severe clinical symptoms with high oxygen demand for
142 more than two weeks. The second highlighted patient contracted the infection in Japan and
143 transferred it to the third case who spread the virus to three family members. The other first cases
144 were infected through family/friend transmission, conference attendance, travel history to
145 Wuhan, Singapore, Thailand and Japan or contact with diagnosed cases (11).

146 In sum, in these Asian countries bordered with China, the transmission of the virus has been
147 predictable due to their proximity to China and the fact that these countries have a large number
148 of populations with Chinese ethnicity who had traveled to China during Chinese New Year
149 Holiday. However, the rapid spread of the virus within two weeks beyond the borders of Asian
150 countries suggest that the COVID-19 is able to spread rapidly from its original source to other
151 countries through human to human transmission regardless of the geographic distance. France,
152 Italy, the United States and Canada are four countries where reported their first cases who
153 originated from travel to Wuhan.

154 France was one of the European countries where reported the first three cases who had history of
155 residence in or travel to China without any exposure to wet market, sick people and live animals
156 during their residence in or travel to China 14 days before the onset of their symptoms.

157 The first case in France was a 48-year-old man who traveled to different cities in China including
158 Wuhan. On the second day of his arrival to China, he visited his family members and friends. He
159 showed the initial symptoms including fever, headache, and cough 6 days before he returned to
160 France. He returned to France via three airports. The next day he visited a GP and was suspected
161 to either severe acute lower respiratory infection or an acute respiratory illness. The patient was
162 transferred to and isolated in a hospital. On the next day, the results of his rt-PCR test for SARS-
163 CoV-2 was positive. The patient demonstrated symptoms after a month with persistent cough
164 and fever.

165 Case 2 and 3 were two Chinese tourists who traveled together to France. Both of them visited a
166 hospital in Wuhan as case 3 had a medical condition that was not relevant to COVID-19 disease.
167 On the day they arrived, case 2, a 31-year old man, developed fatigue, fever, conjunctivitis,
168 chills, and cough. Case 3, a 30-year old woman, also presented similar symptoms except for
169 conjunctivitis 4 days later. On the 6th day of their arrival, they contacted the national hotline on
170 the advice of the China embassy. They were immediately transferred to a regional referring
171 hospital and isolated and sampled for laboratory confirmation of COVID-19. On the same day, it
172 was confirmed that both of them were infected with SARS-CoV-2 (12).

173 Italy has been another country after China which was affected. The first two cases in Italy were a
174 Chinese couple from Wuhan who entered Italy as tourists through Milan and traveled to Rome
175 and accommodated in a hostel in the city center. They were admitted to a specialized hospital in
176 infectious diseases. Not detailed information was provided in the published case report (13).

177 Turning to the Americas, in the United States has currently now the highest number of infected
178 cases. The first infected patient with COVID-19 in the US was a 35-year-old man without any
179 underlying condition who traveled to Wuhan with no visit to the wet market or health care
180 facilities, and no contact with any confirmed patients with COVID-19. On the fourth day of his
181 arrival to the US, he presented cough and subjective fever which lasted 4 days, and then he
182 attended an urgent care clinic. The nasopharyngeal swab specimen tests returned negative for all
183 pathogens test and her chest X-ray revealed no abnormalities. However, on the next day, the
184 patient's nasopharyngeal and oropharyngeal swabs were tested positive for 2019-nCoV by
185 Reverse transcription polymerase chain reaction (RT-PCR) assay. The patient was admitted to a
186 hospital in an airborne-isolation unit. His symptoms were dry cough, history of 2-day nausea and
187 vomiting with no chest pain or shortness of breath and normal vital signs. The patient received
188 supportive care and his signs appeared stable on the 2nd day of hospitalization, but he developed
189 intermittent fevers along with tachycardia, diarrhea and abdominal discomfort. In addition, the
190 non-productive cough and fatigue symptoms were continued. On the next day, the lungs
191 radiography was normal. On day 6 the clinical symptoms improved, and atypical pneumonia was
192 observed in the radiograph. The patient was well on day 8 and remained stable but hospitalized.
193 All symptoms were managed except for a decreasing cough (14).

194 Canada was another country in Americas where a 56-year-old man with non-productive cough
195 and fever and a well-controlled hyper blood pressure visited the Emergency Department in

196 Toronto. One day after he returned from Wuhan, a chest x-ray showed patchy bilateral,
197 peribronchovascular, ill-defined opacities in all lung zones. Considering the clinical presentation
198 of viral pneumonia in a patient with the appropriate epidemiological risk, the patient was
199 admitted as a probable case of COVID-19. The results of the tests were negative for influenza
200 virus A and influenza virus B, parainfluenza virus, respiratory syncytial virus, adenovirus, and
201 human metapneumovirus. PCR showed COVID-19 in both mid-turbinate and throat swabs and
202 sequencing confirmed the 2019-nCoV. One day after admission the patient remained well but
203 developed mild haemoptysis and significant rhinorrhea and intermittent fever which lasted 5
204 days before it was completely managed. The patient discharged home and was on follow up
205 assessments by public health workers. The authors concluded that patients with mild pneumonia
206 who did not require supplementary oxygen and intubation could be isolated at their homes (15).
207 In summary, travel to Wuhan was the main reason for spreading the virus in these countries,
208 regardless of exposure to the known risk factors including the wet market, live animal and sick
209 people. The findings so far suggest that the disease starts with various initial symptoms, which is
210 different from the original idea of manifestation of high body temperature and dry cough. It is
211 not possible to consider a fixed set of symptoms for infected patients with the COVID-19.
212 Further, in cases with negative nucleic acid testing and with a rapid progression of chest
213 imaging, repeated nucleic acid testing is required to confirm the diagnosis of COVID-19.
214 Another important finding was that none of these cases developed severe symptoms. They
215 visited the hospitals as they had seen a health alert from the governments, or they were screened
216 mainly at borders in the airports only because they were traveling. These results highlight the
217 critical role of the early actions of governments and authorities to have policies in place with the
218 purpose of providing valid information for the general population and inform the world without
219 delay and control infection spread in such crises.

220 First reported cases without travel history to China

221 After the outbreak in China, Italy became the secondary source for spreading the disease with a
222 rapidly increasing number of infected cases. Among Latin American countries, Brazil published
223 a report of its first infected case. The first Brazilian case was a 61 years-old man with a 12-day
224 travel history to Lombardy, Italy. On the first day of his arrival to Brazil he presented to the
225 Hospital Albert Einstein in São Paulo, where his initial real-time RT-PCR was positive for
226 SARS-CoV-2. The patient displayed dry cough, fever, coryza, and sore throat. He was isolated at
227 home, received standard precautionary care, and presented mild signs one week after his arrival
228 to Brazil (16).

229 It can be concluded that there might be several similar infected mild cases with COVID-19 with
230 or without flu-like symptoms that have entered into different countries before the authorities
231 started screening for probable infected cases. Considering virulence of the COVID-19, the
232 potential cases contribute to beginning a rapid COVID-19 community transmission. This report
233 emphasizes once more the importance of early action of the authorities in such global emergency
234 situations.

235

236 **Discussion**

237

238 The outbreak of COVID -19 has currently gained a growing focus of the World Health
239 Organization and all sectors around the world to minimize the deadly effects of the disease
240 globally. We reviewed the first cases with COVID-19 reported by 10 countries with a focus on
241 travel history to china in order to suggest the strategies that ensure minimising the spread of the
242 disease. The findings of this study suggest that the lack of prompt action in closing the borders
243 was the main reason for the huge spread of the disease. In support of this assumption, the first
244 cases of 9 out of 10 countries were infected via residence in or travel to Wuhan in China.

245 It should be considered significant that in metropolis cities the spread of contagious infections
246 can be faster than other areas, therefore the place of epidemic can be affective factor on the
247 development of the susceptible people e.g. in the united states and China the spread of COVID-
248 19 can be faster (17). Also, the primary measure to reduce the spread of the COVID-19 is of
249 great importance in which in the early phase of epidemic the spread of the infectious disease can
250 be increased more and more (18).

251 One key factor in controlling the spread of the virus might be using reliable screening strategies
252 in the borders. One of the methods was used in the past months since the pandemic started was
253 measuring body temperature. The results of this review demonstrated that fever was not a
254 definite indicator for diagnosing patients with CoVID-19 as several cases did not develop a
255 fever. The main clinical presentation of most of the reported cases was lower respiratory
256 presentation such as caught, sore throat, and dyspnea, and lung infiltration in CT scan evaluation.
257 In addition, mild cases did not display signs and symptoms except for flu-like symptoms.
258 Missing these cases at the borders is most likely resulting in more infected cases in the
259 communities.

260 Regarding the mild cases, it is possible that the mild symptoms particularly the ones which are
261 not accompanied by shortness of breathing might not be taken seriously by the infected cases.
262 These symptoms might be considered as a common cold or flu by them, while they live their
263 normal daily routine and spread the virus in the communities. One possible strategy is providing
264 people with early public health warnings about the outbreak and the possible early symptoms of
265 the disease. Employing such a strategy also helps authorities in controlling the spread of the
266 virus. One reason that the health authorities were not able to control the disease in a timely
267 manner could be that some countries did not provide valid and timely information to the WHO.
268 Therefore, having some regulation in place by the WHO can be an efficient strategy to ensure all
269 health authorities across the world comply with the regulation and provide them with timely
270 information about emerging deadly diseases. Developing such regulation is a pressing need for
271 future similar situations to prevent entering a pandemic phase from an epidemic phase.

272 Another area of interest might be that most of these cases were diagnosed after clinical
273 manifestation. However, a serologic study reported that a large number of infected cases did not

274 have any clinical presentations. Therefore, several asymptomatic cases have not been diagnosed
275 and live their normal lives in communities while they were carriers. It remained unclear whether
276 symptomatic or asymptomatic cases played a key role in spreading the disease (19).

277 Another critical level of controlling an infectious disease might be early identification and
278 isolation of the new cases or instructing them for quarantine at home. The reported cases
279 presented to the designated hospitals or clinics 5-9 days after the onset of their symptoms. This
280 suggests that before attending the health clinics several individuals in the community were
281 already infected by these new cases that still were not aware of their condition and attended
282 various places around their cities, countries and most importantly other countries and committed
283 to the transmission of the disease. What is important is the prevention of infection, which can be
284 achieved to some extent by knowing how the early cases are infected. In fact, prevention is better
285 than cure. There are many different treatments for COVID-19 today (20), but no definitive cure
286 has been found and sometime antiviral drugs used to treat COVID-19 have renal and liver
287 complications (21). Treatment is much more complicated than follow-up. One interesting finding
288 of this review was that early detection of pneumonia without clinical features may stop the
289 development of severe pneumonia and admission to the intensive care unit. Thus, rapid
290 diagnostic strategies ensure decreasing the spread of disease. To do so the health authorities will
291 need to focus on clinical research for rapid, cost-effective and simple screening of pneumonia for
292 similar future crises.

293 **Conclusion**

294 In conclusion, no consistent set of symptoms was found. However, flu-like symptoms were
295 found to be predictors of new cases. The lack of typical pneumonia is not a reason for postponing
296 chest X-ray or CT scan as there were cases that were diagnosed only because of the early chest
297 CT scans that showed early stages of pneumonia. From a policy-making point of view, analyzing
298 and understanding which strategies are optimal in the prevention of infectious diseases may help
299 to achieve better results in the future. This warrants further investigation and analyzing the
300 lessons taken from the COVID-19 pandemic. Regarding the mild cases, it is possible that the
301 mild symptoms particularly the ones which are not accompanied by shortness of breathing might
302 not be taken seriously by the infected cases

303

304 **Conflict of interest**

305

306 The authors declare that they do not have conflict of interest.

307

308 **Funding**

309

310 This study was supported by Gonabad University of Medical Sciences, Gonabad, Iran.

311

312

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314

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Declaration of competing interest

The authors report no conflicts of interest.

Acknowledgment

This study was supported by Tehran University of Medical Sciences, Tehran, Iran.

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