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

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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?

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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 peerreviewed 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

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

Recently, a new respiratory infectious disease called COVID-19 has emerged and created a 3 global emergency. It was initially linked to the animal-to-human transmission. However, it is 4 now thought that COVID-19 is spreading through human-to-human transmission mainly via 5 droplets. As there is no definite antiviral therapy for the treatment of cases with COVID-19 the 6 best option for slowing down the pandemic and reducing mortality rates is protection against the 7 virus of interest. To achieve this goal obtaining information about how first cases infected with 8 COVID-19 is crucial. Hence, this study aims to review the studies published in peer-reviewed 9 journals to report the first confirmed cases with COVID-19. Herein, we review the origin, 10 symptoms, diagnostic tests, and progress of the disease and possible actions of authorities which 11 would be effective in similar pandemics in the future. This study reviewed 13 cases (5 females 12 and 8 males; 25-61 years old) from 10 countries. All cases have recovered from COVID-19. The 13 results of this review suggested that timely reports of the confirmed cases, notifying World 14 Health Organization and providing information to the general population about the methods of 15 spreading the virus would have decreased the number of infected cases and mortality rates. In 16 17 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 18 19 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 20 advanced screening strategies in the borders and diagnostic strategies for early identification of 21 infected cases. 22

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

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25 Introduction

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

- 32 Organization on 11 March 2020 (3).
- The underlying cause of COVID-19 has not been fully understood. It is thought that the original cause of COVID-19 was linked to bats similar to the previous SARS-Cov and MERS-Cov epidemics. It has also been suggested that snakes can act as intermediate hosts to transfer COVID-19 from bats to humans (1). Given the high incidence and prevalence of the disease, growing human-animal interface, genetic diversity and recombination events across the genomes (3), the outbreak of COVID-19 is likely undertaken by super shaping phenomenon as previously suggested as the main cause for spreading SARS-CoV and MERS-CoV (4). COVID-19 is

40 considered as a multi-organ failure disease in which can involve kidney, respiratory system and41 other organs (5-7).

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

- Given a large number of infected people and mortality rates caused by the COVID-19 crisis, 50 many countries have adopted restrictive measures to minimize the number of cases and death, 51 yet the numbers are still increasing in some countries. The increasing number of cases and death 52 along with the strict restrictive measures together affects people's mental health and well-being. 53 Therefore, it is critical to identify possible modes of transmission to be equipped with efficient 54 precaution recommendations and infection prevention guidelines to minimize infection 55 56 transmission and related consequences on the quality of lives of people in future similar situations. Hence, the present paper reviews all peer-reviewed studies that reported the first cases 57 of COVID-19 disease diagnosed in 11 countries between 05 January 2020 and 09 February 2020. 58 Such an analysis provides a better understanding of the spreading mechanism of the virus and 59 provides information for preparedness, early identification of cases and secondary prevention in 60 future potential epidemics or pandemics, and contributes to improvement in the quality of lives 61 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 Yan'an, China with a history of travel to Wuhan was the first case in the world who spread the 68 COVID-19 virus. The patient visited the emergency department with a chief complaint of 5-day 69 fatigue without any respiratory symptoms. On identifying his 5-day unexplained fatigue a patchy 70 high-density shadow in both lungs was found in his chest CT scan with a negative result for the 71 oropharyngeal swab for COVID-19 on the real-time Reverse Transcription-Polymerase Chain 72 73 Reaction (RT-PCR) assay. Laboratory tests revealed a slight decrease in lymphocyte count and an increase in blood levels for erythrocyte sedimentation rate, C-reactive protein, and high-74 sensitivity C-reactive protein. The white blood cell count and D-dimer were normal. He was 75 admitted to the department of respiratory and critical care medicine and received treatment. Five 76 days after receiving treatments a chest CT scan showed that the dorsal part of the right upper 77 lobe and lower lobe of both lungs developed patchy consolidation with a ground-glass-like 78

real shadow around them and grid shadows along with bronchial inflation. The second oropharyngeal

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

82 clinical symptoms during hospitalization. Det83 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. The first infected patient with COVID-19 virus in Nepal was a 32-year man who was a 85 university student in Wuhan, without any underlying conditions and no history of exposure to 86 Wuhan wet market. In his return to Nepal only 10 days after he originally felt sick in China, he 87 88 was visited at an outpatient department of a tropical and infectious disease hospital with a chief complaint of cough. The patient's throat swabs were tested positive for COVID-19 on real time 89 RT-PCR and the upper lobe of his left lung showed an infiltrate in the chest radiogram. The 90 patient was admitted to the hospital and isolated with 37•2°C temperature and throat congestion 91 and without any other relevant signs or symptoms. Six hours after a protocol of broad-spectrum 92 antibiotics and supportive therapies were provided for him, he had mild difficulties with 93 breathing and decreased oxygen saturation. On the second day of his admission, he presented 94 38.9°C fever followed by more severe breathing difficulties in the supine position along with 95 crepitations in the lower part of the right lung. On the third day of his admission, he did not show 96 97 fever and his clinical symptoms were improved. His lab tests returned normal and he was discharged from the hospital the next day with a self-quarantine instruction at home. All 98 laboratory tests for influenza virus type A and B, dengue viruses, Brucella and scrub typhus were 99 negative at the discharge. His real-time RT-PCR throat swab was negative for COVID-19 on two 100 101 follow up assessments. The patient was categorised as a mild COVID-19 and was recovered in 4 days (8). 102

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

infusion and empiric antibiotic with ceftriaxone (2 gm everyday intravenously and 2 gm loading)
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
- remained negative 6 days later and serial X-ray and chest CT scan revealed tenacious COVID-19
- pneumonia and sequelae. The patient discharged on the 28th day of the illness after 17 days of
- hospitalization when the results of the tests returned negative for SARS-CoV-2 (9).
- Another case was a 25-year-old Vietnamese woman who traveled to Wuhan and stayed there for 124 2 months with two Vietnamese friends. They confirmed that they did not have any exposure to 125 the wet market and contact with sick people. They all returned to Vietnam together on the same 126 date and flight. On the 6th day after they returned to Vietnam, the patient displayed fever, 127 fatigue, coughing, sneezing, and mild chest pain. She visited a local hospital where she was 128 suspected of severe COVID-19 and referred to a relevant hospital. Her two colleagues also 129 displayed similar symptoms and were admitted to a different hospital and tested positive for 130 COVID-19. A nasopharyngeal swab specimen revealed negative results for all relevant 131 pathogens and her nasopharyngeal specimen test was positive for SARS-CoV-2 after 6 days. The 132 clinical symptoms including high fever, chest pain and dry cough remained for 2 days and were 133 managed on day 3 of her admission to hospital followed by an improvement in cough and chest 134
- pain on day 5. The patient discharged on day 9 (10).
- The case report published to report the first cases in South Korea employed a different approach 136 in the report and highlighted three cases among the first 24 cases. The first South Korean patient 137 was a 35 years old woman who developed pneumonia in three days after onset of her symptoms 138 with no pneumonia clinical features, and with a travel history to Wuhan. The reason behind the 139 140 early identification of pneumonia was only scanning her lungs with a high-resolution computed tomography scan. The patient developed severe clinical symptoms with high oxygen demand for 141 142 more than two weeks. The second highlighted patient contracted the infection in Japan and transferred it to the third case who spread the virus to three family members. The other first cases 143 were infected through family/friend transmission, conference attendance, travel history to 144 Wuhan, Singapore, Thailand and Japan or contact with diagnosed cases (11). 145
- In sum, in these Asian countries bordered with China, the transmission of the virus has been predictable due to their proximity to China and the fact that these countries have a large number of populations with Chinese ethnicity who had traveled to China during Chines New Year Holiday. However, the rapid spread of the virus within two weeks beyond the borders of Asian countries suggest that the COVID-19 is able to spread rapidly from its original source to other to other through human to human transmission regardless of the geographic distance. France, 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
- residence in or travel to China without any exposure to wet market, sick people and live animals
- 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

showed the initial symptoms including fever, headache, and cough 6 days before he returned to

France. He returned to France via three airports. The next day he visited a GP and was suspected to either severe acute lower respiratory infection or an acute respiratory illness. The patient was

transferred to and isolated in a hospital. On the next day, the results of his rt-PRC test for SARS-

163 CoV-2 was positive. The patient demonstrated symptoms after a month with persistent cough

- 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.
- On the day they arrived, case 2, a 31-year old man, developed fatigue, fever, conjunctivitis, chills, and cough. Case 3, a 30-year old woman, also presented similar symptoms except for conjunctivitis 4 days later. On the 6th day of their arrival, they contacted the national hotline on the advice of the China embassy. They were immediately transferred to a regional referring 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).
- Turning to the Americas, in the United States has currently now the highest number of infected 177 cases. The first infected patient with COVID-19 in the US was a 35-year-old man without any 178 179 underlying condition who traveled to Wuhan with no visit to the wet market or health care facilities, and no contact with any confirmed patients with COVID-19. On the fourth day of his 180 181 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 pathogens test and her chest X-ray revealed no abnormalities. However, on the next day, the 183 patient's nasopharyngeal and oropharyngeal swabs were tested positive for 2019-nCoV by 184 Reverse transcription polymerase chain reaction (RT-PCR) assay. The patient was admitted to a 185 hospital in an airborne-isolation unit. His symptoms were dry cough, history of 2-day nausea and 186 vomiting with no chest pain or shortness of breath and normal vital signs. The patient received 187 supportive care and his signs appeared stable on the 2nd day of hospitalization, but he developed 188 intermittent fevers along with tachycardia, diarrhea and abdominal discomfort. In addition, the 189 190 non-productive cough and fatigue symptoms were continued. On the next day, the lungs radiography was normal. On day 6 the clinical symptoms improved, and atypical pneumonia was 191 observed in the radiograph. The patient was well on day 8 and remained stable but hospitalized. 192

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

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Toronto. One day after he returned from Wuhan, a chest x-ray showed patchy bilateral, 196 peribronchovascular, ill-defined opacities in all lung zones. Considering the clinical presentation 197 of viral pneumonia in a patient with the appropriate epidemiological risk, the patient was 198 admitted as a probable case of COVID-19. The results of the tests were negative for influenza 199 virus A and influenza virus B, parainfluenza virus, respiratory syncytial virus, adenovirus, and 200 human metapneumovirus. PCR showed COVID-19 in both mid-turbinate and throat swabs and 201 sequencing confirmed the 2019-nCoV. One day after admission the patient remained well but 202 developed mild haemoptysis and significant rhinorrhea and intermittent fever which lasted 5 203 days before it was completely managed. The patient discharged home and was on follow up 204 assessments by public health workers. The authors concluded that patients with mild pneumonia 205 who did not require supplementary oxygen and intubation could be isolated at their homes (15). 206

In summary, travel to Wuhan was the main reason for spreading the virus in these countries, 207 regardless of exposure to the known risk factors including the wet market, live animal and sick 208 people. The findings so far suggest that the disease starts with various initial symptoms, which is 209 different from the original idea of manifestation of high body temperature and dry cough. It is 210 not possible to consider a fixed set of symptoms for infected patients with the COVID-19. 211 Further, in cases with negative nucleic acid testing and with a rapid progression of chest 212 imaging, repeated nucleic acid testing is required to confirm the diagnosis of COVID-19. 213 Another important finding was that none of these cases developed severe symptoms. They 214 visited the hospitals as they had seen a health alert from the governments, or they were screened 215 mainly at borders in the airports only because they were traveling. These results highlight the 216 critical role of the early actions of governments and authorities to have policies in place with the 217 218 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 rapidly increasing number of infected cases. Among Latin American countries, Brazil published 222 223 a report of its first infected case. The first Brazilian case was a 61 years-old man with a 12-day travel history to Lombardy, Italy. On the first day of his arrival to Brazil he presented to the 224 Hospital Albert Einstein in São Paulo, where his initial real-time RT-PCR was positive for 225 SARS-CoV-2. The patient displayed dry cough, fever, coryza, and sore throat. He was isolated at 226 home, received standard precautionary care, and presented mild signs one week after his arrival 227 to Brazil (16). 228

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

236 **Discussion**

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

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

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

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

Another area of interest might be that most of these cases were diagnosed after clinical manifestation. However, a serologic study reported that a large number of infected cases did not have any clinical presentations. Therefore, several asymptomatic cases have not been diagnosed
and live their normal lives in communities while they were carriers. It remained unclear whether
symptomatic or asymptomatic cases played a key role in spreading the disease (19).

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

293 Conclusion

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

- **304** Conflict of interest
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- 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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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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