Revista Habanera de Ciencias Médicas

YEAR 2020
19(2) MARCH-APRIL
ISSN 1729 - 519X

ecimed

CLINICAL AND PATHOLOGICAL SCIENCES
REVIEW ARTICLE

Clinical-epidemiological characteristics of COVID-19

Características clínico-epidemiológicas de la COVID-19

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How to cite this article

Pérez Abreu MR, Gómez Tejeda JJ, Dieguez Guach RA. Clinical-epidemiological characteristics of COVID-19 Rev haban cienc méd [Internet]. 2020 [cited]; 19(2):e_3254_E. Available from: http://www.revhabanera.sld.cu/index.php/rhab/article/view/3254/2506

Received: March 28th, 2020.
Approved: April 11st, 2020.

ABSTRACT

Introduction: COVID-19 is caused by the new coronavirus that was discovered in Wuhan City, Hubei Province, China in the late 2019.

Objective: To describe the clinical-epidemiological characteristics of COVID-19.

Material and Method: A bibliographic review was made from a total of 33 bibliographic references. Articles and information from international organizations such as WHO, PAHO and electronic publications on the topic available from INFOMED were used. The quality, reliability

and validity of the selected articles were analyzed to carry out an adequate review.
Development: The transmission of SARS-COV-2 from an animal source to the first human cases has not been confirmed. The most accepted route of transmission between humans is from person to person via the respiratory route, with an incubation period between 1 and 14 days. In most cases, it presents with a clinical picture corresponding to a self-limited upper respiratory infection with a variety of symptoms according to risk groups, presenting a rapid progression to severe pneumonia and multi-organ failure, generally fatal in the elderly and in people with presence of comorbidities.
Conclusions: We are in the presence of a pandemic in which prevention is the most important means of combating it: to take the necessary measures to stop transmission, to achieve differentiated attention to risk groups, to carry out all relevant actions in order to identify and neutralize the foci of spreading and to get the population to join the health system of each nation and cooperate to combat this disease.
Key words: coronavirus, covid-19, SARS-CoV-2.

RESUMEN

Introducción: La COVID-19 es causada por el nuevo coronavirus que se descubrió en la ciudad de Wuhan, provincia de Hubei, China a finales de 2019.
Objetivo: Describir las características clínico-epidemiológicas de la COVID-19.
Material y Método: Se realizó una revisión bibliográfica a partir de un total de 33 referencias bibliográficas. Se utilizaron artículos e información de revistas nacionales e internacionales de las bases de datos OMS, OPS, Infomed. Se analizó la calidad, fiabilidad y validez de los artículos seleccionados para realizar una adecuada revisión.
Desarrollo: La transmisión del SARS-COV-2 proveniente de una fuente animal a los primeros casos humanos no se ha confirmado. La vía de transmisión entre humanos más aceptada es de persona a persona por vía respiratoria, con un periodo de incubación de 1 a 14 días. Se presenta en la mayoría de casos con un cuadro clínico correspondiente a una infección respiratoria alta autolimitada, con variedad de sintomatología según grupos de riesgo, presentando una rápida progresión a una neumonía grave y fallo multiorgánico, generalmente fatal en personas de la tercera edad y con presencia de comorbilidades.
Conclusiones: Estamos en presencia de una pandemia en la que el pilar más importante para combatirla es la prevención: tomar las medidas necesarias para detener la transmisión, lograr una atención diferenciada a los grupos de riesgo, realizar todas las acciones pertinentes con el fin de identificar y neutralizar los focos de propagación y lograr que la población se una al sistema de salud de cada nación y coopere para combatir esta enfermedad.

Palabras clave: coronavirus, covid-19, SARS-CoV-2, epidemiología.

INTRODUCTION

Health problems with worldwide affectation have occurred since the beginning of the 21st century and Cuba has not escaped from this situation. Many health problems from an increase in microbial resistance and oncological diseases to the appearance of new emerging and reemerging infectious diseases, such as the appearance of COVID-19 in the late 2019 have been occurring.[1.2]

Coronaviruses are an extensive family of viruses that can cause disease in both animals and humans. In humans, several coronaviruses are known to cause respiratory infections that can range from the common cold to more serious illnesses such as Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS).[1]

COVID-19 (coronavirus disease 2019) is caused by the coronavirus 2 of the severe acute respiratory syndrome (SARS-CoV-2); its shape is round or oval and often polymorphic with a diameter between 60 and 140 nm; the spike protein found on the virus surface that forms a rod-shaped structure is the main structure used for classification. The nucleocapsid protein encapsulates the viral genome and can be used as a diagnostic antigen. Both the new virus and the disease were unknown before the outbreak in Wuhan.[2]

It produces flu-like symptoms, including fever, cough, dyspnea, myalgia, and fatigue. Sudden loss of smell and taste (without mucus being the cause) has also been observed. In severe cases it is characterized by pneumonia, acute respiratory distress syndrome, sepsis and septic shock leading to about 3 % of those infected to death, although the mortality rate is at 4,48% and continues to rise.[3]

COVID-19 was first identified on December 1, 2019 in Wuhan City, the capital of Hubei Province in Central China, when a group of people with an unknown cause pneumonia were reported, mainly linked to Wuhan South China seafood wholesale market workers. The number of cases increased rapidly in the rest of Hubei and spread to other territories.[2.3]

The rapid spread of the disease prompted the World Health Organization to declare it a health emergency of international concern on January 30th, 2020. This sanitary emergency was based on the impact that the virus could have on underdeveloped countries with fewer health infrastructures, and it was recognized as a pandemic on March 11th. To the date of April 10th, 2020 a total of 182 countries with positive cases COVID-19, 1 563 857 cases confirmed and 95 044 deaths were reported, for a lethality of 6,08 %.[3]

In the Americas region, 537 678 confirmed cases are reported; 34.4 % of the total cases reported in the world with 19 309 casualties until April 10th, 2020 for a lethality of 3,59 %. The United States of America is the country with the highest number of reported cases surpassing the 501,680 confirmed cases and 18,780 deaths.[2.3]

In Cuba, until April 10th, 2020, 620 cases confirmed with the disease, 16 deaths and 77 recovered patients were reported; 2 415 patients are being clinical-epidemiologically monitored; and other 7 128 persons are being monitored in their homes by their Primary Health Care

physicians. In the province of Holguín, 37 cases of COVID-19 have been confirmed so far.[4]

The number of confirmed cases increases in a daily basis in relation to the number of confirmatory tests performed, while the number of people under surveillance fluctuates as these cases are ruled out due to other pathologies.

Due to the recent emergence of this disease, the situation of world and national alarm and the steady increase in cases and deaths, we decided that our **objective** should be to describe the clinical-epidemiological characteristics of COVID-19.

MATERIAL AND METHODS

A bibliographic review was carried out through the analysis of the sources of information available from The Cuban National Health Care Network and Portal (Infomed); the websites of the World Health Organization and the Pan American Health Organization were consulted.

Articles from national and international journals were retrieved in databases such as Pubmed/Medline, SciELO, Scopus and other open access journals.

The Google Scholar and Web of Science were used as search engines.

The most recently published literature in accordance with this new disease was considered as selection criteria, as well as materials that were in English and Spanish, leaving a total of 33 reviewed references.

The search strategies applied were health science descriptors such as: "coronavirus", "new coronavirus", "COVID-19", "acute respiratory infection", "respiratory distress syndrome coronavirus", "atypical pneumonia coronavirus" and their equivalents in Spanish.

The quality, reliability and methodological validity of the selected articles were analyzed to carry out an adequate review.

DEVELOPMENT

Emerging and reemerging infectious diseases are constant challenges for public health worldwide. Recent cases of pneumonia of unknown cause in Wuhan, China have led to the discovery of a new type of Coronavirus (SARS-CoV-2), which are enveloped RNA viruses, commonly found in humans, other mammals, and birds, capable of causing respiratory, enteric, hepatic and neurological diseases.[4.5]

To date, there are six known Coronavirus species that cause disease in humans. Four of these (229E, OC43, NL63, and HKU1) cause common flu symptoms in immunosuppressed people, and two species (SARS-CoV and MERS-CoV) cause severe acute respiratory syndrome with high mortality rates.[2]

Infection source

A question that continues being investigated is the recognition of the zoonotic origin of the virus, but due to its close similarity to the coronavirus found in bats it is likely that these animals are the primary reservoir of the virus. With the reemergence of this new kind of coronavirus, various studies were carried out in which it was

discovered that the genome level of SARS-COV-2 is 96 % identical to the bat coronavirus; however, other articles rule it out as a possible transmitting agent.[5,6]

Chinese authorities are conducting investigations to determine the source. Regarding the epidemiological characteristics of confirmed cases of COVID-19 in Wuhan City, China, a retrospective cohort study of 41 patients showed that 66% (27 patients) had direct contact with a large seafood and animal market.[6,7]

Given the prevalence and wide distribution of coronaviruses in different animal species, their wide genetic diversity and the frequent recombination of their genomes, it is expected that new coronaviruses will be detected in human cases, especially in contexts and situations where there is a close contact with animals.[7,8]

Animal-human transmission mechanism.

The way in which the virus could be transmitted from the animal source to the first human cases is unknown. Everything points to direct contact with infected animals or their secretions. In studies carried out in animal models with other coronaviruses, tropism has been observed among cells of different organs and systems, mainly producing respiratory and gastrointestinal symptoms, which could indicate that the transmission from the animal to humans could be through respiratory secretions and / or material from the digestive system.[9,10]

Human-human transmission mechanism.

The route of transmission among humans is considered similar to that described for other coronaviruses: through the secretions of infected people, mainly by direct contact with respiratory drops of more than 5 microns (capable of transmitting at distances of up to 2 meters) and by the hands when fomites contaminated with these secretions are followed by contact with the mucosa of the mouth, nose or eyes.[11,12]

Aerial transmission by nucleus of droplets or aerosols (capable of transmitting over a distance of more than 2 meters) has not been demonstrated for COVID-19. However, it is believed that this could occur during and even in the absence of invasive medical procedures of the respiratory tract. During the first SARS outbreak, the presence of the virus could be detected in the air of hospitalized patient rooms. A high in-hospital transmission (40 %) has recently been published in a Wuhan hospital; however, this includes cases since January 1, when the outbreak was under investigation and the causative agent had not yet been identified.[10,11]

During the symptomatic phase, the maximum release of virus by the respiratory mucosa occurs although this may also occur, to a lesser extent, in an asymptomatic stage or during the recovery process.[13]

Transmission through feces is another hypothesis for which there is no evidence in this epidemic up to current date. In animal models, tropism of some coronaviruses has been detected by intestinal cells. The presence of SARS-CoV-2 in stool samples has recently been detected in some infected patients both in China and other locations, without knowing the significance of this finding regarding the transmission of the disease.[14,15]

On the other hand, gastrointestinal clinical manifestations, although present, are not too frequent in patients with SARS-CoV-2 which would indicate that, if this route of transmission exists, it would have a minor impact on the evolution of the epidemic.[14,15]

A son of a mother with COVID-19 was confirmed to have positive throat swabs after 30 hours of birth. This suggests that the new coronavirus may cause neonatal infection through mother-to-child transmission, but more research and scientific evidence is needed to confirm possible mother-son vertical transmission; the virus has not been isolated in amniotic fluid, maternal milk or genital fluids so far.[14]

The authors agree that other routes of transmission could still be unknown or overlooked, for example, through microlesions of the skin or contact with other kinds of mucosa; however, it is a fact that the pertinent measures to prevent the spread of human to human via respiratory tract are showing good results.

Incubation period

According to preliminary data, the most frequent incubation period has been estimated between 4 and 7 days with an average of 5 days, with 95 % of cases occurring 12.5 days after exposure. However, based on the knowledge of other Betacoronaviruses, MERS-CoV and SARS-CoV, and the data of those detected in Europe in this outbreak, it is considered that it could be from 1 to 14 days. One case is reported to have had an incubation period of 27 days.[16]

The World Health Organization recommends isolation for 14 days after hospital discharge because recent studies have shown evidence that the virus can be transmitted after the first 14 days. This is evidenced in a study published by Chinese researchers in February, which found that the period can last as long as 24 days.[8,9]

According to first articles, evidence for transmission from asymptomatic patients or during the incubation period did not exist. Initially, a case of transmission was described from an asymptomatic patient in Germany, although the information was later found to be incorrect and has been corrected by the German authorities.[17]

The information referred to above on the non-transmission of asymptomatic patients does not coincide with the opinion of the authors, since the inability to know if someone is infected makes its transmission possible through daily activities and other elements that under other conditions can be considered normal such as sneezing, touching surfaces and later touching the face or vice versa; also, those young people suffering from allergic rhinitis or chronic pharyngitis, have relatively normal symptomology due to their base pathology, which could mask the presence of the disease, etc.[15,18]

Clinical picture

Regarding the clinical characteristics of the confirmed cases of COVID-19 in Wuhan City, China, a retrospective cohort study of 41 patients showed that the average age was 49 years, with a male prevalence. Important signs and symptoms of COVID- 19 were considered: fever (98 %), dry cough (76 %), dyspnea (55 %), myalgia or fatigue (44 %) and lymphopenia (63 %).[10,18]

Infected people may be asymptomatic or have a

variety of signs and symptoms that vary from mild to very severe depending on the characteristics of each person.[18]

The start of COVID-19 is mainly manifested as fever, but sometimes people only have chills and respiratory symptoms given by mild dry cough and gradual breathlessness in addition to fatigue and even diarrhea. Other very frequent symptoms registered by the World Health Organization (WHO) are expectoration (33 %), sore throat (14 %), headache (14 %), myalgia or arthralgia (15 %), nausea or vomiting (5 %), nasal congestion (5 %).[19]

Fortunately, in 80 % of cases of COVID-19, the disease is mild up to the point of being confused with the flu or common colds. However, 15 % of patients show severe symptoms that require hospitalization and 5 % develop very serious symptoms that must be treated in intensive care units.[9]

The first cases described with mild symptoms correspond to a group notified to the WHO on January 27th, 2020 in Germany. None of the cases presented severe symptoms. The preliminary information describes relatively mild symptoms and good evolution in almost all cases.[9,13]

The authors warn about the importance of the early detection of patients in the asymptomatic stage because the clinical picture can have an unexpected torpid evolution leading the patient to death, and even when a low viral load that does not represent an imminent threat to the patient´s life is present, a correct evaluation is absolutely necessary.

Some infected persons, confirmed through test results, may also be asymptomatic so the authors advise that people in close contact with confirmed infected patients should be isolated and monitored for a specified time to rule out infection.

In this context, the symptoms of the cases that have required hospitalization, therefore the most serious, are fundamentally known, but there is no published information to make a complete clinical description of the milder cases. In other studies, 10,1 % of patients had digestive symptoms (diarrhea and nausea) the days before fever and dyspnea appeared.[11,12,20,21]

In addition, multiple health professionals have also observed that some affected persons lose their sense of smell and taste for several days, an opinion with which the authors agree due to have treated two patients with COVID-19 who have presented taste disorders.

The main clinical forms recognized by the WHO are the following:

Uncomplicated (minimally symptomatic) disease: Nonspecific signs such as fever, cough, sore throat, nasal congestion, slight headache, and malaise might occur. There are no signs of dehydration, dyspnea, or sepsis. Elderly and immunosuppressed patients may present with atypical signs. There may be digestive manifestations such as nausea, vomiting, and diarrhea. It is, in essence, a picture practically indistinguishable from other respiratory viral conditions.[3,12]

Uncomplicated lower respiratory tract infection (mild pneumonia): In addition to the above symptoms, patients may present with fever, there may be a cough which may be productive,

polypnea with wet rales (crackles), or they may present as atypical pneumonia, but without signs of seriousness and with an ambient air SpO2 > 90 %. There are no signs of respiratory failure or seriousness.[5,12]

Severe pneumonia: presence of productive cough, with fever, nasal flaring, tachypnea (respiratory rate > 30 breaths / min), limitation of thoracic expandability, with wet rales (crackles), or presenting as an atypical pneumonia but with signs of severity. There could be intercostal or suprasternal drainage, central cyanosis, with ambient air SpO2 < 90 %, and pleuritic pain. It can also produce and be associated with acute respiratory distress syndrome.[3,12]

Laboratory findings

In case series of hospitalized patients in Wuhan, leukopenia and lymphopenia were the most common hematologic findings. Coagulation disorders, especially D-Dimer and prothrombin time, were more frequent in patients with greater severity. The 37 % of cases also had positive markers of hepatic cytolysis. Severe lymphopenia, high D-dimer, and high nitrogen products were markers related to mortality.[22]

The WHO published several protocols for the diagnosis of the disease in Japan. The test of choice was real-time RT-PCR (or reverse transcription followed by a quantitative polymerase chain reaction). It was performed on respiratory or blood samples. The results were available on January 30th, in a few hours or days. The PCR test can be done because Chinese scientists isolated and published a genetic sequence of the coronavirus.[23]

The objectives of diagnostic tests are to detect the common causes of early pneumonia to support activities for disease control and work with reference laboratories that can perform detection of coronavirus and achieve rapid action on the patients and all their contacts performing an adequate health prevention in the population and avoiding the transmission of the virus as much as possible.[24]

Behavior at pediatric ages

Few references have been published on pediatric cases, two cases of COVD-19 infections in school-age children were reported, one with mild symptoms and the other was asymptomatic. The symptoms described were fever (maximum 38,3 ºC), mild cough, runny nose, nausea, diarrhea, abdominal pain, headache and asthenia; he had leukocytosis, lymphopenia, neutropenia, and elevated C-Reactive Protein with negative procalcitonin. There were no coagulation disorders.[24]

Complications

It is not only the coronavirus that causes death (parasites are not usually interested in killing their hosts), but, in some cases, it is also caused by an uncontrolled immune response (called a "cytokine storm") that can cause multi-organic failure.[25,26]

Clinical research found that a high concentration of cytokines is detected in the plasma of critically ill patients infected with SARS-CoV-2, suggesting that the cytokine storm was associated with the severity of the disease.[27]

The most frequent complications are pneumonia and multi-organ failure that sometimes cause death. Other possible complications described are the respiratory distress syndrome of the

adult, renal failure, acute lung injury, septic shock and ventilator associated pneumonia.[16,27]

Case criteria

Close Contact: It refers to people who have had contact with a confirmed or suspected COVID-19 patient, including the following situations: those who live, study, work, or have other forms of close contact with a patient, medical personnel, family members or others who have had close contact with the patient without taking effective protective measures during diagnosis, treatment, nursing visits; others patients and their companions who share the same room with an infected patient; those who shared the same transport or elevator with the patient or those who are considered as close contact through field investigations.[28]

Suspected cases: It is that patient who classifies into one of these groups of criteria: patient presenting respiratory clinical manifestations with a history of being a traveler or that has been in contact with people from the area of transmission of the disease or any of the countries defined by the Ministry of Public Health (MINSAP by its acronym in Spanish) authorities in the last 14 days; presenting clinical respiratory manifestations with a history of being contact of a confirmed case in the last 14 days; deceased by an severe acute respiratory infection without apparent cause that also meets at the least one of the following conditions: contact with people who have suffered from the disease or to had travelled in the last 14 days to any of the countries that have reported confirmed cases.[3,28]

Confirmed Case: Patient who is positive to the virological study for COVID-19, with or without symptoms.[28]

Confirmed case with admission requirements for intensive care: serious confirmed case that meets the criteria for admission to the Intensive Care Unit (ICU).[28]

Main preventive measures

In the face of this worldwide threat, the main work to be done is preventive. The WHO has issued measures to reduce the spread of the virus. They are similar to those recommended to prevent infection with other coronaviruses and include: frequent washing of hands with soap and water after coughing or sneezing, covering the mouth and nose with the ulnar fossa (the concavity that forms the inner side of the arm when flexed at the elbow).[16,29]

Keep at least a meter away from other people, particularly those who cough, sneeze, and have a fever. Avoid touching the eyes, nose and mouth. Attend to the doctor in case of fever, cough and shortness of breath. Call in advance if you were in areas where the virus is spreading or if the person has visited these places during the last 14 days. Stay home if you start to feel sick, even in the case of mild symptoms such as headache and mild rhinorrhea, until you recover if you are in areas where the virus is spreading or if you have visited them during the last 14 days.[14,30]

To reduce the chances of becoming infected, healthcare organizations recommend to avoid close contact with sick people; wash hands frequently with soap and water; do not touch the eyes, nose or mouth with the hands without

washing; and practice good respiratory hygiene.[14,31]

People who are already infected are advised to stay home, except for medical care, to call ahead of time before visiting a health care provider, to wear a face mask (especially in public), to cover coughs and sneeze with a disposable tissue, wash hands regularly with soap and water, and avoid sharing personal household items. Depending on the legislation of each country, the intentional contagion of the virus is punishable according to the legal system where the event occurs.[15,16]

The authors agree that all people who have had contact with patients who have been classified as probable or confirmed COVID-19, should be monitored for 14 days from the last contact they had with them without protection or when the hygienic-sanitary pertinent measures were not followed properly at the time; in addition, these patients must not be transferred to places outside their place of residence to avoid possible spread.

In general, the use of masks is only recommended when there is exposure to patients with respiratory conditions, like hospitals and clinics.[32]

The authors do not support the previous idea because there can be patients which are asymptomatic and carriers of COVID-19 that become transmission foci, so we recommend the use of protective masks everywhere where there are confirmed cases of COVID-19. The guidelines for the use of the masks must be strictly followed, since the bad manipulation and contact with the hands to the eyes and with the external side of the mask can increase the risks.

Treatment

Meanwhile, numerous research laboratories today continue looking for a treatment that eliminates this virus infection, either with drugs that are already part of the pharmaceutical industry and are used for other diseases, or looking for new, more specific alternatives for the virus.[33]

So far, no fully effective antiviral drug or vaccine has been identified; however, a protocol was developed in Cuba, which is constantly updated to combat the disease and includes the following measures:

General measures in uncomplicated patients: Report of care; vital signs are taken at least every 4 hours; diet according to the patient and comorbidities; reinforcement of protection measures required for the transfer and processing of samples; close observation to look for signs of alarm or worsening of the clinical picture; support measures according to the state of the patient and comorbidities.[28]

Specific measures in Care Centers for Suspected Patients: Oseltamivir capsules (75 mg) every 12 hours for five days. Azithromycin (tablets) 500 mg daily for 3 days. In the absence of contraindications or signs of severity for its administration, Interferon alfa 2b (3 million units, administered intramuscularly, 3 times a week for four weeks). Evaluate the evolution of the disease and determine continuity of this treatment. Base drugs for comorbidities and their compensation status. Natural and Traditional Medicine (Homeopathy and Phyto-apitherapy).[28]

Specific measures in Hospitals: Kaletra (200 Lopinavir - 50 Ritonavir): 2 capsules every 12

hours for 30 days. Chloroquine (250 mg = 150 mg base): 1 tablet every 12 hours for 10 days; in the obstetric patient over 17 years of age with 50 or more kilograms of weight, use 500 mg twice a day for 10 days. In people weighing less than 50 kg, use this dose the first two days and then 500 mg once a day for the next eight days. If there are no contraindications or signs of seriousness for the administration, Interferon alfa 2b, the same dose as above is administered. Broad-spectrum antibiotics should be administered if you suspect bacterial superinfection. Treatment of comorbidities, according to their compensation status.[28]

General measures in ICU: Reported as seriously ill or critically ill; the vital signs are taken every 1 hour; diet and support measures according to the state of the patient and comorbidities; other complementary studies that include (CBC with differential, glycemia, creatinine, coagulation, D-Dimer, LDH, Electrolytes, ABG, Rx -ray, electrocardiogram, study of liver function, ferritin, C-reactive protein and virological studies); Oxygen therapy in prone position, which begins with 5 L/min and increases to the maximum of this therapeutic depending on the capabilities of low flowmeter meter and medium flow meter (10-15 l/min).[28]

Specific measures in the ICU: Kaletra (200 Lopinavir - 50 Ritonavir): 2 capsules every 12 hours for 30 days. Chloroquine (250 mg = 150 mg base): 1 tablet every 12 hours for 10 days. In confirmed cases without contraindications, Interferon alfa 2b (3 million units, administered intramuscularly, every other day, for one month). Broad-spectrum antibiotics if suspected bacterial superinfection. Treatment of comorbidities.[28]

CONCLUSIONS

COVID-19 is associated with high morbidity and mortality in elderly patients and/or with the presence of chronic diseases. In most cases, it presents with a clinical picture corresponding to a self-limited upper respiratory infection; however, in risk groups it has a rapid progression to severe pneumonia and multi-organ failure, generally fatal. The most important pillars for the prevention of the disease are: taking the necessary measures to stop person-to-person transmission, achieving differentiated attention to risk groups and a correct realization of the epidemiological history of confirmed patients in order to identify and neutralize the sources of transmission and get the population to join the health system to combat this disease.

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Conflict of interests

All authors declare no competing interests.

Contribution of authorship

All authors participated in the bibliographic search, the scientific writing, and all of them have approved the final version of the text.