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COVID-19: LITERATURE REVIEW AND ITS IMPACT ON THE PERUVIAN HEALTH REALITY

COVID-19: REVISIÓN DE LA LITERATURA Y SU IMPACTO EN LA REALIDAD SANITARIA PERUANA

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REVIEW ARTICLE

ABSTRACT

Introduction: The disease called COVID-19 is a pandemic caused by the SARS-CoV-2 virus (severe acute respiratory syndrome 2). In Peru, patient zero or first case with COVID-19 was detected on March 6th and since then the virus has continued to spread. The national government fights against this disease on several fronts, but the health situation differs greatly from developed countries. **Objective:** To review the current state of the disease and analyze its possible impact on the Peruvian health system. **Methods:** A bibliographic search of various studies was carried out since the appearance of the disease (December 2019) in different databases (PUBMED, MEDLINE, PLOs, SciELO) and Google Scholar. **Results:** The virus is transmitted mainly by the respiratory route; the average incubation period is 14 days; most patients have mild disease or are asymptomatic but 5% of these will require hospitalization, some will even require intensive therapy with mechanical ventilation; the current treatment is basically symptomatic, though antibiotics, antivirals and antiparasitics have also been used. **Conclusions:** The quarantine with strict measures of isolation and social distancing is accurate given the Peruvian health reality and the imminent contagion of the population.

Key words: SARS-CoV-2; COVID-19; Pandemics; Coronavirus infections; Health systems (source: MeSH NLM).

RESUMEN

Introducción: La enfermedad denominada COVID-19 es una pandemia causada por el virus SARS-CoV-2 (síndrome agudo respiratorio severo 2). En el Perú, el paciente cero o primer caso con COVID-19 fue detectado el último 6 de marzo y desde entonces el virus continúa su propagación. El gobierno nacional lucha contra esta enfermedad desde varios frentes, pero la situación sanitaria difiere mucho con la de países desarrollados. **Objetivo:** Revisar el estado actual de la enfermedad y analizar su posible impacto en el sistema de salud peruano. **Métodos:** Se realizó una búsqueda bibliográfica de diversos estudios desde la aparición de la enfermedad (diciembre 2019) en las diferentes bases de datos (PUBMED, MEDLINE, PLOs, SciELO) y también en Google Académico. **Resultados:** Se encontró que el virus se trasmite principalmente por vía respiratoria; el periodo de incubación promedio es 14 días; la mayoría de los pacientes tienen una enfermedad leve o son asintomáticos pero un 5% de estos requerirán hospitalización, algunos incluso de terapia intensiva con ventilación mecánica; el tratamiento actual es básicamente sintomático, pero tambien prescriben antibióticos, antivirales y antiparasitarios. **Conclusión:** La cuarentena con medidas estrictas de aislamiento y distanciamiento social es precisa, dada la realidad sanitaria peruana y el inminente contagio de la población.

Palabras clave: SARS-CoV-2; COVID-19; Pandemias; Infecciones por coronavirus; Sistemas de salud (fuente: DeCS BIREME).

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INTRODUCTION

On the last day of 2019, China reported 27 cases of pneumonia of unknown cause in the city of Wuhan, which had a close relation to the Huanan market where diverse exotic animals are sold, such as bats, pangolins and snakes[1,2]. The characteristic clinical presentation of these patients included fever, dry cough and dyspnea. A week after the report, the Chinese Center of Disease Control and Prevention discovered that the cause of this disease was a new coronavirus (SARS-CoV-2) that the WHO later denominated COVID-19, from the English acronym "Coronavirus Disease 2019"[3]. Such was the spread of disease that the confirmed cases and deaths kept increasing in China and rapidly COVID-19 reached other countries from various continents until it was considered a pandemic[4].

In the following weeks it was proven that the majority of patients with COVID-19 resolved spontaneously. Likewise, we saw that the disease affects both genders with a slight predominance towards men. Of those affected patients, some require hospital admission and even mechanical ventilation support[5]. These complications are frequent in people with chronic diseases (diabetes mellitus, hypertension, asthma, obesity, etc.) in whom the fatality is greater than the general population[6]. The need for hospitalization and use of intensive therapy converted this pandemic in a real threat for the health systems worldwide.

In Peru, around the middle of March 2020 due to the imminent contagion of the population, the government established healthcare policies similar to those of the Chinese government. This way, quarantine and social distancing measures, the acquisition of new beds and intensive care equipment were established, as well as, the hiring and redistribution of trained professionals in intensive care. However, any strategy applied in another country to counteract the pandemic must be adapted to our reality, since it seems that the quarantine alone is not enough to prevent the spread and the socioeconomic impact of the disease is worrisome. This review was carried out with the objective of determining the current state of the disease and its possible impact on the Peruvian health system.

METHODS

A literature search was performed in PUBMED, MEDLINE, PLOs, and SciELO databases as well as Google Academic; available papers with complete text in Spanish and English were selected with the keywords SARS-CoV-2, COVID-19, pandemics and health systems. The relevant information was extracted from the first reported cases to the present and compared to the current Peruvian health situation.

RESULTS

Etiology and transmission mechanism

COVID-19 is a disease caused by SARS-CoV-2, a virus belonging to the coronavirus family that originated two prior zoonotic epidemics, SARS-Co-V caused Severe Acute Respiratory Syndrome in 2002 and MERS-CoV that caused the Middle East Respiratory Syndrome in 2012[7]. While SARS-CoV-2 is a virus found in snakes, bats and pangolins, apparently one of these animals began the transmission chain in being consumed by various people in Wuhan. However, it is difficult to determine an exact origin of the virus; rather, it seems to have a mixed origin among the diverse animal reservoirs including another unknown one[8,9].

Once the SARS-CoV-2 infection is acquired, the disease has an average incubation period of 14 days, although some reports suggest up to 24 days; which is why the quarantine period should be greater than the latter. A person infected with SARS-CoV-2, even if asymptomatic, could infect 2 or 2.5 people. Although the effective transmission is through large drops via inhalation or contact with oral or ocular mucosa, the virus has also been found in feces, blood and even microdroplets released during a normal conversation; for this reason the general public should wear adequate masks when leaving their home. Furthermore, the transmission associated with medical care reaches over 40%, an important data to reinforce the personal protective equipment in different health establishments. Fortunately, there does not seem to be a perinatal transmission[6,10-12].

Physiopathology

After SARS-CoV-2 exposure, the virus travels through the respiratory tract until reaching the alveolar epithelial cells -pneumocytes- type I and II, that is where it joins the Angiotensin-converting enzyme type 2 (ACE2) receptor. In the normal human lung, the ACE2 is mainly expressed in the type 2 pneumocytes, which produce surfactant, a substance that lowers the surface tension within the alveoli to avoid its collapse. The fact that men have a greater ACE2 level in their pneumocytes explains why they have

a greater possibility of presenting complications and an increase in lethality[13]. The binding of SARS-CoV-2 to the ACE2 receptor is up to 20 times greater than that of SARS-CoV, which explains its greater infectivity. Its binding to ACE2 activates a great expression to said enzyme which leads to the death of the infected alveolar cell and the infection of the contiguous cells. In such way, the virus rapidly injures the lung tissue causing pneumonia. Since it is a virus similar to SARS-CoV and MERS-CoV, the pulmonary histopathology shows similar findings between these pathologies: the hyaline membrane formation in the alveoli and the mononuclear interstitial inflammatory infiltrates with multinucleated giant cells[14].

Clinical presentation and diagnosis

Despite the great transmissibility of SARS-CoV-2, the majority of patients have a mild disease or are asymptomatic. 5% of the infected population requires hospital admission and even some require intensive therapy with mechanical ventilation support[15]. In addition, those who survive the disease could suffer from pulmonary fibrosis, this would be one of the most feared complications after recovery[16].

Furthermore, in symptomatic patients the clinical presentation is mainly fever in over 80%, dry cough in over 70%, dyspnea in over 50%, and also asthenia and myalgias, although less than 50% of cases. Other less reported symptoms are headache, odynophagia, abdominal pain and diarrhea[17].

Two tests are used for diagnosis. A serologic test, also called rapid test because its results are ready in 15 minutes. This test identifies the IgM and IgG antibodies present in the blood or plasma of sick patients. If the test reveals an elevated number of antibodies, the rapid test will be positive, and it is concluded that the person has or recently had the disease. The rapid test has a high specificity, which is useful but requires complementing with the molecular test. This one, also known as PCR-RT, for its English initials, involves a reverse transcriptase polymerase chain reaction and is the test of choice for SARS-CoV-2 diagnosis. It is based on the viral RNA analysis, ideally found in a sample of the lower respiratory tract, although these tests often come from a nasopharyngeal swab[18,19].

Likewise, the most frequent abnormal laboratory findings are lymphopenia, prolonged prothrombin time and elevated lactate dehydrogenase. The thoracic X-rays are characterized by irregular bilateral infiltrates and almost all thoracic computerized tomographies show some alteration such as consolidation or "ground-glass opacity" infiltrates[15,20].

Prevention and treatment

There still does not exist a vaccine to prevent COVID-19, which is why the current treatment is basically symptomatic. Antibiotics, antivirals and antiparasitics have been used with promising results, but the efficacy of these drugs have yet to be verified through large clinical trials. Since we do not count on an effective treatment at this moment, the best way to fight this pandemic is through control of possible sources of infection including asymptomatic patients, early diagnosis and notification, social distancing and support therapies. Also, protective measures for the general population is based on improving personal hygiene, wearing masks -preferably disposable ones- and keeping spaces well ventilated[20].

Table 1. Summary of some relevant articles about COVID-19 up to April 12, 2020.

Articles	Results	Conclusions
[6] Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China.	Out of a total of 138 patients with COVID-19, 36 patients (26.1%) were in the intensive care unit (ICU): 22 with acute respiratory distress syndrome (61.1%), 16 with arrythmia (44.4%) and 11 with shock (30.6 %). The median time from the first symptom until dyspnea was 5 days, until hospital admission 7 days and until ARDS 8 days. Patients treated in ICU (n = 36), compared to those patients not treated in ICU (n = 102), older adults (average age, 66 years) and had more probability of having underlying comorbidities.	Of 138 patients hospitalized with pneumonia due to 2019-nCoV: 41% had a possible hospital transmission, 26% were seen in ICU and mortality was 4.3%.
[7] Paules CI, Marston HD, Fauci AS. Coronavirus Infections—More Than Just the Common Cold.	The coronavirus (nCoV-2019) causes fever, cough, dyspnea and/or watery diarrhea. Up to 30% of infected patients required mechanical ventilation and 10% died, the highest mortality rates were related to patients with greater comorbidities.	La outbreak path and the appearance of the nCoV-2019 recurrence is unpredictable, therefore, early diagnosis and effective isolation is required.
[8] 2020 Cross-species transmission of the newly identified COVID-19.	After analyzing 276 coronavirus genomes, the nCoV-2019 sequence seems to be a recombination between bat coronavirus and others from unknown origin, located within the glycoprotein spikes that recognizes cell surface receptors. Likewise, the nCoV-2019 genetic makeup is similar to that of the bat coronavirus and especially to the snakes in China.	The results suggest that a homologous recombination could occur that contributes to the transmission of cross species with nCoV-2019.
[9] Presumed Asymptomatic Carrier Transmission of COVID-19.	A family group of 5 patients with fever and respiratory symptoms admitted to the Quinto Hospital Popular de Anyang, China was reported. Patient 1 asymptomatic was isolated and observed, but never presented symptoms. The PCR-RT test results, Chest tomography x-rays were normal at first, just as was the C-reactive protein and lymphocyte count. Patients 2 to 6 developed nCoV-2019, 4 were women between 42 and 57 years of age, none had visited Wuhan nor had contact with another individual, except patient 1. Two patients developed severe pneumonia, with opacities in chest tomography and multifocal ground glass images. One patient had subsegmental areas of consolidation and pulmonary fibrosis.	The prevention of an infected asymptomatic nCoV-2019 carrier is a challenge. The mechanism by which the asymptomatic carriers can acquire and transmit the coronavirus nCoV-2019 requires further study.
[10] Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes.	The presence of nCoV-2019 in anal swabs and in blood. Two groups were formed: one collected samples of 39 patients and the second group collected simples of 139 patients, with positive viral nucleotide detection.	nCoV-2019 can be eliminated through multiple routes for which there could be fecal-oral transmission.
[11] Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records.	9 pregnant women between 25 and 40 years of age with history of epidemiological exposure to nCoV-2019 were studied, all in their third trimester with a gestational age range upon admission of 36 to 39 weeks plus 4 days and who underwent a C-section. None of these patients had a chronic underlying disease. One patient had influenza virus infection upon being admitted to the hospital. Seven of nine patients presented fever without chills, but none had a body temperature >39°C. None had the typical thoracic tomography: multiple irregular shadows in ground glass opacity in the lungs.	Clinical characteristics of pneumonia by nCoV-2019 in pregnant women were similar to those reported in non-pregnant adult patients. Currently there is no evidence of perinatal infection by nCoV-2019 at the end of pregnancy.
[12] Single-cell RNA expression profiling of ACE2, the putative receptor of Wuhan 2019-nCov.	According to the WHO, nCoV-2019 has caused 76 392 confirmed cases and 2348 deaths in China as of February 22, 2020. It was reported that SARS-CoV-2 shares with SARS-CoV the same angiotensin-converting enzyme 2 (ACE2) receptor. The expression of this receptor is in the alveolar type II cells (AT2) that are also expressed in other genes that positively regulate the viral entrance, reproduction and transmission.	This study provides a biological support for the future development of the anti-ACE2 therapeutic strategy.
[13] Cryo-EM Structure of the 2019-nCoV Spike in the Prefusion Conformation.	Several SARS-CoV specific monoclonal antibodies were tested and it was found that they did not have a noticeable union to nCoV-2019. Furthermore, it was demonstrated that biophysical and structural evidence that nCoV-2019 attaches to the ACE2 receptor with greater affinity than does SARS-CoV.	The nCoV-2019 structure allows for greater virus infectivity and dissemination.

[14] Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72314 Cases from the Chinese Center for Disease Control and Prevention.	Out of a total of 72 314 registered cases, 44 672 were classified as COVID-19 confirmed cases. The majority of cases were between 30and 79 years of age (87%), 1% had 9 years of age or less, 1% between 10and 19 years of age, and 3% were 80 years or older. The majority of cases were diagnosed in the province of Hubei (75%) and the majority of exposures related to Wuhan (86%). The majority of cases were classified as mild (81%), 14% were severe and 5% were critical. The general fatality rate was 2,3% (1023 deaths in the 44 672 confirmed cases). There were no deaths in the 9 years and younger group and the fatality rate among the critical cases was 49%. Of the 44672 cases, 1716 were healthcare workers (3.8%), 1080 of which were in Wuhan (63%). 14,8% of confirmed cases among healthcare workers were classified as severe or critical and 5 deaths were identified.	COVID-19 spread rapidly in one city of China in just 30 days. The great speed of geographical expansion and the sudden increase in the number of cases surprised and rapidly overwhelmed the health services and public health in China, particularly in the city of Wuhan and the province of Hubei.
[15] Viral Infection Increases the Risk of Idiopathic Pulmonary Fibrosis.	Of 1287 participants, the grouped OR of all viruses indicated that the viral infection could increase the risk of idiopathic pulmonary fibrosis significantly (OR, 3.48; IC 95% 1.61-7.52; p = .001), but not its exacerbation (OR, 0.99; IC 95%, 0.47-2.12; p = 0,988). All the analyzed viruses, including the Epstein-Barr virus, cytomegalovirus, human herpesvirus 7 and human herpesvirus 8 were associated to a significant increase in idiopathic pulmonary fibrosis risk, except human herpesvirus 6.	These findings imply that viral infection could be a potential risk factor for idiopathic pulmonary fibrosis.
[16] Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China.	On January 2, 2020, 41 patients were identified as infected with nCoV-2019. The majority of those infected were men (73%) and less than half had underlying diseases (32%). The median age was 49 years (RIC 41.0 – 58.0). 66% of patients had been exposed to the seafood marked in Huana. The common symptoms at the beginning of this disease were fever (98%), cough (76%) and myalgia or fatigue (44%). Dyspnea developed in 55% of cases and the average time from start of the disease to dyspnea onset was 8 days. 63% of patients had lymphopenia. 41 pacientes had pneumonia with abnormal findings in the thoracic tomography. Complications included acute respiratory distress syndrome (29%), anemia (15%), acute heart failure (12%) and secondary infection (10%). 32% of cases were admitted in ICU and 15% died.	The 2019-nCoV infection caused a severe respiratory disease similar to coronavirus of the severe acute respiratory syndrome. It was associated to a greater admission to ICU and high mortality.
[17] Detection of SARS-CoV-2 in Different Types of Clinical Specimens. JAMA.	1070 samples were collected from 205 patients with COVID-19 who had an average age of 44 years (range, 5-67 years) and 68% were men. The majority of patients had fever, dry cough and fatigue. 19% had an underlying severe disease. The liquid samples of the bronchoalveolar lavage showed the highest positive rates (93%), followed by sputum (72%), nasal swabs (63%), biopsies through fibrobronchoscopic brush (46%), pharyngeal swabs (32%), feces (29%) and blood (1%). None of the urine samples tested positive.	The samples with the highest rates for nCoV-2019 detection were those of the lower respiratory tract (bronchoalveolar lavage), while the simples with greater false negatives were those obtained from pharyngeal swabs, feces and blood.
[18] Clinical characteristics of 2019 novel coronavirus infection in China.	Data from 1099 patients was extracted, the median age was 47 years, and 41.9% were women. Only 1.18% were patients who had direct contact with wildlife, while 31.3% had been in Wuhan and 71.8% had contact with people in Wuhan. Fever (87.9%) and cough (67.7%) were the most common symptoms. The median period of incubation was 3.0 days (range: 0 to 24 days). Upon admission, the typical radiological finding in the thoracic tomography (50%) was ground glass opacity. The most severe cases were diagnosed by symptoms plus reverse transcriptase polymerase chain reaction. Lymphopenia was observed in 8.,1% of patients. 5% of patients were admitted to intensive care units and only 1.36% died.	The nCoV-2019 epidemic spread rapidly through person to person transmission.
[19] The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China.	Since January 10, 2020, 41 patients were diagnosed with 2019-nCoV infection. The onset of disease in these 41 cases ranges from December 8, 2019 to January 2, 2020. Symptoms included fever (over 90% of cases), malaise, dry cough (80%), difficulty breathing (20%), and respiratory distress (15%). Vital signs were stable in the majority of cases, while leucopenia and lymphopenia were common. The 2019-nCoV infection in Wuhan seems to be clinically milder than SARS or MERS en severity and fatality.	The Wuhan outbreak is a clear reminder of the continuing threat of zoonotic diseases on global health security Sharing the experiences of all geographic regions is key to counteract the epidemic.

DISCUSSION

Despite the high transmissibility of SARS-CoV-2, its fatality is apparently low (3%) related to SARS (9.6%) and MERS (34.4%). Likewise, the majority of infected patients are asymptomatic or have few symptoms. The most frequent complication is acute respiratory distress syndrome which requires mechanical ventilation support in 5% of patients[1,6,21]. Upon extrapolating these numbers to almost 32 million of inhabitants in Peru[22], as long as the Peruvian population has the same characteristics as the revised series and without applying any preventive measure, we expect to have 1.6 million hospitalized in the country, of which 48 thousand would die; in addition to a possible national health system collapse which could generate over 5% mortality.

It is difficult for any government to make decisions in an unprecedented global crisis. No health system is prepared to handle this pandemic. Furthermore, a bad public health decision can be devastating for the population and lead to the collapse of the health system in any country. For this reason, in view of the imminent COVID-19 contagion of the population, the Peruvian government enacted a health state of emergency with measures of social immobilization and mandatory home isolation from March 16 to April 26 as a disease containment measure. Undoubtedly, these restrictive measures will generate a great socioeconomic impact, but nothing compared to the loss of hundreds or thousands of human lives. In this way, the national government strategy was to minimize the spread of COVID-19 through "flattening of the curve" of those possibly infected and that way reduce the overload on health services. A logical decision, given that other herd immunity strategies opted by some developed countries implicated the contagion and recovery from viral infection of more than 60% of the population, with the consequent risk that this could bring to the health system. Those countries that began with this last strategy, in the following weeks changed to more restrictive measures, since it seems very difficult to fight the virus due to its high infectivity and that the uncalculated collapse of health system.

The main health problem in Peru is the deficient infrastructure, a fact verified by the Public Defender's Office on April 2018, just as in the last great national census of health infrastructure in 2006 where it was found that 20% of high complexity hospitals (level III) lacked adequate equipment for care. For example, the intensive care units (ICU) of the entire Peruvian health system (MINSA, EsSalud, FFAA, PNP and private clinics) had barely 685 beds, of which only 60 (15%) were available given that the others were already occupied (23). The precarious situation of our health system is clear; if the number of those infected increases, the system will simply collapse. In addition to that, there is also a lack of capacitated human resources: the Colegio Médico del Perú reports a major deficit of 15 thousand medical specialists[24].

In light of this landscape, the Peruvian government's health strategy includes the purchase of new beds in ICU, the suspension of outpatient visits and elective surgeries, reinforcement of emergencies, notification of suspected patients, as well as, the home monitoring of confirmed cases and the transfer of complicated cases to COVID-19 referred hospitals.

On the other hand, the need for diverse materials and medical supplies in the middle of a crisis provoked by the pandemic also limits the acquisition of these. For example, the acquisition of mechanical ventilators for ICU normally is a process that takes around 2 months, Currently the great demand for these worldwide and considering that many countries already placed their importation orders before Peru; it will most probably take longer. For this reason, the national government has coordinated with Peruvian universities the making of mechanical ventilators and in this way attempt to alleviate the demand[25]. All this effort on behalf of the Peruvian government and society does not guarantee success, but not doing so leads to an unnecessary loss of many human lives. Although it might not eliminate COVID-19 in the following months, the rational political response is to fight it now with quarantine.

CONCLUSION

Quarantine with strict measures of social isolation and distancing is precise given the Peruvian health reality and the imminent contagion of the population. These restrictive measures must be evaluated on an ongoing basis in the country to avoid the collapse of the health system. Finally, it is necessary to promote more research on this topic in our reality to obtain first-hand information and make more adequate decisions.

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