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Severe Respiratory Distress Syndrome due to the new Coronavirus SARS-COV-2: A Global and Latin American Perspective

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Abstract

After the initial report of an emerging SARS-like virus in Wuhan in December 2019, many details remain completely unscrambled; such as its origin and its ability to transmit to humans. The number of cases increases, it is less pathogenic than MERS-CoV, but with a greater infectious capacity mostly reflected since its inter-human transmission capacity was demonstrated. Indirectly affected by ignorance of the source of infection, migration. Different case to some influenza type events, in which the knowledge of the infectious source allowed blockages based on their seasonal migratory phenomenon. This viral emergency raises important questions: "What is our ability to respond to emerging germs of great virulence and infectivity? Why have there not been cases in Latin America? Extreme control of travelers? Is the environmental selection of antimicrobial resistance due to industrial use a limitation to the treatment of the event?.

Keywords: *MERS-CoV (Middle East Respiratory Syndrome); 2019-nCoV (New Coronavirus); Migration; Latin America; ELISAP (Latin American Research Team on Infectiology and Public Health)*

Circulating coronaviruses in Colombia, emerging viruses and traveling population

Colombia was the first country in Latin America to obtain the diagnostic molecular test for nCoV - 2019, the coronavirus HKU229, 1E, OC43 and NL63 circulates in our territory; and the Severe Acute Respiratory Syndrome virus (SARS) that emerged in 2002 and the Middle East Respiratory Syndrome (MERS-CoV) of 2012 have not yet circulated to date the new Coronavirus (nCoV - 2019) of China, is not circulating in our country [1] and at this time (February 11, 2020) the number of confirmed cases is 43,146 with 1,018 deaths [2] total. If we analyze that the infection does not cause serious illness, the infected person probably does not consult a health center. Instead, he will go to work and travel; therefore, it will potentially release the virus to its contacts, possibly international [3] and this explains the increasing number of cases already imported in 29 countries; since attempts have been made to carry out epidemiological blockages and border controls [3].

Different studies reveal the great capacity to infect this agent, which compared to other coronaviruses with previous health events of international interest; has lower mortality (Figure 1).

	2019-nCoV	MERS-CoV	SARS-CoV
Date	2019-12	2012-06	2002-11
Place	Wuhan, China	Jeddah, Arabia	Guangdong, China
Age	49 (21-76)	56 (14-94)	40 (1-91)
Man/Woman	2.7/1	3.3/1	1/1.25
Confirmated Cases	4586	2494	8096
Mortality	106 (2.3%)	858 (37%)	744 (10%)
Health personnel	n=16	9.8%	23.1%
Symptoms			
Fever	98%	98%	99%
Cough	76%	47%	29-75%
Dyspnoea	55%	72%	40%
Diarrhea	3%	26%	25%
Throbbing pain	0%	21%	13-25%
MRA	9.8%	80%	20%

Figure 1: *Zhu N, Zang D, Wang W., et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019 - N Zhu., et al. N Engl J Med. 2020. Adapted: Latin American Research Team in Infectology and Public Health ELISAP.*

In a dynamic world of long distances but a moving society, the recent Ebola epidemic in West Africa, the emergence of the Middle East respiratory syndrome coronavirus (MERS-CoV) and the reappearance of Zika and Chikungunya viruses have highlighted the importance of being alert to the possibility that an emerging pathogen is causing a febrile episode. The absolute number of travelers is large and growing. The International Tourism Organization reported 1.2 billion trips in 2015, an increase of 4.4% from the previous year [4].

Migration and impact on local or recipient epidemiology

Defining then, that the population exodus/migration, medical tourism, globalization and international trade; they could have an important role and indirectly influence the behavior of these entities and the lack of positive results to the control measures implemented. Therefore, disease surveillance among travelers provides an important source of information that can provide recommendations before travel and clinical management after the trip [5] and identify sentinel data to detect outbreaks of new diseases and be used to track the global movement of infectious diseases [6].

In a traveler, it is necessary to track their origin, destination and transits during a trip, since the possible causes of fever in the returning traveler are numerous, and a specific diagnosis is often difficult to establish because diagnostic tests for many diseases They work poorly or are not available locally. Even in referral centers with diagnostic experience, approximately 25% of patients never receive a diagnosis (although they generally improve clinically) [6]. But, on the other hand we have the mortality associated with entities linked to travel; Since in most case series involving fever in returning travelers, deaths have been infrequent with a general mortality ranging between 0.2 and 0.5% [7-9].

Fever and death in the traveling traveler

We have that falciparum malaria is the most common serious infection observed in returning travelers and remains the leading cause of death. In areas where falciparum malaria is not endemic, a delay in diagnosis is common and can have fatal consequences. During the recent Ebola epidemic in West Africa, falciparum malaria was the most common diagnosis in patients returning from the affected area [10]. Other causes of death reported include melioidosis, severe dengue, scrub typhus, enteric fever, encephalitis and non-tropical

infections, including influenza, bacterial pneumonia, and septicemia [11]. Regarding the severe dengue event in the Colombian territory, we have that in the epidemiological week 05 of 2020, 4 189 probable cases of dengue were reported with 183 (1.1%) of severe dengue (Figure 2), dengue cases come from 32 departments, 5 districts, 631 municipalities and 5 countries; and 31 probable deaths from dengue have been reported as of 2020 [12].

Reported cases of dengue by territorial entity of origin and classification in Colombia, epidemiological weeks 01 to 05 of 2020.

Territorial entity	Dengue		Serious Dengue		Total	
	n	%	n	%	n	%
Cali	2193	13,5	27	14,8	2220	13,5
Tolima	1921	11,8	9	4,9	1930	11,8
Valle del Cauca	1868	11,5	16	8,7	1884	11,5
Huila	1600	9,9	28	15,3	1628	9,9
Cesar	827	5,1	5	2,7	832	5,1
Santander	766	4,7	4	2,2	770	4,7
Meta	706	4,4	3	1,6	709	4,3
Cundinamarca	615	3,8	4	2,2	619	3,8
Antioquia	601	3,7	6	3,3	607	3,7
Córdoba	596	3,7	5	2,7	601	3,7
Atlántico	563	3,5	10	5,5	573	3,5
Barranquilla	527	3,2	6	3,3	533	3,2
Sucre	496	3,1	20	10,9	516	3,1
Caquetá	370	2,3	9	4,9	379	2,3
Bolívar	327	2,0	5	2,7	332	2,0
Norte de Santander	322	2,0	2	1,1	324	2,0
Cartagena	317	2,0	0	0,0	317	1,9
Putumayo	179	1,1	0	0,0	179	1,1
Casanare	146	0,9	1	0,5	147	0,9
Caldas	141	0,9	5	2,7	146	0,9
La Guajira	141	0,9	2	1,1	143	0,9
Magdalena	136	0,8	5	2,7	141	0,9
Quindío	129	0,8	0	0,0	129	0,8
Risaralda	118	0,7	0	0,0	118	0,7
Cauca	98	0,6	6	3,3	104	0,6
Boyacá	99	0,6	1	0,5	100	0,6
Amazonas	63	0,4	0	0,0	63	0,4
Santa Marta	60	0,4	1	0,5	61	0,4
Nariño	53	0,3	0	0,0	53	0,3
Exterior	51	0,3	0	0,0	51	0,3
Arauca	46	0,3	0	0,0	46	0,3
Guaviare	27	0,2	1	0,5	28	0,2
Chocó	28	0,2	0	0,0	28	0,2
Vaupés	27	0,2	0	0,0	27	0,2
Archipiélago de San Andrés	26	0,2	1	0,5	27	0,2
Buenaventura	19	0,1	0	0,0	19	0,1
Guainía	10	0,1	1	0,5	11	0,1
Vichada	9	0,1	0	0,0	9	0,1
Desconocido	2	0,0	0	0,0	2	0,0
Total	16 223	100	183	100	16 406	100

Figure 2: *Source: Sivigila, National Institute of Health, Colombia. 2020. Adapted: Latin American Research Team in Infectology and Public Health ELISAP.*

New coronavirus, more infectious and less lethal? Its origin

After an apparent trend towards the plateau of the curve of new cases between January 28 and 29, 2020 (from 5578 confirmed cases and 131 deaths to 6125 confirmed cases with 133 deaths respectively), hypothetically attributed to the culmination of the prodromes and history natural disease of the initial cases progressing to recovery or death; we had to witness the vertiginous increase in the

number of cases of severe respiratory distress syndrome by 2019-nCoV; probably attributable to confirmation already of interhuman transmission, among other factors [2].

There is still confusion due to specific details about its origin, infectious source; among other. Although albeit dizzying; Compared to the rapid rearrangement and mutation of avian influenza (H7N9), the degree of diversification of 2019-nCoV is much lower [13,14]. The new coronavirus was isolated for the first time from vendors working in the seafood market in southern China in Wuhan. This market also sells wild animals or mammals, which were probably intermediate hosts of nCoV 2019 that were originally from bat hosts (Figure 3B). It is speculated that intermediate hosts (wild mammals) may have been sold to the seafood market in Wuhan [15].

Regarding its origin, a phylogenomic analysis of the recently published genomic data of 2019-nCoV, showed that 2019-nCoV is more closely related to two CoV sequences similar to severe acute respiratory syndrome (SARS) isolated in bats in 2015 to 2017, which suggests that the Cov of bats and humans 2019-nCoV share a more recent common ancestor (Figure 3A). Therefore, nCoV 2019 can be considered as a virus like SARS. The two viruses were collected in Zhoushan, Zhejiang Province, China, from 2015 to 2017 [16].

According to their phylogenetic relationships, 27 2019-nCoV isolates examined in this study can be divided into at least 6 genotypes (I - VI) (Figure 3C). The 27 isolates are mainly obtained from four different places, three Chinese cities of Wuhan, Zhejiang and Guangdong, as well as from Thailand, and all of them have visited or contacted people from Wuhan. Genotype VI, V and IV (Guangdong and Shenzhen) is found in the basal branch of the 2019-nCoV phylogenetic tree, indicating that patients infected with these CoV genotypes were among the first infected groups. Three genotypes are present in samples from Guangdong Province, indicating that the six strains were infected from different places in Wuhan. Two genotypes are found in Zhejiang Province, suggesting that the two strains were infected from different places in Wuhan. The two Nonthaburi strains detected in Thailand are of the same genotype, perhaps originating in the same place in Wuhan [15].

As for the guest, to date, the intermediate host of 2019-nCoV has not been determined (Figure 3B). Given that intermediate hosts are generally mammals, they are likely to be live mammals sold in the seafood market in southern China [17].

The phylogenomic tree of coronaviruses and the genotypes of the 2019-nCoV chains.

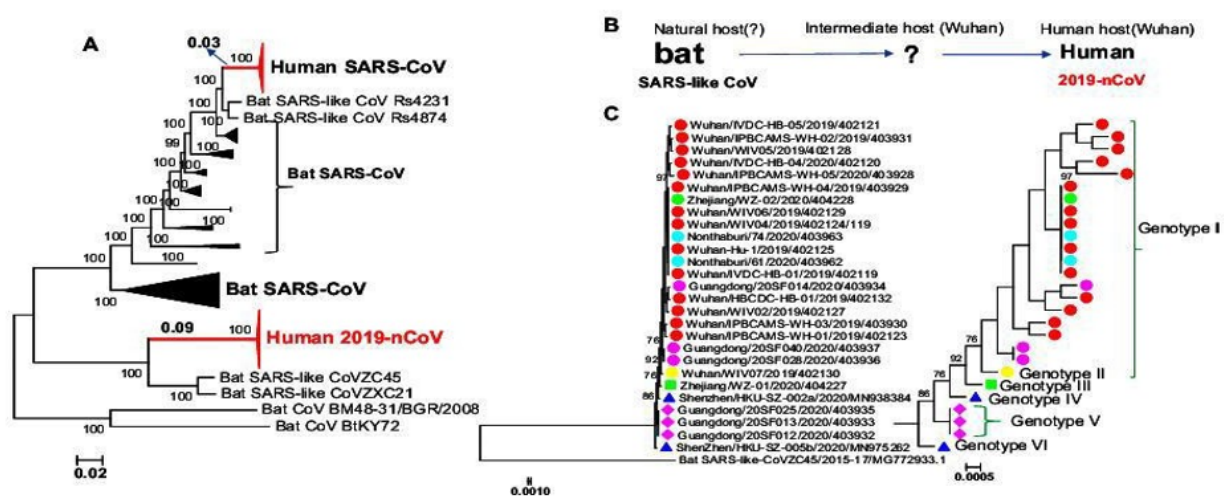

Figure 3: *Liangsheng Zhang, Fu-ming Shen, Fei Chen, Zhenguo Lin, Origin and evolution of the 2019 novel coronavirus, Clinical Infectious Diseases, ciaa112, 03 February 2020 https://doi.org/10.1093/cid/ciaa112. Reproduced with authorization of journals.permissions@oup.com.*

International trade and migration. Why have not documented cases in Latin America and other destinations?

Analysis and Conclusions

The frequency with which these types of infectious agents circulate in the Asian country, China; With a population of 1,395,380,000 people, and a very low percentage of immigration, it is the most populous country in the world (146 inhabitants per Km^2) and the second international economy by volume of Gross Domestic Product GDP (GDP per capita is a very good indicator of the standard of living and in the case of China, in 2018, it was € 8,263, with which it ranks 72nd in the ranking and its inhabitants have a low standard of living in relation to the rest of the 196 countries of the ranking) [18].

With which it is inferred that it is a migrant country by default, 10,732,281 Chinese people live abroad, 0.77% of its population and travel mainly to the United States, where 27.81% go, Hong Kong, 21, 79% and followed by Japan, 7.53% [19]. Allowing us to analyze that in the ranking of the 30 destinations of the Chinese migrant population, only one Latin American country (Brazil) appears and in the position number 25 from 30 countries; being able to raise the low migration to Latin America as a sociodemographic enhancer factor and hypothesis about the non-detection of circulating cases of 2019-nCoV in South America. But more importantly, it allows us to infer that it could favor the entry of cases to Latin America and forces us to focus efforts on surveillance, strategies, epidemiological blocks and other strategies; and direct them to this Latin American destination (Brazil).

It also allows us to ask why there is the distribution of new cases of infection or cases imported to destination countries of the Chinese migrant; bordering and other industrialized.

Clinical spectrum, the search for an effective treatment

The analysis of the spectrum of complications in some patient cohorts has already been analyzed, finding data in a cohort of 41 complicated patients: ARDS 29%, heart failure 12%, acute renal failure 7%, shock 7%, secondary infections 10%. Lymphopenia (< 1000/mm^3) was the most frequent finding in the admission laboratory (63% of cases). Of the 41 patients, 13 (32%) were admitted to an ICU intensive care unit and six (15%) died (mortality of those admitted to the ICU of 38%) [20]. Although the 2019-nCoV mortality is minor, to date already leaves more than 1000 human losses [2]; generating all kinds of alarms regarding therapeutic plans.

As 2019-nCoV is an emerging virus, no effective treatment has been developed for the disease resulting from this virus. Since the combination of lopinavir and ritonavir was already available at the designated hospital, a randomized controlled trial was rapidly initiated to evaluate the efficacy and safety of combined use of lopinavir and ritonavir in hospitalized patients with 2019-nCoV infection [21].

It is an emerging virus, with no current therapeutic chances or established targets. No antiviral treatment for coronavirus infection has proven effective. In a historical control study, the combination of lopinavir and ritonavir among patients with SARS-CoV was associated with a substantial clinical benefit (less adverse clinical outcomes) [22]. And Arabi and his colleagues initiated a placebo-controlled trial of interferon beta -1b, lopinavir and ritonavir among patients with MERS infection in Saudi Arabia [23]. Environmental selection of antimicrobial resistance and its role in the emergence of emerging or re-emerging diseases.

Recall that the effects on the individual by treatment with antibiotics, go beyond it [24]. Emerging (EE) and Reemerging (EREE) diseases are currently a global concern, due to the unusual form of their presentation, as a result of several factors related to changes in local ecosystems that alter the balance between pathogens and their hosts usual. Emerging and reemerging pathogens have great biological flexibility that allows them to take advantage of the epidemiological opportunities that arise in the environment, generating epidemics; Among other consequences. Such is the case of the demonstrated relationship between exposure to environmental mercury and increased antibiotic resistance for isolates of E. coli in different populations [25] and the case of the first report on co-location of a plasmid of a gene that confers resistance to Cadnio/Zinc and resistance genes for aminoglycosides and macrolides [26]; all this in the

context of the environmental selection of antimicrobial resistance. These are clear examples of the ability to adapt Emerging (EE) and Reemergent (EREE) microorganisms, to noxa, whether antibiotic pressure, Environmental or other.

We are then in the arena with an emerging entity of high clinical and epidemiological impact; for which we were not prepared. There is preclinical evidence showing the potent efficacy of remdesivir (a broad-spectrum antiviral nucleotide prodrug) for treating MERS-CoV and SARS-CoV infections [27,28].

Adjuvant therapy to the new Coronavirus?

In order to offer adjuvant measures, it is important to emphasize understanding and determination about the damage or benefit of corticosteroids. Theoretically, corticosteroid therapy could play a role in suppressing pulmonary inflammation; based on that in SARS-CoV infection, such as influenza; Systemic inflammation was associated with adverse outcomes [29]. In SARS, inflammation persisted after viral clearance [30,31] and pulmonary histology in SARS and MERS infections revealed inflammation and diffuse alveolar damage [32].

Historically, corticosteroids were widely used during outbreaks of severe acute respiratory syndrome (SARS) -CoV1 and Middle Eastern Respiratory Syndrome (MERS) -CoV, 2 and are being used in patients with 2019-nCoV in addition to other therapies [21], however, the current internal WHO guideline on the clinical management of severe respiratory syndrome suspected by 2019-nCov (issued January 28, 2020) recommends against the use of corticosteroids, unless otherwise indicated [33].

The future of the epidemic

In the course of the 2019- nCoV event, it is revealed that no effort is tiny, and although the low risk is sustained and there is no confirmed circulation in Latin America; We must incorporate into our mode of operation with the aim of surveillance and control, scenarios such as: transmission mechanisms, signs and symptoms, how is it diagnosed or confirmed? What is the WHO case definition for surveillance? What are the prevention measures for the community and healthcare staff? Risk factors, support measures or treatment.

Frontline medical staff and scientists in China have played a leading role in the fight against the 2019-nCoV associated pneumonia outbreak. The basic and essential strategies that we should follow are early detection, early diagnosis, early isolation and early treatment of the disease. For the enormous efforts of medical professionals to treat patients: substantial prevention and public health measures, accelerated research. We expect the inflection points for new 2019-nCoV cases and the resulting fatal events could come soon [34].

Recently, the Coronavirus Study Group (English CSG) of the international virus taxonomy committee; which is responsible for developing the official classification of viruses, based on phylogeny, taxonomy and established practices; He recognized the new coronavirus as a relative of the Severe Acute Respiratory Syndrome coronavirus (SARS-CoVs) and designated it Coronavirus 2 Severe Acute Respiratory Syndrome (SARS-CoV-2) [35].

Conflict of Interests

The author declares that he is independent with respect to financing and support institutions and that during the execution or drafting of the manuscript no interest or values other than those usually carried out by the research have been affected.

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