IMPACT OF SOCIAL ISOLATION ON PUBLIC HEALTH IN TOCANTINS: A PATHOLOGICAL, ECONOMIC AND SOCIAL ANALYSIS OF COVID-19

Geovane Rossone Reis[1], Waldecy Rodrigues, PhD[2], Marcos Gontijo da Silva, PhD[3], Janne Marques Silveira[4], Marllos Peres de Melo, PhD[5], Érica Eugênio Lourenço Gontijo, PhD[6]

[1,4]M.Sc, University of Gurupi, Brazil
[2,3]Federal University of Tocantins, Brazil
[5,6]University of Gurupi, Brazil
[1]Email: georossone@hotmail.com

Published: 29 April 2020

Abstract

Coronovirus is causing disastrous problems worldwide due to high mortality rates, increased demand from the health sector and the economic impact of social isolation. Based on a review of the pathology of COVID-19, its variation in dissemination capacity in different geographic regions and the capacity of the public health system in the Brazilian state of Tocantins, a non-conclusive analysis is made that the economic impact of social isolation in public health it tends to be greater than the impact caused by the disease itself, since this state is one of the lowest demographic densities in Brazil and with constant temperatures of low survival for SARS-CoV-2. The economic recession caused by social isolation in the state of Tocantins may have more serious consequences, such as increased demand in the public health system and violence due to unemployment.

Keywords: covid-19, economics, social impact, public health.

Cite this article: Reis, G.R., Rodrigues, W., Silva, M.G., Silveira, J.M., Melo, M.P., & Gontijo, É.E.L. (2020). IMPACT OF SOCIAL ISOLATION ON PUBLIC HEALTH IN TOCANTINS: A PATHOLOGICAL, ECONOMIC AND SOCIAL ANALYSIS OF COVID-19. *European International Journal of Science and Technology*, 9(4), 37-47.

1. INTRODUCTION

The coronavirus (COVID-19) has generated far-reaching catastrophic consequences beyond the spread of the disease even in the face of efforts to isolate and quarantine social isolation. As the pandemic spreads across the world, concerns have shifted from productivity and the economy to trying to survive. In the face of the rapidly growing COVID-19 pandemic, a wide variety of models for the progression of this epidemic are being used by public health experts to generate scenarios that are being used to guide decisions and to recommend and impose increasingly isolation measures. severe. In this spectrum, economists are not fully familiar with the quantitative implications of these models and, therefore, are not fully engaged in policy discussions about the tradeoff between public healing and the economic implications of these mitigation and social distance measures (ANDERSEN, 2020; GUAN , 2020).

Coronaviruses are a large family of RNA viruses so named because they have receptors on their surface (protein S), giving them the appearance of a crown (Latin: corona = crown) (Figure 1) when viewed under the electron microscope (Cui, Li and Shi, 2019). Each virus measures 50-200 nm in diameter. They have four structural proteins, known as: protein S (spike), protein E (envelope), protein M (membrane) and protein N (nucleocapsid). Protein N contains the RNA genome and together proteins S, E and M create the viral envelope. Protein S is the protein that allows the virus to bind to the cell membrane of a host cell (Holmes and Rambaut, 2004; Rota et al., 2003).

The pathophysiological characteristics are wide, triggering from a common cold to severe respiratory syndromes. Many disease epidemics caused by these agents have already been described in humans and animals, with varying severity and most of them of limited geographic character (Cui, Li and Shi, 2019; Fan et al., 2019; Zhou et al., 2018) . Before 2019/2020, two major epidemics related to coronaviruses were observed. The first occurred in China in 2002 and was characterized by severe respiratory infections caused by the Severe Acute Respiratory Syndrome - Coronavirus, being named SARS-CoV(Ksiazek et al., 2003). The second epidemic of Acute and Severe Respiratory Syndrome was reported in the Middle East in 2012 and the virus was called the Middle East Respiratory Syndrome - Coronavirus (MERS-CoV) (Doremalen, van et al., 2014).

With an increasing number in the worldwide mortality rates, especially in certain countries whose spread and infectivity of SARS-CoV 2 appear to be greater, whose geographical region is located above the tropics of cancer and its temperature does not maintain between 5 to 11 degrees Celsius at this time of the year. year.According to Anderson et al. (2020), published online in The Lancet, the impact of mitigation measures on the cumulative and peak incidence of the disease over a 12-month horizon, along with concerns that easing early social isolation measures would lead to a resurgence disease. The purpose of the article is to present economists with the quantitative implications of such models for alternative mitigation efforts in certain regions of the world.

This study aims to bring into vogue the real need for social isolation in the Brazilian state of Tocantins, with a tropical climate and dry winter, whose average annual temperatures are 24 to 28 degrees Celsius with maximum values around 38 degrees in August and September.

This is an important forecast of an economic recession generated by social isolation in a region where low population density and high temperatures result in a low probability of spreading the disease. However, the forecast of the increase in unemployment tends to increase the demand for the Brazilian public health system, the single health system (SUS), since a good part of the population, due to the economic crisis generated by social isolation, will no longer have private health plans. For a better development of this analysis, we will address the infectivity of the coronavirus (SARS-

CoV-2), the public health system in Brazil (SUS) and discuss the economic impact of social isolation in the state of Tocantins.

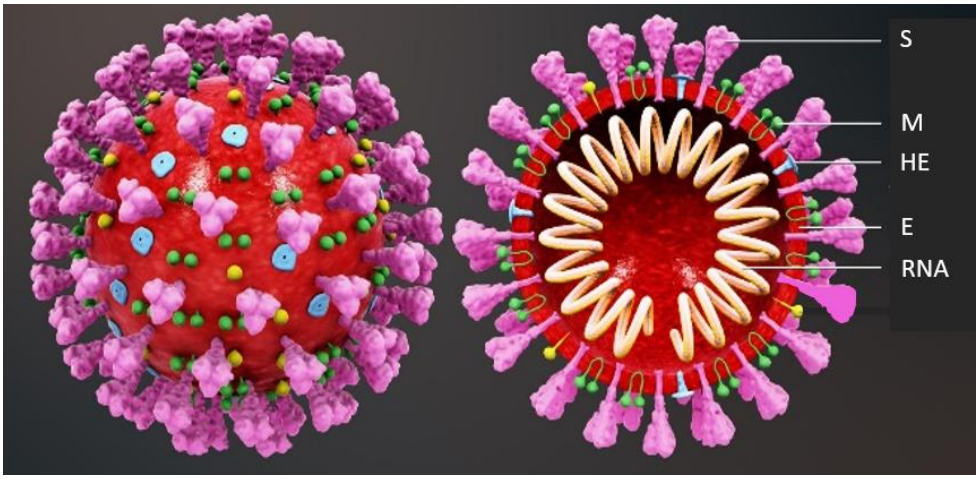

Figure 1: Coronavirus. S: Protein spike; M: Membrane protein; HE: Hemagglutinin; E: Envelope; RNA: Ribonucleic Acid (Photo: Wikimedia Commons) Available at: https://revistagalileu.globo.com/Ciencia/noticia/2020/03/proteina-pode-explicar-por-que-coronavirus-se-espalha-tao-rapido .html.

2.SARS-CoV-2 INFECTIVITY

Spike proteins contain a variable receptor binding domain (RBD). This RBD binds to the angiotensin-2 converting enzyme receptor (ACE-2) found in the heart, lungs, kidneys and gastrointestinal tract of animals, thus facilitating viral entry into target cells. Based on genomic sequencing, the RBD of SARS-CoV-2 apparently this is a mutant of a wild bat virus (Rhinolophusaffinis). Therefore, it is believed that SARS-CoV 2 originated from bats and, after mutation, was able to infect other animals such as Malaysian pangolins (Manisjavanica; an ant-eating mammal and long snout sold illegally for use in medicine) traditional Chinese). The mutation increased the affinity of RBD to ACE-2 in humans, so the pangolin is believed to be the intermediate host of SARS-CoV-2 (Zhu et al., 2020). Since SARS-CoV and SARS-CoV-2 are very similar, the biochemical interactions and pathogenesis are likely to be similar. The binding of SARS-CoV to receptors of angiotensin-converting enzyme 2 (ACE-2) in type II pneumocytes triggers a cascade of inflammation in the lower respiratory tract. The spike protein binds to the ACE-2 receptor, the complex is proteolytically processed by the type 2 transmembrane protease TMPRSS2, leading to the cleavage of ACE-2 and the activation of the spike protein, thus facilitating viral entry into the target cell. The cells in which ACE-2 and TMPRSS2 are present simultaneously are more susceptible to entry by SARS-CoV. Current studies reinforce that the SARS-CoV-2 virus also requires ACE-2 and TMPRSS2 to enter cells (Ksiazek et al., 2003; Kuba et al., 2005; Zhao et al., 2020).

The genomics of SARS-CoV-2 shows an increased binding capacity to the human ACE2 receptor. The SARS-CoV-2 spike protein has a polybasic cleavage site (furin) at the S1 and S2 limit with the insertion of twelve nucleotides which led to the acquisition of three glycans, thus generating a mutant protein (Hoffmann et al., 2020). However, the functional consequence of the polybasic cleavage site in SARS-CoV-2 is unknown, experiments with SARS-CoV have shown that this change in the S1 / S2 junction improves cell-cell fusion. This mutation made the virus more compact and promoted an increase in the strength of its binding force due to five mutations in the receptor binding domain

(RBD) in the SARS-CoV2 spike protein. Thus the evidence that SARS CoV 2 binds more strongly to human cells, in addition to penetrating more effectively than the predecessor virus (Liu et al., 2020; Yamawaki et al., 2019; Zhou et al., 2020).

SARS-CoV-2 enters the body through the nose, mouth or eyes, it can follow the oropharynx and from there to the lungs, it binds via the spike surface protein to the ACE2 protein of the respiratory tree's endothelial cells which is most abundant in pneumocytes type II of the lungs (Hoffmann et al., 2020). The virus binds to the cell by fusing its lipid membrane with the cell membrane and then starts releasing its RNA. The cell reads the viral RNA and begins to produce proteins that inhibit the immune system and help produce new copies of the virus (Glowacka et al., 2011). Each infected cell can produce and release millions of copies of the virus before it dies, infecting new cells and causing respiratory symptoms (Gorbalenya, 2020a).

Viral entry and cell infection trigger the host's immune response, and the inflammatory cascade is initiated by antigen-presenting cells (APC). The process begins with APC performing two functions: presenting the foreign antigen to the auxiliary cells CD 4 + -T (Th1) and releasing interleukin-12 to further stimulate the Th1 cell. Th1 cells stimulate TCD 8 neutrophils and lymphocytes that will target all cells that contain the foreign antigen. In addition, activated Th1 cells stimulate B cells to produce specific antibodies to the antigen (Zhao et al., 2020; Zou et al., 2020).

At this point, the disease can follow two directions, which are: the immune response can control viral proliferation and eliminate the disease, or these cells can overreact by producing more inflammatory proteins, such as cytokines and interferons in a frantic attempt to end viruses, and so on. kill cells in the body itself, inducing exacerbated apoptotic processes that kill epithelial and blood cells, preventing hematosis. As the virus increasingly infects alveolar cells, the disease can progress to severe respiratory failure and death (Cui, Li and Shi, 2019; Kleine-Weber et al., 2018).

The destruction of type 2 pneumocytes almost always results in serious infections, which is the severe acute respiratory syndrome, in which case people get worse, they will almost always have an exaggerated response from the host called, “cytokine storm”, where the lungs fill up with fluid and the lungs fill with fluid and blood. As a result of this process, viral superinfections or disseminated secondary bacterial infections are common, which can trigger generalized sepsis that leads very often to death (Guan et al., 2020).

The virus can also infect heart cells, which are abundant in ACE2, causing heart disease. Respiratory symptoms and prognosis are more severe in patients with cardiovascular disease, which may be associated with greater ACE2 secretion in these patients compared to healthy people. The density of ACE2 in each tissue is correlated with the severity of the disease in that tissue (Zhao et al., 2020). The disease can occur in three stages which are: in the first or initial stage after the virus infects the body, for most people, there is an incubation period associated with mild and non-specific symptoms such as malaise, fever, dry cough which can last from a few days to two weeks with the disappearance of symptoms (Bai et al., 2020; Rabi et al., 2020; Rothe et al., 2020; Wax and Christian, 2020). During this period, the virus multiplies in the respiratory system and can migrate, via hematogenic, to the small intestine. In the second stage, the virus continues to multiply and the inflammation will be located in the lungs, patients develop viral pneumonia with cough and low fever and hypoxia with a feeling of profound tiredness, with bleeding in the lung (Gorbalenya, 2020b; Wax and Christian, 2020). In the third phase, in addition to severe inflammatory processes in the lungs, there is a generalized inflammation process and the uncontrolled immune system, “cytokine storm”, where TCD8 neutrophils and lymphocytes release large amounts of toxic substances that instead of reaching the

virus, they will reach cells, type 2 pneumocytes and vessel endothelial cells, which can lead to shock and lead to death (Guan et al., 2020; Wan et al., 2020).

According to Casanova et al. (2010), in a study carried out with the coronovirus, concluded that there is a rapid inactivation of the same when submitted to a temperature of 40 degrees Celsius, and after 20 degrees the process of inactivation of the same begins.

In research by Wang et al. (2020) it was verified great differences in the transmission capacity of COVID-19 in variations of the climate, whose greatest infectivity occurs when the temperature is between 5 and 11 degrees Celsius and the relative humidity of the air 47 and 79%. Comparing the infected map (John Hopkins University / World Health Organization) in figure 2 with the image from the European Center for Medium-Range Weather Forecasts ERA - figure 3 - which shows exactly the most infectious bands (in yellow), where the real transmission rates are the highest in the world and where temperatures at this time of year vary, exactly between 5 and 11 degrees, there is a visual correlation between temperature and infection rates.

In this plan, and based on the epidemiological data presented, Brazil is geographically located in a region with a low prevalence of the disease, since Sars-COV-2 has low transmission capacity in this climatic zone, which brings to light if the impact in the country cannot bring greater social and health consequences to the population than the spread of the virus itself.

Figure 2: SARS-COV-2 infected map provided by John Hopkins University.

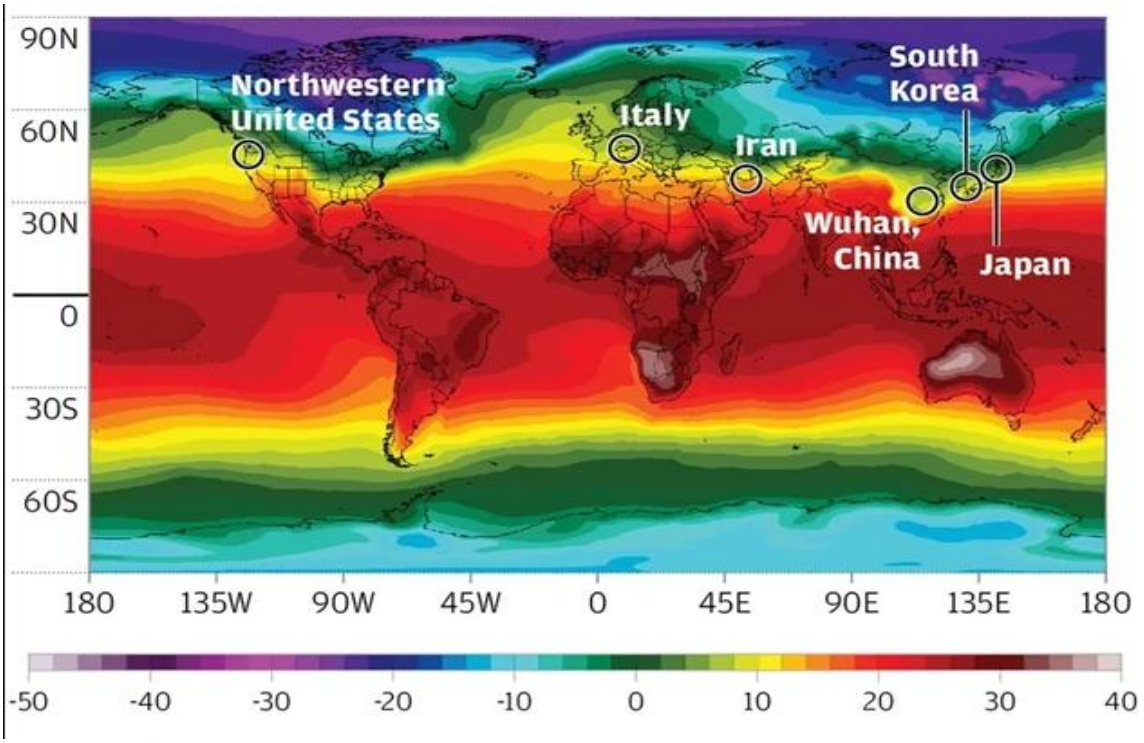

Figure 3: European Center for Medium-Range Weather Forecasts ERA-Interim 1000mb average temperatures from November 2018 to March 2019, provided by John Nicholls research.

3. THE UNIQUE HEALTH SYSTEM AND COVID-19

Brazil's Unified Health System (SUS) reaches 30 years of age and is recognized by the World Health Organization (WHO) as the largest free and universal public health system in the world, ranging from simple blood pressure assessment in Primary Care to organ transplantation.

Its structure includes the FundaçãoInstituto Oswaldo Cruz (Fiocruz), the National Health Foundation (FUNASA), Anvisa, the National Health Agency (ANS), Hemobrás, the Cancer Institute (Inca), the National Institute of Traumatology and Orthopedics (Into) and eight federal hospitals. Considering the rapid spread of COVID 19 infection in various geographical areas worldwide, on March 11, 2020, WHO declares the new Coronavirus pandemic, leading Brazil through the Open University of SUS (UNASUS) to create information and guidelines official reports on the disease in two directions, for the general population and for health professionals, and for the latter, the care protocols are made available by the Ministry of Health in the face of suspicion, diagnosis and referral of the patient to another level of care when necessary.

COVID-19 has an agent that causes a series of pneumonia cases. It is known for its high transmissibility and can evolve to a mild acute respiratory syndrome, in most cases (80%), to very severe cases ranging between 5% and 10%. Its lethality varies, mainly in relation to the increase in the age group.

The clinical picture, typical of a Flu Syndrome, can vary its symptoms from a mild and asymptomatic presentation (the frequency is not known), especially in young adults and children, up to a severe presentation, including septic shock and respiratory failure, with complications and mortality more evident in patients with comorbidities such as diabetes, high blood pressure, cancer , immunosuppressed, transplanted, pregnant and postpartum women. Primary Health Care (PHC) is the gateway to the SUS, playing a fundamental role allowing the early identification of cases,

resolving care in the face of mild cases and handling / forwarding severe cases to other levels of care. Within the protocols of the Ministry of Health on the management of COVID19, the adoption of restrictive measures such as horizontal social isolation, which is a strategy to prevent the virus from being transmitted from person to person in a sustainable manner, is oriented. These contingency measures are for the general population and for patients who have a mild condition to avoid unnecessarily occupying beds.

According to the Ministry of Health, the epidemiological scenario of the disease in Brazil will be unfavorable in April / 2020, indicating that the health system will collapse because there is no time to organize itself, which means when there is financial resources, health insurance, the court order, but hospitals in both the public and private networks will not have enough beds for the care of patients who evolve to a severe form.

In this way, it aims to prevent contamination in a large number of people at the same time and, thus, allow the health system to offer the greatest number of assistance to critically ill patients when necessary, with a lower mortality rate, especially for groups of patients. risk, among them the elderly. In the evidence that the system may become inefficient to meet the demands of serious cases, the State will provide for the adaptation and expansion of beds and hospital areas and the emergency contracting of ICU beds in order to prevent deaths, as is being done in this in the country.

4. ECONOMIC IMPACT OF SOCIAL ISOLATION

Brazil has been following the global guidelines for coping with the disease through investment in health and, above all, in social restraint, which has had a major impact on the economy of many Brazilians, who are progressively losing their jobs and their gains in informality. In this, the question remains about the true impact of COVID-19 in the Brazilian territory, since research shows less infectivity of the new coronovirus in countries with tropical climate.

Shortages of supplies were expected to affect various sectors due to panic buying, increased use of goods to fight the pandemic and disruption of factories and logistics in mainland China. There have been widespread reports of a shortage of pharmaceutical supplies, with many areas seeing panic purchases and a consequent shortage of food and other essential grocery items. The technology industry, in particular, has been warning of delays in shipping electronic products.

In almost all scenarios considered, at the height of the disease's progression, between 10% and 20% of the population (33 - 66 million people) suffer from an active infection at the same time. This level of infection in the population is likely to require a significant shift in the workforce from work to self-quarantine and recovery or to care for these sick individuals for a period of weeks or longer. All of this is likely to happen without adequate support from the health system for those with severe cases of the disease, even if we implement a major investment in health (WHO, 2020)

From the realization of a global pandemic crisis over COVID-19, city halls and governments of Brazilian states adopted measures to restrict social interaction, including the suspension of classes and public and private educational institutions, commercial activities and any means of production that would generate an agglomeration of individuals, which initiated a process of economic crisis with the start of unemployment rates due to the 53% drop in the demand of national companies (CNI, 2020).

Based on research by the national confederation of industry, there is a drop in production in industrial activities, especially in medium and small companies, which has caused an exponential increase in unemployment and income rates.

In Brazil, the health system is divided into public and private establishments. The public health system in Brazil, the largest system in the world, called the single health system, provides assistance in

all possible care, primary, secondary and tertiary, offering comprehensive care to the entire population. However, the same develops with reduced demands because there is also private assistance in the country, governed by health plans, which charge monthly fees to its users, or by private access, which works through direct payment (REIS, 2018) .

Economic crises, associated with reduced employment and income, lead to an increase in the number of users of the single health system, since the increase in unemployment rates corroborates the reduction in the number of members of private health plans.

The main message for economists derived from simulations of this simple model of evolution of COVID-19 in the United States (and probably worldwide) is that it will probably be necessary to take severe measures of social distance, maintained for an entire year or up to 18 months (even a vaccine can be developed) to avoid serious public health consequences.

5. FINAL CONSIDERATIONS

The predictions of the collapse of the health system due to the increased demand from patients with COVID-19 may be harmless in Tocantins (and in other determined regions of the world) due to the low probability of spreading and infectivity of SARS-CoV-2 in regions of high temperature, low relative humidity and low population density. In contrast, the same social isolation in these regions, with the consequent reductions in productivity and a fall in the economy, will culminate in unemployment, misery and greater demand by the public health sector, which can lead to health collapse in the post-pandemic period.

Therefore, this study is an analysis and a forecast, not yet conclusive, of the possible damage to public health in regions whose social isolation may not be necessary.

REFERENCES

[1] ANDERSEN, K. *et al.*The Proximal Origin of SARS-CoV-2 - Novel 2019 coronavirus / nCoV-2019 Evolutionary History - Virological. Disponível em: <http://virological.org/t/the-proximal-origin-of-sars-cov-2/398>. Acesso em: 3 abr. 2020.

[2] BAI, Y. *et al.*Presumed Asymptomatic Carrier Transmission of COVID-19JAMA - Journal of the American Medical AssociationAmerican Medical Association, , 2020.

[3] CASANOVA, Lisa M. et al. Effects of air temperature and relative humidity on coronavirus survival on surfaces. Appl. Environ. Microbiol., v. 76, n. 9, p. 2712-2717, 2010.

[4] CORMAN, V. M. *et al.* Hosts and Sources of Endemic Human Coronaviruses. *In*: Advances in Virus Research. [s.l.] Academic Press Inc., 2018. v. 100p. 163–188.

[5] CNI, Confederação Nacional da Indústria, 2020.

[6] CUI, J.; LI, F.; SHI, Z. L. Origin and evolution of pathogenic coronaviruses Nature Reviews Microbiology Nature Publishing Group, , 1 mar. 2019.

[7] CYRANOSKI, D. Did pangolins spread the China coronavirus to people? Nature, 7 fev. 2020.

[8] DOREMALEN, N. VAN *et al.*Stability of middle east respiratory syndrome coronavirus in milk Emerging Infectious Diseases Centers for Disease Control and Prevention (CDC), , 2014.

[9] FAN, Y. *et al.*Bat coronaviruses in ChinaVirusesMDPI AG, , 1 mar. 2019.

[10] GLOWACKA, I. *et al.* Evidence that TMPRSS2 Activates the Severe Acute Respiratory Syndrome Coronavirus Spike Protein for Membrane Fusion and Reduces Viral Control by the Humoral Immune Response. Journal of Virology, v. 85, n. 9, p. 4122–4134, 1 maio 2011.

[11] GORBALENYA, A. E. Severe acute respiratory syndrome-related coronavirus – The species and its viruses, a statement of the Coronavirus Study Group. bioRxiv, p. 2020.02.07.937862, 2020a.

[12] ___. Severe acute respiratory syndrome-related coronavirus – The species and its viruses, a statement of the Coronavirus Study Group. bioRxiv, p. 2020.02.07.937862, 2020b.

[13] GUAN, W. *et al.* Clinical characteristics of 2019 novel coronavirus infection in China. New England Journal of Medicine, 2020.

[14] HEURICH, A. *et al.* TMPRSS2 and ADAM17 Cleave ACE2 Differentially and Only Proteolysis by TMPRSS2 Augments Entry Driven by the Severe Acute Respiratory Syndrome Coronavirus Spike Protein. Journal of Virology, v. 88, n. 2, p. 1293–1307, 15 jan. 2014.

[15] HOFFMANN, M. *et al.* The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. bioRxiv, p. 2020.01.31.929042, 2020.

[16] HOLMES, E. G.; RAMBAUT, A. Viral evolution and the emergence of SARS coronavirusPhilosophical Transactions of the Royal Society B: Biological Sciences. Anais...Royal Society, 29 jul. 2004

[17] KLEINE-WEBER, H. *et al.* Mutations in the Spike Protein of Middle East Respiratory Syndrome Coronavirus Transmitted in Korea Increase Resistance to Antibody-Mediated Neutralization. Journal of Virology, v. 93, n. 2, 7 nov. 2018.

[18] KSIAZEK, T. G. *et al.* A novel coronavirus associated with severe acute respiratory syndrome. New England Journal of Medicine, v. 348, n. 20, p. 1953–1966, 15 maio 2003.

[19] KUBA, K. *et al.* A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. Nature Medicine, v. 11, n. 8, p. 875–879, ago. 2005.

[20] LAI, M. M. C. Recombination in large RNA viruses: CoronavirusesSeminars in Virology Academic Press Inc., , 1996.

[21] LETKO, M.; MARZI, A.; MUNSTER, V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nature Microbiology, v. 5, n. 4, p. 562–569, 24 fev. 2020.

[22] LIU, Z. *et al.* Composition and divergence of coronavirus spike proteins and host ACE2 receptors predict potential intermediate hosts of SARS- CoV- 2. Journal of Medical Virology, p. jmv.25726, 11 mar. 2020.

[23] MOORE, M. J. *et al.* Retroviruses Pseudotyped with the Severe Acute Respiratory Syndrome Coronavirus Spike Protein Efficiently Infect Cells Expressing Angiotensin-Converting Enzyme 2. Journal of Virology, v. 78, n. 19, p. 10628–10635, 1 out. 2004.

[24] RABI, F. A. *et al.* SARS-CoV-2 and Coronavirus Disease 2019: What We Know So Far. Pathogens, v. 9, n. 3, p. 231, 20 mar. 2020.

[25] REIS, Geovane Rossone. A utilização do uso de evidências científicas como política pública para a otimização na disponibilidade de vagas em UTI no Tocantins. 2018.

[26] ROTA, P. A. *et al.* Characterization of a novel coronavirus associated with severe acute respiratory syndrome. Science, v. 300, n. 5624, p. 1394–1399, 30 maio 2003.

[27] ROTHE, C. *et al.*Transmission of 2019-NCOV infection from an asymptomatic contact in Germany New England Journal of MedicineMassachussetts Medical Society, , 5 mar. 2020.

[28] SHULLA, A. *et al.* A Transmembrane Serine Protease Is Linked to the Severe Acute Respiratory Syndrome Coronavirus Receptor and Activates Virus Entry. Journal of Virology, v. 85, n. 2, p. 873–882, 15 jan. 2011.

[29] VINCENT, M. J. *et al.* Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virology Journal, v. 2, 22 ago. 2005.

[30] WAN, Y. *et al.* Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. Journal of Virology, v. 94, n. 7, 29 jan. 2020.

[31] WANG, Mao et al. Temperaturesignificantchange COVID-19 Transmission in 429 cities. medRxiv, 2020.

[32] WAX, R. S.; CHRISTIAN, M. D. Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patientsCanadian Journal of AnesthesiaSpringer, , 2020.

[33] WORLD HEALTH ORGANIZATION et al. Coronavirusdisease 2019 (COVID-19): situationreport, 72. 2020.

[34] YAMAWAKI, H. *et al.* Camostat Mesilate, Pancrelipase, and Rabeprazole Combination Therapy Improves Epigastric Pain in Early Chronic Pancreatitis and Functional Dyspepsia with Pancreatic Enzyme Abnormalities. Digestion, v. 99, n. 4, p. 283–292, 1 maio 2019.

[35] ZHAO, Y. *et al.* Single-cell RNA expression profiling of ACE2, the putative receptor of Wuhan 2019-nCov. bioRxiv, p. 2020.01.26.919985, 2020.

[36] ZHOU, P. *et al.* Fatal swine acute diarrhoea syndrome caused by an HKU2-related coronavirus of bat origin. Nature, v. 556, n. 7700, p. 255–259, 1 abr. 2018.

[37] ___. Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. Nature, 2020.

[38] ZHU, N. *et al.* A novel coronavirus from patients with pneumonia in China, 2019. New England Journal of Medicine, v. 382, n. 8, p. 727–733, 20 fev. 2020.

[39] ZOU, L. *et al.* SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. The New England journal of medicine, 2020.