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The Coronavirus Brazilian Reality

Sebastião David Santos-Filho

Biosciences department, UFRN, Natal, RN, Brazil

Physiotherapy faculty, UNICEUNA, Natal, RN, Brazil

ABSTRACT

The purpose of this work is to provide a revision of literature about the progress with the treatment of infection caused by coronavirus and to show the reality of the coronavirus disease in Brazil. The number of deaths is up to 3300 and the confirmed cases are more than 50200. The National Health System of Brazil (SUS) involving this disease epidemiology, etiology, diagnosis, treatment, and hospital infection controls. The first advice is to social isolation where the people stay home and some essentials services stay open. The purpose of this work is to present the Brazilian reality on fight this pandemic disease and to show the providences are made to combat it.

***Corresponding author**

Sebastiao David Santos-Filho, Biosciences department, UFRN, Natal, RN, Brazil. Physiotherapy faculty, UNICEUNA, Natal, RN, Brazil. E-mail: sdavidsfilho@gmail.com

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Keywords: Coronavirus, COVID-19, SARS-CoV-2, Remdesivir, Hydroxychloroquine

Introduction

In December 2019, the novel coronavirus (nCoV) was discovered and identified in the viral pneumonia cases occurred in Wuhan, Hubei Province, China, and then was named COVID-19 by the World Health Organization (WHO) on 12 January 2020. In the following months, the Covid-19, quickly spreading inside and outside of Hubei Province, and even other countries. In Brazil it becomes in March 2020 and continues increased the number of deaths until then. Today 24th April 2020, until 16 pm, the number of deaths is up to 3300 and the confirmed cases are more than 50200.

All the health professionals require an up-to-date guideline to follow when an urgent healthcare problem emerging. In response to the requests for reliable advice from frontline clinicians and public healthcare professionals managing COVID-19 pandemics, the National Health System of Brazil (SUS) involving this disease epidemiology, etiology, diagnosis, treatment, nursing, and hospital infection control for clinicians, and also for public health workers and community residents, developed various guidelines strategies to combat the coronavirus.

The first advice is to social isolation where the people stay home and some essentials services are disposable for the population, as supermarkets, pharmacies, bakery and other. It was an effort of Government and Health Minister doing to preserve people and economic alive.

The purpose of this work is to provide a revision of literature about the progress with the treatment of infection caused by coronavirus and to show the reality of the COVID-19 in Brazil.

Methodology

This work is a revision of the literature produced in Brazil about the disease SARS-CORONAVIRUS-2019 named Covid-19 using the keys words coronavirus, COVID-19, SARS, associated to the words clinics, and treatment.

This work was made in April 24, 2020. And the tables, figures and other results were statistic checked on the articles researched. The articles were obtained in the PubMed site using the key-words listened above.

The PubMed site comprises more than 30 million citations for biomedical literature from MEDLINE, life science journals, and online books. Citations may include links to full-text content from PubMed Central and publisher web sites.

As a review of literature exists in this research site it is expressed by a nom personal opinion but the opinion of the researches in Brazil.

Results

Only 6 (six) articles were founded in the PubMed. One is a study review and meta-analyses showing the recent advances founded in various site of publications research, as MEDILINE, Cochrane, EMBASE, Scopus and LILACS. One is the association of the Covid-19 with diabetes. And 3 ones are about solutions of treatment of this disease with some drugs.

The results were expressed in tables and graphics uploaded to the articles data.

All the results were of responsibility of the authors of the articles researched.
The table 1 of Nascimento et al expressed the findings in patients analyzed for Covid-19 [1].
The table 2 extracted of Nascimento et al showed the level of mortality due of the Covid-19 in the studied patients [1].
The figure 1 was extracted to Rosa and Santos that showed the use of different medicine to treat of Covid-19 and their valuable results [2].
Figure 2 showed the principal compounds listed in Ekins et al that were studied and liberated for use in this pandemic by FDA agency [3].

Table 1: Laboratory findingsin patients infected with SARS-CoV-2

Lboratory Test	No. of Studies	Total Patient No	Values in Physlologic Range n(%)	Values > Physlologic Range n(%)	Values < Physlologic Range n(%)	Lost to Follow up n(%)
C-RP	25	1637	427 (26.1%)	900(55.0%)		310(189%)
ESR	7	105	NA	$8(83.8%)		NA
PCT	12	1-163	NA	98(6.7%)	NA	NA
IL-6		99	NA	51(52.0%)	NA	NA
Peripheni blood profile						
Total WBC	32	1747	1109(635%)	155(8.9%)	469(26.8%)	14 (0.8%)
Neutrophils	20	204	143(70.1%)	48(23.5%)	6(2.9%)	7(3.4"-)
Lymphocytes	25	464	159 (34.3%)	47 (10.3%)	256 (55.2%)	2(0.4"-)
Pl;itC'lcts	II	218	NA	64 (29.4%)	25(11.5%)	NA
Blood biochemistry						
ALT	12	1316	NA	211 (16.0%)	NA	NA
AST	18	1420	NA	254 (17.9%)	NA	NA
l.l)H	II	283	NA	157(55.5%)	NA	NA
0-dimcr	16	1573	NA	527(33.5%)	NA	NA

This table is only a copy for Nascimento et al as an illustrative way [1].

Table 2: Summary of findings (SOF') table for all-cause mortality

Outoome	Study Population	"Incidence (95% CI)"	Higgins I2-Test	Certainty of the Evidence (GRADE)
All patients	31 Studies (53,631 patients)	0.3 (0.0-1.0)	83%	(+) very low
Chinese patients	28 studies (5632 patients)	0.5 (0.0-1.4)	85%	(+) very low
PJitients from other countries	3 studies (41 patients)	0.0 (0.0-1.4)	0%	(+) very low

This table is only a copy for Nacimento et al as an illustrative way [1].

Figure 1: extracted at it is in the article publication done by Rosa and Santos [2].

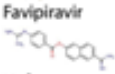
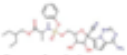
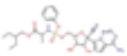
TABLE 1. Clinical trials identified at Clinicaltrials.gov related to drug repositioning for COVID-19 treatment

Intervention	Clinical condition	Sponsor	N° test / Status	Beginning / Estimated end	Phase
Hydroxychloroquine	30 participants with pneumonia caused by 2019-nCoV	Shanghai Public Health Clinical Center	NCT04261517 / Recruiting patients	6-2-2020 / 31-12-2020	3
Chloroquine	10000 participants in a prophylaxis study for COVID-19	University of Oxford	NCT04303507 / Not yet recruiting	May 2020 / May 2022	N/A
Human immunoglobulin	Pneumonia caused by 2019-nCoV with 80 participants	Peking Union Medical College Hospital	NCT04261426 / Not yet recruiting patients	10-2-2020 / 30-06-2020	2 and 3
Remdesivir	Severe respiratory infection caused by 2019-nCoV with 452 participants	Capital Medical University	NCT04257656 / Recruiting patients	6-2-2020 / 31-05-2020	3
Remdesivir	308 participants with mild/moderate respiratory infection caused by 2019-nCoV	Capital Medical University	NCT04252664 / Recruiting patients	05-02-2020 / 27-04-2020	3
Arbidol (umifenovir)	Pneumonia caused by 2019-nCoV with 380 participants	Jieming QU, Ruijin Hospital	NCT04260594 / Not yet recruiting patients	7-02-2020 / 30-12-2020	4
Arbidol or **lopinavir-ritonavir** or **oseltamivir**	400 participants infected with 2019-nCoV	Tongji Hospital	NCT04255017 / Recruiting patients	01-02-2020 / 01-07-2020	4
Arbidol or **lopinavir-ritonavir**	125 participants infected with 2019-nCoV	Guangzhou 8th People's Hospital	NCT04252885 / Recruiting patients.	28-01-2020 / 31-07-2020	4
Darunavir-cobicistat combination	Pneumonia caused by 2019-nCoV with 30 participants	Shanghai Public Health Clinical Center	NCT04252274 / Recruiting patients	30-01-2020 / 31-12-2020	3
TCM combination with **lopinavir-ritonavir**, **α-interferon** via aerosol	150 participants infected with 2019-nCoV	Beijing 302 Hospital	NCT04251871 / Recruiting patients	22-01-2020 / 22-01-2021	N/A
Recombinant human interferon α2β	328 participants with COVID-19	Tongji Hospital	NCT04293887 / Not yet recruiting	01-03-2020 / 30-06-2020	1
Carrimycin or **lopinavir-ritonavir** or **arbidol** or **chloroquine phosphate**	520 participants with COVID-19	Beijing YouAn Hospital	NCT04286503 / Not yet recruiting	23-02-2020 / 28/02-2021	4
Danoprevir-ritonavir and **interferon** inhalation or **lopinavir-ritonavir** or **TCM** plus **interferon** inhalation	50 participants with pneumonia caused by 2019-nCoV	The Ninth Hospital of Nanchang	NCT04291729 / Recruiting	14-02-2020 / 30-04-2020	4
Xiyanping or **lopinavir-ritonavir-interferon** inhalation	384 participants with pneumonia caused by 2019-nCoV	Jiangxi Qingfeng Pharmaceutical Co. Ltd.	NCT04275388/ Not yet recruiting	19-02-2020 / 14-12-2020	N/A
Xiyanping combined with **lopinavir-ritonavir**	80 participants with COVID-19	Jiangxi Qingfeng Pharmaceutical	NCT04295551 / Not yet recruiting	14-03-2020 / 14-04-2021	N/A
Combinations of **oseltamivir, favipiravir,** and **chloroquine**	80 participants with COVID-19	Rajavithi Hospital	NCT04303299 / Not yet recruiting	15-03-2020 / 30-11-2020	3
Thalidomide	40 participants with COVID-19	First Affiliated Hospital of Wenzhou Medical University	NCT04273581 / Not yet recruiting	18-02-2020 / 30-05-2020	2
Thalidomide	100 participants with pneumonia caused by 2019-nCoV	First Affiliated Hospital of Wenzhou Medical University	NCT04273529 / Not yet recruiting	20-02-2020 / 30-06-2020	2
Vitamin C	140 participants with severe pneumonia caused by 2019-nCoV	ZhiYong Peng	NCT04264533 / Recruiting	14-02-2020 / 30-09-2020	2
Methylprednisolone	80 participants infected with 2019-nCoV	Peking Union Medical College Hospital	NCT04244591 / Recruiting patients	26-01-2020 / 25-12-2020	2
Pirfenidone	294 participants with severe pneumonia caused by 2019-nCoV	Huilan Zhang	NCT04282902 / Recruiting	04-02-2020 / 01-06-2020	3
Bromhexine hydrochloride	60 participants with suspected and mild pneumonia caused by 2019-nCoV	Second Affiliated Hospital of Wenzhou Medical University	NCT04273763 / Enrolling by invitation	16-02-2020 / 30-04-2020	N/A
Bevacizumab	20 participants with severe COVID-19 pneumonia	Qilu Hospital of Shandong University	NCT04275414 / Recruiting	February 2020 / May 2020	2 and 3
Fingolimod	30 participants with COVID-19	1° Affiliated Hospital of Wenzhou Medical University	NCT04280588 / Recruiting	22-02-2020 / 01-06-2020	2

COVID-19, coronavirus disease 2019; 2019-nCoV, novel coronavirus 2019; TCM, traditional Chinese medicine

Figure 2: Obtained to Ekins et al. as an illustrative form [3].

Compounds screened *versus* SARS-CoV-2: Vero E6 cells were infected with nCoV-2019BetaCoV/Wuhan/WIV04/2019 at a multiplicity of infection (MOI) of 0.05 [14]

Molecule	Class	EC_{50} (μM)	CC_{50} (μM)	SI	FDA status
 Ribavirin	Antiviral for hepatitis C	109.5	>400	3.65	Approved
 Penciclovir	Antiviral for herpesvirus	95.96	>400	4.17	Approved
 Favipiravir	Broad-spectrum antiviral	61.88	>400	6.46	Experimental
 Nafamostat	Anticoagulant agent	22.50	>100	4.44	Approved
 Nitazoxanide	Anthelmintic agent	2.21	35.53	16.76	Approved
 Remdesivir	Antiviral agent	0.77	>100	129.87	Phase II/III
 Chloroquine	Antimalarial agent	1.13	>100	88.50	Approved

Discussion

As showed in their work, Nascimento & collaborators, a total of 61 studies were included (59,254 patients) [1]. The most common disease-related symptoms were fever (56%-99%; n = 4410), cough (39%-81%; n = 3985), muscle aches and/or fatigue (18%-55%; n = 3778), dyspnea (12%-41%; n = 3700), headache in 12% (4%-23%, n = 3598), sore throat in 10% (5%-17%, n = 1387) and gastrointestinal symptoms in 9% (3%-17%, n = 1744). Laboratory findings were described in a lower number of patients and revealed lymphopenia (0.83-1.03 × 109/L, n = 464) and abnormal C-reactive protein (21.54-45.91 mg/dL; n = 1637). Radiological findings varied, but mostly described ground-glass opacities and consolidation. Data on treatment options were limited. All-cause mortality was 0.3% (0.0%-1.0%; n = 53,631). Epidemiological studies showed that mortality was higher in males and elderly patients. The majority of reported clinical symptoms and laboratory findings related to SARS-CoV-2 infection are non-specific. As the situation imposed by SARS-CoV-2, in January 31st of 2020, the Brazilian Health Ministry made the Emergency Interministerial work group in public health of National and International importance to following of the situation and definition of action protocols for the vigilance of the SARS-CoV-2 in the Country. The protocol established the obtained of two samples for all the patients attended on public health clinics that attend the definition of case, that take care not only the characteristic symptomatic square, as also the recent trip historical to regions that presents direct transmission and/or contact historical with suspect or confirmed case. The collected samples must be processed by specific organs to test for respiratory virus that do part of the vigilance of Syndrome Respiratory Acute Disease, staying the criteria of the states establish also the local test for Covid-19. Beside this, to minimize the impact of the layer of notification and digitation, was stablished also priority ways of notification, without necessity of hierarchical notification, and platform of rapid visualization for the suspects cases divulgation, the Vigilance Integrated Platform in Health (plataforma.saude.gov.br/novocoronavirus/) [4].

In their work, Hussain, Bhowmik and Vale Moreira, describes the clinical spectrum of COVID-19 as heterogeneous, ranging from mild flulike symptoms to acute respiratory distress syndrome, multiple organ failure and death [5]. Older age, diabetes and other comorbidities are reported as significant predictors of morbidity and mortality. Chronic inflammation, increased coagulation activity, immune response impairment, and potential direct pancreatic damage by SARS-CoV-2 might be among the underlying mechanisms of the association between diabetes and COVID-19. No conclusive evidence exists to support the discontinuation of angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers because of COVID-19 in people with diabetes. Caution should be taken to potential hypoglycemic events with the use of chloroquine in these subjects. Patient tailored therapeutic strategies, rigorous glucose monitoring and careful consideration of drug interactions might reduce adverse outcomes. Suggestions are made on the possible pathological mechanisms of the relationship between diabetes and COVID-19, and its management. This disease is not primarily a metabolic disease, but metabolic control of glucose, lipid levels and blood pressure are key in these patients. This approach is important to address the well-established metabolic and cardiovascular complications of this primary comorbidity. Moreover, effective control of these metabolic parameters might represent and ameliorate the acute effects of this virus by reducing the local inflammatory response and blocking its entry into cells [6].

Rosa and Santos identified 24 clinical trials, involving more than 20 medicines, such as human immunoglobulin, interferons, chloroquine, hydroxychloroquine, arbidol, remdesivir, favipiravir, lopinavir, ritonavir, oseltamivir, methylprednisolone, bevacizumab, and traditional Chinese medicines (TCM) [2]. Although drug repurposing has some limitations, repositioning clinical trials may represent an attractive strategy because they facilitate the discovery of new classes of medicines; they have lower costs and take less time to reach the market; and there are existing pharmaceutical supply chains for formulation and distribution. No proven effective therapies for this virus currently exist. The rapidly expanding knowledge regarding SARS-CoV-2 virology provides a significant number of potential drug targets. The most promising therapy is remdesivir, that has potent in vitro activity against the virus, but it is not US Food and Drug Administration approved and currently is being tested in ongoing randomized trials [7].

The strategies for prevention consider the safety of hydroxychloroquine for a short period of time, demonstrated

antiviral effect and its low cost and accessibility. In the context of the COVID-19 epidemic, if clinical evidence from prospective controlled clinical trials confirms the positive impact, its implementation will be urgently need. Early HCQ administration to all people at risk of infection from close contact with a positive patient is one of the most reasonable choices. Moreover, it is a choice that could potentially have a consider impact on the early termination of the COVID-19 epidemic. However, its administration should be done under medical control to avoid potential side effects and to prevent an uncontrolled use leading to supply shortages [8]. Chloroquine, a widely-used anti-malarial and autoimmune disease drug, has recently been reported as a potential broad spectrum antiviral drug. Chloroquine is known to block virus infection by increasing endosomal pH required for virus/cell fusion, as well as interfering with the glycosylation of cellular receptors of SARS-CoV. The assays developed in our laboratory demonstrated that chloroquine functioned at both entry, and at post entry stages of the 2019-nCoV infection in Vero E6 cells. Besides its antiviral activity, chloroquine has an immune-modulating activity, which many synergistically enhance its antiviral effect in vivo. But it is widely distributed in the whole body, including lung after oral administration [9].

Although there are already several drugs being assessed clinically for SARS-CoV-2, there is still a need to identify additional treatments as alternatives and possibly discover molecules with increase efficacy, safety and cost effectiveness. If Ebola, ZIKV, MERS-CoV and SARS-Cov outbreaks are anything to go by this SARS-CoV-2 pandemic will be far more significant. Having multiple effective treatments available for SARS-CoV-2 that can be rapidly delivered to patients could save lives. The sense of déjà vu will probably be repeated again and again with the next virus outbreaks until we develop broader spectrum antivirals [3].

Conclusion

This pandemic disease will be in the beginning form and the researches about it are scarce in front of the researches do about other ills. In Brazil, the government does an effort to do the best to combat this pandemic. Social isolation and economic measures still be made to solve the problem at Country level, because the Brazil is a continental Country with different and peculiar regions dominated by any differences as climatic as social. I wish that it will be solved. Future is construct by the efforts of all to the beneficiate of all.

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