One year after the WHO alert for COVID-19: what is next?

Um ano após o alerta da OMS para COVID-19: o que vem a seguir?

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ABSTRACT
In December 2019, an outbreak of atypical pneumonia was discovered, later revealed to be due to a new virus identified as SARS-CoV-2, responsible for causing the coronavirus disease (COVID-19). The purpose is brings the main changes and discoveries, after a year that PHEIC was declared. We argue that after one year since PHEIC was declared, a lot has changed since then, in this sense, carried out a bibliographic review. We conducted a survey of articles published in the PUBMED and Google Scholar databases, from January 2020 to January 2021, which released data from studies related to transmission, treatment, vaccines, new variants for COVID-19. After the novel virus spread to other countries and caused hundreds of deaths, the World Health Organization issued its alarm on January 30, 2020, known as PHEIC. After a year that the alarm was given a lot has changed. The first major change was the beginning of a COVID-19 pandemic on March 11, 2020. Many discoveries were made, from a better understanding of transmission, treatment, vaccines and challenges with new strains that arose after selective pressure.

Keywords: COVID-19, Coronavirus, Pandemic, Sars-CoV-2, WHO.

RESUMO
Introdução: Em dezembro de 2019, foi descoberto um surto de pneumonia atípica, posteriormente, revelado ser devido a um novo vírus identificado como SARS-CoV-2, responsável por causar a doença coronavírus (COVID-19). O objetivo se baseou em trazer as principais mudanças e descobertas, após um ano que o PHEIC foi declarado. Argumentamos que após um ano desde que o PHEIC foi declarado, muita coisa mudou desde então, nesse sentido, realizou-se uma revisão bibliográfica. Depois que o novo vírus se espalhou para outros países e causou centenas de mortes, a Organização Mundial da Saúde emitiu seu alarme em 30 de janeiro de 2020, conhecido como PHEIC. Depois de um ano que o alarme foi dado, muita coisa mudou. A primeira grande mudança foi o início de uma pandemia de COVID-19 em 11 de março de 2020. Muitas descobertas foram feitas, a partir de um melhor entendimento da transmissão, tratamento, vacinas e desafios com novas cepas que surgiram após pressão seletiva.

Palavras-chave: COVID-19, Coronavírus, Pandemia, SARS-CoV-2, OMS.

1 INTRODUCTION

In December 2019, there were the first reports of outbreaks resembling viral pneumonia, with possible onset of contagion in the Central Market of Wuhan, in the province of Hubei, China, but so far its real origin is uncertain. Novel virus is known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is responsible for causing coronavirus disease 2019 (COVID-19), named by World Health Organization (WHO) (LI et al., 2020).

With the growing number of cases and the virus already spreading to almost 20 countries, on 30 January 2020, WHO raised its alarm: Public Health Emergency of International Concern (PHEIC). This alarm, when sounded, may be related to a possible pandemic. This alarm has been declared six times since its creation (2005), and two alarms

have occurred pandemics: H1N1 (2009) and the current experienced COVID-19 (2020) (MAXMEN, 2021).

Main symptoms corresponding to the pathogenesis of the novel coronavirus are cough, fever and dyspnea, with the possibility of progression to severe acute respiratory distress, pneumonia, renal failure and systemic failure (ITA, 2021). As it was an unknown virus in the scientific community, there were no safe and effective drugs for prevention and treatment. Thus, the first measures used at the beginning of the pandemic were the restriction of air and land traffic, social distance and temporary closure of trade considered non-essential (HARTLEY; PERENCEVICH, 2020).

These implemented actions brought positive results in the containment of the novel coronavirus, reducing the evolution of new cases, but it also generated socioeconomic impact on countries, especially those that do not have public health policies aimed at facing respiratory epidemics and are more fragile both health system as well as financial resources (RUEBUSH, 2021).

It has been a year since PHEIC was given and a lot has changed since then. Here we bring the scenarios related to transmission, treatment, vaccines, new variants and perspectives after a year of the PHEIC of COVID-19, a disease that has already caused the death of more than 2 million people.

2 METHODOLOGY

We conducted a study from a descriptive and qualitative review of the literature. The research was based on articles published in the PUBMED and Google Scholar databases, from January 2020 to January 2021, which released data from studies related to transmission, treatment, vaccines and new variants for COVID-19.

3 TRANSMISSION

The main proven route of transmission of COVID-19 has been through aerosol, infected individuals come into contact with healthy people and are responsible for the general contamination through infectious droplets present in the air. This transmission is more common in symptomatic than asymptomatic and the transmission rate varies from each place (PACHECO et al., 2020a; POLLOCK; LANCASTER, 2020).

At the beginning of the pandemic, it was also believed that contamination by surfaces was one of the main ways to become infected with COVID-19, however despite

the existence of hundreds of studies on the subject, none has yet been able to effectively prove this route of transmission (LEWIS, 2021; VAN DOREMALEN et al., 2020).

Only one study shows, in a better way, this transmission by contaminated surfaces, but even so it is not possible to be sure. This study reported the case of a building resident, infected with COVID-19, who pressed the elevator button after blowing his nose. Immediately afterwards, another resident pressed the same button and put a toothpick in his mouth to use as dental floss and ended up being infected. However, without the virus sequence of each of these people, it is not possible to rule out that the resident who brought the toothpick to his mouth was infected by another person (XIE et al., 2020).

Even without concrete proof, at the end of 2020, the surface disinfectants sector sold US $ 4.5 billion in products, more than 30% than the previous year. Some studies even recommend that expenses should be higher for ventilation or air purification instead of decontamination of surfaces (LEWIS, 2021).

However, even without effective evidence of the transmission of the coronavirus (SARS-CoV-2) on surfaces, it is essential to wash hands and continue with all the care, since the coronavirus is not the only pathogen harmful to human health.

4 TREATMENT

Numerous treatments against COVID-19 have been tested with low efficacy, however there is still much controversy about which is the best treatment. The only one widely accepted is the use of corticosteroids in stage 3 of the disease due to a large randomized study using dexamethasone, but there are treatment protocols with hydroxychloroquine, azithromycin, lopinavir/ritonavir, nitazoxanide, ivermectin, remdesivir and others (PACHECO et al., 2020a; JAN et al., 2020; BEIGEL et al., 2020; GAUTRET et al., 2020; HILL et al., 2021).

Another treatment option for COVID-19 corresponds to convalescent plasma therapy, a passive immunization practice that has been used since 1890 in infectious diseases and, more recently, in the case viral pneumonia as severe acute respiratory syndrome coronavirus (SARS-CoV, 2002-2003), H1N1 pandemic (2009) and middle east respiratory syndrome coronavirus (MERS-CoV, 2012) (RAJENDRAN et al., 2020; DUAN et al., 2020), however, its effectiveness against covid-19 still needs to be proven and its use considered safe, since this type of therapy was related to the emergence of new variants (KEMP et al., 2020).

5 VACCINES

In less than a year since the COVID-19 pandemic was declared, there are already 6 vaccines approved against COVID-19. The first to be approved for emergency use was that of Sputinik V on August 11, 2020, in Russia, even without the final tests. The first to complete the final tests, in record time, were those of Pfizer / BioNTech and Moderna and are already being administered in different populations worldwide (PACHECO et al., 2020b). The others approved, even for emergency use, are those of Sinopharm, Coronavac and Oxford / AstraZeneca (WHO, 2021).

Pfizer / Biontech and Moderna vaccines were made using the modified coronavirus (mRNA) genetic material and carried by nanoparticles18. The vaccine from SinoPharm and Coronavac, both from China, were made using the technology with the virus inactivated. The vaccines from Russia (Sputinik V) and Oxford/Astrazeneca use the technology with coronavirus subunits being carried by non-replicating adenovirus (PACHECO et al., 2020b).

Protection against COVID-19 is mediated in large part by an immune response directed against the coronavirus Spike protein (S). S-protein is responsible for binding the virus to the cell and is the target of virus-neutralizing antibodies (NAbs). Through vaccination, NAbs are induced against COVID-19. They bind to S-protein in or near the receptor-binding domain (RBD); in doing so, NAbs prevent the virus from attaching itself to the ACE2 receptor on human cells. However, some new strains have presented a challenge in the effectiveness of vaccines, as they present mutations of biological importance in the spike protein, target of the technology of many vaccines, which can cause evasion of the immune system (WANG et al., 2021; MOORE; OFFIT, 2021).

6 VARIANTS

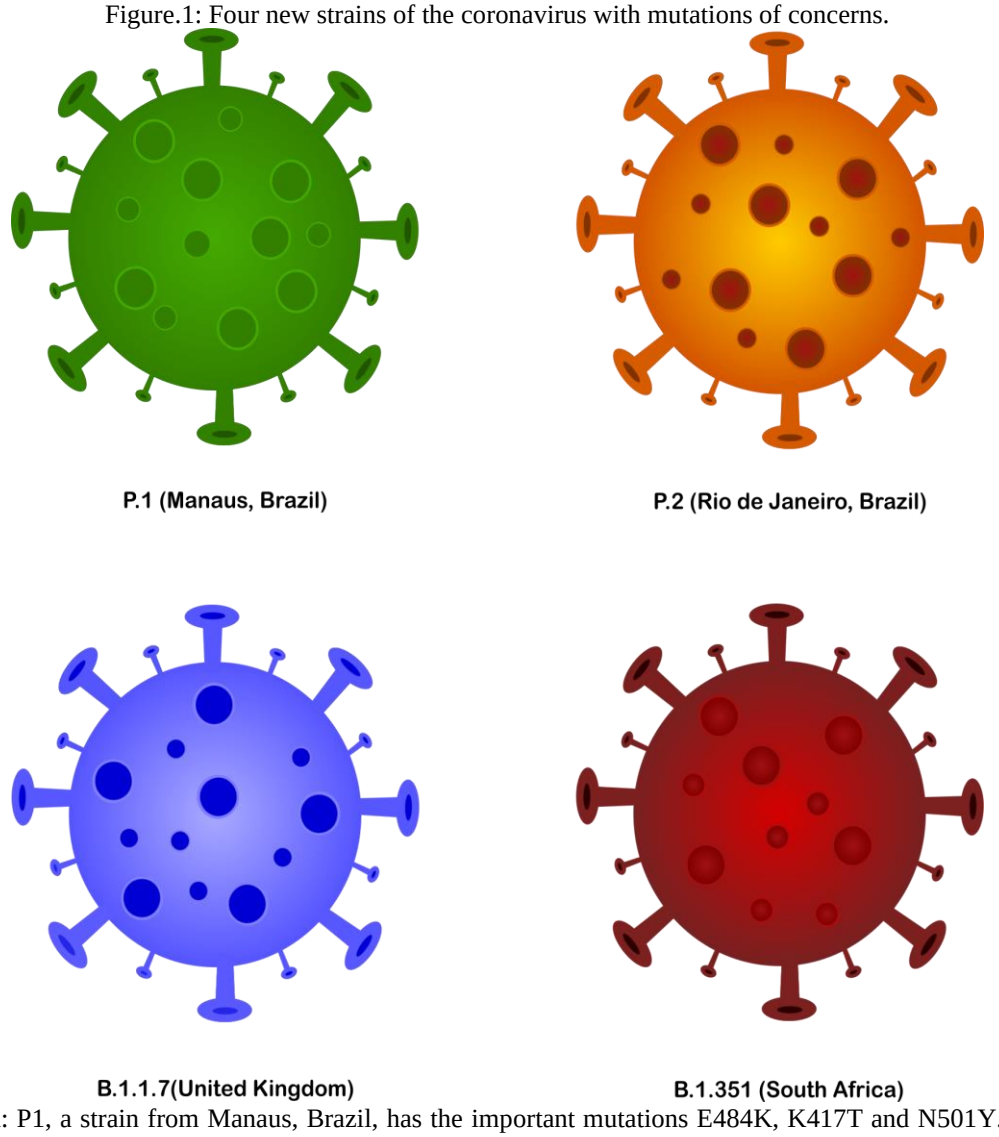
Coronaviruses have a crown-like appearance and can evolve by homologous or non-homologous mutation and recombination, justified by the huge single-stranded RNA (+ssRNA) genome that correspond approximately 30 kilobases, nonsegmented and positive sense. These characteristics facilitate the amplitude of host exchange, crossing of barriers between species, genetic recombination between coronaviruses (FELSENSTEIN et al., 2020; CASCELLA et al., 2020).

There are currently four strains of the coronavirus that raise concerns due to new mutations. P1, from Manaus, Brazil, contains a unique constellation of lineage-defining mutations, including mutations of known biological importance in the RBD, such as

E484K, K417T and N501Y. P.2, which originated recently in Rio de Janeiro, Brazil, also has the mutation E484K (VOLOCH et al., 2020; SABINO, 2021) (figure 1).

The United Kingdom lineage (B.1.1.7), among the 17 mutations detected, there are eight in the gene that encodes the spike protein on the viral surface, two of which are of particular concern. One, called the N501Y, the same of P.1. The other, called 69-70del, which leads to the loss of two amino acids in the spike protein and was found in viruses that escaped the immune response in some immunocompromised patients (KUPFERSCHMIDT, 2020) (figure 1).

Figure.1: Four new strains of the coronavirus with mutations of concerns.



Legend: P1, a strain from Manaus, Brazil, has the important mutations E484K, K417T and N501Y. P.2, a variant from Rio de Janeiro, Brazil has the mutation E484K. B.1.1.7 Lineage from the United Kingdom, has the mutations of N501Y and 69-70 del. B.1.351 has the same important mutation of P.1 from Brazil: E484K, K417T and N501Y.

Finally, strain 501Y.V2 or B.1.351 (South Africa) is characterized by eight strain-defining mutations in the spike protein, including three in important residues in the receptor-binding domain (K417N, E484K and N501Y), the same than the Brazilian lineage, P1. This strain from South Africa has already been shown to be resistant in convalescent sera almost 48% of the people tested and also to be highly resistant against vaccines that were more than 95% effective against the original virus (SHI et al., 2021; CALLAWAY, 2021a; CALLAWAY, 2021b)

The E484K and N501Y mutations occur in the receptor-binding domain (RBD) and are in the motif receptor-binding that the virus uses to bind to the human ACE2 receptor. E484K and N501Y correspond to one of the six main amino acid residues that determine a strong interaction of the SARS-CoV-2 receptor (RBD) binding domain with its angiotensin-converting enzyme cell receptor (ACE2). The K417T mutation also occurs in RBD, but it appears to have a minimal effect on binding to human ACE2, but it can contribute to immune evasion by decreasing key interactions with neutralizing antibodies (MOORE; OFFIT, 2021; TEGALLY et al., 2020).

The mutation called E484K is largely responsible for part of the unwanted effects of new strains, such as immune evasion, and the strain of Brazil and South Africa share this mutation. Therefore, the spread of this strain is of great concern to all countries in the world (KUPFERSCHMIDT, 2021).

7 CONCLUSIONS

After a year of the WHO PHEIC alarm, although there is no effective treatment against COVID-19, we already have effective vaccines, however these vaccines are not yet available to the entire world population, so the ways to prevent them are still a major challenge and treatment. Furthermore, the new variants of the coronavirus are of great concern, especially the strains from Brazil and South Africa, P.1/P.2 and 501Y.V2, respectively, which carry the E484K mutation and may hinder the effectiveness of available vaccines or possible treatments.

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