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A review of the emergence of the new variants of the SARS-CoV-2 in the world

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Abstract: A new infectious disease responsible for the emergence of respiratory syndrome and caused by the virus called coronavirus (SARS-CoV-2) was detected in late 2019 in Wuhan. Coronaviruses are a group of viruses, belonging to the family *Coronoviridae* of the order *Nidoviridales* and are responsible for causing, mainly, respiratory and gastrointestinal tract infections. SARS-CoV-2, despite predominantly infecting birds, has been responsible for the third major coronavirus outbreak in the last 20 years. In March 2020 the World Health Organization (WHO) declared the outbreak of COVID-19 cases to be a pandemic, and in October of the same year more than 1.04 million deaths were recorded.

Keywords: SARS-CoV-2. Coronavirus. Epidemic.

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1. Introduction

Since the coronavirus family was discovered, they have caused problems in society, initially with SARS-CoV, causing respiratory syndrome in Guangzhou, China, along with SARS-CoV-2 that caused a worldwide pandemic beginning in Wuhan- China in December 2019. Currently researchers have their attention focused on the new variants of concern of SARS-CoV-2. These variants cause outbreaks in places that consequently spread to the rest of the world, causing closures of borders, shops, schools and other public environments. With the emergence of vaccines, there was a decrease in mortality by Covid-19, which allowed populations to return to their former pre-pandemic normality. At the same time there is a contingent of people who do not believe that vaccines help to reduce the spread of the virus, which is one of the causes of why new variants of SARS-CoV-2 (TABIBZADEH *et al* .2021) still emerge.

In late December 2019, authorities reported the first case of coronavirus disease 2019 (COVID-19) in China, caused by a new type of coronavirus called severe coronavirus respiratory syndrome2, (SARS-CoV-2). COVID-19 has consequently led to the global pandemic we are currently experiencing; according to a situation report released by the World Health Organization (September 9), there are 27.4 million cases and almost 900. 000 deaths in total (World Health Organization, 2020). SARS-CoV2 was placed under the genus beta coronavirus, closest relatives being bats and coronavirus of pangolins (Zhu, N. *et al*.,2020) (Andersen, K. G.,2020).

It is important to highlight that little difference was observed globally in recent samples even in the face of increased mutations in relation to the specified reference sequence. Thus, it has been suggested that sequence-based analyses should opt for a consensus presentation to adequately cover the genomic variation observed to accelerate the diagnosis and production of the vaccine. It is noteworthy that at the moment, the GISAID database established that the SARS-CoV-2 population consists of six main clades: G, GH, GR, L, S and V 16. There are an increasing number of studies on the genetic variability of SARS-CoV -2 in relation to the reference genome (Maitra *et al*, 2020) (Kim *et.al*, 2020).

2. Methodology

A narrative literature review was conducted for retrospective observational study. As a first stage, a bibliographic survey was made in order to obtain all the references found on the theme addressed. The references used were websites, scientific articles, dissertations and doctoral theses described in lilacs, PubMed., SciELO and Portal “Periódicos Capes”, Science Direct. The health descriptors used in Health Sciences (DeCs) were: "SARS-CoV-2"; "CORONAVIRUS", "PANDEMIC COVID-19", "EVOLUTION”, “VARIANTS OF SARS-CoV-2". The literature consulted was published from 2019 to 2021, using as inclusion criteria studies in Portuguese and English and some studies with a date prior to the publication period. Therefore, studies that did not meet these criteria were excluded. From this survey, we contextualized the problem and the analysis of the possibilities present in the literature consulted for the conception of the theoretical framework of the research. From this survey, a narrative review was elaborated to establish relationships with previous scientific productions, identify recurrent themes and point out new perspectives, aiming at the construction of an updated work.

3. Results and Discussion

Coronavirus genomes have a variable number of open reading structures (ORF). 3´ ORF, which corresponds to only 1/3 of the genome, consists of genes encoding accessory and structural proteins (KHAILANY *et al*,2020). In addition, SARS_CoV-2 has 6 accessory proteins encoded by the genes ORF3a, ORF6a, ORF7a, ORF8 and ORF10: its functions are still unexplored (WU *et al*,2020 and KHAILANY *et al*,2020). When performing a comparative analysis of the SARS-CoV-2 genome sequence, striking similarities were identified with Bat-CoV, suggesting the possible origin in bats (Benvenuto *et al*,2020). The rapid evolution of virus populations can lead to the accumulation of amino acid mutations, which in turn can affect the transmissibility of the virus and pathogenicity (CACCURI, 2020).

Coronavirus is relatively stable due to a mechanism that operates during replication, but some genomic studies have revealed some changes in its genomes. The D614G mutation in the Spike protein of SARS-CoV-2 quickly became the most propagated variant of SARS-CoV-2 (PACHETTI *et al*, 2020), (KORBER, 2020). Several other mutations were found, and allowed the classification of several SARS-CoV-2 strains (ANDERSEN, 2020). While the D614G variation provides a selective benefit to the fitness of SARSCoV-2, the biological importance of other mutations to date is unknown. The results suggest the evolution of a possible near-viral species, however more data will be needed to conclude this hypothesis (CACCURI, 2020). From previous viral outbreaks, it is known that, as part of the natural evolution of a virus, subpopulations of subpopulations that can affect the severity of a disease emerge and alter the trajectory of a pandemic 21. (Harvala, H. *et al*., 2020). Being explained that; although the two main structures of proteins, S and capsid nucleus protein (N) are rich in episodic selection sites, ORF3a and ORF8 they also showed to carry many mutations (Benvenuto, D. *et al*.2020). In this study, we investigated the genetic variability of SARS-CoV-2 genomes in the Netherlands until mid-2020, against the background of the global viral population with a particular focus on the later phases of the first pandemic wave (from early April to late May). The most variant proteins in the SARS-CoV-2 genome were identified, as well as the most frequent mutations in the Netherlands, which also showed high dominance in the rest of the world.

To evaluate the mutational landscape and its impact as the pandemic progressed, dominant mutations were investigated over time in the viral population. This monitoring is of paramount importance to observe changes in the genome of SARS-COV-2, to identify conserved sites relevant both to the conception of therapeutics and vaccines, as well as to study viral evolution during the pandemic. Currently each new sample has on average ten mutation sites compared to the Reference Wuhan-Hu-1 (IDNC access 045512.2). In particular, S and N proteins have been reported as the most variant proteins in SARS-CoV-2 (Benevenuto *et.al*, 2020); (Zhou. *et.al* .2020).

In a recent study, new information about S and N proteins and their known epitopes were combined to identify regions in the SARS-CoV-2 genome that could potentially serve as epitopes for B and T cells (Koyama *et al*, 2020).

In order to determine the specific primers for diagnosing patients with RT-PCR tests and also for designing new initiator/probe sequences, variations in nucleotide sequences should be considered, as they play an important role for a precise test (Wang, C., Liu, Z., Chen, Z., Huang, X., Xu, M., He, T., *et.al* 2020) (Laha, S. *et.al* 2020). Protein (N) is recommended as a screening assay and is used in many countries (WHO, 2020).

We see a diverse mutational landscape in Australia, India and Spain, the viral population in China remained relatively homogeneous and with few variants compared to the reference Wuhan-Hu-1 the most frequent mutation is ORF8: L84S, which defines that apparently the S-wand is disappearing, the one that has been circulating since the beginning of the pandemic. Recently, a possible link between two mutations, ORF8: L84S and NSP4: S76S, was suggested, as it was observed that it occurred several times outside Europe, in China, USA, Australia and Canada (Tang *et.al* 2020).

The study the authors researched more than 29,503 SARS-CoV-2 genomes in the Netherlands, where they began analyzing their genetic diversity in the population, sequenced between April and May. Even with the measures of restrictions for social distancing, new mutations arose after the initial response and to obtain an effective survey, presented 3 factors: (1) before the first case was reported, (2) from the first case reported until the beginning of screening of health professionals and (3) the period since the introduction of more rigid measures along with events and large agglomerations of people being prohibited until March 15, when the stricter phase of blocking began with the closure of the retail and catering industries, as well as schools and day care centers. (Urhan, A., Abeel, T, 2021). Four mutations were identified: N: P383P, NSP14: D390D, NSP14: S374A and ORF7a: F87F, the authors state that these changes are unique to the Netherlands and affirm in their research that in the future they can be used to track possible transmissions of the disease.

In mutation N: P383P, (Urhan, A., Abeel, T, 2021), they say: "a silent mutation in the N protein is quite exclusive to the Netherlands", in this sense, the reading shows that this mutation has been in circulation for a while, well before the onset of the pandemic. This mutation was found in several provinces in sequence studies, found that more than 50 in total. In the second mutation identified, the authors found it difficult to interpret, because it was present in 9 genomes, and identification occurred in the Netherlands with 7 samples and 2 in the United Kingdom. In the third, he found that it would be the only non-silent and probably a small association. In the fourth mutation, the authors in their studies, claim "it is also incredibly rare, as it was observed only in Gelderland, in the Netherlands from late April to early May, and less than five times in any other country. It takes place in only one sequence in Canada on April 13, twice in the US at the end of March and four times in the UK in mid-April. In this context of analysis of the literary work, the authors offer a broad view of their research through a diversity of data by the population surveyed, especially in the Netherlands. This study enables future research with consolidated data and covering a look at the genetic variation of SARS-CoV2, this information is of paramount importance to understand the dynamics of mutations and perform covid-19 screening. In order to fully understand the potential of genomic epidemiology, we need routine sequencing of viral DNA established in parallel with the COVID-19 test. (Urhan, A., Abeel, T, 2021). There are already numerous genetic variations of the original covid-19-causing virus, but not all are lethal or contagious. At the beginning of the pandemic, the Variants of SARS-CoV-2 were named after the region where they had been described and the more opportunities a virus has to spread, the more likely it will have to replicate and change. The mutation is a natural and evolutionary process, especially if the organism in question has ribonucleic acid (RNA, the genetic material of the virus), as is the case of SARS-CoV-2. These different paths give rise to different strains of a virus and some specific arise from the appearance of new viral variants, which typically present one or more different mutations from the other variants circulating in a population, and which can pass this information for several generations on. Therefore, sometimes new variants appear and disappear, while other new variants may arise and persist. In one study it was seen that after the analysis of the polymorphism of the SARS-CoV-2 gene, it was observed that several mutations happen independently and are related to the increase in the number of infections, mortality and hospitalization by OC than the wild strain. In relation to *Delta*, infected individuals have twice the possibility of hospitalization and mortality due to the risk for the development of serious diseases than the CoV variants (TIAN, *et al*,2021).

The Lambda variant became responsible for the increase in cases in Peru, Chile and Argentina, which caused new peaks of COVID-19. Thus, this variant presents great capacity for the emergence of new pandemics. However, a study conducted by the University of Chile showed that Coronavac vaccine reduced by 67% the neutralization activity of the Lambda variant (TIAN, *et al*, 2021).

Finally, we see the presence of the Ômicron variant and little bit it is still known which viral characteristics facilitated its expansion. The Ômicron variant of SARS-CoV-2 shows more than 30 mutations leading to amino acid changes in the Spike protein sequence,15 of them located in the receptor-binding domain (RBD), which is fundamental forace-2receptor-mediated cell-virus interaction. Inferences to determine the transmission rate were attempted from the genetic sequence of Spike at Ômicron. These data reported a set of mutations at the S1-S2 site, which may increase viral infectivity. In addition, coupling studies have shown that a combination of mutations in RBD would produce a high binding affinity with human ACE2 of this variant. *In vitro* studies are needed to confirm these hypotheses (Ferré *et al*,2021).

4. Conclusions

In general, mutations modify the biological performance of variants, enabling a higher number of transmissions, hospitalization, mortality and mechanism of immune escape compared to the wild strain. Therefore, the Delta variant that was considered the most transmissible and with a higher risk of hospitalization and mortality than the other variants of SARS-CoV-2, now has its position occupied by the Ômicron variant, which has not been causing the same risks of hospitalization and mortality, by the action of vaccines.

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