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General Genetic Analysis of the COVID19 Pandemic

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ABSTRACT

COVID-19 pandemic has introduced a shift in accepted and routine handling of elective cases in hospital administration. This shift introduced a delay in the treatment of all non-COVID-19 cases, including cancer patients. Usually, non-complicated cases of cancer do not require immediate surgery, but procrastination is not an option. The pandemic is taking a longer time to be defeated as previously thought, and medical infrastructure is overwhelmed in many countries. Therefore, procrastination for non-COVID-19 cases became a reality. To this, we must add that there are specific cancer problems that require urgent resolution. The problem is having a heavy toll on almost all the involved continents. South and Central America are no exception. Unfortunately, South and Central America do not have all the resources available to the developed world, and this makes the issue of timely cancer surgery even more troublesome. A distressed hospital system needs a systematic approach to deliver cancer care in time. This paper has the intention to show the genomic impact of the severity of this new disease.

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Introduction

For 12 months, the planet has been immersed in the context of a pandemic phenomenon that has cycles approximately every 100 years, usually due to infectious causes and at this time has caused more than 1.4 people died worldwide and approximately 62 million infected globally [1].

The cause of this infection is a new coronavirus detected in China since December 31, 2019, in the city of Wuhan, China. This event coincided with the Chinese New Year, as a result of the massive population migration from different continents to and from China, which favored the spread of the phenomenon worldwide. Gorbalenya, with a geometric expansion, high contagiousness, and multiple transmission routes due to the particular genetic characteristics of the virus [2].

Our intention is to make a subjective analysis of different genetic aspects of the pandemic, based on the available information generated worldwide.

Generalities

Cyclically every 100 years a pandemic has occurred. The most recent was in 1920 with the death of 50 million human beings, caused by H1N1, which appeared again on the planet in 2009, becoming a seasonal disease.

At the beginning of the current pandemic, 27 cases of an acute respiratory syndrome were found, which was determined to be caused by a new virus discovered and reported on January 7, 2020, by China called SARS-2 CoViD-19 (Severe acute respiratory syndrome coronavirus 2 or severe acute respiratory syndrome by coronavirus type 2) [3]. This forced the quarantine of this city of 11 million people, with the consequent restriction of mobility and radical measures to stop its expansion, contagion, and virulence [4].

The Atlanta CDC raised the possible origin of the infection as probable in a market for the sale of live animals in Wuhan, apparently due to the ingestion of bats, or pangolin meat [5]. Another hypothesis suggests that it was from a bio-research laboratory close to that market, because patient zero worked in that institution, but frequently attended that market [6].

In India, in January 2020 it was reported (Prashant) in bioRxiv by the Indian Institute of Technology, through analysis by powerful computer software resources, that the genetic structure of the virus contained 4 sequences similar to those of the HIV virus and that Analogously, it allows it to enter the host by infecting it and giving it the possibility of multiple transmission routes, different from other types of coronavirus, which in practice has occurred [7].

This disease manifests itself with respiratory and systemic symptoms involving many organs and can be severe or cause death, especially if there are previous illnesses [8,9]. The disease produced by the COVID19 virus initially looks like a cold, but in addition to the respiratory symptoms, there are generalized symptoms that produce multisystemic damage to the brain, heart, kidney, liver, testicles (causing infertility), conjunctivitis, otitis, deafness, hepatitis, myocarditis, failure kidney, Guillan Barre syndrome, psychiatric and neurological disorders, cognitive deficit, seizures, Disautonomía, depression, infertility, kidney failure, gastroenteritis, myopathy, Kawasaki-like syndrome in children, etc. It has been observed that it can manifest mild, moderate, severe, fatal, and without symptoms [3].

The two aspects that affect severity are the presence of generalized inflammation that causes death due to a storm of cytokines or bradykinins, according to new research, and the second cause of death is massive dissemination of clots that cause stroke, heart attack, clots in the lungs, limbs, etc. [9].

Population Genetics Analysis

From its inception, based on observations made in the John Hopkins University real-time database, we were struck by a persistent pattern of certain countries, which compared to others had lower mortality, even with a number equivalent of infected [1]. For example, initially, India considering its population of approximately 1 billion people had few cases. In a cut to October 2020 when India had 7.6 million infected and the United States 8.2 million, the mortality of the former is only 115,914, but that of the USA is 221,694, that is, almost double, despite the fact that the US health system It is better than its counterpart and the poverty and overcrowding conditions in India are high, in addition to the possible lack of personal protection measures for the population.

Likewise, South Africa and the United Kingdom, both at that time with approximately 700.00 cases, but showed important differences since Africa had 18,700 deaths and the United Kingdom 44,248 deaths. In this case, we could suggest that the great geographical distances of Africa and its poor population density vs the overcrowding of the cities of the United Kingdom could explain this important mortality figure or perhaps genetic protection factors.

On the other hand, countries like Italy with 449,648 cases and 36,832 deaths, if we compare it with countries in relatively close ranges of the number of infected people such as Iraq, the latter only had 10,418 deaths, Bangladesh 5,723, Philippines 6,747, Turkey 9,513, Saudi Arabia 5,235, Pakistan 6,692, and Israel 2291.

We also observe this phenomenon in countries with lower figures from 150,000 to 100,000. For example, Ecuador with 154,115 cases and 12,404 deaths and Bolivia with 8,526 when compared with Nepal, which had 791 deaths, Qatar 225, Arab Emirates 472, Kuwait 721. Possibly the conditions of the health system in Ecuador and Bolivia, the shortcomings and lack of preparation for this health system influenced this rapid and deadly expansion of these developing countries. Other places with a low incidence of deaths were Lebanon 536, Uzbekistan 534, Ghana 312 deaths 6 cases, Singapore with 28 deaths and 57,000 infected. However, Sweden, with fewer cases at that time approximately 107,355 and that tested the herd immunity system, that is, no use of masks or other measures, or confinement, had 5929 deaths, reflecting very high mortality, which was similar to all countries of the Scandinavian peninsula together, which attracted a lot of attention.

This data presented above made us wonder if there are protection genes or susceptibility to severe clinical spectra or high mortality from COVID-19 depending on ethnicity, in addition to environmental factors (epigenetic) that are known to give a risk of poor evolution, such as male, elderly, having previous diseases such as hypertension, previous heart, lung or kidney problems, diabetes, pulmonary fibrosis, etc.

We then put forward our hypothesis that genetic factors affect the clinical expression (mild, moderate or severe of COVID-19) and the possibility of being carriers without symptoms or, on the contrary, having a high risk of dying.

Comparison of genetic concepts and clinical expression of COVID19

In an analysis from the genetic point of view of the pandemic, we observed that there is genetic heterogeneity, which means that the same clinical phenotype can have different genetic causes. In this case, making a comparison with the clinical spectrum of the current coronavirus, it presents similarities to the symptoms produced by other viruses.

There is also the variability of expression, which means the observation of symptoms with a very wide spectrum of presentation in different people, even in the same family group, and we clearly observe this phenomenon in the current pandemic.

On the other hand, the Degree of Expressiveness, which means that the clinical entity manifests itself with a different intensity in each person and can be mild, moderate, or severe, is analogous to the expression of mild, moderate, severe, asymptomatic symptoms of coronavirus disease (same as HIV) and fatal cases which we observed in the case in question [7].

The Asymptomatic expression modality parallels the genetic concept of Penetrance, which is the ability to express a gene in the phenotype, that is, it means that symptoms may or may not be present. It is clear that although all continents have positive cases, there are certain countries despite reporting a significant number of cases, there is very low mortality compared to other countries that had a similar number of affected, but high mortality and possibly the presence of asymptomatic patients has influenced this expansion.

This observation led us to wonder if there were genes determined by ethnicity that regulate predisposition to these differences in Variability of clinical expression, Degree of intensity, or penetrance, which apparently appear in all ages, sex, and races at a global level in those affected. In addition, how and when we express it (incubation period of 14 to 30 days) and degree of possibility of infecting others (superspreaders where 1 single person has infected up to 1000 more people) [1].

Epigenetics, on the other hand, corresponds to environmental factors that predispose or worsen the clinical picture such as deficiency of vitamin D, zinc or predisposing diseases such as diabetes, asthma or hypertension, pulmonary fibrosis, etc. However, it is clear that, in certain populations such as India, Africa, Arab countries, or some parts of Asia, despite a large number of people affected as well as other latitudes, mortality is not comparable, but much lower than in countries of Caucasian origin, whether we analyze it from the point of view of the population of each country or if we determine the rate per 100,000 inhabitants and compare it.

Trying to analyze the possible causal factors of these differences, we observe, for example, in Mongolia, a region also in China, a low incidence of cases and mortality, but we attribute it to geographical factors since there are giant cities in that location, but almost no there is population.

In Germany, we initially observed little mortality, but we consider that it was probably due to the radical measures taken at the beginning, like Australia, with the immediate closure of its borders, the early applied personal protection, and social distancing measures.

In Japan, culturally, the regular use of masks in respiratory processes possibly explains the quite acceptable control of the infection, but in the previously mentioned countries, we find no explanation and that is why the approach is that if the genes determined by ethnicity are the causes of this differences.

Phylogenetic Analysis

In the review of the literature, researchers found that people who inherited a sequence of ancestral genes of 50 kilobases, derived from Neanderthal man, are those who are at risk of making the severe clinical picture of high mortality [10]. It is present in 50% of Asians and 16% of Europeans, but we do not know in Panama or America, if it is present in our indigenous or Afro-descendants, mestizos, or Native Americans, etc., and in what percentage, which would be our objective to be carried out in the second phase of this analysis with local DNA studies.

The current human is Homo sapiens, sapiens. The extinct Neanderthal man or Homo sapiens neanderthalensis, inhabited from 28,000 to 230,000 years ago in Europe and Western Asia in the Middle Paleolithic period and in the Pleistocene. The current humans descended from him are those who are at risk of having a severe clinical picture or dying from COVID-19.

The causes of the ethnic variability of Panama are the migratory process as a link between North and South America, the presence of the Panama Canal, the trans-isthmian railway in the time of the Gold Rush of California, which implied the massive arrival to our country of citizens from all over the planet, for being a country of transit. Therefore, we consider that our population can be a significantly rich sample of genomes representative of the world, in the search for ethnic groups at risk and subsequent DNA analysis, to determine if any of our 7 indigenous groups, Caucasian, Asian, Indian, European, etc. possess this ancestral gene of Neanderthal man in order to capture these risk people early and protect them.

Considering the particular characteristics derived from the geographical position of Panama as a transit country, we would try to extrapolate this population variability of our Panama as a melting pot of races, where people of approximately 24 ethnic groups coexist, as a fertile field of research in the sense of the possibility of having a pool or genetic load of different ancestral origins and observe if there are differences by population groups indirectly representative of the planet's population.

In Panama the pandemic was declared on March 9, 2020, by the health authorities and as of today there are 163, 453 infected and 3039 deceased according to Gisanddata [1]. Due to the significant amount of human capital that has been dying, the Panamanian Government established sequential measures to reduce infection rates in the country, save time and optimize health resources to have the capacity to massively serve the population.

It is important to highlight that the GWAS group of severe COVID discovered a greater susceptibility to respiratory failure in people with blood group A and lower risk in group O. Franke A, GWAS consortium and 6 candidate genes located in the chromosome 3, short arm and are SLC6A20, LZTFL1, CCR9, FYCO1, CXCR6, and XCR1, related to important functions with COVID-19 [11].

Reducing the risks in Susceptibles

Due to its high mortality, expansion, and virulence, it is necessary to determine what are the most appropriate measures to reduce this high spread and if what we have done so far as citizens of the world has worked. To decide new State policies worldwide and give recommendations to educate the population, it is necessary to know the characteristics of this infection, such as that its incubation period ranges from 14 to 30 days, that there may be reinfection, that the sites closed are the riskiest and that all human body fluids can transmit it.

To protect the susceptible, thinking about environmental factors, that is, epigenetics, we must know the possible infection routes reported in the literature and these can be by air, aerosols, body secretions, respiratory, blood, perinatal, etc., therefore washing hands, social distancing and the use of masks reduce its transmission [12].

When a person coughs or sneezes, the droplets with the virus can spread up to 8 meters and can be recycled in the air by air conditioning that does not have a protective HEPA filter or settle on surfaces. Closed places such as cinemas, nightclubs, churches, elevators, restaurants, transportation, and public bathrooms, are places of the high risk of infection because infectious secretions such as saliva, tears, sweat, semen, urine, feces, blood, etc. can be there.

Additionally, it has been reported that it can be transmitted from pregnant women to babies and through sexual intercourse [13].

In the air, the risk of transmission is through droplets with the virus or aerosols that are smaller and contain the viral particles. When coughing or sneezing, the flush is spread according to studies with infrared rays, for about 8 meters of distance, being trapped on different surfaces or on people's skin [3].

Therefore, the places with the highest risk of infection are closed places, without ventilation, elevators, public transport, and places where air conditioning, which does not contain HEPA filters, allows it to retain the virus and recycle it into the surrounding air. , sending it directly to the people in the room, including walls, ceilings, and fomites.

In cruise ships there was cross-transmission, determining that it was due to air conditioning and feces that can be infectious for up to 30 days [14]. Today we know that the virus has been found positive in tears, saliva, sweat, semen, blood and could be acquired through the eyes, ears, nose, mouth, sexual intercourse, perinatal, through feces, when sneezing, coughing, speaking, or singing [15].

One of the biggest dangers that despite wearing a mask is getting infected by touching the face or the front of the masks, not having protective glasses because the virus can get through the eyes, or by touching infected surfaces that keep the virus for days since it has been found viable in skin 9 hours, hair, clothing. In-wood 2 days, plastic 3 days, 4 days in metal, plastic, wallets, masks, bills, on the asphalt 8 days, floating in the air 8 hours, corpses 7 days and on cell phones at 20 degrees centigrade 28 days [16-19].

We know that the virus measures approximately 100 microns and the mesh of the masks can generate holes of different sizes [20,21]. Fabric mask holes are approximately 1000 microns, surgical ones 300 microns. There are three masks that have filters that give 95% particle filtering and are synonymous: the N95 (American), the KN95 (Chinese), and the FFP3 (European) have holes of approximately 20 to 100 microns [22]. They only protect the last three bidirectionally. The virus is transmitted along with the carrier secretions and this is a factor to consider.

Studies have determined that cloth masks are not safe, nor are surgical masks, since the user is not protected, it only reduces the spread of secretions in the air when coughing or sneezing over long distances and reduces the risk of If the person is infected, spread it to others, but they do not avoid it 100%. A fact demonstrated in ophthalmological offices, where aftercare daily to patients, it was cleaned with quaternary ammonium and still viral RNA of coronavirus was found floating in the air [19-21,23].

The only ones that protect the wearer and others are the three with a 95% protection filter (N95, KN95, and FF3) and if the susceptible person is not protected with the correct protection and with protective glasses, their risk of infection will increase as an environmental factor, in addition to genetic risk, if it exists. A few months ago it was not easy to find surgical masks, nor N95 for sale, and people used cloth, which is currently prohibited in Spain, due to the above-explained since October 2020 [24,25]. In France, cloth masks were banned on flights.

Our proposal is that the industry concentrates on the worldwide mass production of N95, KN95, or FFP3 masks so that these are the ones used by the entire world population, not only health personnel, as it is obvious that this would reduce the rate of the infection.

In theory, with only one month of global quarantine, considering the incubation period of 14 to 30 days, if all citizens of the world were guaranteed food, services, education, economic resources, and the entire planet would use the protective filter masks 95% without a valve, the pandemic could be stopped and world economic activity could return because the sick and asymptomatic would already be limited and in better health in that period of 30 days and if no one leaves, only the necessary personnel, the number of people who they could relay the infection. This would only occur under the precept of global solidarity, discipline, and citizen awareness and a policy of world governments that protects the interests of the country, because if there are no infected, the expenses for sick and intensive care are reduced, allowing States to restart the life we used to have.

In a small survey that we carried out on social networks through a virtual survey, with a sample of 100 people over 18 years of age, we determined that 15% of our sample had suffered COVID19 in the period from March to October 2020.

Most of those surveyed use surgical masks in 67% of cases, 18% masks with an N95 filter and 8% made of cloth, however, at the time of infection, 54% of those affected were using surgical masks. Our explanation is because the virus measures 100 microns and the surgical holes allow the virus to pass to the person who uses it, just like the cloth ones, due to the aforementioned, therefore in both cases, the virus passes easily. The objective of surgical masks is to reduce the expansion of secretions from a patient or asymptomatic to others, but it does not protect the person and this is relevant because of the more exposure, the more viral load, and the more severe clinical picture.

Future risks

At this point, we meditate on some hypotheses to rule out or check in the future, regarding this pandemic. Making an analogy with other viral diseases such as infectious mononucleosis, which in the African population can give a risk of Burkitt's lymphoma, or the HIV-AIDS disease, which can occur with Kaposi's sarcoma, we consider the possibility that in certain susceptible individuals, can give the mutation of proto-oncogenes of the cell cycle or the activation of oncogenes by effects of the virus.

Considering the asymptomatic and making a parallel with AIDS, we wonder if, in the future, the presence of the virus deposited or stored in multiple organs will be determined, and that for example, due to its neurotropism, reactivations of this latent and hidden state may be suffered, which allow the micro RNA machinery of the CoVID19 virus to act on healthy cells and promote their malignancy since we still do not have enough data and answers for all the questions about the mechanisms of action, genomic integration or integrase analogs, as well as potentialities chronicity of this new virus or other unknown long-term effects.

We also wonder if, despite the fact that malformations have not been properly reported in children born from the pandemic, from the point of view of Genetics, it seems to us that it is important and different, the moment that their pregnant mothers suffered COVID19, either in the critical period of teratogenesis that corresponds to the first 4 months of pregnancy, due to the relevance of neurodevelopment or after that moment where all the anatomy, cells and tissues are already formed.

The question is, what effects will the presence of viruses in these individuals chronically have on their organs in the future? If this mechanism can occur and if so, will this produce modifications to the genome in the long term, putting them at risk of cancer or other effects in their adult lives? or on the contrary, it will confer them a special long-term immunity, including their stem cells.

We consider, according to our genetic approach, that efforts should be concentrated on drugs that reduce the possibility of integration and replication of the virus in humans, due to the risk that its permanence and interaction with our genes could represent, considering the effects produced by transposons and the jumping genes, and because by rapidly reducing the symptoms, they would shorten the infectivity period and the possible sequelae, if they are treated early.

For safety and to verify the presence and viability of the virus in the blood in secondary reservoirs such as mosquitoes, appropriate measures must be taken to avoid the possibility that this new virus shares genetic information with other viruses on resistance, integrase, virulence, degree of affectation, etc.

Conclusion

The urgency of controlling this event is because it is decimating the population of all ages, children, the future of humanity, young people of reproductive ages, the human capital that works, and our elderly with morbidities, valuable people in our community.

In conclusion, based on our hypothesis that genetic factors affect the clinical expression (mild, moderate, or severe of COVID-19) and the possibility of being carriers without symptoms or, on the contrary, having a high risk of dying, if we determine the existence of this genetic susceptibility and those genes, the impact would be extraordinary when capturing people at risk to protect or treat them early, reducing the risk of mortality and sequelae, impacting the negative global outcome of the pandemic, benefiting humanity, reducing social damage, emotional, psychological, economic, personal, business and Government by reducing expenses for illness and mortality, which reduces the main resource of the countries, that is, their human capital that suffers the consequences that imply a reduction of capacities, produces disability work and sequelae with disabilities that merit costly medical attention, investment of time and State expenses do.

Recommendations

1. Do strict surveillance of those who suffered COVID 19, to determine if, in the long term, they suffer a greater risk of cancer than the population that did not suffer from it.
2. Concentrate the vision of the industry on the local mass production of N95, KN95, or FFP3 masks for universal use throughout the world population, since this small investment will benefit the collective, by reducing the infection rate global, allowing us to rejoin life before normality and facilitating a better global economic reopening with less risk of second waves.
3. Long-term surveillance of the children of the pandemic, to determine risks of malformations, cancer, chronic meningitis due to viral neurotropism or other effects.
4. Concentrate the efforts of the pharmacological industry, on drugs that quickly control the infection to reduce the period of contagion due to secretions and avoid the permanence of viruses in cells, avoiding the interaction of our genome with the virus, as far as possible by risks of carcinogenesis.
5. Analysis of vectors or other reservoirs that could facilitate infection in humans or favor reinfection.

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