Folia Cardiologica 2021 vol. 16, no. 2, pages 168–176 DOI: 10.5603/FC.a2021.0020 Copyright © 2021 Via Medica ISSN 2353-7752 e-ISSN 2353-7760

# What have we learned about COVID-19 in 2020? Ten hypotheses explaining the differences in incidence and mortality from COVID-19 between countries

Czego dowiedzieliśmy się o COVID-19 w 2020 roku? Dziesięć hipotez wyjaśniających różnice w zachorowalności i śmiertelności z powodu COVID-19 między krajami

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#### Abstract

Coronavirus disease 2019 pandemic is one of the most difficult challenges for modern medicine and health care. Since the beginning of its outbreak in different regions of the world, researchers have noticed differences in incidence and mortality rates. We herein present ten hypotheses that were a topic of scientific discussions and might explain this observation. Cultural, demographic, sociological characteristics of societies, differences in healthcare systems and vaccination schedules, genetic polymorphism, and other factors can serve as variables affecting the course of the pandemic in different regions of the world. Further study of those hypotheses might provide us with valuable insight and broaden knowledge in this unprecedented epidemiological situation.

Key words: COVID-19, epidemiology, One Health, pandemic

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#### Introduction

Severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) human-to-human transmission was confirmed on January 20<sup>th</sup>, 2020, and declared a pandemic by the World Health Organization on March 11<sup>th</sup>, 2020 [1, 2]. The year has passed since we are aware of the coronavirus disease 2019 (COVID-19) and the virus noted in almost every country of our globe [3].

From the very beginning of the COVID-19 pandemic, there have been significant differences in morbidity and mortality between countries. The natural development of pandemic, transmission from one area to the other, or the data analysis time could not merely explain this fact. All of it led to the formulation of several hypotheses – summed up and discussed more widely in our textbook – explaining why the epidemical situation differs between countries [4].

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At the beginning of the pandemic, Poland has noted a relatively low number of deaths with a high incidence rate. This observation was similar for most countries in Central and Eastern Europe, in contrast to Western Europe and America. Unfortunately for Poland, the tendency has changed due to poor control of the pandemic. It led to the healthcare system's paralysis and severe growth in mortality, with the highest number of almost one thousand deaths on 8<sup>th</sup> April (Figure 1).

Hereby we describe the most important contemporary hypotheses, explaining partially why the epidemic reports suggested that the course of COVID-19 was milder in some areas, and the percentage of deaths from COVID-19 was significantly lower.

#### Hypothesis 1

# The hypothesis of the initial demographic and health status of the infected population

In this hypothesis, society's different demographic structure can cause the virus's heterogenic spread, the other morbidity and mortality rates. Countries with a higher proportion of young people have a milder incidence of infections, whilst countries with a high proportion of the elderly experience more deaths and hospitalization due to COVID-19 [5]. This theory perfectly explains the low incidence and mortality of COVID-19 in the continent with the youngest population in the world – Africa. Factors modifying these correlations may be individual societies' health status – the prevalence of additional risk factors such as smoking, obesity, diabetes, cancer, and respiratory system diseases [6]. Those factors can increase susceptibility to SARS-CoV-2 infection and mortality from COVID-19. Initially, this hypothesis explained the relatively low mortality from COVID-19 in China, compared with the other country that became the epicenter of the pandemic — Italy. However, this model cannot explain the significant difference in mortality from COVID-19 in societies with a similar demographic structure (e.g. Italy and Germany).

### Hypothesis 2

# The hypothesis of cultural and sociological differences

The hypothesis of cultural and sociological differences tried to fill this gap, explaining differences in the development of the epidemic in Asia and countries of Western Europe [7, 8]. In these countries, the pandemic spread more quickly and had higher mortality (Italy, Spain). There is a possible correlation between the easier spread of the virus and cultural behaviors, which differ between Mediterranean and Asian societies. In Southern Europe, people live very active social life: spending much time in restaurants and pubs, celebrating meals, enjoying feasts and parties, taking pleasure from the time shared (Italian la dolce vita, Spanish fiesta); when Asians are thought to be more focused on work and study and are significantly less social. There is a clear distinction between such simple day-to-day gestures as greeting - hugs and kisses of people regardless of gender in southern Europe versus keeping distance and nodding head in Asian countries. The rapid transmission of the infection could



Figure 1. Daily deaths in Poland (na podstawie: https://www.worldometers.info/coronavirus/country/poland/)

significantly affect multi-generational families living in the same household.

Additionally, the traditional model of an Italian family with a late independent young generation being a vector of infection to the oldest members of the family living together could also play a role in transmitting disease [9]. However, this hypothesis still does not fully explain the high mortality rates from COVID-19 in the rich countries in Northern Europe — the Benelux countries: Belgium and Luxembourg. Nevertheless, cultural and sociological differences may have been related to seemingly trivial behavior in individual societies and be important in the initial stages of the virus's transmission.

Even difference in simple social habits concerning hygiene can play a role in the transmission of COVID-19. The results of a study carried out five years before the outbreak of the pandemic (WIN/Gallup International, 2015, assessed 30.12.2020 - https://www.statista.com/chart/4111//do-europeans-wash-their-hands-after-using-the-toilet/) determined the percentage of Europeans routinely washingtheir hands with water and soap after leaving the toilet.The percentage was the highest in some Islamic-mainlycountries (Turkey, Bosnia and Herzegovina – 94 and 96%respectively), high in some countries (Germany – 78%,Sweden – 78%, Finland 76%, Great Britain – 75%), medium in other (Ukraine – 71%, Poland – 68%), and low inthose highly impacted with COVID-19 five years later (France – 62%, Spain – 61%, Italy – 57%, Netherlands – 50%).

#### **Hypothesis 3**

#### The hypothesis of the efficiency of health care systems and the early implementation of preventive measures

The hypothesis of the efficiency of health care systems and the early implementation of preventive measures adds to the previous observations important factors modifying the spread of the virus. In an excellent organization, the health system's proper funding and efficiency could result in the low mortality rate from COVID-19 in countries such as Germany. Contrary, the absence or the late implementation of a 'lockdown' strategy in Sweden and the United Kingdom explains very high mortality rates from COVID-19 [10]. The general practice of wearing masks, social isolation and distancing in public are factors that could possible explain the relatively stable control of the pandemic in countries such as South Korea, Singapore, Taiwan, Japan and Hong Kong. Studies emphasized that those societies wore masks long before the epidemics outbreak and continued to do it during and afterwards [11]. People in those countries wore masks because of previous viral epidemics, but also due to air pollution. Thus, Asian countries quickly and effectively implemented preventive and protective methods. Other elements limiting transmissions have also been introduced more easily: for instance, frequent handwashing. Quickly introduced control of tourism and journeys could explain success achieved in Australia and New Zealand.

Assuming that the Chinese morbidity and mortality data are accurate, this country has managed the epidemic very well [12]. It was possible by using severe forms of 'lockdown': locking citizens in their homes and putting them under strict control, isolating certain cities and provinces, preventing the movement of people within these zones. These measures were a very troublesome strategy, but it is undoubtedly more effective than just reporting danger in individual districts without any control over the movement of people between them (a strategy implemented in Poland with so-called 'yellow' and 'red' districts). Sociologists also point out that effective methods of preventing pandemics in the population dimension are paradoxically easier to introduce in countries with authoritarian power than in liberal democracies.

Furthermore, the testing strategy and its testing capacity played a significant role in the pandemic's adequate control. In Poland, problems related to this matter might provide us with a possible explanation of the excess-all cause of mortality rate during the second and third wave [13]. The high rate of positive SARS-CoV-2 test - exceeding 20% with a peak of 50.3% - suggests that COVID-19 was underdiagnosed in the second and third wave period [14]. Consequently, patients died because of COVID-19 and its complications before diagnosis was made or were tested during screening in the emergency units of general hospitals, where they were admitted because of deterioration of COVID-19 and other somatic conditions. Diagnosis of CO-VID-19 in hospitalized patients impacted majorly on operations, as it led to the quarantine of medical personnel and closures of whole wards, limiting access to health services for the most severely ill people [13].

Furthermore, focusing on COVID-19 cases, many health professionals had to abandon their previous obligations with severe limitations of direct patient-doctor contact. Apart from the current issues related to the pandemic, there is a need to sustain the proper level of medical care in the whole system: efficient oncological diagnostics (7% decrease of fast-track oncological cards in Poland in 2020 vs. 2019) [15], cardiological services (15% decrease of myocardial infarction hospitalizations in Greater Poland region in 2020 vs. 2019) [16], brain stroke management (25% decrease in stroke patients treated with mechanical thrombectomy in Lesser Poland region in January-May 2020 vs. January-May 2019) [17], and managing an observed deterioration of the population's mental health are expected to be major significant challenges for the following months of the ongoing pandemic [18].

### Hypothesis 4

# The hypothesis of population density and accelerated transmission of infections

The hypothesis of population density and accelerated transmission of infections. Population density could be the main element explaining the differences in pandemic development in individual countries. It is a simple parameter that correlates with the risk of SARS-CoV-2 infection. The Scandinavian countries in Europe have become an excellent model to prove this hypothesis. In this hypothesis, we cannot compare the data from Sweden, where the authorities decided not to apply the 'lockdown' strategy but to opt for population immunization. Other countries -Norway, Denmark, Finland - have a similar socio-cultural picture with high economic growth, a similar healthcare organization, and a preventive and lockdown policy. These countries have almost identical populations (5.4-5.8 million citizens), but their population density varies Norway 15, Finland 15, Denmark 138 people/km<sup>2</sup>. The reported mortality from COVID-19 is twice as high in Denmark as in Finland or Norway [19]. It is worth pointing out that also in Poland, the regions of the dense population - the Silesian agglomeration, Mazavia and Lesser Poland – had the highest morbidity rate of SARS-CoV-2.

The epidemiological literature also emphasizes the role of local communities that can increase virus transmission regardless of population density in large industrial factories, mines, military barracks, schools, educational institutions, dormitories, monasteries, temples. Similarly, the infection can be easily transmitted in crowded places: concerts, religious rites, weddings, funerals, large sports events. The conditions of contact can alter the effectiveness and the scale of transmission. Analyses suggest a higher chance of infection indoors than in open air, especially in the smaller spaces, when there is a closed air circuit, and there is no possibility of regular ventilation with opening windows [20, 21]. The hypothesis of the accumulation of transmission can also explain the accelerated and highly unfavorable initial course of the Italian Lombardy and Veneto epidemics. Some epidemiologists believe that it is no coincidence that the epidemic started there between February and March. This region is significantly industrialized and has high economic development due to numerous business contacts with Asian countries. January 2020 was when many people from China came to Italy after celebrating the Chinese New Year; similar migrations were also observed in Chinese provinces [22]. According to one of the hypotheses, some of these people could have been carriers of the coronavirus, thus forming a particular population of 'zero patients', which, by further transmitting the virus, caused an extreme progression in the number of infected people.

## Hypothesis 5

# The hypothesis of variable virulence of different strains of the virus

The hypothesis of variable virulence of different strains of the virus. At the beginning of the COVD-19 pandemic, studies analyzed the genetic variability of SARS-CoV-2. It was necessary because the newly discovered coronavirus showed a relatively high potential for genetic variability, which enabled it to break down the species barrier and switch from animals to humans. Many different mutations in SARS-CoV-2 have been described so far [23]. Currently, the most common subtype is D614G, which is commonly called G strain. It mutated into GR and GH clades at the end of February 2020. Studies show that the prevalence of G, GH and GR clades is continuously increasing worldwide. The 'old' S strain exists in some restricted areas in the US and Spain. The L and V strains are gradually disappearing.

Four other SARS-CoV-2 genetic clusters were identified as super-spreaders (SS) variants. They are also responsible for triggering the primary COVID-19 pandemic outbreaks in different countries. The SS1 cluster was widespread in Asia and the US, and it was probably responsible for the outbreaks in Washington and California and South Korea, and the SS4 cluster contributed to the pandemic in Europe. The British variant of SARS-CoV-2 has also been reported in December 2020 [24]. At present, there is no conclusive data that would enable to establish correlations between a specific genetic variant of SARS-CoV-2 and mortality. Significantly, none of the found mutations seems to affect the antigenic structure of the new coronavirus. This lack of antigenic mutation is an important facilitation in the design of vaccines directed against SARS-CoV-2, available since the end of December 2020.

### **Hypothesis 6**

### The hypothesis of genetic polymorphisms

The hypothesis of genetic polymorphisms always arises when a pandemic involves different countries, nations and societies. Since the beginning of the COVID-19 pandemic, attention has been drawn to the possible impact of genetic polymorphisms within the renin-angiotensin system, resulting in a different expression of ACE2 – a protein essential in entering host cells [25]. There were claims that people with specific ACE polymorphisms using ACE/sartan inhibitors may prevent severe alveolar damage. It has been emphasized that genetic polymorphism if affects mortality from COVID-19, should be linked to a gene located on chromosome X, thus would explain the higher mortality rate in men with one copy of this chromosome. Studies showed that the course of COVID-19 is particularly severe in individuals with mutations of the TLR7 gene in chromosome X. which would affect the expression of genes for interferon. There is also a hypothesis that the poor prognosis of CO-VID-19 is related to the gene's polymorphism for glucose 6-phosphate dehydrogenase (G6PD). Favism, associated with a deficiency of G6PD, is a disease that affects approximately 200 million people worldwide. Poland is one of the countries with a low prevalence of G6PD deficiency (0.1% of the population); higher percentages of people with this genetic defect are observed in Italy, Spain, the USA, India and southern China. That could explain higher morbidity and/or mortality in the course of COVID-19.

Other studies highlight the possible link between the prognosis of COVID-19 and gene polymorphism in:

- already mentioned genes encoding ACE2 some genetic polymorphisms of ACE2 may favor the occurrence of neurological complications. Interestingly, the ACE2 polymorphisms rs35803318 and rs2285666 occur at a completely different frequency in the Italian population than in other parts of the world [26];
- genes encoding ACE1: where ACE1 II polymorphism is associated with higher mortality from COVID-19 and higher ACE1 I/D ratio would be associated with better prognosis [25, 27];
- genes encoding interferon-induced helicase 1 (IFIH1): which may involve the lower expression of INF-beta in some populations with a specific mutation of the single nucleotide IFIH1 (Afro-Americans in the USA) [28];
- a gene encoding the expression of a receptor the TMPRSS2 serine protease – that is responsible for the attachment to the host cell: it was found that out of four alleles responsible for the expression of TMPRSS2 in the alveoli, those associated with increased expression of TMPRSS2 are more common in the European and American than in the Asian population [29];
- genes encoding dipeptidyl-peptidase-4 (DPP4) –
  CD26 protein, which may explain a worse prognosis in
  COVID-19 in people with diabetes [30];
- genes encoding glutathione s-transferase [31];
- genes encoding the major histocompatibility system HLA (human leukocyte antigens): type HLA- DQB1\*06 increases the risk of SARS-CoV-2 infection, and types HLA-A\*02, HLA-B\*44 and HLA-C\*05 have a potential protective role;
- genes encoding interferon-induced transmembrane protein 3 (IFITM3); its specific polymorphisms may be associated with a worse prognosis of COVID-19 [32];
- genes encoding the blood group system, with lower susceptibility to SARS-CoV-2 infection of people with blood group 'O' and higher susceptibility of people with blood group 'A' [33].

# Hypothesis 7

The hypothesis of unspecific cellular immunity induced by tuberculosis vaccination. has gained many supporters and

resonated with the public. Tuberculosis vaccination was introduced in 1921 (after the 'Spanish flu' epidemic) to prevent tuberculosis. The vaccine is produced from the BCG strain (Bacille Calmette-Guérin) — a mutant bovine bacillus deprived of virulence by multiple passages. The hypothesis of the protective effect of tuberculosis vaccination was proposed by observing large differences in SARS-CoV-2 infections and mortality from COVID-19. East Germany (former GDR — German Democratic Republic, a socialist state existing until 1989) mortality rates were lower compering to West Germany (former Federal Republic of Germany) [34]. The former GDR used the BCG vaccine until 1990; thus, all people over 30 years old are still immunized. In West Germany, due to the low risk of tuberculosis, citizens were not vaccinated with the BCG vaccine [34].

Similarly, studies showed significant differences in mortality rates between post-communist Eastern and Western Europe: Spain (BCG has not been vaccinated since 1981) and Portugal (BDG vaccinations until 2017 - 36 years longer) [35]. Other countries that do not carry out the mandatory BCG vaccination have experienced significant problems in controlling the epidemic: Great Britain, the USA, France, Belgium, the Netherlands, Denmark, Italy, Luxembourg, Spain, Australia, and Israel. Similarly, the high mortality rate from COVID-19 in Ecuador (no BCG vaccination) in comparison with Peru (BCG vaccination obligatory since 1945) and Colombia (BCG vaccination obligatory since 1960). Studies correlate the number of cases of COVID-19 with the lack of obligatory BCG vaccination [35]. Data indicate that the earlier in the life of an individual the BCG is given, the lower is the risk of death from COVID-19. It appears that there were fewer infections and fewer deaths during the first 30 days of the epidemic in countries where BCG vaccination was compulsory at least until 2000. In Poland, the Brazilian strain has been used since 1955 to 2005, on all children and infants with the birth-weight above 2000 grams (the first dose - given right after birth, and the second - at the age of seven). According to the information provided to us by the Polish national consultant in Pediatrics - prof. Teresa Jackowska - the BCG infant vaccination rate in Poland is over 90%. It could explain low mortality from COVID-19 in Poland. One dose of the BCG vaccine leads to anti-tuberculosis immunity for at least 15-20 years. The BCG vaccine does not stimulate the production of specific antibodies but activates T CD4 lymphocytes to produce cytokines. Increased INF-gamma production in vaccinated individuals has been found even after 10 to 30 years since the last vaccination. However, we still do not know if the BCG vaccine itself could be a protective factor against SARS-CoV-2 and whether it is worth giving an additional dose of BCG vaccine to people who have been vaccinated in the past or the first dose to people who never received BCG vaccine. The results of ongoing randomized clinical trials, including the Australian BRACE (BCG vaccination to Reduce the impact of COVID-19 in Australian healthcare workers following Coronavirus Exposure) and the Dutch BCG-CORONA (Reducing Health Care Workers Absenteeism in COVID-19 Pandemic Through BCG Vaccine), will resolve this issue [36, 37]. Studies also suggested that BCG vaccination's protective effects against the COVID-19 may also apply to other early child-hood vaccines, such as MMR vaccine [38, 39].

# **Hypothesis 8**

# The hypothesis of other factors inducing immune protection against SARS-CoV-2

Possibly, a vast number of other coronaviruses, symptomatically or asymptomatically infecting humans, may induce resistance to the coronavirus SARS-CoV-2 via the humoral and/or cellular pathway. Studies showed that the memory T cells, which have previously recognized the cold-causing coronaviruses, can also recognize the SARS-CoV-2 proteins (including the S protein responsible for its association with human cells). It may explain why some people have a milder course of the disease. Studies showed that 40% and 60% of people who have never contacted SARS-CoV-2 have memory T cells capable of responding against the virus. These cells recognize parts of the virus with which they have never been in contact before. Observations confirming this fact were conducted in the Netherlands, Germany, the UK, and Singapore. Flu and infections of the upper respiratory tract – more frequent in Central and Eastern Europe than in warm Mediterranean countries - could also, paradoxically, contribute to better protection in pandemic times. The mechanism explaining this phenomenon may be the occurrence of "cross-reactivity" - the presence of lymphocytes that can fight a dangerous virus due to the similarity of a previously recognized, less virulent one. This mechanism can be triggered by contact with 'animal' coronaviruses and to produce a protective immune system. According to anecdotal that veterinarians and pet owners - people who have frequent contact with animals - had a milder course of SARS-CoV2 infection [40]. However, these reports need to be verified.

Interestingly, Oxford University scientists promote the hypothesis that exposure to 'animal' coronaviruses can modify people's immune response against SARS-CoV-2. They prove that SARS-CoV-2 or a very similar coronavirus, long before the pandemic erupted in 2020, infected people in South-East Asian countries (Vietnam, Laos, Cambodia, Burma, Thailand). In these countries – contrary to South China – bats are the most common reservoir of many coronaviruses, including the species considered to be the one from which the SARS-CoV-2 infection started. These countries — including Indonesia — are characterized by the highest biodiversity of bats. According to this hypothesis, SARS-CoV-2 has repeatedly infected these countries' populations, making them immunologically protected. Then, the virus infected the pangolin and was dragged to Wuhan's province, where the population was 'immunologically unprepared'. This theory explains the very low incidence and mortality rate of COVID-19 in Vietnam, Laos, Cambodia, Burma or Thailand — countries very close to China with dense population and without strict lockdown restrictions. The cross-over SARS-CoV infections between humans and animals are not fully understood until now [41, 42].

# **Hypothesis 9**

### The hypothesis of additional lung damage and the impact of an industrially altered environment

The hypothesis of additional lung damage and the impact of an industrially altered environment was gaining supporters at the beginning of the US epidemic after observing the increased mortality rate from COVID-19 in regions with increased air pollution [21, 43-46]. It seems that an atmosphere with a high PM2.5 and PM10 content favors the transmission of the virus by transporting it on dust particles over long distances. PM2.5 and PM10 particles also induce inflammation in the lungs, which may increase the risk of infection and exacerbate the course of COVID-19 [47-51]. The rapid development of the pandemic in Italian Lombardy may also have depended on air pollution in Italian cities in the region [21]. If these concepts are valid and have clinical implications, they are bad news for Poland's epidemic - one of the most polluted countries in Europe. The coal-based economy leads to high annual concentrations of PM2.5 and PM10, especially in Silesia and Lesser Poland. Some experts emphasize that the 'lockdown' applied in Europe has resulted in significant air pollution reductions in March-April 2020, which would be crucial for reducing virus transmission [21]. Further observations of these dependencies and their impact on pandemic control are necessary.

# Hypothesis 10

### The climatic hypothesis

The climatic hypothesis suggests that the transmission of the virus and its infectivity depends significantly on the climatic conditions. At the very beginning of the pandemic, scientists suspected that the SARS-CoV-2 virus would disappear or significantly weaken with time — similarly to other coronaviruses causing flu and respiratory infections. It could probably happen in the summer period, characterized by higher temperatures and more sunlight [52]. The higher temperature limits the transmission of the virus since it promotes aerosol droplets' drying on which the virus can spread or remain active on surfaces for longer [53]. Unfortunately, the effects of temperature and sunlight in high humidity conditions are unlikely to be significant. Studies show that UVC light can neutralize SARS-CoV-2, used to decontaminate surfaces, rooms and personal protective equipment [54]. The atmosphere of Earth stops the UVC radiation - it does not reach the ground surface and does not affect the virus. The significance of UVA and UVB radiation against the SARS-CoV-2 virus is not entirely clear. However, some data suggest that the pandemic development from February to May 2020 inverselv correlates with the amount of UVA and UVB radiation. i.e. sunlight. It may suggest a lower number of SARS-CoV-2 infections in the northern hemisphere during the summer, with an increased incidence of COVID-19 in the southern hemisphere at the same time (Brazil, Australia). It is also consistent with the observations made in Bangladesh. India and Pakistan. Despite the hot climate, the epidemic is growing because monsoon clouds block solar radiation and high humidity. The correlation of the course of the epidemic and the climate requires further research. If such dependence exists, it is undoubtedly influenced by other modulating factors (mentioned above). These factors - easing of restrictions, holiday tourism, failure to follow recommendations, 'pandemic lassitude' - may have caused an increase in summer infections in a hot, sunny Europe in August 2020.

#### Conclusions

Many explanations exist that partially could answer why some world regions are differentially affected with the SARS-CoV-2 pandemic. In this paper, we have grouped those hypotheses into ten possible areas of impact. Nevertheless, we must emphasize that all the factors can interact, thus have a different impact on the course of the COVID-19 around the globe. It is worth remembering that the state of knowledge about SARS-CoV-2 and the COVID-19 pandemic remains highly speculative, controversial and difficult to verify, and the real explanation of the differences in morbidity and mortality from COVID-19 is probably the result of many factors. We cannot also reject the hypothesis of the difference morbidity and mortality, which says that different strategies of testing, the capacity of the health system, ability to track infections and eligibility criteria of COVID-19-related deaths vary from country to country, thus could create a false picture of the dynamics of the pandemic. The publicly available data from the European Centre for Disease Prevention and Control (ECDC) show a clear correlation between GDP per capita and the number of deaths per COVID-19 per million population in each country. It would indicate that wealthier countries are testing more, identifying more cases, and better qualifying COVID-19-related deaths. Nevertheless, this paper should stimulate others to do more research on the subject.

#### **Conflict of interest**

The authors declare that there is no conflict of interest.

#### Streszczenie

Pandemia choroby koronawirusowej 2019 jest jednym z najtrudniejszych wyzwań dla współczesnej medycyny i systemów ochrony zdrowia. Od początku jej wybuchu w różnych częściach świata zaobserwowano różnice w zapadalności i śmiertelności. W artykule omówiono 10 hipotez, które były tematem dyskusji naukowych i mogą wyjaśniać tę obserwację. Czynniki kulturowe, demograficzne oraz socjologiczne, różnice w systemach opieki zdrowotnej i harmonogramach szczepień, polimorfizm genetyczny mogą stanowić zmienne wpływające na przebieg pandemii w różnych regionach świata. Dalsze badanie tych hipotez może dostarczyć cennych informacji i poszerzyć dostępną wiedzę w tej bezprecedensowej sytuacji epidemiologicznej.

Słowa kluczowe: COVID-19, epidemiologia, One Health, pandemia

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