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COVID-19: THREE PHASES OF THE PANDEMIC
Dynamics of cases, deaths and tests related to SARS-CoV-2
A systematic analysis of 213 countries and territories

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Mary Jo Takach, No Cure for that Cold?
"The common cold is like the weather – everybody talks about it but no one can do much about it ... A new group of viruses has also been isolated. These are called 'human coronaviruses' and they also cause typical colds... Dr. James Spray estimates that there are at least 200 cold viruses ... The U.S. National Institutes of Health (NIH) closed down its Board of Vaccine Development last year, deciding it was a waste of time and money". [This World (San Francisco, CA), 1972, Oct 8, Sun, N 41: 28].

Abstract

Background

Since the previous study dealing with the case fatality ratio and infection fatality ratio caused by COVID-19, the author has received many comments that prompted the question: "Why did an optimistic prognosis fail?" To answer this question, a more detailed and expanded analysis was carried out in a new study.

Objective

To evaluate the dynamics of monthly numbers of cases, deaths, tests and CFR worldwide during three phases of the COVID-19 pandemic.

Material and Methods

Twenty three sets of databases, dated the 22nd of each month from January 2020 to November 2021, for 213 countries were collected from the Worldometer website. The number of cases, deaths, tests, CFR, IFR, etc. were counted for various periods of time for each of the 213 countries, then results related to different periods of time were compared.

Results

The analysis of the main epidemiological parameters led to the division of three phases of the global pandemic evolution. The first phase (23.01.20-22.07.20), the second phase (23.07.20-22.01.21) and the third phase (23.01.21-22.07.21) were different in terms of the number of tests performed, new cases, and mortality due to COVID-19. By the end of the second phase, the worldwide statistics indicated the imminent end of the pandemic, but the third phase was characterized by a sudden rise in the number of new cases and deaths that could not be explained rationally. The most dramatic evolution of the epidemic curve occurred in the countries where doctors had successfully battled COVID-19 during the first two phases of the pandemic.

Conclusions

Despite the decrease in overall death numbers during the latest months analyzed, additional study is necessary to identify the cause for the increase in the number of new cases and deaths during the third phase of the pandemic.

Only complete information regarding the positive and negative impact of medical and non-medical methods of diagnostics and prophylaxis of COVID-19 can help to organize effective measures to end the current pandemic and prevent a similar one from occurring in the future.

Presumably, there are several causes of the negative evolution of the current pandemic, including the overreliance on PCR tests, application of non-specialized premises for quarantine and treatment, decrease in herd and individual immunity, inadequate change of therapeutic protocols, and ignoring prophylactic treatment.

It can be suggested that the use of immunemodulatory drugs, for example, thymus extract or thymic peptides, in groups of people with compromised immunity is necessary, and prophylactic and therapeutic protocols should be changed from the 'standard' types to 'personalized' ones.

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Background

Since the previous study dealing with the case fatality ratio and infection fatality ratio caused by COVID-19,[1] the author has received many comments that prompted the question: "Why did an optimistic prognosis fail?" To answer this question, a more detailed and expanded analysis was carried out in a new study.

1. Introduction

1.1. Initial and current state of the COVID-19 pandemic narrative

On December 31, 2019, the WHO's China Country Office was alerted to cases of pneumonia of unknown cause detected in Wuhan City, Hubei Province of China.[2] On January 3, 2020, the first complete genome of the novel coronavirus (2019-nCoVs) was identified.[3] On February 11, 2020, a new disease was named "the coronavirus disease 2019" or CoViD-19.[4] Further studies revealed that SARS-CoV-2 was circulating in various countries, including Spain,[5] Italy,[6] India,[7] France,[8] USA,[9] etc. before the outbreak of the epidemic in China.[10-11]

During the initial stage of the COVID-19 pandemic two well-known discoveries, namely: "Unique inserts in the 2019-nCoV spike protein" and "Reduction and functional exhaustion of T-Cells" in COVID-19 patients,[12-13] were published. These discoveries demonstrated structural and functional similarities between two viruses and prompted a common sense question about the origin of SARS-CoV-2.[14-15] Questions about the origins of the virus resurfaced in December 2020 when production of an Australian vaccine was discontinued as healthy vaccinated people became tested positive for HIV.[16]

Other issues related to the epidemic curve that had anomalous evolution include:

(1) *New patterns*:

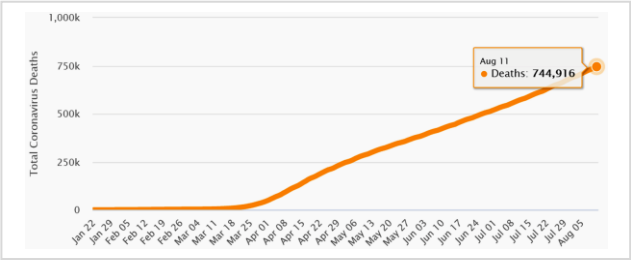
In April 2020, an expert in epidemiology, Prof. Vladimir Nikiforov mentioned: "if the virus followed the 'classical pattern', the epidemic would have ended within three months, but now we are faced with something new".[17]

(2) *Data adjustments*:

During the first half of the pandemic there were many cases of local number adjustments that affected the worldwide statistics related to COVID-19.[18] (Fig. 1)

On April 26, 2020, a cumulative report of Palestine was reduced by 153 cases; on May 25, 2020, a report of Spain was reduced by 1915 deaths; on June 3, 2020, a report of France was reduced by 37,895 cases; on June 20, 2020, a report of Mayotte was reduced by 787 cases; on August 13, 2020, a report of the United Kingdom was reduced by 29,726 cases and by 5,319 deaths.[18] (Fig. 2)

(a)



(b)

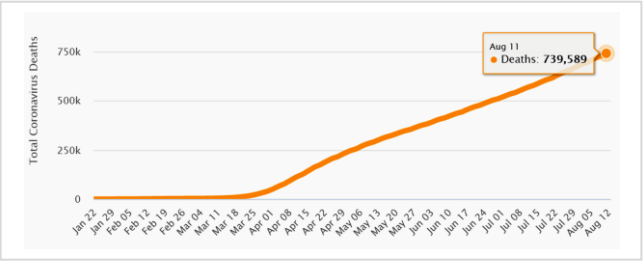


Figure 1. Worldometer: Adjustment of the worldwide cumulative number of deaths.[18]
These are two screenshots dated (a) August 12, 2020, 07:27 GMT; and (b) August 13, 2020, 09:18 GMT.
The total number of deaths decreased suddenly from 744,916 to 739,589 cases.

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(a) (b)

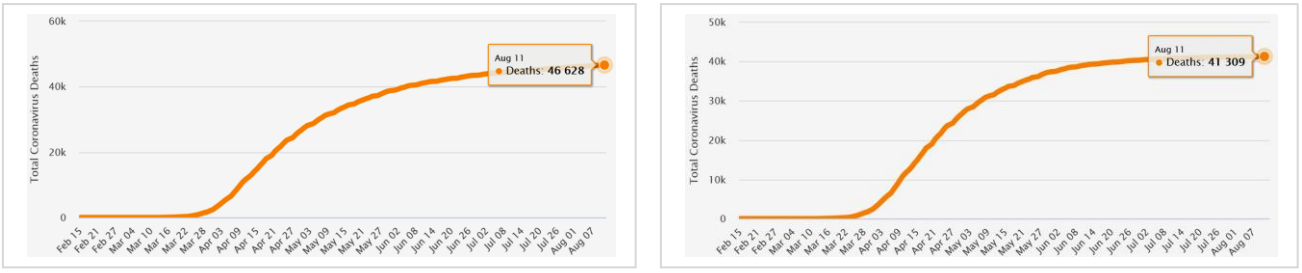

Figure 2. Worldometer: Adjustment of cumulative number of deaths in the United Kingdom.[18]
These are two screenshots dated (a) August 12, 2020, 07:34 GMT; and (b) August 13, 2020, 08:19 GMT.

(a) (b)

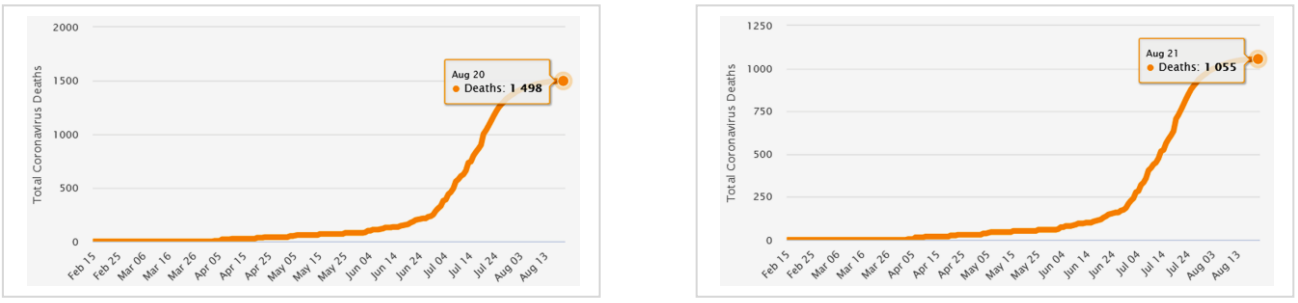

Figure 3. Worldometer: Adjustment of cumulative number of deaths in Kyrgyzstan.
These are two screenshots dated (a) August 21, 2020, 08:21; and (b) August 22, 2020, 08:04 GMT.[18]

On August 14, 2020, a report of Peru increased by 3,935 new deaths; on August 21, 2020, the number of deaths in Kyrgyzstan, decreased by 443 cases (Fig. 3); on September 24, 2020, a record of Liberia, decreased by 133 cases,[18] etc. Similar adjustments took place during the later period of the pandemic: on July 2, 2021, it was reported, "Santa Clara County's COVID-19 death toll drops by 505",[20] and so on.

(3) *A synchronization-like phenomena*:

The first example of synchronization was a weekly mortality cycle which was noticed in June 2020,[21] later this anomalous cycle of daily death became obvious and steady.[22] A comparison of the percentage of fatal cases on different days of the week for a period of 100 weeks (26.01.20-25.12.21) revealed almost identical distribution as described in a previous study.[22] (Fig. 4).

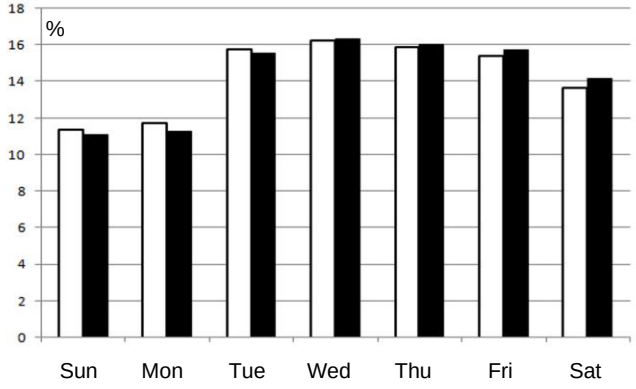

Figure 4. Global mortality due to COVID-19 on various days of the week: white columns - period of 100 weeks (26.01.20-25.12.21); black columns – period of 40 weeks (01.03.20-05.12.20). The vertical axis shows percentages; the horizontal axis shows days of the week.

There is another example of synchronization related to the daily new cases of COVID-19. During 1.5 years of the pandemic the highest number of daily new cases in the United States and the United Kingdom were recorded on the same day, on January 8, 2021; together they accounted for 44% of the total number of new cases worldwide.[18]

(4) *A Strange evolution of the pandemic*:

In mid December 2021, a well-known expert in infectious diseases, Dr. Anthony Fauci, said: "it's 'unprecedented' how long the COVID-19 pandemic has lasted globally, with many countries enduring multiple major waves of infections since it was declared in March 2020".[23] So, a pertinent question that pops up is: why, despite unprecedented control measures to prevent the spread of a new virus, including worldwide quarantines, isolation, movement control order, curfew, social distancing, wearing of masks and mass vaccinations, the epidemic curve still has a 'wave-like' or 'propagated' shape instead of going down? Were preventive measures effective, or simply useless or harmful?

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1.2. Infectious disease – a battle between the human body's defense and viruses or bacteria

History of the battle against viruses and bacteria goes back at least several thousand years. Ancient physicians already knew about external pathogens which could cause acute febrile diseases. They also knew that an evolution of any clinical case depended on the health status of the patient before the onset of the disease, so they talked about "body defense".[24] At the beginning of modern microbiology the importance of body resistance was confirmed by a Prof. Max von Pettenkofer, who swallowed the entire contents of a tube filled with germs of cholera, but nothing happened to him. So he claimed: "The important thing is the *disposition* of the individual!"[25]

Despite a variety of external pathogens, the human body has a limited number of defense mechanisms, which is accompanied by a few clinical syndromes, consisting of common symptoms, such as fatigue, chills or hot feeling, headache, cough, shortness of breath, nausea, vomiting, diarrhea, skin rashes or discoloration of the skin, etc.

In ancient times the mechanism of the onset of fever was differentiated into two main groups based on the presence of thirst, sweating, chills, or feelings of heat; and the choice of individual treatment was determined by the type of fever. According to the modern view on fever, which commonly accompanies infectious diseases, one can define only two mechanisms leading to an increase in temperature: one is an increase in heat production and another, a decrease in heat transfer, or their combination.[26] Thus ancient and modern explanations of fever are quite similar, and two types of antipyretic medicines are necessary and sufficient to manage any case of excessive fever. Similarly, 2-3 mechanisms can be identified that underlie each of the remaining symptoms of any acute viral disease, so, a small group of commonly used drugs would be sufficient to manage any infectious diseases, including *old* and *new* ones.

After the discovery of bacteria and viruses as a cause of infectious diseases the main emphasis was changed from supporting the body resistance to the fighting against pathogens. It was successful in the majority of bacterial infection cases, but it was almost useless when disease was caused by a virus.

Therefore, if there is no etiotropic treatment, then there is no need to identify a *new* viral disease. All pharmaceutical and non-pharmaceutical therapeutic modalities would be addressed to the well-known protective mechanisms of the human body, and treatment should be based on the leading syndromes and symptoms, using the principle called *off label* therapy.

1.3. The classical foundation of medicine is wisdom, which is evergreen

Multiplication tables, the Pythogorean theorem, Archimedes' law, ideas of inertia and atomic structure of matter appeared several thousand years ago. In the course of history ancient knowledge developed and improved until it turned into higher Mathematics and quantum Physics, however, the multiplication table, Archimedes' law and other basic knowledge have not lost their value in our time.

Similarly, ancient medicine also had its own canon, preserved within the framework of traditional Chinese medicine. The most important law of that canon was postulate: to strengthen or reinforce that which is *deficient*, and drain or sedate that which is *excessive*.[27] Over the centuries, it has taken on new forms, and was introduced in the theory of *asthenic* and *sthenic* diseases by Dr. John Brown.[28] At the beginning of the 20th century, two physiologists presented this postulate in the form of theories of *parabiosis*[29] and *dominant*.[30] In the 1930s, Hans Selye discovered a dynamic interaction between excess and deficiency, and described General Adaptation Syndrome theory, which distinguished the *alarm phase* (= excess, sthenic disease, dominant) and *exhaustion phase* (= deficiency, asthenic disease, parabiosis).[31-32]

At the beginning of organotherapy[33-34] doctors used extracts of animal organs to treat various age-related problems, nowadays called *frailty*.[35-36] Later a modern branch of organotherapy, taking the form of hormonotherapy, became a powerful tool to treat various diseases caused by hormonal insufficiency.[37-38] They followed the first part of the ancient postulate: *to strengthen or reinforce that which is deficient*. When antibiotics were discovered, physicians got a tool to inhibit bacterial growth.[39] Application of antibiotics was an example of following the second ancient postulate: *drain or sedate that which is excessive*. But further development of medicine did not follow the basic canon.

Nowadays despite the fact that *deficiency* patterns are the causes of the majority of chronic diseases, especially among elderly people, antagonists, blockers, or inhibitors, such as α-blockers, β-blockers, calcium channel blockers, ACE inhibitors, PDF-5 inhibitors, and H2 antagonists are used for therapy. Before prescribing sedative therapy patients are not tested whether the corresponding target is in an excited state or not. So, a rational medical sense is ignored and patients have to take medication for all their life.

The same problem has arisen with the treatment of COVID-19. The main pathologic target was T-cell immune-deficiency,[13,40-41] nevertheless a lot of attention was paid to the cytokine storm which was a consequence, but not a primary cause. According to basic medical law, treatment should be focused more at restoring T-cell immunity,[42] and less against increased activity of certain components of the immune system.

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1.4. Treatment of patients suffering from acute infectious diseases

About 1800 years ago, Dr. Zhang Zhongjing summarized the results of research from previous generations and developed a theory of acute infectious diseases, which explained therapy based on leading clinical symptoms and syndromes.[43] According to this theory, there could be only 6 phases, and certain phases could have 2-3 variants. Thus, the whole variety of clinical syndromes related to infectious diseases was limited to 10-12 variants, each having specific treatment and prevention. (Fig. 5.b)

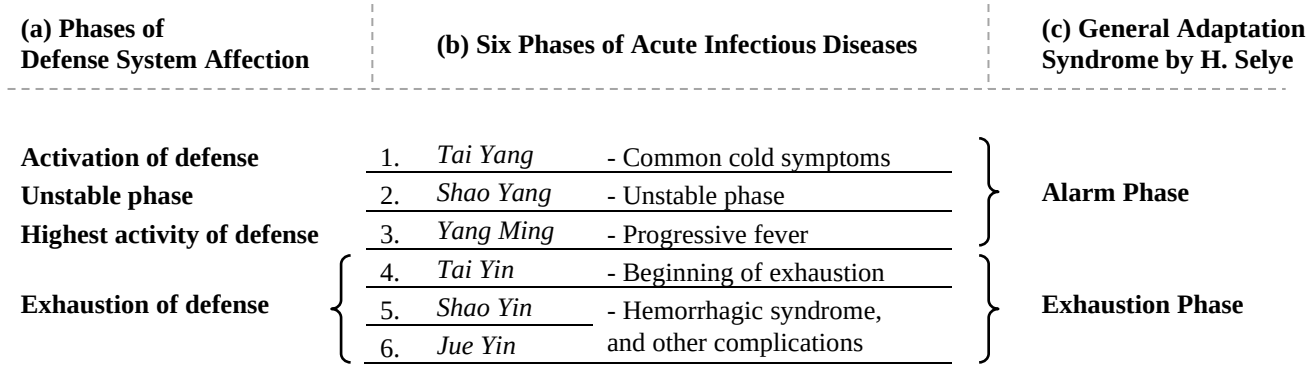

Figure 5. A comparison between various theories which describe phase evolution of acute infectious diseases:
(a) Four phases of diseases caused by external physical or biological pathogens called "excessive heat".[44]
(b) Six phases of diseases caused by various external physical, chemical or biological pathogens.[43]
(c) Two phases of diseases according to the general adaptation syndrome discovered by Hans Selye.[31-32,45]

There are some examples of treatment of the initial phases of infectious diseases: in the case of initial fever with general cold feelings without sweating – *Herba Ephedrae* was recommended; if there is initial fever with general hot feelings – *Folium Mori Albae* or *Herba Menthae Haplocalycis* should be used; if there is initial fever with intensive sweating or tension in the muscles – *Ramulus Cinnamomi Cassiae* was recommended; in the case of fever with alternating cold and hot feelings – *Radix Bupleuri*, was used, etc.[43] (Fig. 5.b). A change in symptoms pointed to a change in the phase of the disease and required an adjustment of therapy. If a patient has a severe fever with hemorrhagic symptoms, skin rashes, kidney and liver impairment, delirium, etc. – *Radix of Isatis tinctoria* should be applied.[44,46] (Fig. 5.a)

It would be useful for modern pathophysiology to distinguish between various types of the fever and choose antipyretic medicines (paracetamol, ibuprofen, etc) based on the pharmacodynamic of these popular drugs, but not empirically, as they are usually used.[47]

During later centuries, protocols of infectious disease treatment were updated according to the new scientific discoveries of that time. Excepting deadly epidemic diseases (plague, smallpox, or cholera), therapy of other infectious diseases was effective and successful. Theoretically, modern medicine having a long history in the past and advanced pharmaceutical science nowadays must be able to treat any problem more effectively than our predecessors, but the helplessness of the modern medical system during the current pandemic was beyond common sense,[48] and raised a question about the quality of medical education of the distinguished leaders and their followers.

1.5. Treatment of COVID-19 at initial phase of pandemic

At the beginning of the pandemic, WHO encouraged doctors to use well-known medicines as *off-label* treatment of a new disease since there were no approved drugs yet for the treatment of COVID-19.[49] The majority of knowledgeable and experienced doctors who received high quality medical education treated patients suffering from COVID-19 with great success. They recommended using anticoagulants, such as dipyridamole[50] or heparine;[51] antiviral and anti-inflammatory drugs, including ivermectin,[52-53] colchicine,[54-55] methylene blue,[56-57] chloroquine and hydroxychloroquine;[58-60] immune-modulators, such as thymic extracts,[61] thymic peptides,[62] solution of Formaldehyde,[63] melatonin[64] and common adjuvants.[65] A group of physicians, who had identified the similarity between COVID-19 and toxic damage to red blood cells, recommended to use therapeutic protocol which was effective in cases of acute intoxication.[66] Other experts recommended an inhalation with ethanol vapor[67-68] and helium-oxygen mixture,[69] since those methods had already been applied to similar cases before.[70-72] Plant derived medicines, including extracts of Artemisia, Isatis or Colchicum as well as green and black tea, and various complex prescriptions were also used either for prophylaxis or for combined therapy.[73-78]

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During the early days of the COVID-19 epidemic, doctors in Russia used their own treatment protocols, that resulted in very low mortality, and even raised questions and skepticism from the international medical community.[79-80] For example, in April-June 2020, in a hospital attached to the Moscow State University, 420 out of 424 indoor patients suffering from COVID-19 were successfully treated with routine medication. Effectiveness of the therapy was around 100%.[81]

As basic medicines these doctors used Colchicine, Dipyridamole, Bromhexine, and Spironolactone; additional application of certain anticoagulants and corticosteroids depended on a particular case.[82] Thus, common medical knowledge and experience were enough to treat the infectious disease caused by the *new* virus.

Every doctor knows that effective therapy of any patient requires individual approach due to the natural difference between even two *similar* cases, especially if a patient suffers from COVID-19.[83] Following standard protocols without dose adjustment and individual correction of used medicines in certain clinical trials resulted in decreasing or even losing effectiveness of the drugs that had been used by other doctors earlier on.[84] Nevertheless knowledgeable doctors continued their successful and effective treatment.[65,85-86] The therapeutic effects of the medicines mentioned above have been proven in further clinical trials and the results were published in peer-reviewed journals.[87]

After recent discussions on therapeutic protocols taking place between various experts, Dr. Peter A. McCullough recommended to his colleagues to treat COVID-19 patients according to their own knowledge and experience.[88] One can only deduce there is no common sense for doctors to follow the protocol of an expert or a country where mortality was high, otherwise they will gain the same high mortality among their patients.

1.6. Clinical trials

Early in the 18th century, homeopathic doctors, who studied *pathogenesis* of new remedies, introduced extensive and multi-centered clinical trials to the medical public. They needed to differentiate the primary and secondary symptoms, and to separate important symptoms from non-important ones, and so on. According to the demand of homeopathic pharmacy, there was a rationale for using large groups of people. Nevertheless extensive trials were criticized by Dr. Rudolf Virchow, the father of modern Pathology. He insisted that despite certain similarities in pathology discovered in different patients with a similar disease, each patient has his/her individual disease, so instead of using statistics collected from large groups of patients, doctors should pay more attention to detailed analysis of every particular case.[89]

As far as acute infectious diseases are concerned, their pathological condition is not stable, but has several phases. Each of the phases requires the use of different medicines and patient care. It would be illogical to look for the treatment of COVID-19 in general, but each phase of the disease requires an appropriate group of medicines. Then a doctor should choose one or two medicines taking into account the main symptoms of a certain patient. Multiple attempts to find a unique medicine against 'COVID-19' have failed. That means treatment of COVID-19 or any further new acute viral infectious diseases should be managed by means of routine drugs applied as *off label* therapy.

When COVID-19 was announced as a new disease,[4] healthcare worldwide was challenged to conduct new clinical trials to find medicines that were safe and effective in treating COVID-19 and comorbidities. After Dr. T. A. Ghebreyesus expressed an opinion about the pandemic,[48] all patients suspected of being infected with SARS-CoV-2 were automatically made participants of clinical trials which were the most extensive in the history of mankind.

Since all the pathogenic mechanisms encountered in COVID-19 were already well-known before April-May, 2020, the treatment of COVID-19 should not have been difficult.

Moreover, since some routine medicines had already been used successfully, the main goal of further clinical trials was to design the most effective and adjustable protocols, but not to reject the effects of the used medicines. That is why it is crucial that ongoing clinical trials should focus more on adjusting protocols to enhance the efficacy of the tested medicines, rather than adhering to some standard approach. Adhering to such rigid protocols might render the treatment of COVID-19 ineffective, not due to the ineffectiveness of the medicine per se but due to the inappropriate protocols applied. The trials also tested the ability of doctors to form homogeneous groups, taking into account the leading pathogenic mechanisms, presented among the patients in the group of study and the main therapeutic action of the studied medicine. Unfortunately, many ongoing clinical trials have ended up demonstrating insufficient knowledge and experience of the physicians conducting the research.

For experienced physicians with a solid background, clinical trials were not necessary. Since they knew the pathogenesis of COVID-19 and pharmacodynamic of the medicines used, in their clinics efficacy of therapy must be around 100%.[65,82,85,86] But results of clinical trials were very important and useful for beginners, since standard protocols help them to reduce the number of adverse reactions of their treatment.

1.7. Paradoxes of Clinical trials

There were some facts that would be worth paying attention to, since they could indicate possible causes of high mortality at the initial phase of the COVID-19 pandemic.

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In January-April, 2020, mortality among CoViD-19 patients who were treated with invasive mechanical ventilation (IMV) was higher than 80%, including, 81%,[90] 88.1%,[91] 92%,[92] and even 97%.[93] According to a review by G. Bellani, et al. published in 2016, the highest mortality among the severest cases of patients with Acute Respiratory Distress Syndrome (ARDS) of various origin, who were treated with IMV, was around 50%.[94]

After comparing the results of IMV application among COVID-19 patients with the results presented in the review on IMV (2016), one may conclude that IMV had no therapeutic value among patients with ARDS caused by SARS-CoV-2. The lack of a therapeutic effect of IMV was explained by systemic endotheliitis and coagulopathy which led to micro and macro-thromboses in various organs including the lungs.[95] Nevertheless, IMV is still in use to treat COVID-19 patients with ARDS.

From the outset of the COVID-19 pandemic, it was known that there would be a high risk group, comprising mainly of aged people with compromised immunity and comorbidities. The main parameter that could point to the risk of severe cases was lymphopenia.[93] Prognostically unfavorable signs of COVID-19 were: a decrease in the number of lymphocytes in general, a decrease in sub-populations of T-lymphocytes (CD4+, CD8+) and, as a consequence, a dysfunction of B-lymphocytes and dys-regulation of their production of Ig-M and Ig-G. The number of T-lymphocytes, including CD4+ and CD8+, was especially reduced among patients requiring treatment in the intensive care unit.[13] The severity of the case and outcome of COVID-19 largely depended on a patient's age, that correlated with a decrease in T-cells, due to the thymus atrophy.[40,96] The risk of COVID-19 hospitalization rises exponentially with age, inversely proportional to T-cell production.[41] In COVID patients, thymus enlargement was frequent and associated with increased T-lymphocytes production that appears to be a beneficial adaptation to virus-induced lymphopenia. The loss of thymic reactivation might contribute to a worse prognosis.[97] Despite great importance of immunological dysregulation caused by T-cell deficiency, there were only a few studies with application of thymus derived medicines,[42,61,98] although the immune-modulating and protective effect of thymus extract has already been known for more than two hundred years.[99]

On June 16, 2020, Professor Peter Horby said, that dexamethasone "is the only drug so far that has been shown to reduce mortality – and it reduces it significantly".[100] It reduced deaths by one-third in patients receiving invasive mechanical ventilation, by one-fifth in patients receiving oxygen without invasive mechanical ventilation, but did not reduce mortality in patients not receiving respiratory support at randomization.[101] The later conclusion on the efficacy of corticosteroids was pessimistic: "There is no evidence that corticosteroids are safe and effective on the treatment of severe acute respiratory infection when COVID-19 disease is suspected".[102] The key point of these controversial claims was a wrong approach to use corticosteroids on patients with COVID-19. The corticosteroids should be recommended as a replacement therapy to the patients with bacterial or viral infectious disease being in the phase of exhaustion according to the general adaptation syndrome described by Hans Selye.[31-32,45] (Fig. 5.c) Thus, blood tests on cortisol and aldosterone must be obligatory routine analyses before prescription of corticosteroids therapy, especially in the case of COVID-19.

1.8. Case fatality ratio and infection fatality ratio

There are two most important characteristics of infectious diseases: the first is a case fatality ratio (CFR) and the second, an infection fatality ratio (IFR). Case fatality ratio is the proportion between the number of patients who died from COVID-19 and the number of confirmed cases of COVID-19, while infection fatality ratio is the proportion between the number of patients who died from COVID-19 and the number of estimated cases infected with SARS-CoV-19.[103]

To identify the total number of infection prevalence, tests were carried out for the presence of the viral genome – Polymerase chain reaction (PCR), or for specific antibodies against SARS-CoV-2 virus (IgM and IgG). Due to the fact that PCR provided positive results for a limited time after infection, and specific antibodies were produced and circulated in the blood of an infected person from several months up to a year,[104-105] the percentage of seroprevalence would always be lower than the real one, and, therefore, IFR from COVID-19 would be always overestimated.

In a study published by J. Ioannidis (2020), at the end of October 2020, the number of infected people worldwide reached 10%.[106] Similar proportion of infected people in October 2020 was calculated for Belgium, Brazil, and the United States.[107] In December 2020, the number of infected people in the United States was estimated at 50 million, or around 15%.[108]

On January 29, 2021, the Mayor of Moscow, Sergei Sobyanin announced that "half of Moscow's 12 million residents have had Covid-19" and recovered.[109] That estimation was based on a trial where antibodies to the SARS-CoV-2 virus were found in more than half of the blood samples taken randomly from a thousand *healthy* residents of Moscow.[110]

Thus, one may conclude that since the beginning of the pandemic, major populations of large cities have already been infected with SARS-CoV-2 and have some amount of circulated antibodies or have memory about this virus stored in the T-cells.[111-113]

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1.9. Databases were collected from Worldometer website

Information on cumulative numbers of the total cases and deaths due to COVID-19 is available at the Worldometer website from January 21, 2020.[18] (Fig. 6) On January 23, 2020, a controversial article on RT-PCR tests was published,[114] and a historical session of the World Economic Forum devoted to Wuhan Coronavirus took place in Davos.[115] Despite the fact that there was no cause for alarm yet,[116] January 23, 2020 was chosen as the first day of the current study.*

To provide an overall and detailed analysis of the COVID-19 pandemic, one year and a half was divided into three phases: (23.01.20-22.07.20), (23.07.20-22.01.21) and (23.01.21-22.07.21). Twenty three sets of databases, dated the 22nd of each month from January 2020 to November 2021, were collected. Raw data included more than 20,000 figures in total. Only simple calculations using MS Excel easily understandable by any doctor have been used.

The databases related to each month for every country were calculated by subtracting the previous month's data from the analyzed month's data. For example, in China on 22.02.20 there were 76,923 cases, and 2,441 deaths, and on 22.01.20 there were 571 cases and 17 deaths. Subtracting the second from the first, one gets that from 23.01.20 to 22.02.20 there were 76,352 cases and 2,424 deaths, and so on. The same method was used to count the database related to each phase for every country. Since only 213 countries† were affected by COVID-19 during the first phase, these 213 countries were analyzed during the current study.

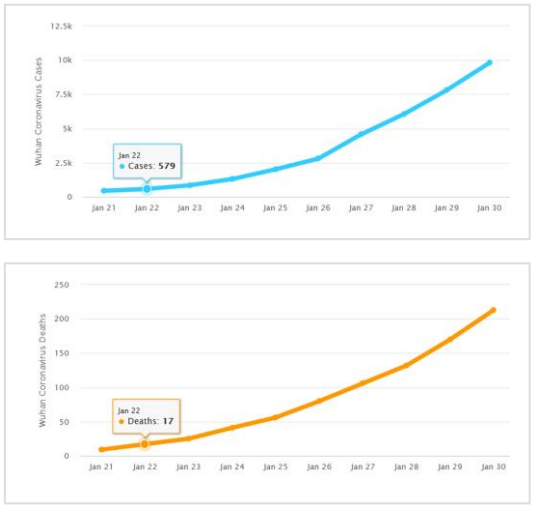

Figure 6. Cumulative numbers of the total cases of COVID-19, and the total deaths due to COVID-19 started on January 21, 2020; daily counts of both parameters have been available since January 22, 2020. [A part of the screenshot of the Worldometer website dated January 31, 2020, 21:35 GM].

* On January 23, 2020, Dr. Peter Salama, an expert in epidemiology, the former director of WHO's Health Emergencies Program, who organized a successful battle against the Ebola virus in the D.R.C., died suddenly.[117]

† Here and below 'Countries' means 'Countries and Territories'.

2. One and a half years of the pandemic: Case fatality ratio and infection fatality ratio

Objective

To evaluate CFR and IFR in 213 countries during one and a half years of COVID-19 pandemic.

2.1. Calculation of CFR among COVID-19 patients in 213 countries

Material and Methods

To calculate the CFR and IFR worldwide, the databases of 220 countries dated as July 22, 2021, 23:49 GMT, were collected at the Worldometer website. In these countries there were 193,349,043 confirmed cases of COVID-19; 4,150,541 deaths due to COVID-19; and a total population of 7,838,783,871 people.

Since in the first phase of COVID-19 pandemic (23.01.20-22.07.20) only 213 countries were affected, so databases of only these 213 countries were used for this study. Seven countries, including Marshall Islands, Micronesia, Saint Helena, Samoa, Solomon Islands, Vanuatu, and Wallis and Futuna, with 479 confirmed cases, 8 deaths, and population of 1,412,031 people were excluded from the study. In 213 countries there were 193,348,564 cases and 4,150,526 deaths.

A case fatality ratio was calculated by dividing the number of deaths by the number of confirmed cases.

Results

The overall case fatality ratio for 213 countries, counted by dividing the number of deaths (n=4,150,526) by the number of confirmed cases (n=193,348,564), was 2.147 %. The overall case fatality ratio for 220 countries was 2.147 % too.

2.2. Calculation of CFR among COVID-19 patients in 175 countries

Material and Methods

To increase the homogeneity of the main group of study, 38 countries with death numbers of fewer than 50 were excluded from further analysis. Thus, the main group of study decreased to 175 countries, with a total population of 7,734,426,580 people. These countries had 193,207,132 confirmed cases and 4,149,944 fatal cases. For each country, the CFR was calculated by dividing the number of deaths by the number of confirmed cases.

Results

The overall case fatality ratio for 175 countries was 2.148 %. In this group the CFR ranged from 0.267 % in Qatar to 19.597 % in Yemen, and the average value of CFR was 2.146±1.965%. Based on the calculated CFR values, all countries were divided into 16 groups as shown in Fig. 7.

The first group (n=7) where CFR was less than 0.500 %, included Qatar (0.267%), Maldives (0.285%), UAE (0.286%), Cyprus (0.418%), Seychelles (0.490%), Mongolia (0.495%), and Vietnam (0.498%).

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