UDC 578.72
DOI 10.17721/1728.2748.2022.89.39-45

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PATTERNS OF THE INFLUENCE OF VACCINATION ON THE DYNAMICS OF DIFFERENT SARS-COV-2 VARIANTS SPREAD. TWO-YEAR ANALYSIS

The new coronavirus, now known as SARS-CoV-2, has attracted the attention of thousands of scientists around the world. This attention is primarily due to the significant impact of this pathogen on the economic and social aspects of the existence of a large number of people. Rapid and powerful anti-epidemic measures in most countries have led to a slowdown in the pandemic. And with the creation of a number of effective vaccines against SARS-CoV-2, we have learned to counteract its spread in the field of resistance of each individual. Which obviously created an additional selection factor. And according to the classical concept of the host-parasite system, human impact on SARS-CoV-2 theoretically requires appropriate adaptive changes of the latter.

In this work, by analyzing the statistical data available in open sources, we try to identify and study the existing patterns of the impact of vaccination on the dynamics of the spread of different SARS-CoV-2 variants for the period from the beginning of the pandemic to November 2021.

Keywords: SARS-CoV-2, variant Delta, coronavirus, vaccination.

Introduction. SARS-CoV-2 is a new coronavirus believed to have originated in late 2019 in Wuhan (People's Republic of China). The virus spread rapidly around the world and on March 11, 2020, the World Health Organization (WHO) officially declared a pandemic [1]. As of November 29, 2021, the number of reported cases of COVID19 exceeds 261 million (of which 5.2 million died) worldwide [2]. Ukraine ranks 6th in the world in terms of the number of registered cases of this disease (3,595,410 cases and 90,673 deaths). Just for comparison, the SARS-CoV virus in 2002–2003 infected about 8,500 people in 27 countries and caused 866 deaths [3].

Due to the rapid and steady spread of this pathogen, there is a need for effective means to combat it. Accordingly, effective vaccines were developed fairly quickly [4]. The mechanism of action of which is to modulate the immune response of each vaccinated person, which gradually leads to an increase in resistance to SARS-CoV-2 in the entire population, although, in most cases, immunity is short-lived. However, along with the obvious advantages of this approach (especially over inactivity), such as the gradual reduction of morbidity and mortality, vaccination is an additional potent positive selection factor for this virus that can potentially further stimulate SARS-CoV-2 to evolve toward counteracting the immune response [5, 6]. At the same time, we observe different rates of increase in the level of vaccination of the population for different countries. There may be populations with a low level of group immunity along with highly resistant populations. And given the degree of development of the modern transport system, even distant populations are, to some extent, close [7]. Thus, SARS-CoV-2 faces a very heterogeneous host population. In such conditions, the formation of new strains of the already known virus is a logical and probable phenomenon [8]. However, the further direction of the development of such variants remains unpredictable, due to the huge number of factors that may affect this process.

Moreover, analysis of available statistics has the potential to improve our understanding of the prevailing evolutionary developments to which SARS-CoV-2 is exposed as it expands in the human population.

As of November 2021, the Delta is the most common variant of SARS-CoV-2, which in most cases completely supplanted other variants of this virus, which was not typical for other strains [9]. This behavior of the Delta strain indicates a qualitatively new step in the process of adaptation of this virus to the human population.

Thus, in this study, the regularities of the influence of vaccination on the dynamics of the spread of different SARS-CoV-2 variants are studied by means of a comparative analysis of information on changes in the epidemic situation and the peculiarities of the dynamics of detection of the Delta variant along with other strains from the beginning of the pandemic to November 2021.

Approach. The following resources were used as the main source of statistically significant information: CoVariants, The Johns Hopkins Coronavirus Resource Center and Our World in Data [10, 2, 11]. Each selected country was analyzed according to four parameters: the dynamics of the spread of different variants of SARS-CoV-2 and their interaction, the dynamics of the epidemic situation in the country, the speed and features of vaccination of the population and anti-disease measures, which were followed by changes in population mobility. Google COVID-19 Community Mobility Reports was used to evaluate the latter [12].

Results and discussion. Three countries were selected as the object of the study: India, Germany and Ukraine. Each of them was chosen based on their socio-economic characteristics. Germany is a representative of economically developed countries. Its economy is the most powerful among the countries of the European Union [13]. Ukraine and India are developing countries. However, they differ greatly in demographic, cultural and social parameters. In addition, India was one of the first countries where the Delta strain was discovered [14].

Analysis of the dynamics of the spread of SARS-CoV-2 strains in India, showed that the Delta variant was registered for the first time in India in August 2020. However, its appearance in that period did not lead to the displacement of other strains. On the contrary, he was ousted. Further, in October-November there was a slight increase in the share of sequences of this variant (Fig. 1).

ISSN 1728-2748

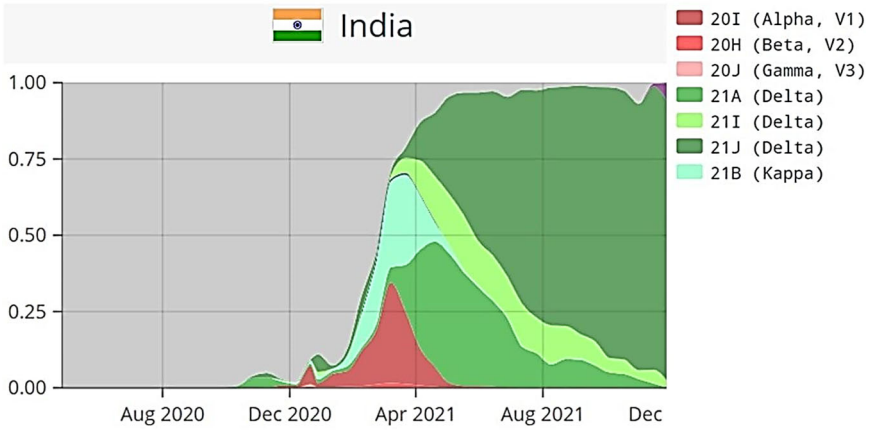

Fig. 1. Changes in the proportion of sequences of different variants of SARS-CoV-2 in India [10]

This rise lasted for a relatively short period of time and was quickly replaced by another rise in December 2020 – January 2021. Here, along with the Delta variant, the Alpha variant began to spread. You can see how both of these variants coexist in one period of time. A similar situation is observed in the next rise, which lasted from the end of the previous one to May 2021. The only difference is in the scale – dominant strains almost completely supplanted the other variants, as well as the Kappa variant, which for some time was more represented in the SARS-CoV-2 population than the Delta variant. However, as early as mid-March, the latter began to displace other strains – first Alpha, and then Kappa.

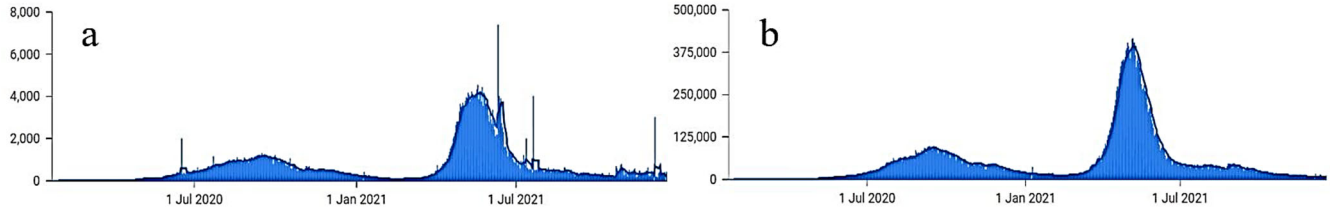

Fig. 2. Dependence of mortality (a) and morbidity (b) on time in India [2]

As can be seen from Fig. 2 at the time of the research, India has experienced two waves of aggravation of the epidemic situation. The first lasted from June to January 2020 and was caused by the original variant of SARS-CoV-2. The second wave was characterized by a much higher level of morbidity and mortality and lasted from late March to June 2021. It was during this period that the Delta strain began to displace other variants. Its spread has led to such an exacerbation of the epidemic situation in this country.

Vaccination in India began in early March (Fig. 3) (the first dose was received by >1 % of the population) and from the beginning was characterized by a significant gap in the number of people who received two doses of vaccine and those who received one. At the time of the study, the gap between the two numbers is a quarter of the country's population. Actually, the dynamics of vaccination is characterized by a fairly low rate of increase in population resistance.

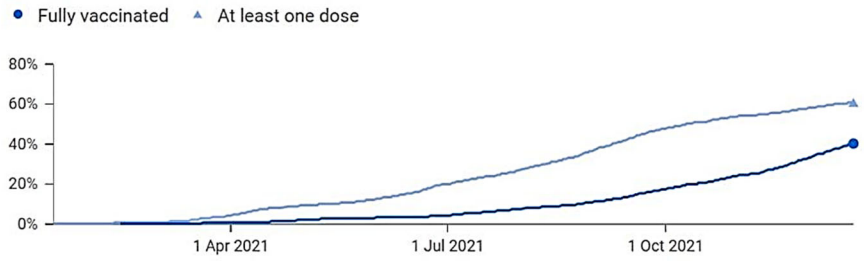

Fig. 3. Increasing the share of vaccinated population over time in India [11]

Almost from the beginning of the pandemic, India introduced powerful anti-COVID measures (Fig. 4), which during the first wave led to almost complete immobilization of the population at the time of active spread of the pathogen. In the future, these measures were apparently weakened and starting from October 2021 population movements have reached baseline.

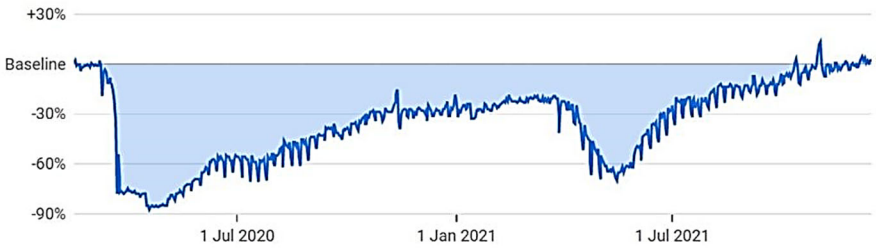

Fig. 4. Changes in population mobility over time in India [12]

Thus, two waves of exacerbation of the epidemic situation in India were caused by different variants of SARS-CoV-2. In addition, they differed in the degree of danger – the first was characterized by a relatively slow increase in morbidity and mortality and the same slow decline, the second progressed rapidly and was several times more powerful, although also shorter. The behavior of the first wave can be explained by a sharp decrease in the effectiveness of the spread of the pathogen in the host population. This was caused by powerful anti-COVID measures introduced before the mass distribution of SARS-CoV-2 among the population [15]. In some respects a different situation is observed in the case of the second wave. In the months leading up to its inception, anti-epidemic measures were significantly weakened, leading to the rapid spread of Alpha, Kappa and Delta variants among the population, which, however, did not cause an increase in morbidity [15]. Only from March 2021 a sharp rise in morbidity can be seen. It was during this period that the Delta strain began to actively displace other variants. However, another interesting fact is that a few weeks before the aggravation of the situation, the population of India started vaccination. After the start of the second wave, tougher anti-COVID measures were returned to the country, as well as accelerated vaccination of the population. That together with the gradual increase in population resistance due to the rapid natural transmission of the infection resulted in a rapid attenuation of the outbreak [16].

Therefore, taking into account the peculiarities of the spread of the Delta variant, the epidemic situation and vaccination, it is possible to observe a certain coincidence between the dominance of the mentioned variant and the beginning of vaccination. A scenario in which variants more vulnerable to a vaccine-induced immune response pave the way to a less vulnerable one seems likely [17].

Analysis of the dynamics of the spread of strains in Germany (Fig. 5), showed that the Delta variant in this country was sequenced in late April 2020 for the first time. Like in India, this strain did not displace all other variants immediately after invasion. And, to some extent, it was replaced by other, obviously more successful in specific conditions, variants [17]. Moreover, in this case, the Delta strain was almost not observed in the host population for a long period of time. Between October 2020 and May 2021, strains Alpha, EU1 and EU2, as well as variants 98F and 439K dominated. Then, starting from June 2021 the Delta variant very quickly, literally at one point, supplanted the Alpha strain main at the time and became dominant.

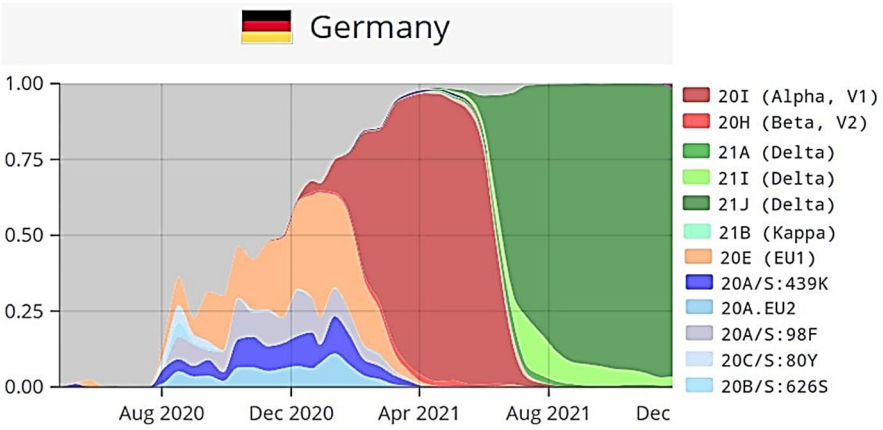

Fig. 5. Changes in the proportion of sequences of different variants of SARS-CoV-2 in Germany [10]

As can be seen in Fig. 6 the first wave of morbidity in Germany was short-lived and mild, with mortality disproportionately high during this period. This wave lasted from March to April 2020. The next rise in morbidity began in October 2020 and lasted with varying intensity until June 2021. Despite the similar level of morbidity in the two sub-peaks that make up this wave, the mortality rate differed several times – the first part was much more intense. At the time of the study, Germany is experiencing the third wave, which began in August 2021 and in terms of morbidity, it several times exceeded all previous outbreaks. However, the mortality rate has not experienced such a serious increase and is generally at the level of the second part of the second wave.

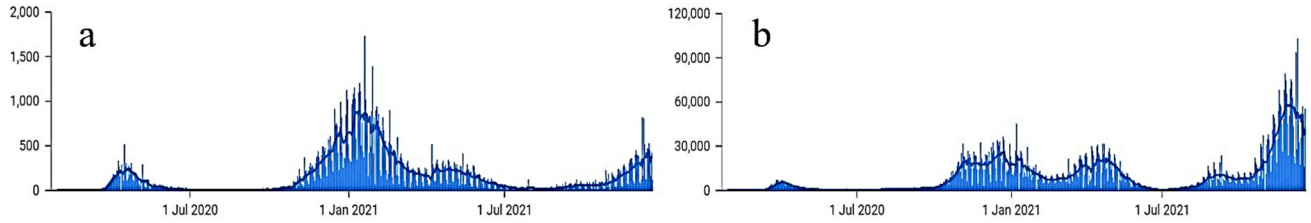

Fig. 6. Dependence of mortality (a) and morbidity (b) on time in Germany [2]

Vaccination in Germany began in February 2021 and was characterized by a rapid increase in the number of vaccinated persons. From April to August, both doses were given to 50 % of the population. After that, this indicator began to grow more slowly and at the time of the research was 70 % (Fig. 7).

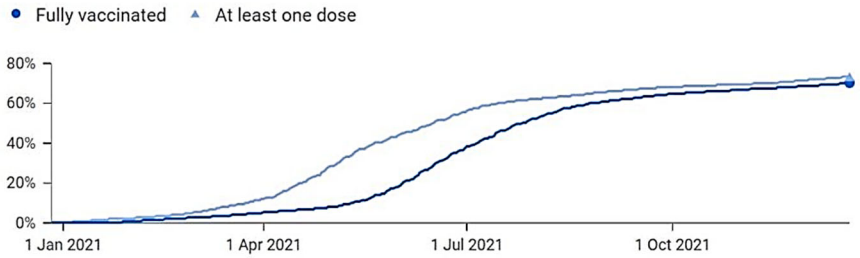

Fig. 7. Increasing the share of vaccinated population over time in Germany [11]

Similar to India, Germany has imposed strong anti-epidemic measures from the beginning (Fig. 8). Which led to a significant reduction in population movements. After the first lockdown, which occurred in the first wave of the disease and lasted from March to July 2020 for three months, population mobility has reached close to baseline levels. With the beginning of the second wave began the second lockdown, which lasted until June 2021. Closer to the time of the research Germany no longer imposed significant restrictions on movement.

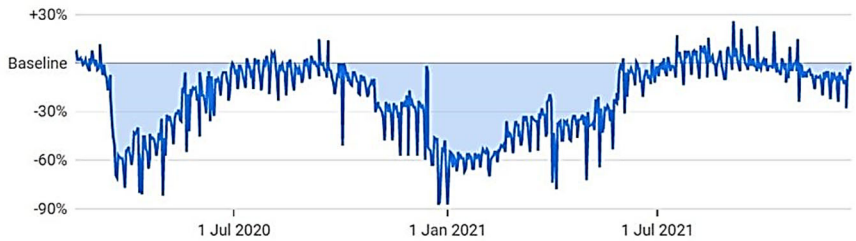

Fig. 8. Changes in population mobility over time in Germany [12]

Thus, in Germany, as in India, all waves of disease were caused by different variants of SARS-CoV-2. The first, short one, was observed during the initial penetration of the virus into the human population and was relatively insignificant due to powerful and effective anti-COVID measures introduced in the country since the beginning of the pandemic [15]. The second wave was much larger and at the same time heterogeneous. The first powerful and dangerous rise was caused by EU1, EU2, 98F and 439K variants. After that, there was some reduction in morbidity with subsequent rise. During this period the Alpha variant became widespread. In addition, this period marks the beginning of an active vaccination program in Germany. Therefore, it is clear that there is a significant difference in the duration and danger of the end of the second wave compared to its beginning. The massive increase in population resistance has mitigated the effects of each individual's infection and has led to the cessation of the spread of the pathogen [16]. In the process of extinguishing this outbreak, the Delta variant quickly supplanted the Alpha variant and remained the only strain circulating in Germany. A few months later, after a significant easing of anti-epidemic measures, this option caused the third, most powerful wave of morbidity, which, however, is characterized by a relatively low mortality rate. What can be explained by analogy with the Alpha variant by the presence of a significant level of individual resistance obtained as a result of vaccination.

In this case, the Delta variant, like in India, also did not dominate the population immediately after its appearance. Moreover, it was completely displaced for a long time. Until the beginning of the growth of group immunity accelerated by the use of vaccines. The high immunity of the population despite the spread of the Delta variant led to the suppression of the spread of SARS-CoV-2 in general [16]. However, over time, the weakening of post-infectious immunity, increasing mobility of the population and the approach of the winter period in which the pattern of human contact changes, the Delta strain has aggravated the epidemic situation [18].

According to Fig. 9 until December 2020 Ukraine has not encountered any of the variants that require special supervision. Since the beginning of winter, when in Europe and, in particular, in Germany, variants EU1, 98F and 439K have become widespread. In our country, they were represented by a very small proportion and were short-lived.

Starting from January 2021 the Alpha variant rapidly supplanted other strains and became dominant until June. When, in turn, was replaced by the Delta variant. At the same time, in the summer months of 2021 after the complete displacement of the Alpha variant, there is a short-term increase in its share in the pool of sequences of Ukrainian origin in GISAID [19]. What can be attributed to the seasonal increase in labor and tourist migration of the population of our country [20].

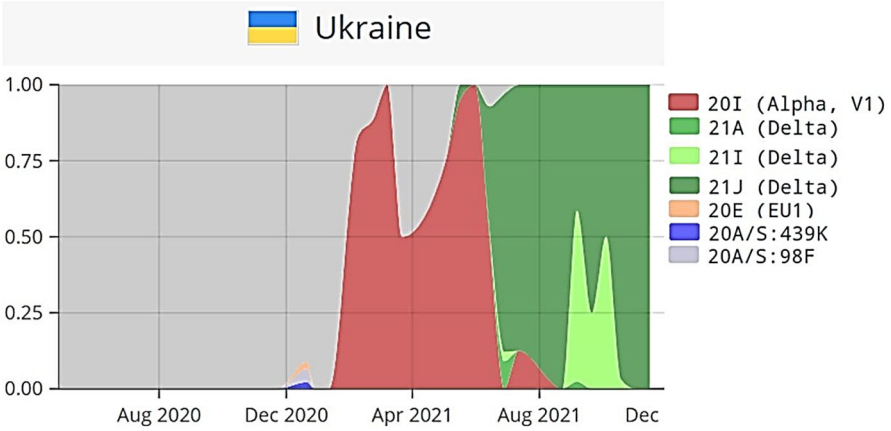

Fig. 9. Changes in the proportion of sequences of different variants of SARS-CoV-2 in Ukraine [10]

In terms of the dynamics of the epidemic situation, the first wave of morbidity in Ukraine began in September and ended in January 2020. It was characterized by a significant increase in both morbidity and mortality. Without reducing to baseline, it moved to the second one, which in turn lasted from February to May 2021. Mortality parameters were corresponding. After a long period of significant reduction in morbidity in the summer months, the third wave began – more powerful and dangerous than in the past. It continues at the time of the study, although it is clearly on the decline (Fig. 10).

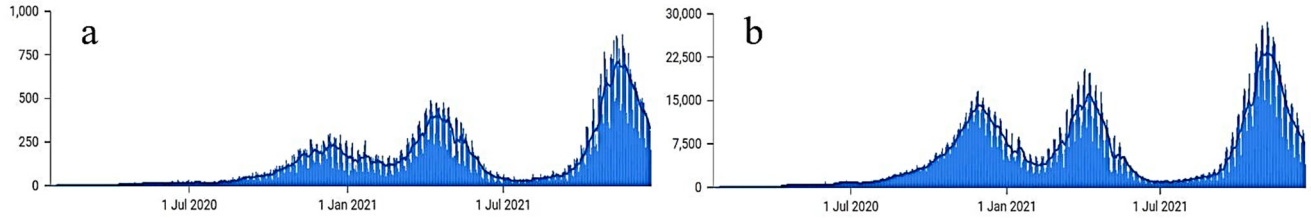

Fig. 10. Dependence of mortality (a) and morbidity (b) on time in Ukraine [2]

Active vaccination in Ukraine began in late June 2021 (Fig. 11). It is characterized by a slow increase in the number of vaccinated persons, a relatively small gap between those who received one dose of vaccine and those who received two. In general, at the time of the research, only a quarter of the population of our country has received full vaccination, which is quite low compared to European countries.

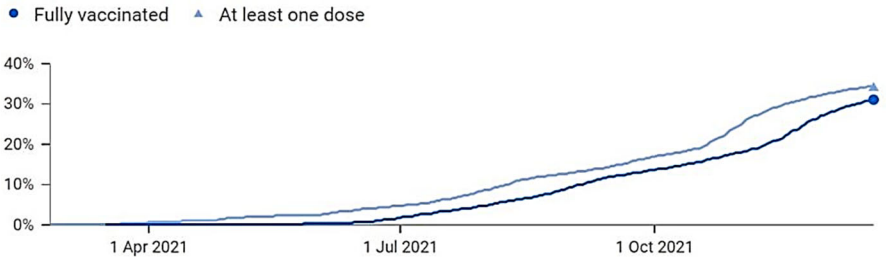

Fig. 11. Increasing the share of vaccinated population over time in Ukraine [11]

Even before the active spread of SARS-CoV-2 on the territory of the country, Ukraine introduced powerful anti-COVID measures. This is confirmed by the dynamics of changes in population mobility (Fig. 12). However, after the pandemic escalated, these measures were almost completely lifted. And renewed only after the increase in morbidity during the first and second waves. The situation was repeated and quarantine was suspended again until the incidence of the third SARS-CoV-2 outbreak in the country increased.

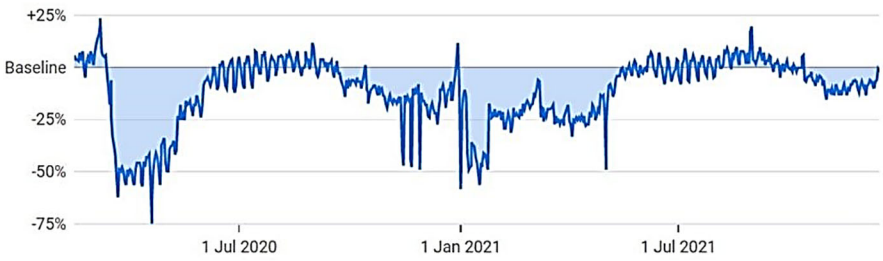

Fig. 12. Changes in population mobility over time in Ukraine [12]

Thus, due to timely and powerful anti-epidemic measures introduced in Ukraine at the beginning of the pandemic, it was possible to avoid a significant increase in the incidence of SARS-CoV-2, similar to that observed in Germany. Nevertheless, the original strain caused an outbreak a little later – in the fall of 2020. It was preceded by a long period of lack of control over population movements, which was probably the cause of high rates of both morbidity and mortality [15]. Without a significant improvement in the epidemic situation, the first wave passed into the second. The second wave, however, was caused by another strain – the Alpha, which very quickly supplanted the original version. Anti-COVID measures introduced at the beginning of the first wave, the increase in collective immunity and the approach of the summer period led to a significant reduction in the morbidity. As the epidemic situation improved, the Delta strain began to displace the Alpha variant. It should also be noted that, although this variant (Delta) was not registered in Ukraine long before the appearance of other strains (as in the case of India and Germany), for the first time it was sequenced in May 2021 – one month before the active displacement of other variants. Which, however, coincides with the beginning of the strengthening of collective immunity due to vaccination. The third wave began rapidly, after several summer months of high mobility of the country's population. There were no significant restrictions on the movement of citizens in the past, which is probably one of the reasons for the higher morbidity that we can observe at the time of the study [15]. In addition, the contribution of a relatively low level of vaccination of the population seems likely – the low level of resilience of each individual is a probable cause of high mortality in this case [15].

Generalization. In the case of each of the countries considered, the Delta strain was present in their territory before the beginning of its active dominance. It did not displace other variants immediately. And in the case of Germany, it disappeared from the population of circulating variants for more than half a year, giving way to other strains. However, with increasing population resistance due to vaccination, we have been able to observe a consistently rapid and confident displacement of all other SARS-CoV-2 strains by the Delta variant. This behavior, in our opinion, indicates the emergence of a significant advantage in this variant over others in the presence of a certain proportion of the vaccinated population in the country. This is highly likely to be due to the lower suppressive effect of post-vaccination immunity on this particular strain compared to others, which is primarily manifested in a greater number of so-called breakthrough infections [21]. At a more fundamental level, this may be related to the distinct, possibly unique, antigenic profile characteristic of the Delta variant. The one that allows avoiding the effect of vaccination-induced individual resistance on a qualitatively new level. In parallel, in the case of Germany and Ukraine, with an increase in the share of the Delta variant, we can observe an overall decrease in morbidity. Consistent with the proposed hypothesis – the Delta variant, due to less vulnerability to post-vaccination immunity is able to circulate for a longer time in the host population. In the case of India, the displacement of all other strains by the Delta variant was accompanied by an increase in morbidity, which can be explained by cultural characteristics and high population density [22]. In addition, the low level of morbidity during the first wave (and consequently post-infection immunity) and vaccination multiplied by the increase in population mobility, in our opinion, were crucial.

The situation in the case of Germany is interesting. The first and second parts of the second wave, in addition to being caused by different variants of SARS-CoV-2 and having relatively similar morbidity rates, differed significantly in mortality. Relatively low mortality rates are observed in this country in the third wave as well. This feature of the dynamics of the epidemic situation can be explained by a sharp increase in the number of vaccinated people. Thus, despite perhaps not so significant effects on morbidity in general, vaccination can reduce the mortality several times – significantly reduce the manifestation of life-threatening consequences of COVID19.

However, this effect is observed only at a high level of vaccination of the population. In the case of its low level, as in the case of Ukraine and India, we can observe a comparable proportion of deaths. Thus, in our opinion, depending on the cultural, economic, demographic and other characteristics of the country, there is a certain state of the population when vaccination is sufficient to give preference to the Delta along with other variants and not enough to effectively reduce mortality from this strain.

Conclusions. The studying of the dynamics of the spread of different variants of SARS-CoV-2 and comparative analysis of the data with the dynamics of the epidemic situation in the country, the peculiarities of vaccination and changes in mobility allowed to identify the following patterns:

1. The rapid displacement of all other variants of SARS-CoV-2 by the Delta strain in all cases was accompanied by the beginning of active vaccination of the population.
2. The high level of vaccination has had little effect on the spread of SARS-CoV-2, but has been accompanied by a significant reduction in mortality.
3. There is a certain level of post-vaccination resistance of the population, which is sufficient to displace of other variants by the Delta strain and at the same time insufficient to seriously reduce the likelihood of death.

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Надійшла до редколегії 16.05.22
Отримано виправлений варіант 17.06.22
Підписано до друку 17.06.22

Received in the editorial 16.05.22
Received version on 17.06.22
Signed in the press on 17.06.22

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ЗАКОНОМІРНОСТІ ВПЛИВУ ВАКЦИНАЦІЇ НА ДИНАМІКУ ПОШИРЕННЯ РІЗНИХ ВАРІАНТІВ SARS-COV-2. ДВОРІЧНИЙ АНАЛІЗ

Новий коронавірус, нині відомий як SARS-CoV-2, привернув до себе увагу тисяч науковців по всьому світу. Передусім така увага пов'язана зі значним впливом цього патогену на економічні та соціальні аспекти існування великої кількості людей. Швидкі та потужні антиепідемічні заходи більшості країн уповільнили темпи пандемії, а зі створенням пулу ефективних вакцин проти SARS-CoV-2 людство навчилося протидіяти його поширенню і у сфері резистентності кожної окремої людини, тим самим, очевидно, створивши додатковий фактор добору. За класичною концепцією системи господар – паразит вплив людини на SARS-CoV-2 теоретично потребує відповідних пристосувальних змін останнього. Шляхом аналізу наявних у відкритих джерелах статистичних даних автори пропонованої статті намагалися ідентифікувати й вивчити закономірності впливу вакцинації на динаміку поширення різних варіантів вірусу SARS-CoV-2 за період від початку пандемії до листопада 2021 р.

Ключові слова: SARS-CoV-2, варіант Дельта, коронавірус, вакцинація.