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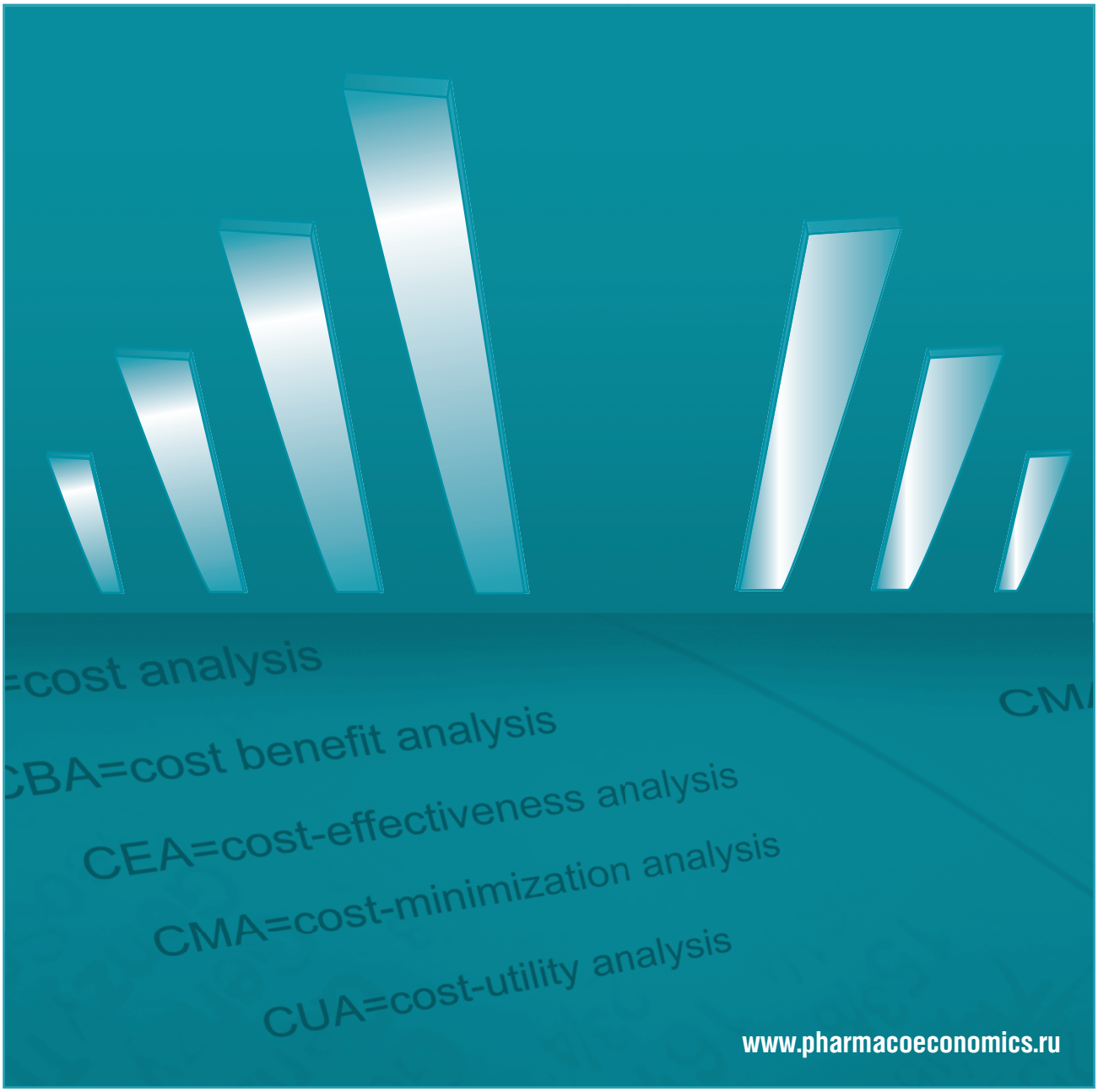

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Dietary factors influencing the COVID-19 epidemic process

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SUMMARY

Objective: to analyze the role of diet in the epidemiological parameters of the SARS-CoV-2 Coronavirus and identify factors that correlate with the reduction in the severity of the consequences of COVID-19 disease, namely the rate of prevalence (RPr) and infection fatality rate (IFR) in different regions.

Material and methods. The information and data required for this study were found in scientific publications and the media available on the Internet, as well as obtained from statistical databases using specific keywords, both for a single tag and in various combinations of them. Statistical samples were managed from sources and facts available on the Internet. Pearson correlation coefficient (r) was used to understand a statistical relationship between two variables.

Results. The relationship between nutritional factors and the impact of the 15-month COVID-19 pandemic in different regions was investigated using various available statistics for five continents and 47 countries. A clear relationship was found between the outcomes of the SARS-CoV-2 epidemic (RPr and IFR) and the amount of consumed essential nutrients, with correlations in the negative range r=–0.98 and r=–0.66 for plant proteins and with correlation coefficients r=0.92 for animal proteins. Also, excessive sugar consumption increased the severity of COVID-19 with correlation coefficients in the range of r=0.99–0.72 in the representative samples.

Conclusion. Statistical analysis presented that the number of diagnosed patients with SARS-CoV-2 (RPr) and deaths from COVID-19 (IFR) was significantly lower in regions where more plant foods were consumed than animal products. A detailed study of the relationship between the Coronavirus and the host as well as the metabolism of protein and sugar may reveal the diet factors responsible for resistance to the pathogen. Edible plants can contain components responsible for suppressing the replication cycle of the SARS-CoV-2 virus. Biochemical investigation of these components would help in the development of etiological oral administrated anti-COVID-9 medicine.

KEYWORDS

Coronavirus SARS-CoV-2, COVID-19 pandemic, epidemic, pathogenesis, diet, risk factors.

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Conflict of interests

The author declares she has nothing to disclose regarding the conflict of interests with respect to this manuscript.

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Диетические факторы, влияющие на эпидемический процесс COVID-19

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РЕЗЮМЕ

Цель: проанализировать роль рациона питания в эпидемиологических параметрах коронавируса SARS-CoV-2 и выявить факторы, коррелирующие со снижением тяжести последствий заболевания COVID-19, а именно частотой заболеваемости (англ. rate of prevalence, RPr) и смертности (англ. infection fatality rate, IFR) в разных регионах.

Материал и методы. Информация и данные, необходимые для этой работы, были найдены в научных публикациях и средствах массовой информации, доступных в Интернете, а также получены из баз статистических данных с использованием определенных ключевых слов для одного тега или в различных их комбинациях. Статистические выборки были сформированы из источников и фактов, доступных в Интернете. Корреляция для двух переменных определялась как коэффициент Пирсона.

Результаты. Взаимосвязь между факторами питания и влиянием 15-месячной пандемии COVID-19 в разных регионах была исследована с использованием различных доступных статистических данных по пяти континентам и 47 странам. Обнаружена четкая связь между исходами эпидемии SARS-CoV-2 (RPr и IFR) и количеством потребленных основных нутриентов с корреляциями в отрицательном диапазоне r=–0,98 и r=–0,66 для растительных белков и коэффициентом корреляции r=0,92 для белков животного

происхождения. Также чрезмерное потребление сахара увеличивало тяжесть течения COVID-19 с коэффициентами корреляции в диапазоне r=0,99–0,72 в репрезентативных выборках.

Заключение. Статистический анализ показал, что количество диагностированных пациентов с SARS-CoV-2 (RPr) и смертей от COVID-19 (IFR) было значительно ниже в регионах, где потреблялось больше растительной пищи, чем продуктов животного происхождения. Детальное изучение взаимосвязи между коронавирусом и хозяином, а также метаболизма белков и сахаров поможет выявить факторы питания, ответственные за устойчивость к патогену. Съедобные растения могут содержать компоненты, ответственные за подавление цикла репликации вируса SARS-CoV-2. Биохимические исследования этих компонентов помогут в разработке этиологических пероральных препаратов против COVID-19.

КЛЮЧЕВЫЕ СЛОВА

Коронавирус SARS-CoV-2, пандемия COVID-19, эпидемия, патогенез, диета, факторы риска.

Статья поступила: 01.04.2022 г.; в доработанном виде: 20.10.2022 г.; принята к печати: 16.12.2022 г.

Конфликт интересов

Автор заявляет об отсутствии необходимости раскрытия конфликта интересов в отношении данной публикации.

Для цитирования

Пономаренко С.В. Диетические факторы, влияющие на эпидемический процесс COVID-19. *ФАРМАКОЭКОНОМИКА. Современная фармакоэкономика и фармакоэпидемиология.* 2022; 15 (4): 463–471 (на англ. яз). https://doi.org/10.17749/2070-4909/farmakoekonomika.2022.135.

Highlights

What is already known about the subject?

- Epidemiological data on morbidity and mortality from SARS-CoV-2 in different countries or regions may differ by 2–3 orders of magnitude, i.e. there are populations more resistant to this infection
- To date, the availability of effective targeted anti-covid drugs has not been confirmed. It is necessary to identify factors influencing resistance to SARS-CoV-2 virus infection
- Type of diet is one of the factors affecting the development and outcome of COVID-19

What are the new findings?

- An analysis of statistics from the COVID-19 pandemic shows that populations consuming staple foods high in protease inhibitors have low rates of virus infection and mortality from COVID-19
- The pathogenesis of the disease directly depends on the type of diet: in populations resistant to SARS-CoV-2, people consume predominantly plant-based, low-calorie, and low-protein foods
- The severity of COVID-19 development correlates with excessive consumption of sugars and animal proteins. It is necessary to study the anti-covid effect of some components in products of plant origin

How might it impact the clinical practice in the foreseeable future?

- To increase individual resistance to the SARS-CoV-2 virus, the type of nutrition should be controlled at an early stage of infection
- A detailed study of the relationship between the SARS-CoV-2 pathogen and the host as well as the biochemistry of protein and sugar metabolism, will reveal the direct factors responsible for resistance to infection
- Analysis of natural molecules directly responsible for the suppression of Coronavirus replication will help in the development of an etiological therapeutic

Основные моменты

Что уже известно об этой теме?

- Эпидимиологические данные о заболеваемости и смертности от вируса SARS-CoV-2 в разных странах или регионах могут отличаться на 2–3 порядка, т.е. существуют популяции, более резистентные к этой инфекции
- К настоящему времени не подтверждено наличие эффективных таргетных антиковидных препаратов. Необходимо выявить факторы, влияющие на резистентность к инфекции вируса SARS-CoV-2
- Тип питания является одним из факторов, влияющих на развитие и исход COVID-19

Что нового дает статья?

- Анализ статистических данных показывает, что в популяциях, потребляющих основные продукты с высоким содержанием ингибиторов протеаз, зарегистрированы низкие показатели инфицирования вирусом и смертности от COVID-19
- Патогенез заболевания напрямую зависит от типа диеты: в популяциях, резистентных к SARS-CoV-2, люди потребляют преимущественно растительную, низкокалорийную и низкобелковую пищу
- Тяжесть развития COVID-19 коррелирует с избыточным потреблением сахаров и животных белков. Следует изучить антиковидное действие некоторых компонентов в продуктах растительного происхождения

Как это может повлиять на клиническую практику в обозримом будущем?

- Для повышения индивидуальной резистентности к вирусу SARS-CoV-2 следует контролировать тип питания на ранней стадии инфекции
- Детальное изучение особенностей взаимотношения между патогеном SARS-CoV-2 и хозяином, а также биохимии обмена белков и сахаров может позволить найти непосредственные факторы, отвечающие за устойчивость к инфекции
- Анализ природных молекул, непосредственно отвечающих за подавление репликации коронавируса, поможет в разработке этиологичного терапевтика

INTRODUCTION / ВВЕДЕНИЕ

The current COVID-19 pandemic was announced by World Health Organization (WHO) on March 11, 2020 [1]. The disease was caused by the highly transmitted from person to person SARS-CoV-2 coronavirus. COVID-19 (Corona Virus Infectious Disease) was detected in China at the end of 2019, and a newly discovered coronavirus was identified moreover, the genome of SARS-CoV-2 was rapidly sequenced [2–4]. This is a very dangerous infectious disease that affects a huge number of people on all continents and countries [5, 6].

Epidemiologists and virologists have suggested that global infection with the highly pathogenic SARS-CoV-2 virus will continue for more than three years. The COVID-19 pandemic is a global health, medical, social, and economic challenge now and as well as in the future. Many diverse factors increasing the onset and course of COVID-19 disease have been evaluated and analyzed [5, 7–17].

This review analyzes the influence of dietary factors on the development of the SARS-CoV-2 epidemic process on five continents and in some of their regions to assess the effectiveness of factors that can reduce the consequences of severe infectious disease.

MATERIAL AND METHODS / МАТЕРИАЛ И МЕТОДЫ

Expected information was methodically investigated on the Internet using selected keywords. The keywords were managed as a single tag or in tags compositions. The statistical population groups were made from data from 47 countries. Most of the statistics were acquired from the following special and reliable databanks: World Health Organization[1], Worldometer[2], Food and Agriculture Organization[3], Our World in Data[4], The World Bank Open Data[5], International Monetary Fund[6].

The rate of prevalence (RPr) or infection fatality rate (IFR) of the virus was calculated as a ratio between the quantities of all cases and the total population. Case fatality rate (CFR) was the ratio between total COVID-19 deaths and the registered infection cases in %. The relationship between statistical data was calculated as a Pearson correlation coefficient (r).

RESULTS AND DISCUSSION / РЕЗУЛЬТАТЫ И ОБСУЖДЕНИЕ

Basic views about the etiology and pathogenesis of SARS-COV-2 / Основные представления об этиологии и патогенезе вируса SARS-COV-2

Discovered at the end of 2019, the new virus was announced by the International Committee on Taxonomy of Viruses as SARS-CoV-2. The large and combined RNA virus belongs to the genus Beta-coronavirus, the Coronaviridae family. Coronaviruses cause respiratory tract infections in birds and mammals. Betacoronaviruses are highly transmissible, enveloped, heavyweight, and complex RNA viruses that cause several acute respiratory infections in humans [2–4, 18]. The SARS-CoV-2 Beta-coronavirus is extremely contagious to humans, and pathogen virions spread among people through aerosol-generated particles and primarily enter type 2 pneumocytes attaching to the host angiotensin-converting enzyme (ACE2) [2, 3, 19, 20].

Conventionally, the life cycle of pathogenic viruses transmitted by airborne droplets is determined by the main stages: infection, replication, release, and transmission of virions. The stage of infection includes the following phases: the presence of a sensitive object in the environment; invasion of the respiratory tract; transport to sensitive tissues and endocytosis into host cells. The replication stage consists of the following phases: synthesis of viral polypeptides and RNA; the formation of a protovirus; assembly of virion components. The third stage is: the exit of daughter virions from the cell, departure from the host, and spread. The genome of Coronaviruses encodes the structure of several proteases that are important for the successful invasion and productive pathogen replication [2–4].

COVID-19 is currently known as a very dangerous infectious disease that causes fatal pathogenic symptoms. Five main variants of the severity of COVID-19 disease have been identified: asymptomatic, subclinical, acute with convalescence, chronic, and lethal [5, 7, 8]. The predominantly clinical manifestation of COVID-19 is pneumonia, which can lead to SARS and critical lung damage in a very short time. Moreover, the virus is toxic and destructive to other human organs. The SARS-CoV-2 virus can destroy tissue and cause multiple organ failure during infection [7, 8, 21, 22], as well as cause a dangerous post-COVID syndrome called Long-COVID [5, 7, 23, 24]. In the current conditions of a pandemic, it would be very useful to find natural factors that prevent the development of a serious illness.

Consequences of the pandemic: fifteen months later / Последствия пандемии: пятнадцать месяцев спустя

On Thursday, June 10, 2021, 15 months have passed since the WHO announced the COVID-19 pandemic [1], but no clear scientific prediction of the end date has yet been made. By this time, cases of infection have been confirmed in all countries and several thousand circulating variants of the SARS-CoV-2 virus have been identified [5–7]. New mutants with higher transmission rates are emerging in different regions, indicating that, there are no signs of weakening of the global pandemic. Most likely, the number of cases of infection will continue to increase in the form of growing waves.

This review discusses the COVID-19 pandemic data collected over the study period, March 11, 2020, to June 10, 2021. During the 15 months of the study-period, about 175.6 thousand cases of viral infection were confirmed globally, which is 2.25% of the world's population [5, 6]. The largest number of infected patients on this date was observed in Europe and Asia, together lived on these continents 57% of global infected with the virus SARS-CoV-2 [6].

In North America (NA), the majority of those infected were in the United States of America (USA), South America in Brazil, Europe in France, Asia in India, and in Africa in South Africa [5, 6]. In these five countries, almost 50% of the globally detected cases of the SARS-CoV-2 virus with the spread of special variants [5–7] were reported. However, the relative number of deaths in these countries from different continents varies considerably [6].

On this date, about 4 million deaths were registered in the world, which was 2.16% of all infected patients. Until June 10, 2021, data on mortality from COVID-19 disease in the world grew in the form of four growing waves [6]. As the number of people infected increases, the number of deaths will rise on all continents. Reducing the number of incidences and deaths from COVID-19 is an urgent task in the fight against coronavirus. To do this, it is important to analyze the epidemiological data and determine the factors that can reduce the pathogenesis of the SARS-CoV-2 virus.

Infection or mortality rates vary greatly from region to region and from country to country. These data may differ by a factor of a hundred or a thousand, which is why some publications question the fact that statistical information on epidemiological processes from different countries was reliable [25]. Despite the opinion that the analysis of a large database has its drawbacks, which are especially evident with a heterogeneous sample [26], for greater reliability, the influence of socio-economic factors on the course and outcomes of the SARS-CoV-2 coronavirus was analyzed using a large number of representative statistics and a long study period [27–29].

[1] https://www.who.int.
[2] https://www.worldometers.info.
[3] http://www.fao.org.
[4] https://ourworldindata.org.
[5] https://databank.worldbank.org.
[6] https://www.imf.org.

Risk factors for the epidemic process COVID-19 / Факторы риска развития эпидемического процесса COVID-19

The pathogenic coronavirus SARS-CoV-2 has paralyzed all human activities around the world, making it impossible to resolve the global health and economic crisis. The number of confirmed infected cases was growing every day and rising in the next fifth wave [6]. Decisions about the course of each epidemic are based on an analysis of statistics on circulating infection in the population over the period described. Epidemiologists, infectious disease specialists, clinicians, and other experts analyze primarily the risks of an epidemic (pandemic) and their factors [5, 8–17, 27–29]. The following available sources differentiate or assess risk factors for severity or mortality from COVID-19 [5, 7].

The elevated mortality rate among high-incomed patients suffering from COVID-19 has been unexpectedly recognized [12, 29]. A similar trend was found in statistical populations of continents [28].

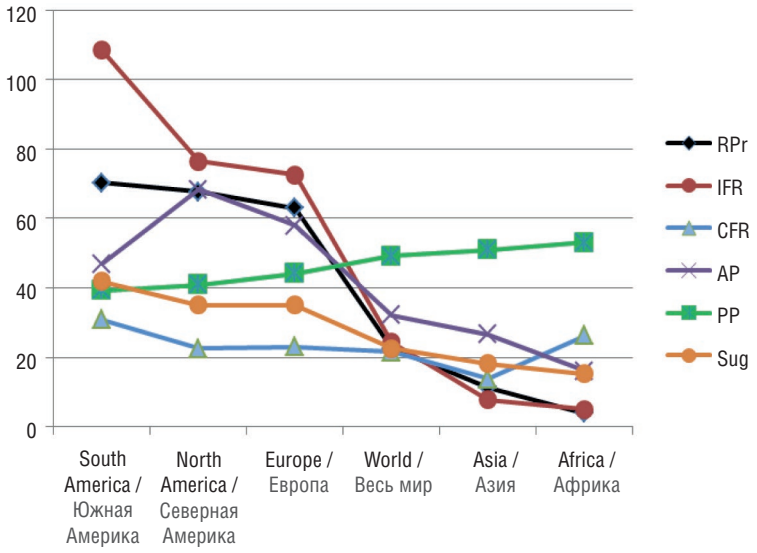
Africa is characterized by a low standard of living: gross domestic product is 32 times, consumption of high-calorie foods is 2.2 times, protein intake is 1.6 times lower than in NA [30, 31]. In Africa the RPr was 18 times and the IFR 22 times lower than in NA [6, 15, 28]. This difference between NA and Asia was less contrasting (Fig. 1) but also significant; accordingly, the infection fatality rate (IFR) and rate of prevalence (RPr) were several times lower in Asia, than in NA [6, 28].

It was investigated the influence of socio-economic factors on the pathogenesis of the virus and shown that the level of consumption of fats and total protein could be a reliable factor influencing the pathogenesis of the SARS-CoV-2 virus [28]. In the non-white (black and South-Asian) groups in the USA or Great Britain population, the rates of incidence and mortality were higher than in the white group [11, 12, 16]. These studies supported the idea that eating habits rather than ethnicity were the risk factors for COVID-19.

Relation between dietary habits and progress of SARS-COV-2 infection / Связь между пищевыми привычками и развитием инфекции SARS-COV-2

Many publications and reviews have suggested that a person's diet plays an important role in the development of COVID-19 outcomes [34–42]. For a long time, nutritionists believe that an optimal diet helps in the fight against diseases, including infectious ones, since proper nutrition improves the immune system and strengthens the body's defenses [34, 40–43]. Nutritional deficiencies and low metabolic rates have been suggested to exacerbate the disease and increase mortality [34, 36, 38, 44]. Therefore, patients with COVID-19 were recommended, an enriched diet with all essential nutrients, vitamins, and minerals [5, 38, 40, 44, 45]. It was suggested, that a Mediterranean diet could reduce the risk of severe SARS-CoV-2 disease and COVID-19 mortality [46]. Several studies have shown that COVID-19 disease was worsening not only due to malnutrition, but also due to obesity [35–39]. To combat the infectious COVID-19 disease, excessive consumption of fatty and protein foods was recommended [40]. Opposite assumptions were the following: a plant-based diet was beneficial for recovery from COVID-19 [47] and the severity of the development of the epidemic process of SARS-CoV-2 in humans directly depends on the amount of fat and protein consumed, as has been shown for populations of continents and different regions [28].

Proteins are vital macronutrients for the animal body. People get animal and plant proteins from food. On the continents of Asia and Africa, plant food (**Fig. 1**) predominates (66% and 76% of the total protein, respectively). Nations in Europe and America consumed more fat and protein than in Asia or Africa for decades (Fig. 1), and this is also much more than the WHO recommendation [43, 48]. The diet of Europeans and North Americans is dominated by animal proteins



Correlation coefficients (r) between COVID-19 outcomes and different factors of diet / Коэффициенты корреляции (r) между исходами COVID-19 и различными факторами питания

Factor / Фактор	RPr	IFR	CFR
IFR	0.97		
CFR	0.46	0.60	
AP	0,92	0,80	0,17
PP	–0.98	–0.98	–0.49
wP	0.84	0.69	0.03
Sug	0.99	0.99	0.52

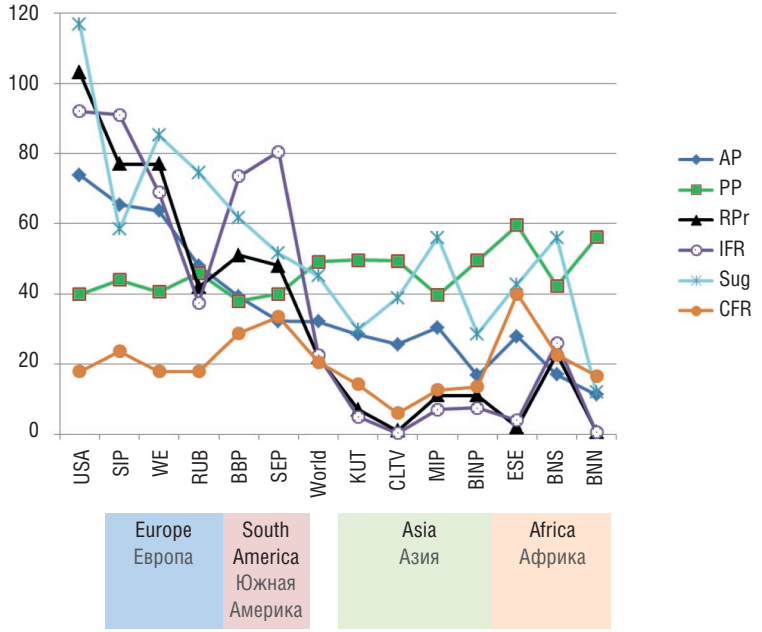
Figure 1. Relation between outcomes of the COVID-19 pandemic and diet factors on five continents (compiled by the author).
Correlation between rate of prevalence (RPr), infection fatality rate (IFR) or case fatality rate (CFR) of the SARS-CoV-2 infection and amount of consumed animal protein (AP), plant protein (PP), whole protein (wP) or sugar (Sug).
AP, PP, wP – in protein g/day/person [31], Sugar – in Kg/year/capita [32], RPr – total amount infected/1000 population (as of June 10, 2021) [6], IFR – total amount deaths/50 000 population (as of June 10, 2021), CFR – relative mortality in %.
World Health Organization recommendation: maximum 50 g sugar and its products per day per capita [33]

Рисунок 1. Связь между последствиями пандемии COVID-19 и факторами питания на пяти континентах (составлено автором).
Корреляция между уровнем распространенности (англ. rate of prevalence, RPr) и смертности (англ. infection fatality rate, IFR) или относительной летальности (англ. case fatality rate, CFR) от инфекции SARS-CoV-2 и количеством потребляемого животного белка (англ. animal protein, AP), растительного белка (англ. plant protein, PP), общего белка (англ. whole protein, wP) или сахара (англ. sugar, Sug).
Белки – г/сут на человека [31], сахар – кг/год на душу населения [32], RPr – общее количество инфицированных на 1 тыс. населения (на 10.06.2021) [6], IFR – общее количество смертей на 50 тыс. населения (на 10.06.2021), CFR – относительная летальность в %.
Рекомендация Всемирной организации здравоохранения: не более 50 г сахара и продуктов его переработки в день на душу населения [33]

(58 and 68 g/person/day), namely 57% of the total protein consumed. Inhabitants of Africa consume 4.2 times and Asia 2.6 times less animal protein than in NA. At the same time, the maximum difference in the amount of vegetable protein consumed by a person on different continents ranges from 25% to 30% (in NA 41, in Asia 51, and Africa 53 g/day). People in some Asian countries consume less fat, and in Africa, much less protein than the WHO recommendation [43, 48]. The inhabitants of these two continents consume significantly less animal protein than the world average. Fig.1 shows a direct association between RPr or IFR on five continents and the amount of animal protein consumed, with correlation coefficients r=0.92 for incidence or r=0.8 for mortality. These correlation coefficients for total protein were smaller: 0.84 or 0.69, respectively, for the same continents (Fig. 1) [28]. All indicators of SARS-CoV-2 for continents: RPr, IFR, and case fatality rate (CFR) show a higher correlation for vegetable protein than for animal protein with r=–0.98, r=–0.98, and r=–0.49. The correlation between the severity of COVID-19 and the amount of plant or animal proteins eaten is more pronounced (Fig. 1) than between total dietary protein [28]. A direct correlation between the level of manifestation of viral pathogenesis and the consumed quantity of plant proteins on the continents was obtained for both RPr and IFR (Fig. 1).

A similar analysis was carried out for the selected groups of countries [28] on each continent. It was analyzed the epidemiological data of grouped countries from each continent, and the relationship presented for most of these countries: lower consumption of fat and total protein correlates with less severe pathogenicity of the SARS-CoV-2 [28, 47]. A side effect of COVID-19 is an increase in plasma cholesterol in patients [49]. A diet rich in fat amplifies the circulating ACE [50], which explains the positive correlation between fat intake and RPr or IFR of COVID-19 [28, 51]. Here, the same groups of countries [28] have used to analyze risk factors for infection with SARS-CoV-2 (**Fig. 2**).

The tendency of the dependence of the severity of COVID-19 on the amount of consumed animal proteins revealed for the continents (Fig. 1) also manifests itself (Fig. 2) for the previously selected groups of countries [28]. In Ethiopia and Nigeria, from ESE and BNN groups (Fig. 2), the population consumes 12 and 10 times less animal-based protein than in the USA, and, accordingly, the frequency of infection



Correlation coefficients (r) between COVID-19 outcomes and different factors of diet / Коэффициенты корреляции (r) между исходами COVID-19 и различными факторами питания

Factor / Фактор	RPr	IFR	CFR
IFR	0.94		
CFR	0.16	0.35	
AP	0.92	0.8	0.06
PP	–0.66	–0.7	0.07
Sug	0.86	0.72	0.07
AP/PP	0.95	0.85	0.06
wP	0.69	0.45	0.16

Figure 2. Relation between outcomes of the COVID-19 pandemic and diet factors in different country groups of five continents (compiled by the author).
Correlation between rate of prevalence (RPr), infection fatality rate (IFR) or case fatality rate (CFR) of the SARS-CoV-2 infection and amount of consumed animal protein (AP), plant protein (PP), whole protein (wP) or sugar (Sug).
AP, PP, wP – in protein g/day/person, sugar – in Kcal/day/capita [31], RPr – total amount infected/1000 population (as of June 10, 2021) [6], IFR – total amount deaths/50 000 population (as of June 10, 2021), CFR – relative mortality in %.
On abscissa axis are names of country groups taken from [28]: USA – United States of America; SIP – Spain, Italy, Portugal (Mediterranean Europe); WE – Western Europe (Austria, Belgium, France, Germany, Netherlands, Switzerland); RUB – Russia, Ukraine, Belarus (Eastern Europe); BBP – Bolivia, Brasil, Paraquay (North-West of Southern America); CEP – Colombia, Ecuador, Peru (South-East of Southern America); KUT – Kyrgyzstan, Uzbekistan, Tajikistan (Central Asia); CLTV – Cambodia, Laos, Thailand, Vietnam (Mainland South-Estern Asia); MIP – Malaysia, Indonesia, Philippines (Maritimeland South-Estern Asia); BINP – Bangladesh, India, Nepal, Pakistan (South Asia); ESE – Egipt, Ethiopia, Sudan (North Nile region); BNS – Botswana, Namibia, South Africa (Southern Africa); BNN – Benin, Niger, Nigeria (Eastern part of West Africa)

Рисунок 2. Связь между последствиями пандемии COVID-19 и факторами питания в различных группах стран пяти континентов (составлено автором).
Корреляция между уровнем распространенности (англ. rate of prevalence, RPr) и смертности (англ. infection fatality rate, IFR) или относительной летальности (англ. case fatality rate, CFR) от инфекции SARS-CoV-2 и количеством потребляемого животного белка (англ. animal protein, AP), растительного белка (англ. plant protein, PP), общего белка (англ. whole protein, wP) или сахара (англ. sugar, Sug).
Белки – г/сут на человека, сахар – ккал/сут на человека [31], RPr – общее количество инфицированных на 1 тыс. населения (на 10.06.2021) [6], IFR – общее количество смертей на 50 тыс. населения (на 10.06.2021), CFR – относительная летальность в %.
По оси абсцисс приведены названия групп стран [28]: США – Соединенные Штаты Америки; SIP (англ. Spain, Italy, Portugal) – Испания, Италия, Португалия (Средиземноморская Европа); WE (англ. Western Europe) – Западная Европа (Австрия, Бельгия, Франция, Германия, Нидерланды, Швейцария); RUB (англ. Russia, Ukraine, Belarus) – Россия, Украина, Беларусь (Восточная Европа); BBP (англ. Bolivia, Brasil, Paraquay) – Боливия, Бразилия, Парагвай (северо-запад Южной Америки); CEP (англ. Colombia, Ecuador, Peru) – Колумбия, Эквадор, Перу (юго-восток Южной Америки); KUT (англ. Kyrgyzstan, Uzbekistan, Tajikista) – Кыргызстан, Узбекистан, Таджикистан (Центральная Азия); CLTV (англ. Cambodia, Laos, Thailand, Vietnam) – Камбоджа, Лаос, Таиланд, Вьетнам (материковая часть Юго-Восточной Азии); MIP (англ. Malaysia, Indonesia, Philippines) – Малайзия, Индонезия, Филиппины (приморская часть Юго-Восточной Азии); BINP (англ. Bangladesh, India, Nepal, Pakistan) – Бангладеш, Индия, Непал, Пакистан (Южная Азия); ESE (англ. Egipt, Ethiopia, Sudan) – Египет, Эфиопия, Судан (регион Северного Нила); BNS (англ. Botswana, Namibia, South Africa) – Ботсвана, Намибия, Южная Африка (юг Африки); BNN (англ. Benin, Niger, Nigeria) – Бенин, Нигер, Нигерия (восточная часть Западной Африки)

with the virus was 44 and 129 times lower. In addition, inhabitants of these two African countries consume 7.5 and 5.6 times less sugar than residents of the USA (Fig. 2). In countries with low consumption of sugar and its derivatives, the incidence of SARS-CoV-2 virus infection was usually lower. The correlation coefficients of the dependence of RPr or IFR on the amount of sugar eaten were for selected groups 0.8 or 0.7 respectively (Fig. 2). To reduce the risk of glucose in COVID-19 development, recommended the use of non-physiological glucose analogues for therapy. A review by F. Paoli et al. suggested that elevated blood glucose suppresses the antiviral response, and stimulates the expression of ACE2 receptors in animal tissues, increasing the severity of COVID-19 [52]. The trend in the severity of COVID-19 across country groups matches the consumption of both animal-based protein and sugar with its derivatives (Fig. 2).

Although there may be exceptions in the correlation for some countries, in which, in the short period before the study day of the pandemic, the number of infected patients increased sharply due to the penetration of new variants of the SARS-CoV-2 virus with very high infectivity. So has happened in May and June of this year in Peru, Brazil, and India [5–7]. At the end of April 2021, such a phenomenon was recorded in a group of Central European countries (Czech, Poland, and Slovak Republics) [6, 28], whose residents consume less fat, sugar, and animal proteins [6, 48] but the data on infection and mortality rates (RPr and IFR) were significantly higher than in neighboring West-Europe [6, 28]. In the South Africa Republic, also in the BBP and CEP groups from Southern America, in contrast to other countries, mortality jumped out of the trend of dependence on the amount of fat and protein consumed. In these countries, the escalation of the pathogenic process of the SARS-CoV-2 virus may be influenced by more contagious of the virus variants (Beta- and Gamma) [5, 7]. The influence of dietary factors on the number and rate of transmission of virions, or the basic reproduction number (Ro), should be principal minimal.

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The other two country groups, RUB (Russia, Ukraine, Belarus) and CLTV (Cambodia, Laos, Thailand, Vietnam), were well outside the trend line in terms of the rates of infections (RPr) or deaths (IFR) (Fig. 2). In the countries of these two groups, people consume less protein and fat than Europeans [28, 47]; moreover, the intervals between waves of infection were much longer than the world average [6]. Thus, in the RUB group, the numbers of RPr and IFR were 70% and 55% of the average data for Europe.

In the CLTV region, RPr and IFR values were extremely lower than the average for Asia (928 and 6 per million, respectively) [6], although the inhabitants of this region consume fats and animal proteins, almost equal to the average for Asian continent [28, 48]. The consumption of sugars in this group is not lower than [32, 33, 48] in other regions of Asia (Fig. 2).

The diet in the CLTV region is plant-based with a high consumption of soy products (**Table 1**). The average world consumption of soybeans is 0.77 g/day/person [48]. Thus, in Vietnam with a high population density (314 people/sq. Km) [30, 31] the incidence of coronavirus infection and mortality were among the lowest in the world (Fig. 1, 2; Table 1). In this state, residents consume the largest amount of soy protein per capita (9.14 g per day) [48]. Also, in Taiwan, with its very high population density (673 persons/sq. Km [30, 31]), infection and mortality rates were among the lowest in Asia [6, 28]. The inhabitants of this island eat about 8 g of soy protein per day.

Despite the high heterogeneity of data in the group of Asian countries with high consumption of soybeans, the revealed relationship between the consumption of plant proteins and RPr or IFR remains higher than for fat, sugar, or animal proteins.

The Asian population, which consumes a lot of soy products, has the lowest infection rate not only in the world but also in Asia (Fig. 1, 2), even with high consumption of fatty or protein foods and a very high population density [6, 28, 30, 48]. There was no relationship between RPr or IFR and level of consumption of fat, sugar, and soy in these countries (**Table 2**), which have been easy throughout the COVID-19 pandemic [6]. This reason for the very mild outcomes of the SARS-CoV-2 coronavirus needs to investigate. Soybeans contain a wide variety of serine and other proteases inhibitors, the activity of which was minimally reduced after prolonged boiling [53–55]. Are soybeans virucidal or food protease inhibitors able to disrupt the activity of viral enzymes important for the infectious process? The question of whether soy products help to block the development of the SARS-CoV-2 virus can be resolved after serious research.

Table 1. Diet factors and the outcomes of COVID-19 in South- and South-East Asia countries (compiled by the author)

Таблица 1. Факторы диеты и последствия COVID-19 в странах Южной и Юго-Восточной Азии (составлено автором)

Country / Страна	Factor / Фактор							
	RPr	IFR	Soy	AP	PP	Soy/AP	F	Sug
Vietnam / Вьетнам	100	0.6	**9.14**	36.8	53.2	24.84	79.0	108
Taiwan / Тайвань	512	15.0	**8.70**	42.5	43.3	20.47	127.0	275
Japan / Япония	6089	110.0	**8.20**	48.1	38.5	21.30	88.0	242
Cambodia / Камбоджа	2165	18.0	**4.42**	19.2	46.2	23.02	34.0	216
Pakistan / Пакистан	4021	90.0	**2.55**	27.9	38.4	9.14	72.0	238
Thailand / Таиланд	1890	12.0	**1.90**	26.2	34.8	7.25	64.0	387
Laos / Лаос	268	0.4	**0.88**	20.1	63.1	4.38	49.0	64
World average / В среднем глобально	22 529	486.0	**0.77**	32.1	49.1	2.40	82.8	136

Note. *RPr – rate of prevalence; IFR – infection fatality rate; Soy – soy protein; AP – animal protein; PP – plant protein; F – fat; Sug – sugar. Soy, AP, PP, F – in g/day/person [31], Soy/AP – in %, Sug – in Kg/year/capita [32]. RPr – total amount infected/1mln population (as of June 10, 2021) [6]; IFR – total amount deaths/1mln population (as of June 10, 2021).*

Примечание. *RPr (англ. rate of prevalence) – уровень распространенности; IFR (англ. infection fatality rate) – уровень смертности; Soy (англ. soy protein) – соевый белок; AP (англ. animal protein) – животные белки; PP (англ. plant protein) – растительные белки; F (англ. fat) – жиры; Sug (англ. sugar) – сахар. Белки и жиры – г/сут на человека [31], Soy/AP – %, сахар – кг/год на душу населения [32]. RPr – общее количество инфицированных на 1 тыс. населения (на 10.06.2021) [6]; общее количество смертей на 50 тыс. населения (на 10.06.2021).*

Table 2. Pearson correlation coefficients (r) between COVID-19 outcomes and different food components in South- and South-East Asia countries (compiled by the author)

Таблица 2. Коэффициенты корреляции Пирсона (r) между последствиями COVID-19 и различными компонентами питания в странах Южной и Юго-Восточной Азии (составлено автором)

Factor / Фактор	wP	AP	PP	F	Sug	Soy
Soy	0.69	**0.83**	–0.10	0.67	–0.05	
RPr	–0.18	**0.35**	–0.63	0.09	0.36	0.04
IFR	–0.04	**0.45**	–0.56	0.18	0,24	0.12

Note. *wP – whole protein; AP – animal protein; PP – plant protein; F – fat; Sug – sugar; Soy – soy protein; RPr – rate of prevalence; IFR – infection fatality rate. Correlation coefficients were calculated from data in the Table 1.*

Примечание. *wP (англ. whole protein) – общий белок; AP (англ. animal protein) – животные белки; PP (англ. plant protein) – растительные белки; Sug (англ. sugar) – сахар; Soy (англ. soy protein) – соевый белок; RPr (англ. rate of prevalence) – уровень распространенности; IFR (англ. infection fatality rate) – уровень смертности. Коэффициенты корреляции рассчитаны на основе данных, приведенных в таблице 1.*

The RUB group has the lowest population density in the selected Europe clusters [6, 28, 30]. In the countries of this group, RPr was much lower, and IFR was slighter than the European average (Fig. 1, 2). In this RUB region, residents consume less fat and protein than other Europeans [28, 48]; however, the largest amount of potatoes in the world (6.17 g of protein per day per capita, or 13.4% of plant proteins eaten). In Belarus, on average, each inhabitant intakes 8 g of potato proteins per day, or 18.6% of all consumed vegetable proteins [28, 48]. This country had the lowest rates of both infection (RPr) and mortality (IFR) from COVID-19, not only in Europe, but also in the group [6]. Potatoes and soy are similar in protease inhibitors producing and digestion affecting, and uptake of nutrients in the gastrointestinal tract. Potato tubers contain a wide range of different protease inhibitors with mass variations of 5–160 KDa. Potatoes synthesize a large amount of protease inhibitors which are relatively thermostable and have low Ki [55–57]. Interested researchers should investigate whether potato products can directly suppress infection or reduce the severity of COVID-19 disease.

In traditional medicine, especially in Asian countries, numerous herbs or natural remedies are widely used to fight various infections, including Coronavirus [55, 58, 59]. The structure and mechanism of action of different synthetic inhibitors of viral proteases are known [55, 58], and the role and anti-viral effect of other components have been analyzed [49, 55, 60–63]. In light of these studies, the effect of plant foods should be investigated.

CONCLUSION / ЗАКЛЮЧЕНИЕ

After 15 months of the COVID-19 pandemic, the global community has learned some key lessons. A quantitative analysis was carried out, using large statistical samples, of the influence of the staple food components on the development of infection with the SARS-CoV-2 virus and the severity of the COVID-19 disease. A direct correlation was found between the severity of the development of COVID-19 and the quantity of dietary proteins, fats and sugars consumed.

Analysis using big epidemic data showed that in the case with the minimum rate of SARS-CoV-2 pathogenic outcomes, the level of ingested fats, sugars, and proteins of animal origin was low or not significantly higher than the WHO recommended. Countries with high consumption of soy or potato products had lower morbidity and mortality rates from COVID-19 than neighbors. A high intake of plant-based proteins was correlated with low severity of COVID-19. Perhaps, not only soy or potatoes, but also other dietary vegetables contain substances to help an organism resist pathogens, including the SARS-CoV-2 virus.

The established relationship between nutritional factors and the outcomes of SARS-CoV-2 infection requires detailed study. The over-consumption of essential nutrients may not be critical to the stages of transmission of infection, but to remove the reproduction of the Coronavirus. From the publications cited and this analysis of statistical data, it follows that the type of diet may be a decisive factor in development of the COVID-19 pathogenesis. Consequently, a specific recommendation arises to combat the pandemic. Models of national food-based dietary guidelines need to be developed.

The nature of found effects of dietary factors on the host-pathogen interaction should be proved by methods of nutritional biochemistry and molecular biology of metabolism.

Research using modern methods will help identify dietary components that can inhibit the replication cycle of the pathogenic SARS-CoV-2 virus. Establishing the nature and molecular structure of the antiviral factor will help in the rapid creation of the required etiotropic therapeutic agent.

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