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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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DIABETES MELLITUS AND COVID-19: TODAY'S CHALLENGES

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Abstract.

Patients with diabetes have more complications and higher mortality from COVID-19. This is due to the fact that diabetes impairs the immune response. Hyperglycemia causes a violation of the immune response, which in turn cannot control the spread of pathogenic microorganisms and therefore patients with diabetes are more susceptible to infections. The purpose of the work – analysis of bibliometric databases of literature on new developments in diabetes and COVID-19 and focused on clinical recommendations for patients with diabetes infected with COVID-19. The search methods included a literature review of scientific articles that studied diabetes and COVID-19. According to the results of the analysis of the articles obtained as a result of the search in the PubMed, SCOPUS, Web of Science, MedScape databases, a combination of the terms “diabetes and SARS-CoV-2”, “diabetes and COVID-19”, “pathogenesis of diabetes in case of COVID-19”, "pancreas", "clinical features", "diagnosis", "treatment", "clinical recommendations", we found 32 messages from 2020 to 2022. The main parameters of the study were outpatients and inpatients with diabetes and COVID-19 of middle and elderly age starting from 46 years and up to 82 years of age in France, China, the USA, Great Britain, in which a nationwide, retrospective, population-based study was conducted. The following concomitant diseases are included in the main studies: arterial hypertension, cardiovascular diseases, heart failure, chronic kidney disease, chronic obstructive pulmonary disease, myocardial infarction, cerebrovascular diseases. Issues of pathogenetic mechanisms in DM and COVID-19, as well as management of patients with DM and COVID-19 are highlighted.

Key words. Diabetes mellitus, COVID-19, SARS-CoV-2, angiotensin-converting enzyme-2, cytokines.

Introduction.

In November 2019, the epidemic that arose in China in the city of Wuhan exceeded all previous epidemics in terms of its scale [1]. The new respiratory disease was named - COVID-19 (Coronavirus Disease 2019) [2]. The causative agent is the SARS-CoV-2 coronavirus [3]. In Ukraine, for the first time, COVID-19 was registered in Chernivtsi on February 29, 2020, in a man who had visited Italy the day before [4-6].

As of March 23, 2023, there are more than 680 million confirmed cases of COVID-19 worldwide, including 6,824,670 deaths. The updated number of cases of the disease in English-language sources in the form of an interactive map with coverage of confirmed cases around the world is presented on the websites of the World Health Organization (WHO) and the European Center for Disease Prevention and Control (European Center for Disease Prevention and Control , ECDC) [7].

In most medical recommendations regarding COVID-19, it is emphasized that diabetes - is one of the categories of high risk of the disease, because data from Chinese scientists showed an increased mortality rate in this category of patients [8].

Given the high prevalence of cardiovascular changes, obesity, and hypertension in patients with DM, it is not fully understood whether DM is an independent risk factor in patients with COVID-19 or whether there is a combined adverse effect of one or more diseases in addition to the primary disease.

Given the high rate of deaths in DM and COVID-19, clinical recommendations for such patients are necessary, for understanding which it is necessary to clarify the pathogenetic mechanisms of DM and COVID-19, which became the subject of our search.

Search strategy.

The search methods included a literature review of scientific articles that studied diabetes and COVID-19. According to the results of the analysis of the articles obtained as a result of the search in the PubMed, SCOPUS, Web of Science, MedScape databases, a combination of the terms “diabetes and SARS-CoV-2”, “diabetes and COVID-19”, “pathogenesis of diabetes in case of COVID-19”was used -19", "pancreas", "clinical features", "diagnosis", "treatment", "clinical recommendations", we found 32 messages from 2020 to 2022. The inclusion criteria for literature sources were information on changes in the body of diabetes patients infected with SARS-CoV-2 coronavirus to summarize new advances in diabetes and COVID-19 and to focus on clinical recommendations for patients with diabetes.

We also got the full text relevant cross-references by search results. In addition, we obtained access to currently available scientific literature and recommendations on the websites of the World Health Organization and the Centers for Disease Control and Prevention (CDC). Literary data related to morbidity, pathogenesis, clinical features, diagnosis, and treatment were studied and summarized.

Discussion.

In November 2002, in the south of China, in the village of Foshan, atypical pneumonia was first detected, which spread to 37 countries. In March 2003, the WHO defined this disease as an acute respiratory syndrome - SARS (Severe Acute Respiratory Syndrome). Since this syndrome was clinically similar to known atypical pneumonias, SARS was called atypical pneumonia. For the first time, the term "atypical pneumonia" was used in 1938 by a virologist, Hobart Rayman, describing lung inflammation caused by mycoplasmas, chlamydia, and legionella [6]. In 2002, the causative agent of the disease was the SARS-CoV virus

from the Coronaviridae family, which previously also caused the SARS epidemic in 2002 and the MERS epidemic in 2008 [2-5].

In Ukraine, for the first time, COVID-19 was registered in Chernivtsi on February 29, 2020, in a man who had visited Italy the day before [7]. The People's Republic of China submitted information about the SARS-CoV-2 virus to the WHO at the end of December 2019 [8], and Chinese scientists published the sequence of the SARS-CoV-2 genome [9]. This made it possible to start work on diagnostics and the creation of vaccines to fight against COVID-19. Given the high prevalence of cardiovascular changes, obesity, and hypertension in patients with DM, it is not fully understood whether DM is an independent risk factor in patients with COVID-19 or whether there is a combined adverse effect of one or more diseases in addition to the primary disease.

According to the results of the Chinese Center for Disease Control and Prevention, as of February 11, 2020, among 73,215 cases of COVID-19, the number of men and women among patients was- 49% to 19.51%, respectively. Therefore, men are more prone to COVID-19 [10]. COVID-19 is observed in all age groups, the average age of patients is 47-59 years, and a more severe course is observed with comorbid conditions [11,12].

COVID-19 and glucose metabolism.

Hyperglycemia increases SARS-CoV-2 replication, and glycolysis supports SARS-CoV-2 replication through production of mitochondrial reactive oxygen species and activation of hypoxia-inducible factor 1α 20. Thus, hyperglycemia supports the proliferation of the virus. DM is a predictor of morbidity and mortality in patients with SARS. In such patients, regulation of the immune response is disturbed, which leads to severe and extensive lung pathology [13]. The presence of complications of DM, CVD, HF, and CKD increase mortality from COVID-19. National and retrospective cohort studies conducted in Europe and the USA are presented in Table 1.

A nationwide cohort study conducted in France showed that the average age of patients was 69.8±13.0 years, the number of men was 2 times higher compared to women, with a glycemic status of 8.1±1.9, arterial hypertension prevailed among concomitant diseases (77%), cardiovascular diseases (41%), chronic kidney disease (33%) and death occurred on the 7th day in 29% of patients. A retrospective cohort study conducted in China showed that the mean age of patients was 64.0 years, the largest number of patients (24%) had a glycemic profile of >9.0, hypertension (57%) and cardiovascular diseases were also predominant among comorbidities (21%), 18% of patients were in the intensive care unit, while only 8% without diabetes, mortality was 20%. A retrospective cohort study conducted in the USA showed the average age of patients to be 67.9±13.7, the number of women and men was almost the same (649/630), the glycemic profile was 7.5±2.0, among concomitant diseases hypertension prevailed (91%), cardiovascular diseases (59%) and mortality was 33%.

Summarizing the results of the conducted research, we can say that patients with a high risk of a severe form of COVID-19 are elderly, male, have hypertension and cardiovascular diseases among the concomitant diseases. National and retrospective cohort studies in Europe and the United States have shown that cardiovascular disease and diabetes are common among patients with COVID-19 who are hospitalized in the intensive care unit.

Pathogenetic mechanisms in diabetes and COVID-19.

To date, the pathogenesis of COVID-19 is unknown, but it may be similar to the pathogenesis of the SARS-CoV virus. Although the pathophysiological mechanisms have not yet been studied, it has been noted that fatal cases of COVID-19 have been observed in elderly people with concomitant diseases, in particular, in the presence of CVD, diabetes, and chronic lung diseases [13]. According to the results of the WHO, the mortality rate among patients with hypertension is 8%, among patients with diabetes - 9%.

Research published in the journal The Lancet Respiratory Medicine links this to taking drugs that change the shape of cells and make those cells more vulnerable to the SARS-CoV-2 coronavirus. The virus penetrates into such cells more easily, damages them more often, the course of the disease is more severe, and the risk of fatal consequences increases [14]. ACE blockers help lower blood pressure, but at the same time, by increasing the expression of ACE-2, they attract more new viruses. Interacting with ACE-2, the virus depletes it, developing symptoms of deficiency of this enzyme.

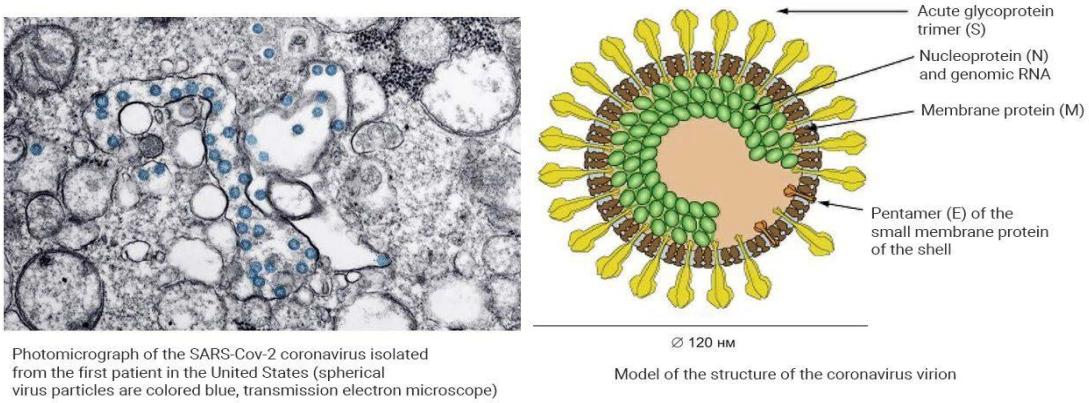
DM causes high morbidity and mortality worldwide. Such changes are caused by macro- and microvascular complications [15]. Influenza and pneumonia are often serious complications in elderly people with type 2 diabetes [16]. However, data on whether DM contributes to the susceptibility of the body to disease upon exposure to the virus and affects the outcome of infection or whether CVD and renal disease, which are often associated with DM, are the main causes of mortality remain controversial [17].

For SARS-CoV-2, a molecular mechanism of entry into the cells of the human body has been established. It has been studied that the coronavirus consists of 4 proteins: spike (S), membrane (M), nucleocapsid (N) and envelope protein (E). Spike protein (S) binds to receptors on the host cell membrane (Figure 1) [18].

In figure 2 shows the period of functioning of the SARS-CoV 2 virus. Upon entering the host cell, the carrier of genetic information - sense RNA is included in the translation process without the participation of additional enzymes. RNA is placed in the center and surrounded by structural proteins. S-type proteins have appendages (spikes) that look like a crown under a microscope, which is why the Coronaviridae family was so named. On the surface of the infected cell, the S-protein of the virus (acute glycoprotein trimer) binds to the ACE 2 receptor [19]. Subsequently, the stage of transformation (rearrangement) of the spike glycoprotein occurs with the help of the cell's own proteases (TMPRSS2, cathepsins, HAT, furin). After that, the ORF1a/b gene translation process begins. As a result of translation, polyproteins of large molecular weight are formed, which are subjected to chemical reactions, as a result of which the molecules are divided into parts by viral proteases. After that, 16 non-structural proteins are formed, which are responsible for virus replication. A replication complex is formed on vesicles with a double membrane. The replication complex produces genomic RNA of the virus and subgenomic RNAs, which encode structural proteins S, E, M, N, as well as additional

Table 1. *Clinical characteristics and outcomes in patients with diabetes and COVID-19.*

Region	Research design	Age (years; mean or median)	Number (women/ men)	Glycaemic status, HbA_{1C} (%) (proportion)	Comorbidities (%)	Main findings
Diabetes mellitus						
France	Nationwide observational cohort study	68,9±13,0	1317 (462/ 855)	8,1±1,9	HTN (77) CVD (41) HF (12) CKD (33) COPD (10)	Primary outcome (MV, death on day 7): 29% Risk factors for primary outcome: BMI Risk factors for mortality: older age, microvascular and macrovascular complications
China	Retrospective cohort study	64,0 (56,2-72,0)	153	<7,0 (16%) 7,0-8,0 (13%) 8,0-9,0 (12%) >9,0 (24%)	HTN (57) CVD (21) CKD (4) COPD (5)	ICU admission: 18% (non-DM 8%) In-hospital death: 20% (non-DM 11%) Risk factors for mortality: age ≥70 years, HTN
USA	Retrospective cohort study	67,9±13,7	1276 (649/ 630)	7,5±2,0	HTN (91) CVD (59) CKD (43) COPD (14)	Death: 33% Risk factors for mortality: insulin treatment before admission, COPD, male sex, older age, higher BMI
T1DM						
UK (England)	Population-based cohort study	46,6±19,6	264390 (114710/ 149 680)	<6,5 (7%) 6,5-7,0 (8%) 7,1-9,9 (50%) >10,0 (12%)	HTN (SBP >140 mmHg (17); antihypertensive agents (44)) CKD (10) MI (1) Stroke (1) HF (3)	COVID-19-related deaths: 464 Risk factors for mortality: male sex, older age, renal impairment, non-white ethnicity, socioeconomic deprivation, previous stroke, previous HF, HbA_{1c} ≥10.0% (reference range 6.5–7.0%) BMI (U-shaped, reference range 25.0–29.9 kg/m^2)
France	Nationwide observational cohort study	56,0±16,4	56 (25/31)	8,4 (7,6 -9,5)	Microvascular complications (49) Macrovascular complications (33) CKD (29) COPD (4)	Primary outcome (MV, death on day 7): 23% (age <55 years 12%; 55–74 years 24%; ≥75 years 50%)
T2DM						
China	Retrospective cohort study	62 (55-68)	952 (442/ 510)	Glucose 8.3 mmol/l (6.2–12.4 mmol/l)	HTN (53) CHD (14) CeVD (6) CKD (5) COPD (1)	Well-controlled versus poorly controlled T2DM
UK (England)	Population-based cohort study	67,5±13,4	2874 020 (1267590/ 1606430)	<6,5 (25%) 6,5-7,0 (21%) 7,1-7,5 (13%) 7,6-9,9 (25%) ≥10,0 (11%)	HTN (SBP >140 mmHg (67); antihypertensive agents (76)) CKD (18) MI (2) stroke (2) HF (5)	COVID-19-related deaths: 10,525 Risk factors for mortality: male sex, older age, renal impairment, non-white ethnicity, socioeconomic deprivation, previous stroke, previous HF, HbA_{1c} ≥7.5% or <6.5% (reference range 6.5%–7.0%), BMI (U-shaped, reference range 25.0–29.9 kg/m^2)



Photomicrograph of the SARS-Cov-2 coronavirus isolated from the first patient in the United States (spherical virus particles are colored blue, transmission electron microscope)

Model of the structure of the coronavirus virion

Figure 1. *Photomicrograph of the SARS-CoV-2 coronavirus and Model of the structure of vibrio coronaviruses.*

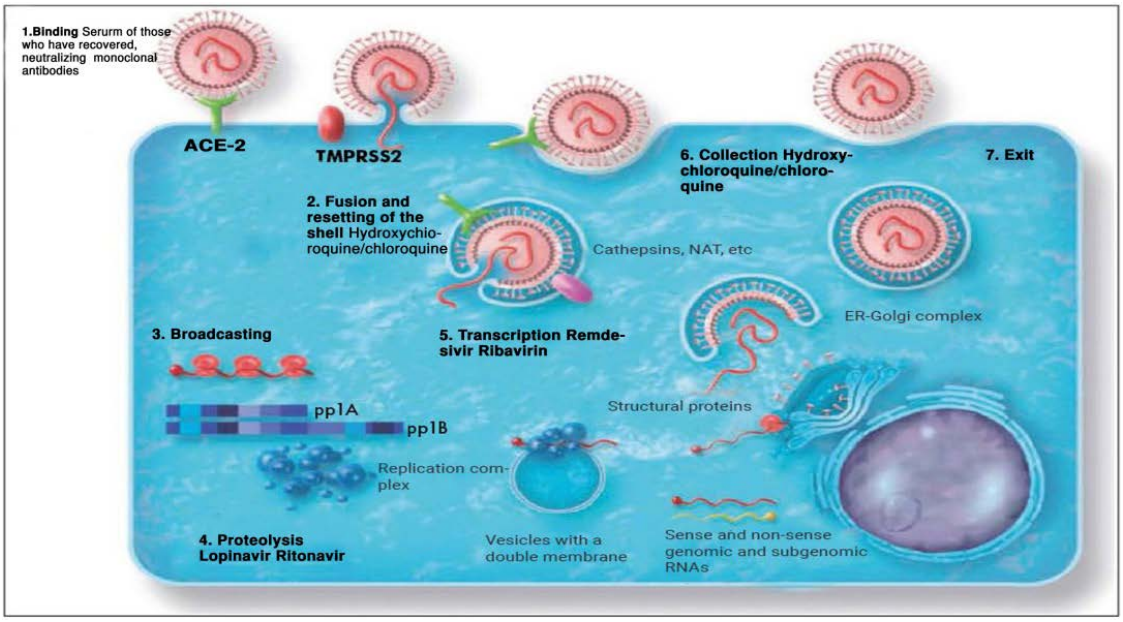


Figure 2. *Term of functioning of the SARS-CoV 2 virus.*

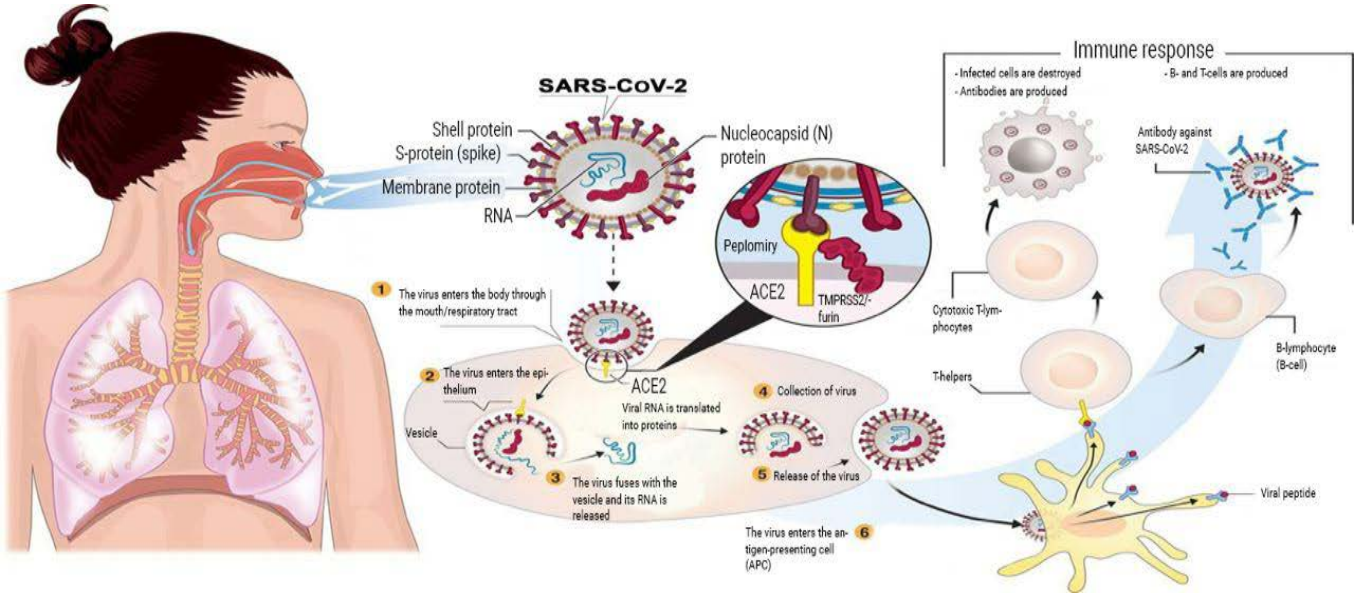


Figure 3. *Functioning of the SARS-CoV 2 virus in the host's body.*

ORF genes that play the role of modulators of the immune response. New viral particles are collected on the membranes of the endoplasmic reticulum and the Golgi apparatus, after which they are pushed out of the cell as its secretory products.

The SARS-CoV 2 virus penetrates and multiplies in the cells of the respiratory epithelium. The variety of clinical manifestations varies from an asymptomatic infection to the development of severe lung damage and acute respiratory distress syndrome (ARDS), requiring mechanical ventilation [20]. The severity of the disease is determined both by the direct damaging effect of the virus and by the nature of the host's immune response [21]. The functioning of the SARS-CoV 2 virus in the host's body is presented in figure 3. When S-glycoproteins bind to ACE 2 receptors, the virus causes a decrease in receptor function, which leads to an imbalance of the renin-angiotensin system and causes the development of diffuse alveolar damage.

Multiple metabolic and vascular disorders occur in diabetes, which delay the reaction to pathogenic microorganisms [22]. Hyperglycemia suppresses the immune system [23,24]. SARS-CoV-2 infects circulating cells of the immune system and increases the programmed cell death of lymphocytes (CD3, CD4 and CD8 T cells), which causes lymphocytopenia [25]. Decreased T-cell function and hyperfunction of neutrophils lead to hyperproduction of a number of pro-inflammatory cytokines (IL1β, IL-2, IL-6, IL-7, IL-8, IL-17, MCP1, TNFα, etc.), which is called the "cytokine storm" syndrome [26].

The presence of spike-like protein in patients with DM causes hypercytokinemia, a "cytokine storm" [27]. Hyperglycemia and insulin resistance increase the secretion of pro-inflammatory cytokines [28]. WHO identifies three main conditions that put people at higher risk of complications and death - heart disease, lung disease, and diabetes.

Infection with the SARS-CoV 2 virus leads to an increase in the level of inflammatory mediators in the blood, including lipopolysaccharides, inflammatory cytokines, toxic metabolites. Alteration of natural killer cell activity and IFNγ production increases interstitial and/or vascular permeability to proinflammatory products, increases reactive oxygen species (ROS) production, leading to pulmonary fibrosis, acute lung injury, and acute respiratory distress syndrome (ARDS). Increased expression of angiotensin II leads to activation of the renin-angiotensin-aldosterone system by the virus. In turn, reactive oxygen species and the renin-angiotensin-aldosterone system activated by the virus cause insulin resistance, hyperglycemia, damage to the vascular endothelium, which leads to the development of cardiovascular complications, thromboembolism, and disseminated intravascular coagulation (DIC). Infection also causes an increase in fibrinogen and D-dimer, which leads to an increase in blood viscosity, damage to the endothelium of vessels, cardiovascular complications, thromboembolism and disseminated intravascular coagulation (DIC) (Figure 4).

Recently, there have been reports of caution in patients with CVD when taking ACE inhibitors. Since ACE-2 receptors are the "entrance gate" for the coronavirus, taking ACE inhibitors and ARBs increases the risk of contracting a coronavirus infection.

Many elderly people use ACE inhibitors and ARBs to lower blood pressure, which causes an increase in the number of ACE-2 receptors, so such people are much more susceptible to the virus. This explains the high infection and mortality rates in the elderly with concomitant hypertension who use ACE inhibitors, which cause the proliferation of ACE-2 receptors, which are targets for COVID-19. In addition, the elderly often have

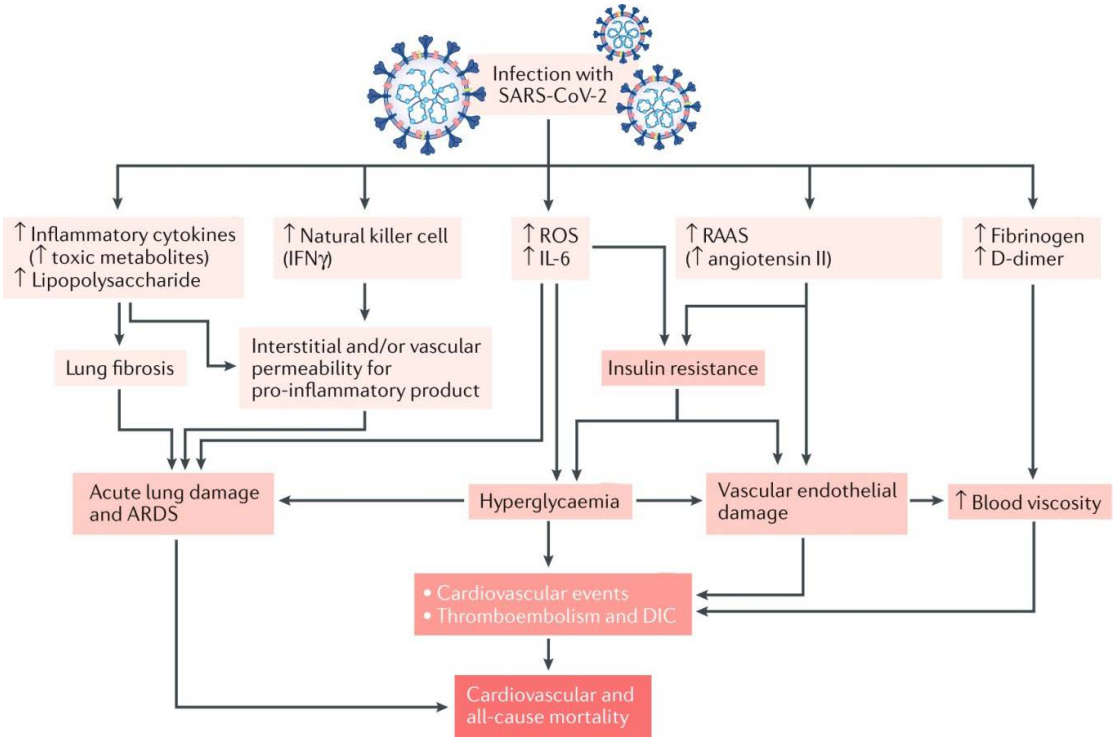


Figure 4. *Pathogenetic mechanisms in diabetes and COVID-19.*

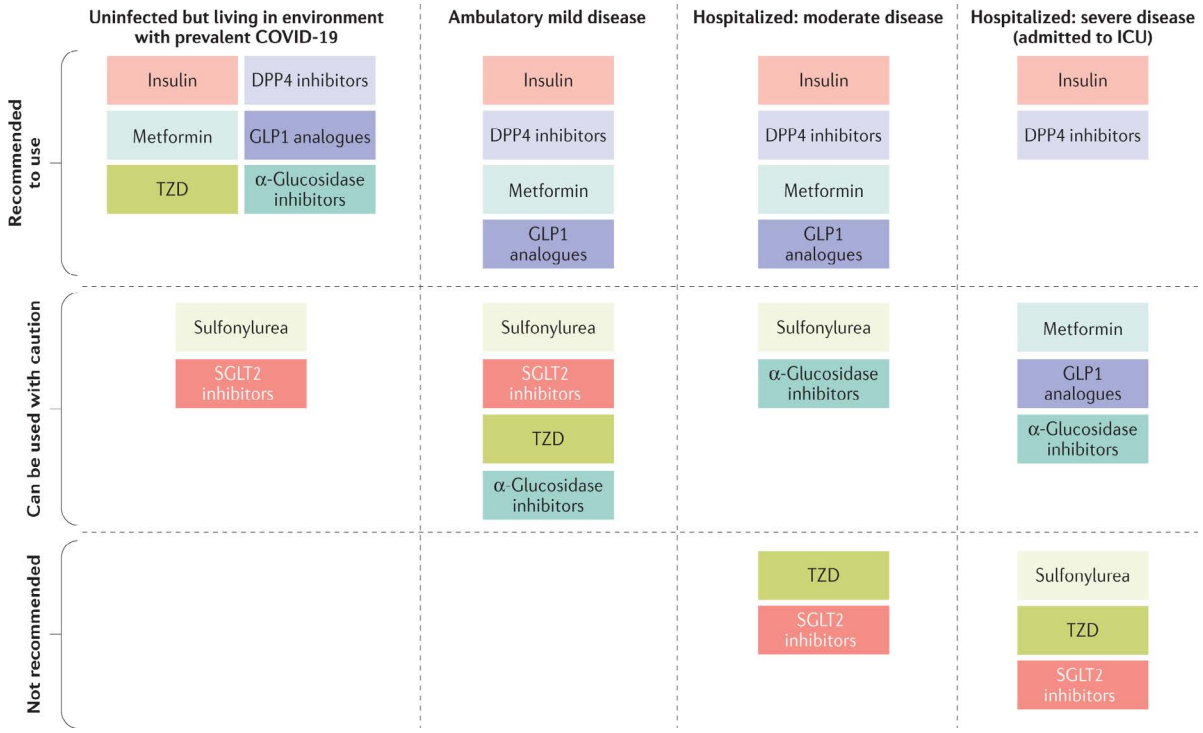


Figure 5. *Use of antidiabetic medications in patients with DM and COVID-19.*

chronic diseases: heart, blood vessels, liver, kidneys, often in combination with diabetes. Accordingly, a significant increase in the load on them in the presence of a viral infection causes negative consequences.

Management of DM.

An extremely important element of development is ACE-2, which plays the role of the SARS-CoV-2 receptor [29,30]. There is an assumption that insulin can cause excessive expression of ACE receptors [31,32], which increases the risk of developing complications during infection in patients with diabetes (Figure 5).

Acute hyperglycemia is possible in patients with DM when combined with COVID-19, which may be exacerbated by insulin resistance associated with inflammation, thus prompt and effective provision of appropriate glycemic control is necessary [26]. According to Drucker's review, analogs of dipeptidyl peptidase DPP4 and glucagon-like peptide GLP1 are recommended for patients with mild and moderate symptoms, as these drugs have proven glucose-lowering effectiveness in hospital settings, as well as in outpatient clinics [27]. However, there are insufficient data to support the use of these drugs instead of insulin in critically ill patients with diabetes and COVID-19 [28].

Thiazolidinediones are agonists of the γ receptor, which regulates the transcription of genes involved in glucose and lipid metabolism. In animal studies, thiazolidinediones have been found to reduce insulin resistance. In a review of randomized controlled trials comparing thiazolidinediones with placebo for the prevention of stroke and vascular disease in stroke survivors, treatment with thiazolidinediones reduced the incidence of recurrent stroke compared with placebo [29].

Sodium-glucose cotransporter 2 (SGLT2) inhibitors work on the kidneys to lower blood glucose levels and are used to treat type 2 diabetes. SGLT2 reduces the infiltration of inflammatory cells into arterial plaques and decreases the mRNA expression of some cytokines and chemokines, such as TNF, IL-6, and monocyte chemoattractant protein 1 (MCP1) [24].

Currently, many scientists are reviewing the prescription of drugs that reduce sugar levels in patients with diabetes and COVID-19. Insulin remains the only therapy for people with diabetes [25]. Metformin and sulfonylurea drugs do not interact with ACE-2, ADAM17, so they can be safely used in mild cases of COVID-19 [26]. The use of GLP-1 receptor agonists should be discontinued in patients with hemodynamic instability, renal and gastrointestinal dysfunction. Such therapy can cause hypovolemia and regurgitation [27]. With a severe course of COVID-19, the use of sulfonylurea drugs requires control of the level of glucose in the blood. Therefore, sulfonylurea drugs are replaced by insulin [28]. Thiazolidinediones cause fluid retention and increasing systemic edema. They are contraindicated in patients with high/low blood pressure, high/low heart rate (pulse), loss of consciousness/confusion, impaired liver, or heart function [29].

To date, the risks associated with taking aspirin have not been described. However, myocardial damage is a serious manifestation of COVID-19, acute myocardial ischemia has not been clearly described [25].

Currently, there is no direct evidence regarding the use of statins in patients with diabetes and COVID-19 [26]. There is information about increased liver and muscle enzymes associated with COVID-19 [27]. Therefore, individual therapy of patients with diabetes mellitus and COVID-19 is currently being used, considering indications for the appointment of statins, interactions with antiviral drugs [28].

Over the past 2 years, new information has emerged regarding the use of dexamethasone in critically ill patients

with COVID-19 who are on mechanical ventilation, which has shown good results in reducing mortality in such patients [29].

According to a published report in the journal Nature, remdesivir prevents the infection of human cells by SARS-CoV-2 in vitro [30]. Previously, the US Food and Drug Administration (FDA) approved the use of remdesivir only for use in patients with severe COVID-19 to improve quality of life. Currently, the FDA has approved the emergency use of remdesivir, which shortens the course of the disease in patients with less severe forms of the disease. Remdesivir, a nucleotide analog inhibitor of RNA-dependent RNA polymerase, increased glycemia and increased insulin resistance in mice fed a high-fat diet [31]. In contrast, the increase in blood glucose levels was similar between the remdesivir and placebo groups in two randomized clinical trials with multiethnic groups and Chinese patients [31]. Thus, more evidence is needed to clarify its effects on glucose metabolism.

The antiviral drug favipiravir, developed by Fujifilm Toyama Chemical in Japan, has shown results in treating mild-to-moderate COVID-19. It has been used in Japan to treat influenza and has been approved as an experimental treatment for COVID-19. The drug likely shortens the duration of the virus and also improves the condition of the lungs in patients with COVID-19. The clinical effectiveness of this drug continues to be investigated [32]. However, the search for drugs to treat COVID-19 is ongoing, and these drugs may affect glucose metabolism in diabetes.

Conclusion.

1. Patients with DM and comorbid conditions are at high risk of progression and severe course of COVID-19.
2. SARS-CoV 2 increases the level of inflammatory mediators in the blood, increases the production of reactive oxygen species, which leads to acute lung damage and acute respiratory distress syndrome.
3. In severe cases of COVID-19, insulin, and dipeptidyl peptidase 4 inhibitors are recommended; metformin and sodium-glucose cotransporter 2 inhibitors should be discontinued.
4. Patients with diabetes and COVID-19 should follow general prevention rules, monitor glucose levels more often, eat well, and control other risk factors.

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