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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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RELATIONSHIP BETWEEN SOME INFLAMMATORY MARKERS AND BACTERIAL INFECTIONS AMONG COVID-19 PATIENTS

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Abstract. Fifty blood samples were collected from patients who were confirmed to have COVID-19 by conducting a diagnostic test using real-time RT-PCR for the direct qualitative detection of the Coronavirus when the patients attended the private clinics at Al Rabeea Private Hospital in Mosul for the period from the beginning of March to the end of May 2021. The patients' ages range from17-59 years, with 23 males (46%), and 27 females (54%). The blood samples were taken before giving any type of treatment for blood culture, biochemical, and immunological tests. Bacteremia is investigated to determine the types of bacteria that cause bacteremia, biochemical tests such as D-dimer, S. Ferritin, CRP, Protein S, Protein C, FBS, LDH, Blood Urea, Serum Creatinine, SGOT & SGPT, and immunological tests such as blood group, IgG & IgM, IL-1B, IL-6, TNF-α alpha, ASOT, ESR, C3, and C4. In this study, the relationship between bacteremia and the types of biomarkers used is determined in addition to the relationship of bacteremia to the patient's age, sex, SPO2, and body temperature. More accurate comparison is also accomplished in cases of bacteremia by adopting the types of bacteria isolated if they were gram-positive or gram-negative. The results of this study show an increase in the severity of COVID-19 disease caused by a secondary bacterial infection. This is determined by measuring several biomarkers used in this study and also by performing bacteriological tests to document bacteremia by blood culture. Also, these results can be adopted in future studies concentrating on the molecular level to determine the genetic changes associated with viral infection with or without secondary bacterial infection to develop an effective treatment protocol.

Key words. COVID-19, Blood culture, Bacteremia, Biomarkers.

Introduction.

The first appearance of infection with Coronavirus in Wuhan City in China was in December 2019, which was initially named by Chinese scientists as SARS-COV-2, and after the disease spread all over the world, the name COVID- 19 was given by the World Health Organization (WHO) in February 2020 [1,2]. According to the statistics of WHO about confirmed COVID-19 cases and confirmed deaths due to worldwide infection, it is documented that there were more than 160 million confirmed cases of infection and more than 3 million confirmed deaths. The most serious symptoms are difficulty in breathing, shortness of breath, difficulty in speaking and movement, and chest pain [3-5]. It should be noticed that data and reports indicate not only the infection with COVID-19 is the reason for the disease to develop into severe infections, but also secondary bacterial infection [6,7]. One of the difficulties that physicians face is the ability to distinguish between symptoms of COVID-19 and bacteremia or sepsis, due to the similarity of symptoms such as fever, cough, and muscle pain[8-10]. One of the most important complications of bacteremia is a multi-organ failure, which can lead to patient's death, and as indicated by one of the studies, the patients' death by COVID-19 is due to infection with *Staphylococcus aureus* bacteria for 14-30 days after the first positive blood culture [11]. The complications of secondary infections associated with COVID-19 and the variation in disease sign that the doctors are in the biggest challenge in managing the development of the clinical case and choosing the treatment protocols because bacterial infections are an essential element in enhancing the severity of the disease and the high mortality rate; and on the other hand, the challenge is the heterogeneity among the patients in many respects, such as different age groups, gender, and blood group and the incidence of chronic diseases in the elderly [12,13]. Despite, the use of some biomarkers for measuring the levels in normal and pathological conditions becomes beneficial, and the levels of these biomarkers in cases of COVID-19 and secondary bacterial infections may be useful in determining the severity of the disease, treatments used, and evaluation response to treatments [14].

This study aims to determine the relationship between some biomarkers and the severity of COVID-19 disease. The different levels of biomarkers were also measured and evaluated in the case of bacteremia, also it was measured in different types of bacteria, whether they were Gram-positive or Gram-negative. The biomarkers identified and selected in this study are the biochemical tests such as D-dimer, S. Ferritin, CRP, Protein S, Protein C, FBS, LDH, Blood Urea, Serum Creatinine, SGOT & SGPT, and immunological tests such as Blood group, IgG & IgM, IL-1B, IL-6, TNF-α alpha, ASOT, ESR, C3, and C4. In addition to measuring the rates of biomarkers according to the patient's different risk factors such as gender, age, and blood groups.

Materials and Methods.

In this study, 50 blood samples were collected from patients who were confirmed to have COVID-19 by conducting a diagnostic test using real-time RT-PCR (RIDA®GENE SARSCoV-2) technology for the direct qualitative detection of the Coronavirus when they attended private clinics at Al Rabeeh Private Hospital in Mosul after symptoms appearance during the period from the beginning of March to the end of May in 2021 for 50 patients, their ages range between 17-59 years, and the number of men was 23 (46%) and the number of women was 27 (54%). Venous

blood samples were taken before giving any type of treatment used in the treatment protocols. And blood samples were taken from each patient, sufficient for bacteremia, biochemical, and immunological tests, according to the internationally approved methods. The three types of tests (biochemical, immunological, and bacteriological) are considered Biomarkers. Bacteremia was investigated following the method of Buckland, Kessock-Philip, and Bascomb (1983) [15], biochemical tests D-dimer (Guangzhou KOFA Biotechnology Co., Ltd), S. Ferritin, CRP, (BIOGENIX INC. PVT. LTD), Protein S (LSBio- LS-F12426), Protein C (Chromogenix Coamatic® Protein C), FBS, LDH, Blood Urea, Creatinine (Anamol Laboratories Pvt. Ltd), SGOT (MAX WIN HEALTH CARE PVT. LTD.) & SGPT (Anamol Laboratories Pvt. Ltd)], and immunological tests [Blood group (Max win health care Pvt ltd), IgG & IgM (Cygnus technologies), IL-1β, IL-16 & TNF-α (Beijing Solarbio Science & Technology Co., Ltd), ASOT (MAX WIN HEALTH CARE PVT. LTD.), C3 (LSBio- LSF4278) & C4 (LSBio- LS-F22483)].

In this study, the relationship between bacteremia cases and reading the ranges of biochemical and immunological tests is determined in addition to the relationship of bacteremia to the patient's age, sex, and blood groups of the patients. A more accurate comparison is also made in cases of bacteremia by adopting the types of bacteria isolated in this study whether they were gram-positive or gram-negative bacteria by reading the ranges of biomarkers.

Statistical analysis.

Two proportional Z-tests are used to compare the significance of the difference between bacteremia and different biomarkers. The $\chi 2$ test is used to assess the association of blood groups with different biomarkers. The level of statistical significance was set at level 5% with an alpha error of <0.05.

Results.

The studied biomarkers were divided into three categories of risk factors such as age, gender, and blood type, biochemical tests represent the second section of biomarkers, and the last section is immunological tests. The effect of COVID-19 infection on the studied biomarkers, as well as the effect of secondary bacterial infections on biomarkers in COVID-19 patients, was determined.

Regard the difference in sex and the difference in age groups did not show any significant difference, neither in the case of infection with Covid 19 nor the case of bacterial concomitant infection, while the number and percentage of people with blood group A are 24 (48%) in COVID 19 patients with a statistically significant difference at (P<0.0001), more than blood group B and O being 12 (24%) for each type, and blood group AB are 2 (4%) as shown in Table (1).

Complications of COVID-19 infection, especially secondary bacterial infections, are of important concern and they resemble evidence of bacterial contamination in the blood (bacteremia) of an infected person with COVID-19. This is a strong indicator of secondary infection.

The results show that 32 (64%) of the cases infected with COVID-19 developed secondary infections, which were mostly bacterial, and gave a significant difference at (P<0.04) as shown in Table (2).

Table 1. Relationship between blood group types and the percentage of COVID-19 patients.

Blood group	Number	%	*P* value
A	24	48.0	**0.0001**
B and O	12	24.0	
AB	2	4.0	

Table 2. The rate of bacteremia (Secondary infection) between COVID-19 patients.

Bacteremia	Number	Percentage	*P* value
Absent	18	36.0	**0.04**
Present	32	64.0	

In this study, the percentage of bacteremia in COVID-19 patients has been determined according to different age groups, sex, and blood groups, as well as its percentage with normal and abnormal ranges for the Biomarkers, studied in this research, calculated out of the total number of samples. Infections with bacteremia show a significant difference between normal and abnormal ranges in the Biochemical Biomarkers (SGOT) and immunological Biomarkers (IgM and IL-6) as shown in Tables (4&5).

In addition, the incidence of Gram-positive bacteria of 26 (52%) and Gram-negative bacteria of 6 (12%) are calculated from the total number of samples. The incidence of bacteremia with gram-positive bacteria is 26 (81.25%) and the incidence of gram-negative bacteria is 6 (18.75%) out of the number of bacteremia cases. There is a significant difference between normal and abnormal ranges in the Biochemical Biomarkers (S. Ferritin, CRP, FBS, SGOT and, SGPT) and immunological Biomarkers (IgM, SPO2, body temperature, ESR, IL-6 and, ASOT,) as shown in Tables (4&5).

Discussion.

Viral infections are often associated with secondary bacterial infections [16], and this is what some studies have indicated that infection with viruses that infect the respiratory tract, including COVID-19, may lead to interference in clinical, biochemical, and immunological features, and expose patients to the risk of secondary infection. Thus, it is considered one of the complications of COVID-19, and this is what complicates clinical findings, diagnosis, and treatment [7]. However, there is little data regarding bacteremia rates, due to the treatments used to treat COVID-19 patients including antibacterial [9]. For this reason, the blood samples were taken in this study from patients before starting treatment. According to the findings of this study, 64 % of COVID-19 patients were infected with secondary bacterial infections, with a significant difference at (p<0.04) as shown in Table (2), and the percentage of infection with gram-positive bacteria (84.38%) including coagulase-negative bacteria with (18.75%) and Staphylococcus aureus with (65.63%), while the percentage of infections with gram-negative bacteria constituted (15.62%). These results are close to the results of some studies that confirmed that infection with Gram-positive bacteria including Staphylococcus aureus, is more common among cases of COVID-19, followed by the other types including Pseudomonas aeruginosa. Staphylococcus aureus is one of the causes of secondary pneumonia, and the

Table 3. The Relationship between Bacteremia in COVID-19 patients and risk factors.

Risk factors		**Range**	**Bacteremia+ No (%)**	**Bacteremia- No (%)**	***P* value**	**Bacteremia No (%)**		***P* value**
						gr^+	gr^-	
1	**Age**	**17-30 Y.**	10(20%)	5(10%)	0.9	9(28.12%)	1(3.125%)	0.4
		30-45 Y.	7(14%)	8(16%)	0.2	5(15.63%)	2(6.25%)	0.5
		> 50 Y.	15(30%)	5(10%)	0.3	12(37.5%)	3(9.375%)	0.9
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
2	**Sex**	**Male**	12(24%)	10(20%)	0.2	10(31.25%)	2(6.25%)	0.8
		female	20(40%)	8(16%)		16(50%)	4(12.5%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
3	**Blood group**	**A**	15(30%)	7(14%)	0.6	11(34.38%)	4(12.5%)	0.3
		B	9(18%)	4(8%)	0.4	8(25%)	1(3.125%)	0.5
		AB	3(6%)	1(2%)	0.6	2(6.26%)	1(3.125%)	0.5
		O	5(10%)	6(12%)	0.1	5(15.62%)	0.0(0.0%)	0.2
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	

Table 4. The Relationship between Bacteremia in COVID-19 patients and Biochemical tests.

Biochemical Biomarkers		**Range**	**Bacteremia+ No (%)**	**Bacteremia - No (%)**	***P* value**	**Bacteremia No (%)**		***P* value**
						gr^+	gr^-	
1	**D-dimer**	**N.R.* up to 500 ng/ml.**	8(16%)	5(10%)	0.8	5(15.625%)	3(9.375%)	0.1
		> N.R.*	24(48%)	13(26%)		21(65.625%)	3(9.375%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
2	**S. Ferritin**	**N.R.* In male: 15-300 ng/ml In female: 15-200 ng/ml**	11(22%)	6(12%)	0.9	7(21.875%)	4(12.5%)	0.06
		> N.R.*	21(52%)	12(24%)		19(59.375%)	2(6.25%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
3	**CRP**	**N.R.* 9-800 pg/ml.**	9(18%)	7(14%)	0.4	5(15.625%)	4(12.5%)	**0.02**
		> N.R.*	23(46%)	11(22%)		21(65.625%)	2(6.25%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
4	**Protein S**	**N.R.* 70-140%**	21(42%)	16(32%)	0.8	16(50%)	5(15.625%)	0.3
		< N.R.*	11(22%)	2(4%)		10(31.25%)	1(3.125%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
5	**Protein C**	**N.R.* 60 -150 %**	25(50%	16(32%)	0.3	20(62.5%)	5(15.625%)	0.7
		< N.R.*	7(14%)	2(4%)		6(18.75%)	1(3.125%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
6	**FBS**	**N.R.* 60 - 120 mg/dl.**	8(16%)	7(14%)	0.4	4(12.5%)	4(12.5%)	**0.009**
		> N.R.*	24(48%)	11(22%)		22(68.75%)	2(6.25%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
7	**LDH**	**N.R.* 140 – 280 U/L**	10(20%)	4(8%)	0.5	7(21.875%)	3(9.375%)	0.3
		> N.R.*	22(44%)	14(28%)		19(59.375%)	3(9.375%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
8	**Blood Urea**	**N.R.* 140 – 280 U/L**	3(6%)	2(4%)	0.5	2(6.25%)	1(3.125%)	0.5
		> N.R.*	29(58%	16(32%)		24(75%)	5(15.625%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
9	**Serum Creatinine**	**N.R.* In male : 0.74 to 1.35 mg/dL In Female : 0.59 to 1.04 mg/dL**	16(32%)	9(18%)	0.8	13(40.625%)	3(9.375%)	1
		> N.R.*	16(32%)	9(18%)		13(40.625%)	3(9.375%)	
	Total		32(64%)	18(36%)		**26(81.25%)**	**6(18.75%)**	
10	**SGOT**	**N.R.* 8 – 45 U/L**	32(64%)	18(36%)	**0.0001**	26(81.25%)	6(18.75%)	**0.0000 1**
		> N.R.*	**0.0**	**0.0**		0.0(0.0%)	0.0(0.0%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
11	**SGPT**	**N.R.* 7 – 56 U/L**	32(64%)	17(34%)	0.2	26(81.25%)	6(18.75%)	**0.0000 1**
		>N.R.*	0.0(0.0%)	1(2%)		0.0(0.0%)	0.0(0.0%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	

**N.R.=Normal range*

Table 5. The Relationship between Bacteremia in COVID-19 patients and Immunological tests.

Immunological Biomarkers		**Range**	**Bacteremia+ No (%)**	**Bacteremia- No (%)**	***P* value**	**Bacteremia No (%)**		***P* value**
						gr^+	gr^-	
1	**IgM**	**< 1.0 IU/L**	0.0	0.0	**0.0002**	0.0(0.0%)	0.0(0.0%)	**0.0000 1**
		> 1.0 IU/L	32(64%)	18(36%)		26(81.25%)	6(18.75%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
2	**IgG**	**< 1.0 IU/L**	8(16%)	6(12%)	0.5	7(21.875%)	1(3.125%)	0.6
		> 1.0 IU/L	24(48%)	12(24%)		19(59.375%)	5(15.625%	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
3	**SPO2**	**90 – 100 %**	14(28%)	5(10%)	0.3	9(28.125%)	5(15.625%)	**0.03**
		< 90 %	18(36%)	13(26%)		17(53.125%)	1(3.125%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
4	**Body temp.**	**37-37.5 °C**	6(12%)	4(8%)	0.3	3(9.375%)	3(9.375%)	**0.03**
		> 37.5 °C	26(52%)	14(28%)		23(71.875%)	3(9.375%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
5	**ESR**	**N.R.* In male: 1-15 mm/h. In female: 1-20 mm/h.**	6(12%)	3(6%)	0.8	3(9.375%)	3(9.375%)	**0.03**
		> N.R.*	26(52%)	15(30%)		23(71.875%)	3(9.375%	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
6	**IL-1β**	**N.R.* 3-120 pg/ ml.**	28(56%)	16(32%)	0.9	22(68.75%)	6(18.75%)	0.3
		> N.R.*	4(8%)	2(4%)		4(12.5%)	0.0(0.0%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
7	**IL-6**	**N.R.* 2-80 ng/L**	32(64%)	18(36%)	**0.0001**	26(81.25%)	6(18.75%)	**0.0000 1**
		> N.R.*	0.0	0.0		0.0(0.0%)	0.0(0.0%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
8	**TNF-α**	**N.R.* 20-400 ng/L**	30(60%)	18(36%)	0.2	25(78.125%)	5(15.625%)	0.2
		> N.R.*	2(4%)	0.0		1(3.125%)	1(3.125%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
9	**ASOT**	**N.R.* 80-200 IU/L**	9(18%)	7(14%)	0.4	5(15.625%)	4(12.5%)	**0.02**
		> N.R.*	23(46%)	11(22%)		21(65.625%)	2(6.25%)	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
10	**C3**	**N.R.* 90-207 mg/dl.**	22(44%)	14(28%)	0.5	9(28.125%)	1(3.125%)	0.4
		< N.R.*	10(20%)	4(8%)		17(53.125%)	5(15.625%	
	Total		**32(64%)**	**18(36%)**		**26(81.25%)**	**6(18.75%)**	
11	**C4**	**N.R.* 17.4 -52.2 mg/dl.**	26(52%)	16(32%)	0.5	5(15.625%	1(3.125%)	0.9
		< N.R.*	6(12%)	2(4%)		21(65.625%)	5(15.625%)	
	Total		**32(64%)**	**18(32%)**		**26(81.25%)**	**6(18.75%)**	

**N.R.=Normal range*

spread of these bacteria and others in the lungs is attributed to a group of changes in immune responses including the production of cytokines that create suitable and attractive conditions for Staphylococcal and other bacteria by changes such as tissue damage and raise body temperature, for example, the changes in body temperature and a set of signals transfer the bacteria "Staphylococcus aureus" from the nasal environment into the lung, and this requires attention to modify treatment protocols [17], also, for Pseudomonas aeruginosa, it is an opportunistic bacteria that exploits the changes resulting from infection with COVID-19 and is responsible for infections in the upper respiratory tract [18]. In addition, recent studies have demonstrated that type I and III IFNs that are produced after bacterial infection may promote the persistence of SARS-CoV-2 infection due to the ACE-2 receptor used by the virus being a gene stimulated by interferon [19].

Studies have demonstrated that bacterial infections associated with COVID-19 infection are a fatal complication associated with worse health outcomes because of their impact on all body functions and delaying treatment may lead to septic shock [20]. One study confirmed that the death rate rose among patients with coronavirus and those with a secondary bacterial infection to 12.6% compared to 8.7% with influenza without an accompanying bacterial infection. The secondary bacterial infections associated with influenza were documented with increased mortality in the influenza pandemic of 1918, H2N2: 1957, H3N2:1968-1969, and H1N1: 2009-2010, in fact, due to pulmonary embolism and impaired breathing resulting from secondary bacterial infections, which may also lead to inhibition of activation of the host's immune defenses [17,21].

On the other hand, the results of this study showed that the most affected biomarkers among COVID19 patients with concomitant secondary bacterial infection compared to COVID-19 patients without secondary bacterial infection as shown in Tables (4 and 5). It has been proven that the following biomarkers were affected in the case of bacteremia (IgM, IgG, SPO2, Blood groups "A, B, and AB", body temperature, ESR, D-dimer, S-ferritin, IL-1β, TNF-α, CRP, ASOT, C3, C4, protein s, protein c, FBS, HDH, Blood urea, and serum creatinine), While the following markers were not affected or deviated from their normal levels in the case of bacteremia (IL-6, SGOT, and SGPT). However, it was found from the results that both types of infection with COVID-19 with or without bacteremia, didn't show a significant difference between them.

Both types of COVID 19 infection with or without bacteremia led to an effect on the deviation of biomarkers from their normal ranges, although in the case of COVID-19 infection associated with the secondary bacterial infection, the rates of deviation are greater and statistically significant at (<p 0.0 5 - 0.00001). Some biomarkers as shown in Tables (4&5) can be relied upon in diagnosing the severity of the disease and its development into more serious pathological complications, and also these results can be adopted in determining the direction of future studies on the molecular level to determine the genetic changes associated with viral infections and secondary bacterial infections to differentiate between viral infection and bacterial infection or combined infections to develop effective treatment protocols.

It is worth noting that the results of this research show that blood type O protects people from COVID-19 infection, while blood type A makes individuals more susceptible to infection. These results are in line with those of much other research. As with blood type O, it can be stimulated by natural antibodies against antigens that act as part of the innate immune response to neutralize virus particles. Alternatively, blood group A antigens can act as additional receptors for viruses, and those who can express these antigens on epithelial cells (exudates) are more likely to develop COVID-19 [22,23]. Although the results of our study are consistent with many studies, the generalization of these results and their dependence on blood type as part of the predictive model and a mechanism for sorting viral diseases and severity of disease or mortality but is not reliable because it needs to conduct large-scale surveys to make a database with Taking into account population differences in blood types and testing protocols.

One of the important results that were reached in this study is that infection with Covid-19 is a strong qualifying factor that makes the patient more predisposed to infection with bacteremia. The results of this study showed that the severity of Covid-19 disease is caused by secondary bacterial infection, which was determined by measuring many indicators Vital and also by performing bacteriological tests by culturing a blood sample to determine bacteremia.

Conclusion.

In conclusion, it is complicated to reveal the three-dimensional biological relationship between viral infection, secondary bacterial infection, and changes in host functions such as "biomarker rates, clinical, immunological and physiological pathway" in viral infection with or without bacterial infection. This study is the first in the city of Mosul that attempts to find the shortest way to diagnose and adopt the best treatment protocols based on the results of this study.

REFERENCES

1. Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A. The role of biomarkers in diagnosis of COVID-19–A systematic review. Life sciences. 2020;254:117788.
2. Zhou F. Y u T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395:1054-1062.
3. Ontario Ministry of Health and Long-Term Care. "COVID-19 Reference Document for Symptoms v7.0.". 2020: 19-22.
4. Larsen JR, Martin MR, Martin JD, Kuhn P, Hicks JB. Modeling the onset of symptoms of COVID-19. Frontiers in public health. 2020;8:473.
5. Aiyegbusi OL, Hughes SE, Turner G, Rivera SC, McMullan C, et al. Symptoms, complications and management of long COVID: a review. Journal of the Royal Society of Medicine. 2021;114:428-442.
6. Nag VL, Kaur N. Superinfections in COVID-19 patients: role of antimicrobials. Dubai Medical Journal. 2021;4:117-126.

7. Ippolito M, Simone B, Filisina C, Catalanotto FR, Catalisano G, et al. Bloodstream infections in hospitalized patients with COVID-19: a systematic review and meta-analysis. Microorganisms. 2021;9:2016.
8. Lardaro T, Wang AZ, Bucca A, Croft A, Glober N, et al. Characteristics of COVID-19 patients with bacterial coinfection admitted to the hospital from the emergency department in a large regional healthcare system. Journal of Medical Virology. 2021;93:2883-2889.
9. Hughes S, Troise O, Donaldson H, Mughal N, Moore LS. Bacterial and fungal coinfection among hospitalized patients with COVID-19: a retrospective cohort study in a UK secondary-care setting. Clinical Microbiology and Infection. 2020;26:1395-1399.
10. Bayo SM, Ruíz MP, Hijazo MM, Usón MC. Bacteremia during COVID-19 pandemic in a tertiary hospital in Spain. Enfermedades Infecciosas y Microbiología Clínica. 2022;40:183-186.
11. Cusumano JA, Dupper AC, Malik Y, Gavioli EM, Banga J, et al. Staphylococcus aureus bacteremia in patients infected with COVID-19: a case series. In Open forum infectious diseases 2020;7:ofaa518.
12. Oldoni E, van Gool A, García Bermejo L, Scherer A, Mayrhofer MT, et al. Biomarker Research and Development for Coronavirus Disease 2019 (COVID-19): European Medical Research Infrastructures Call for Global Coordination. Clinical Infectious Diseases. 2021;72:1838-1842.
13. Zhang H, Zhang Y, Wu J, Li Y, Zhou X, et al. Risks and features of secondary infections in severe and critical ill COVID-19 patients. Emerging microbes & infections. 2020;9:1958-1964.
14. Samprathi M, Jayashree M. Biomarkers in COVID-19: an up-to-date review. Frontiers in pediatrics. 2021;8:607-647.
15. Buckland AN, Kessock-Philip ST, Bascomb SH. Early detection of bacterial growth in blood culture by impedance monitoring with a Bactometer model 32. Journal of clinical pathology. 1983;36:823-828.
16. Rajni E, Garg VK, Bacchani D, Sharma R, Vohra R, et al. Prevalence of bloodstream infections and their etiology in COVID-19 patients admitted in a Tertiary Care Hospital in Jaipur. Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine. 2021;25:369.
17. Shafran N, Shafran I, Ben-Zvi H, Sofer S, Sheena L, et al. Secondary bacterial infection in COVID-19 patients is a stronger predictor for death compared to influenza patients. Scientific reports. 2021;11:1-8.
18. Mulcahy ME, McLoughlin RM. Staphylococcus aureus and influenza a virus: partners in coinfection. MBio. 2016;7:e02068-16.
19. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. cell. 2020;181:271-280.
20. Timsit JF, Ruppé E, Barbier F, Tabah A, Bassetti M. Bloodstream infections in critically ill patients: an expert statement. Intensive Care Medicine. 2020;46:266-284.
21. Bengoechea JA, Bamford CG. SARS-CoV-2, bacterial co-infections, and AMR: the deadly trio in COVID-19?. EMBO molecular medicine. 2020;12:e12560.
22. Shokri P, Golmohammadi S, Noori M, Nejadghaderi SA, Carson-Chahhoud K, et al. The relationship between blood groups and risk of infection with SARS-CoV-2 or development of severe outcomes: A review. Reviews in medical virology. 2022;32:e2247.
23. Kim Y, Latz CA, DeCarlo CS, Lee S, Png CM, et al. Relationship between blood type and outcomes following COVID-19 infection. In Seminars in Vascular Surgery 2021;34:125-131.