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Diagnosis of bacterial infection in patients with COVID-19: is it a simple task? (literature review)

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ABSTRACT

Diagnosing bacterial infection in patients with novel coronavirus infection (COVID-19) is not an easy task. Available data suggest that bacterial infection in patients with COVID-19 is rare and occurs in less than 10% of cases. At the same time, data of individual studies and systematic reviews indicate that more than 70% of patients with COVID-19 receive mainly empirical antimicrobial therapy with broad-spectrum antibiotics often before the diagnosis of COVID-19 has been verified. Therefore, this widespread empirical use of antibiotics is not supported by data on the need for their use.

The article discusses the literature data on the significance of commonly accepted methods for diagnosing bacterial infection, with an emphasis on laboratory presence / absence tests. In everyday practice, the likelihood of bacterial coinfection in patients with COVID-19 is assessed by clinical presentation of the disease and the results of standard laboratory tests and imaging methods. However, when viral respiratory infection develops, this approach does not always allow to diagnose bacterial coinfection with sufficient significance. This issue may be handled by available modern test systems, the use of a combination of signs or additional laboratory criteria (for example, procalcitonin), and the analysis of the overall clinical presentation by the doctor using knowledge about patient risk groups.

Keywords: COVID-19, bacterial infection, diagnosis

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Диагностика бактериальной инфекции у больных COVID-19: так ли все просто? (обзор литературы)

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РЕЗЮМЕ

Проблема диагностики бактериальной инфекции у больных новой коронавирусной инфекцией (НКИ) представляет не такую простую задачу, как выглядит на первый взгляд. Имеющиеся данные свидетельствуют, что бактериальная инфекция у больных COVID-19 встречается редко и составляет менее 10%. При этом данные отдельных исследований и систематических обзоров свидетельствуют, что более 70% пациентов

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с НКИ получали антибактериальную терапию, преимущественно препараты широкого спектра и часто эмпирически, нередко до получения подтверждения НКИ. Таким образом, это широко распространенное эмпирическое использование антибиотиков не подтверждается данными о необходимости их применения.

В статье обсуждаются литературные данные о значимости общепринятых методов диагностики бактериальной инфекции с акцентом на лабораторное подтверждение ее наличия/отсутствия. В повседневной практике сочетание клинического течения болезни и результатов стандартных лабораторных исследований, данных методов визуализации являются ведущими в оценке вероятности бактериальной коинфекции у пациентов с COVID-19. Однако в условиях развития тропной к респираторной системе вирусной инфекции такой подход не всегда позволяет с достаточной степенью достоверности диагностировать бактериальную коинфекцию. Помочь в этом могут имеющиеся современные тест-системы, использование комбинации признаков или дополнительных лабораторных критериев (например, прокальцитонина), а также анализ врачом общей клинической картины заболевания с использованием знаний о группах риска пациентов.

Ключевые слова: COVID-19, бактериальная инфекция, диагностика

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INTRODUCTION

2019 novel coronavirus infection (2019-nCoV), COVID-19, is an infectious disease that emerged in late 2019 and quickly spread around the world, having a significant impact on all sectors of healthcare. Since the beginning of the pandemic, doctors have faced various problems, the main of which were occasional lack of tests for prompt diagnosis and lack of commonly accepted treatment methods. This resulted in the situation when doctors frequently prescribed empirical antimicrobial therapy with broad-spectrum antibiotics to patients with lung lesions as part of COVID-19 treatment, despite the lack of evidence of bacterial coinfection. Empirical antibiotic therapy was often prescribed to critically ill patients when bacterial infection was suspected as the underlying cause. Viral lung disease may lead to bacterial superinfection, causing structural damage to lung tissue and weakening of host immunity. During previous influenza pandemics, the development of bacterial coinfection and superinfection was associated with increased mortality [1, 2]. Severe COVID-19 infection manifested itself by clinical and radiological symptoms and laboratory test results, mimicking those of bacterial pneumonia, so empirical antimicrobial therapy was a common practice early in the pandemic.

At the same time, available data indicate that bacterial infection in patients with COVID-19 is rare, occurring in less than 10% of cases [3–8]. However, the frequency of superinfection, especially in patients hospitalized in intensive care units, increased to 14% and, according to some data, up to 54% [4, 6, 9]. At the same time, data from individual studies and systematic reviews indicated that over 70% of patients with novel coronavirus infection received empirical antimicrobial therapy with broad-spectrum antibiotics often even before the diagnosis of COVID-19 infection has been verified [4, 6, 10–16]. Therefore, empirical antimicrobial therapy was prescribed although their necessity was not confirmed by the tests.

Given high frequency of antimicrobial therapy in COVID-19 (with such a low incidence of bacterial infection), it is yet to be understood what criteria are used by the doctor to make a decision to prescribe antibiotics to patients with this pathology. Several surveys of practicing physicians were conducted, which demonstrated the following results. A survey of 414 Italian doctors revealed that prescribing antibiotics to patients with novel coronavirus infection was due to accompanying comorbidities (bone marrow transplantation, presence of bronchiectasis), certain microbial isolation (positive test for pneumococcal urinary antigen or pneumococcal shedding), elevated levels of procalcitonin (PCT) (> 0.5 ng / ml), radiographic and ultrasound impressions of the thoracic cavity (presence of lobar consolidation), hospitalization in the intensive care unit (ICU), or mechanical ventilation [17].

In a survey of 166 physicians from 82 different hospitals in 23 countries, clinical presentation was recognized as the most important cause for initiating antimicrobial therapy, followed by laboratory markers of inflammation and X-ray findings. PCT was recognized as the most important factor among the laboratory inflammatory markers, followed by neutrophil and leukocyte counts and C-reactive protein (CRP) level [18].

According to Spanish researchers, fever (> 38 °C), cough, dyspnea, arthralgia, fatigue, anorexia and gastrointestinal symptoms, oxygen saturation < 90%, tachypnea or tachycardia, and wheezing on auscultation of the lungs were associated with prescribing antibiotics [15]. The decision to initiate antimicrobial therapy was made following elevated levels of conventional inflammatory markers, such as CRP (odds ratio (OR) 2.14, 95% confidence interval (CI) 1.91–2.41; $p < 0.05$), PCT (OR 1.73, 95% CI 1.28–2.35; $p < 0.05$), or leukocytosis (OR 1.18, 95% CI 1.01–1.38; $p < 0.05$), as well as increased levels of inflammatory markers associated with COVID-19, such as lactate dehydrogenase (OR 1.30, 95% CI 1.16–1.47; $p < 0.05$), interleukin 6 (OR 1.73, 95% CI 1.16–2.59; $p < 0.05$), or ferritin (OR 1.93, 95% CI 1.59–2.35; $p < 0.05$). The presence of any infiltrate on X-ray was also the reason for initiating antimicrobial therapy ($p < 0.05$).

A number of guidelines also set the criteria for antimicrobial therapy prescription. For instance, in order to detect fungal or bacterial pneumonia in patients with novel coronavirus infection, as well as to make a decision on the use of antibiotics, the recommendations by the National Institute for Health and Care Excellence (NICE) proposed to conduct the following [19]:

– complete blood count;

– thoracic imaging (radiography, computed tomography (CT) or ultrasound);

– bacterial culture tests of respiratory and blood samples (e.g. sputum sample or tracheal aspirate, blood culture);

– Pneumococcal and Legionella urinary antigen tests.

Russian guidelines recommend prescribing antimicrobial therapy only if there are convincing signs of bacterial infection: increased PCT (> 0.5 ng / ml), purulent sputum, leukocytosis (> 12×10^9 / l in the absence of previous use of glucocorticoids), and an increase in the proportion of band neutrophils (> 10%) [20].

Therefore, it is critical to conduct comparative studies to identify patients with COVID-19 who are candidates for empirical antimicrobial therapy, thereby reducing the widespread overuse of antibiotics.

The aim of our analysis was to summarize the results, risk factors, and methods of diagnosing bacterial infection in COVID-19 patients.

The review was prepared by searching relevant publications in PubMed, ResearchGate, and eLibrary databases, using the following keywords: COVID-19, SARS-COV2, diagnosis, and bacterial infection. The presented review is based on original research articles that discussed the evidence and significance of bacterial infections in COVID-19 patients and the conducted antimicrobial therapy. The review also included case studies, case series, observational studies, meta-analyses, and systematic reviews published from late December 2019 to May 2022.

RESULTS

It should be noted that, regardless of novel coronavirus infection, the diagnosis of a clinically suspected bacterial infection (especially pneumonia) is not always an easy task [21]. COVID-19 is a viral infection, but its clinical manifestations may be similar to those of bacterial pneumonia. Patients often have respiratory symptoms, including fever, cough, and dyspnea, and unilateral / bilateral changes in the lung tissue according to thoracic imaging. The most common radiological findings in these patients are ground-glass opacity, consolidation, and a combination of these two with a predominantly peripheral distribution. However, there are no specific radiological signs distinguishing between viral and bacterial pneumonia, especially atypical bacterial pneumonia. For example, one of the studies did not reveal significant differences in clinical symptoms and CT data in patients with novel coronavirus infection and a positive / negative urine test for pneumococcal infection [22]. This creates difficulties in differential diagnosis, especially before COVID-19 is verified.

A study conducted on patients with novel coronavirus infection compared the incidence of clinically established bacterial infection (bacterial pneumonia, urinary tract infections, ventilator-associated pneumonia (VAP), and bloodstream infections) with microbiological data [23]. In approximately 20% of COVID-19 hospitalizations, patients were diagnosed with bacterial pneumonia, and nearly all cases were community-acquired. In 9% of COVID-19 hospitalizations, patients were diagnosed

with community-acquired urinary tract infections. When microbiological results were used to detect bacterial infections, only about 7% of hospitalized COVID-19 patients had positive results for respiratory, blood, and urine cultures. Microbiological culture is a relatively insensitive method, especially during antimicrobial therapy [24].

Diagnosis of bacterial respiratory tract infection by bacterial culture test has two disadvantages: a significant waiting time (usually about 72 hours) for obtaining the result of a susceptibility test and low sensitivity of microbiological culture, which does not always make it easy to distinguish bacterial colonization from infection [25–28]. It is impossible to ignore the fact that the identification of bacterial pathogens does not explain the causal relationship. Some patients may be carrying large numbers of potentially pathogenic bacteria either in their respiratory tract or in the endotracheal site during intubation without developing any clinically significant bacterial infection [29]. For instance, according to the study by S. Khurana et al. (2021), only 60% of samples obtained from patients with novel coronavirus infection and clinical signs of bacterial infection tested positive for bacterial culture, including samples classified as contaminants [28].

According to C. Huang et al. (2020), 98% of patients with COVID-19 had bilateral lung lesions on chest X-ray, and only 28% of patients provided sputum for Gram stain or culture [30]. Concerns about performing aerosol-generating procedures (e.g. bronchoalveolar lavage) further limit the ability to obtain satisfactory sputum samples for bacterial culture tests and other microbiological tests [31–32]. It should also be taken into account that in a number of countries, guidelines for management of patients with community-acquired pneumonia do not recommend routine staining and culture of sputum in patients with non-severe chronic obstructive pulmonary disease (COPD) or in patients without the risk of multiple drug resistance due to low sensitivity of these tests [32]. Urine sampling for Legionella and pneumococcal antigen is not common in Russia due to its high cost, while microbiological testing of respiratory samples is routinely performed in patients hospitalized for COVID-19. Consequently, the possibility to diagnose bacterial infection in outpatients with novel coronavirus infection is significantly limited.

Standard laboratory methods are too slow to make initial decisions on prescription of antibiotics, requiring the use of rapid point-of-care testing. This technology which is promoted as a solution to future rational use of antimicrobials is now available and can provide comprehensive panel results for respiratory viruses, including SARS-CoV-2, within 45 minutes. Recently developed rapid tests can improve both the speed and sensitivity of examination [26, 33, 34]. Before the emergence of novel coronavirus infection, the US Food and Drug Administration approved the use of many multiplex PCR panels to aid in early diagnosis of possible respiratory pathogens, including Luminex xTAG RVP v1 (Luminex Corporation), Luminex xTAG RVP Fast (Luminex Corporation), FilmArray respiratory panels (BioFire Diagnostics), BioFire FilmArray Pneumonia / Pneumonia plus (BioFire PN/PNplus; BioFire Diagnostics, LLC, Salt Lake City, UT), eSensor RVP (GenMark Diagnostics), Verigene Respiratory Pathogens Flex Test (Luminex Corporation), Luminex NxTAG Respiratory Pathogen Panel (Luminex Corporation), and ePlex Respiratory Pathogen Panel (GenMark Diagnostics) [35].

During the COVID-19 pandemic, SARS-CoV-2 was quickly incorporated into pre-existing syndromic multiplex panels, such as QIAstatDx Respiratory 2019-nCoV (Qiagen, Netherlands) and BioFire FilmArray RP-2.1 (BioFire FilmArray Respiratory Panel-2 plus SARS-CoV- 2; bioMerieux, France) [35]. The panels are molecular multiplex PCR tests that increase the sensitivity of detecting causative agents of pneumonia and significantly reduce the risk of misdiagnosis of coinfection during the COVID-19 pandemic. Some studies have already discussed using some of them to diagnose the bacterial coinfection in patients with novel coronavirus infection [9, 36, 37]. According to Z. Dhesi et al. (2020), the FilmArray Pneumonia Panel revealed bacterial infection in 54% of patients, while the microbiological culture data detected it in only 28.2% of cases [9]. In another study, early bacterial coinfection in patients with acute respiratory distress syndrome was reported in 13 (27.7%) patients with COVID-19: in 12 people following a PCR test and only in one individual following conventional bacterial culture test [38].

A systematic review and meta-analysis involving the results of seven studies (558 patients with novel coronavirus infection admitted to the ICU) demonstrated that the FilmArray Pneumonia panel detected bacterial infection in 33% of cases (95% CI 0.25–0.41, I2= 32%), while bacterial culture test revealed it in only 18% of patients (95% CI 0.02–0.45; I2=93%) [26]. Similar data on greater information value of multiplex panels were reported by other authors [37]. In another study, a rapid PCR test panel (ABI 7500 Real-Time

PCR System, Applied Biosystems, USA) detected 31 more respiratory pathogens, including *P. aeruginosa, E. coli, M. catarrhalis, H. influenzae*, *S. pneumonia*, and *S. pyogenes*, than conventional bacterial culture tests [39].

The need to obtain a high-quality sputum sample limits the use of such panels outside the ICU, which is not always possible in non-intubated patients, e.g. due to the absence of cough. In addition, a number of authors reported complicated interpretation of the test results, limitations of the panel in the detection of gram-negative bacteria, and sometimes overdiagnosis of MRSA [36], albeit such panels could help resolve the issue of distinguishing infection from colonization via semi-quantitative results [26]. Although the prospects of these tools for diagnosing infectious diseases are great, their superiority over conventional mainstay approaches, such as bacterial culture tests, has not yet been unequivocally confirmed.

Another method aimed directly at the detection of pathogens is microbial metagenomic sequencing (MS). This is a rapidly developing technology that allows to identify pathogen and microbiome information simultaneously within 24 hours [5, 40]. Based on previous studies, it can be concluded that MS has higher detection sensitivity than conventional microbiological tests, which makes this method more advantageous in modern microbial surveillance [5, 41]. A microbiome analysis is increasingly used in clinical microbiology laboratories to identify rare and hard-to-detect pathogens and coinfections directly from clinical samples [40]. Characterization of the respiratory microbiome was performed in various respiratory diseases.

In VAP, sequencing of 16S rRNA amplicons expanded microbiological diagnosis by complementing standard culture and demonstrated its potential use as a prognostic marker, since the composition of the microbiome during intubation can predict subsequent development of VAP [40]. MS of COVID-19 respiratory samples demonstrated minimal differences in the microbiome between patients with different prognosis and patients with different duration of mechanical ventilation. At the same time, bronchoalveolar lavage samples are comparable in the information value with samples obtained following endotracheal aspiration [5, 40]. In a small Danish study (34 patients), potential pathogens were detected in 7 patients (21%) by the bacterial culture test, in 4 patients (12%) by the microbiome analysis, and in only 1 patient (3%) by the respiratory panel. The authors considered that there was a reasonable agreement between the results of the bacterial culture test and the microbiome analysis, as 6 / 7 (85%) of the cultured microorganisms in the aspirates were identified during the microbiome analysis. When combining the results of the microbiome analysis and conventional bacterial culture tests in endotracheal aspirate samples, the prevalence of bacterial / fungal coinfections increased from 21 to 33% [40].

The increased sensitivity of multiplex panels and 16S metagenomic analysis for the detection of pneumonia-inducing pathogens, compared with bacterial culture tests, was demonstrated in the European multicenter study BioFire PNplus, Curetis Unyvero [34]. The scope of application of the microbiome analysis in respiratory specimens in the clinical setting is yet to be determined, but its routine use requires reduced processing time and cost.

PREDICTORS (BIOMARKERS) OF BACTERIAL COINFECTION AND SECONDARY INFECTIONS

Studying the predictive capability of various clinical and laboratory tests as predictors of bacterial coinfection and secondary infections is relevant. PCT is recognized as the most promising indirect test in terms of diagnosing bacterial infection in patients with novel coronavirus infection [6, 20, 42, 43]. PCT, a precursor of the hormone calcitonin, is stimulated by IL-6, tumor necrosis factor, and cytokines associated with bacterial infection and is inhibited by interferon gamma, which is associated with viral infections [44]. Expression of PCT is elevated in the epithelial layer of cells when infected with bacterial infection. A landmark article published in 1993 reported on the ability of PCT to distinguish between bacterial and viral infections [45]. A number of studies showed that PCT surpasses CRP in distinguishing between bacterial and viral infections [46], but the role of PCT measurement in antimicrobial management is controversial. PCT testing is approved by the US Food and Drug Administration for the treatment of sepsis and respiratory tract infections; but in the UK, current guidelines of the National Institute for Health and Care Excellence (NICE) do not include PCT testing due to insufficient evidence [47].

Many studies showed that antimicrobial therapy with the control of PCT levels yields good results in patients with acute respiratory disease, exacerbation of COPD, and sepsis [24, 44, 48, 49]. Numerous studies demonstrated a higher level of PCT in patients with

COVID-19 and bacterial coinfection compared with patients with COVID-19 without signs of bacterial infection, as well as changes in PCT after the initiated antimicrobial therapy [24, 50–52].

During the first wave of the COVID-19 pandemic, there was widespread use of PCT level detection in NHS hospitals (UK). The number of hospitals using PCT detection for emergency / acute hospital admissions increased from 17 (11%) to 74 / 146 (50.7%), and its use in ICUs increased from 70 (47.6%) to 124 / 147 (84.4%). This increase occurred predominantly in March and April 2020, before the release of the NICE guidelines. Approximately half of the hospitals used PCT measurement as the only test to decide on discontinuation of antimicrobial therapy, and half of the hospitals used repeated measurements [47].

In their study, M. van Berkel et al. (2020) investigated PCT and CRP levels as prognostic markers of possible bacterial coinfection in COVID-19 patients in the ICU. It was noted that CRP levels tend to increase, while PCT is often low in patients with novel coronavirus infection at admission [53]. Other authors presented similar data on PCT as a prognostic marker in COVID-19 [24].

In the study by G.P. Drewett et al. (2021), changes in serum PCT levels were associated both with the initiation of antimicrobial therapy in patients with novel coronavirus infection and with the transition from intravenous to oral drug delivery [54]. All patients with high PCT levels (> 0.5 ng / ml) received antibiotics in hospital, while 20% of patients with moderate PCT levels (0.07– 0.5 ng / ml) and 40% of patients with low PCT levels (< 0.07 ng / ml) did not receive any antimicrobial therapy. These results highlight the potential utility of PCT testing. Similar data on lower frequency of prescribing antibiotics (21%) in the absence of an increase in PCT level (< 0.25 ng / ml) were obtained by the authors of another study [52].

The most appropriate threshold for PCT has not been determined yet [19]. It was indicated that a PCT level of more than 0.5 ng / ml could be used to confirm bacterial infection, while a level of < 0.25 ng / ml was not associated with bacterial infection [43]. According to M. van Berkel et al. (2020), the negative predictive value in patients with PCT levels < 0.25 μg / l was 81%, whereas PCT >1.00 μg / l had a positive predictive value of 93% for the development of bacterial infection [53]. Data from another study suggested that the use of PCT levels as a marker for reducing the use of antibiotics actually decreased the duration of their use by two days in patients with novel coronavirus infection [55].

However, not all studies confirmed the diagnostic value of PCT [8, 44, 56, 57]. In a retrospective analysis of the data from 60 patients with COVID-19, no significant difference was found between peak PCT levels in patients with positive and negative bacterial culture tests [58]. Another case–control study demonstrated that no difference was observed between PCT levels in COVID-19 patients with and without bacterial coinfection (p = 0.883) [56]. Besides, an increase in PCT levels can be detected in patients with novel coronavirus infection without bacterial coinfections, which would serve as a basis for prescribing antibiotics. For instance, in one study, microbiologically confirmed bacterial infection was present in only 12% of patients with a PCT level of > 0.5 ng / ml [32].

Therefore, the significance of PCT in detecting bacterial coinfection is not so clear, and further research is needed to develop an accurate predictive model or a method for diagnosing coinfection in patients with novel coronavirus infection. The NICE guidelines (UK) state that there is not enough evidence for introducing a PCT level examination for making decisions on prescription of antibiotics [19]. In October 2020, the study on the significance of PCT levels in antibiotic use in hospitalized patients with COVID-19 (PEACH), commissioned and funded by the National Institute of Health Research (NIHR), started [59].

Therefore, the significance of an elevated PCT level in confirming the presence of bacterial infection in patients with novel coronavirus infection is not undoubtful: its increase may represent bacterial infection or immune dysregulation, or actually be a marker of the disease severity. However, low or normal PCT levels may be useful to avoid prescription or early discontinuation of empirical antimicrobial therapy in non-critically ill patients. Besides, serial measurements of PCT provide the insight into inflammatory changes in the patient, where a secondary increase should make the physician suspect a bacterial superinfection [60]. Finally, PCT levels can be controlled after the initiation of antimicrobial therapy to reduce the duration of treatment [60].

Some authors emphasized the diagnostic value of leukocytosis (especially neutrophilia) in patients with COVID-19 in relation to bacterial infection [7, 8, 51, 61–64]. The results of another study indicated that the

level of leukocytes less than 8.2×10^9 cells / l allowed to exclude bacterial infection in 46% of patients with COVID-19 [25], while other authors recommended focusing on a level $\geq 10 \times 10^9$ / l [65].

Regarding the level of CRP, there are recommendations that its high values in patients with novel coronavirus infection do not necessarily imply the presence of bacterial infection; however, its low level characterizes a low probability of bacterial coinfection [19, 53, 66]. In a study by German researchers, patients with COVID-19 and confirmed coinfections had higher levels of CRP and PCT than patients without infection [67]. In bloodstream infections, the increase in CRP and PCT levels was more pronounced than in respiratory infections.

The study by P. Hedberg et al. (2022) showed that the predictors of bacterial coinfection in patients with COVID-19 were CRP levels of ≥ 50 mg / l, CRP levels of ≥ 150 mg / l, leukocyte count of over 12.0×10^9 cells / l, PCT levels of ≥ 2.00, and the neutrophil-to-lymphocyte ratio exceeding 20.0 [68].

H. Chen et al. (2021) considered prescribing antibiotics only if the infiltrate was visible on chest X-ray and the leukocyte count was $\geq 10 \times 10^9$ / l, or in severe illness requiring intensive care in the ICU. If the CRP level was < 60 mg / l or the PCT level was < 0.5 ng / ml, they recommended to refrain from prescribing antibiotics [65]. According to the authors, only 4 out of 114 patients would qualify for antibiotics during a 14-day period.

It should be noted once again that serological markers of inflammation usually associated with bacterial infection, such as elevated PCT and CRP levels, may appear in patients with novel coronavirus infection without bacterial coinfection [69, 70].

RISK FACTORS FOR BACTERIAL INFECTION

It is often difficult to determine which patients should be given antibiotics and which patients may not benefit from them. The possibility of identifying a probable bacterial pathogen in a large number of admitted patients with novel coronavirus infection is significantly limited. Therefore, it is necessary to understand and identify risk factors for the development of bacterial infections in hospitalized patients with COVID-19 and reveal markers of a bacterial coinfection in order to form clearer indications for antimicrobial therapy. All of these would contribute to rational antibiotic use aimed at improving the quality and safety of their application.

Risk factors for the development of bacterial infection include age over 60 years, prolonged hospital stay, need for mechanical ventilation, stay in the ICU (severe course of COVID-19), chronic bacterial infections in the past medical history (primarily those of the respiratory tract), administration of steroids and / or immunosuppressive therapy prior to and / or during COVID-19 therapy, chronic renal failure with a need for hemodialysis, and immunodeficiency (e.g. chemotherapy for cancer; bone marrow or organ transplantation; primary immunodeficiency; poorly controlled HIV or AIDS) [3, 4, 16, 20, 29, 32, 50, 51, 66, 67, 71–74]. It is also impossible to ignore the increased risk of catheter-associated bacterial infection in patients with a severe course of novel coronavirus infection following even short-term placement of a central catheter [27, 75].

CONCLUSION

Therefore, the problem of diagnosing bacterial infection in patients with COVID-19 appears quite complicated. In routine practice, the combination of the clinical course of the disease with the results of standard laboratory tests and data provided by imaging methods are foremost in assessing the likelihood of bacterial coinfection in patients with novel coronavirus infection. However, this approach does not always allow to diagnose bacterial coinfection with a sufficient degree of certainty when a patient develops viral respiratory infection. Substantial assistance in this matter could be provided by available modern test systems along with a combination of symptoms and additional laboratory criteria (e.g. PCT), supplemented with the analysis of the overall clinical presentation of the disease performed by a physician with the knowledge of the patient risk group. Furthermore, the data on extremely rare incidence of bacterial infection in outpatients and its rare incidence in patients in the first 5–10 days of hospitalization are very helpful in this regard.

If the doctor doubts the presence of bacterial coinfection, empirical antimicrobial therapy is possible upon admission of the patient to the hospital (in the first 24–48 hours). However, after receiving laboratory test results, antimicrobial therapy should be reviewed and immediately discontinued if there are no criteria for its prescription. Consequently, young patients and patients without concomitant pathologies who are prescribed antibiotics for dry cough, fever, flu-like symptoms, interstitial infiltrates, or elevated CRP levels are likely to receive antimicrobial therapy

without indications. Therefore, in the absence of alternative data indicating the need for its use, antimicrobial therapy should be suspended.

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