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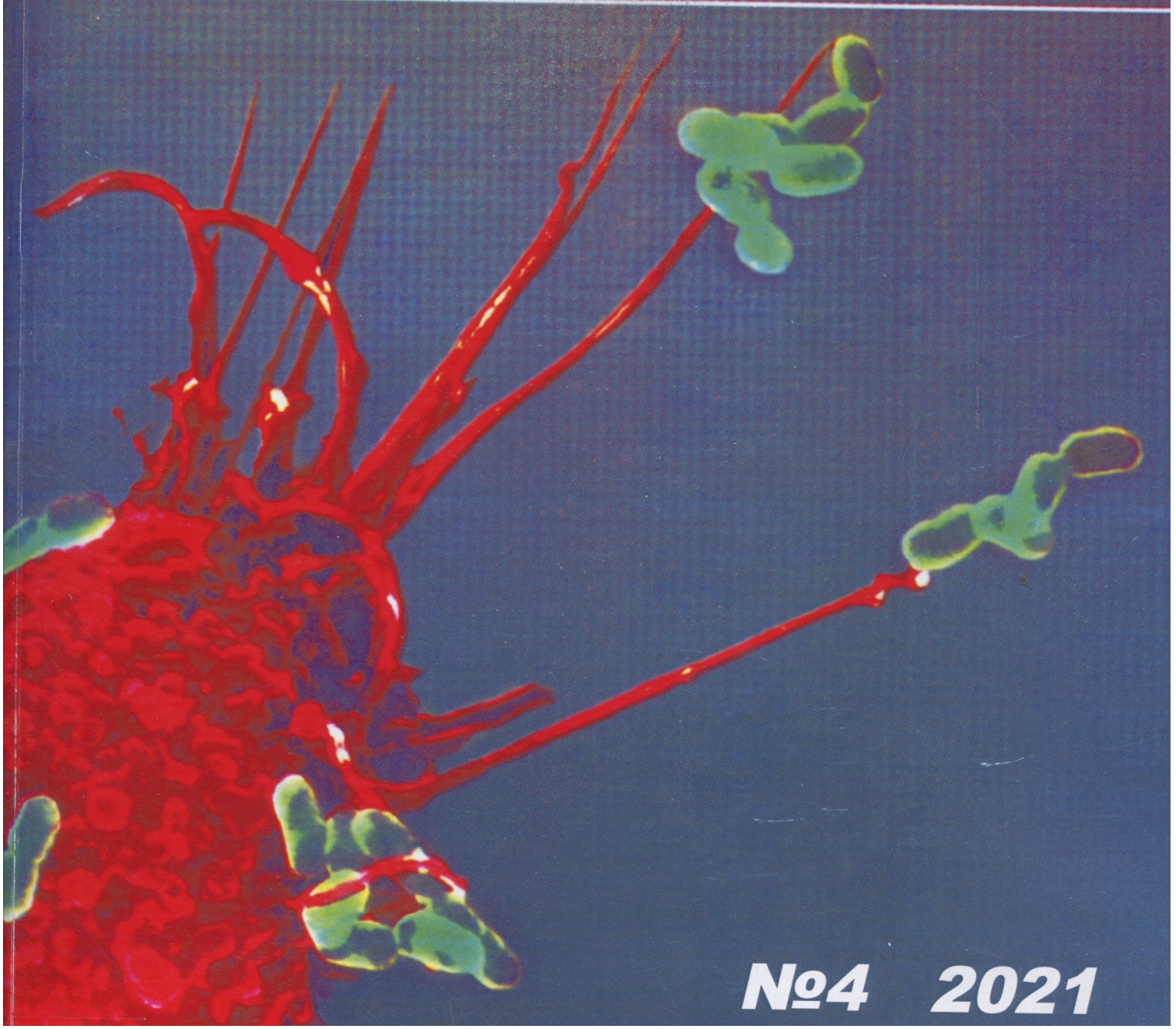

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ИНФЕКЦИЯ, ИММУНИТЕТ и ФАРМАКОЛОГИЯ

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CASE OF CARDIOVASCULAR DISEASES IN PATIENTS WITH COVID-19

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Introduction: In face of the pandemic of the novel coronavirus disease 2019 (COVID-19), the management of patients with cardiovascular risk factors and/or disease is challenging. The proper care of patients with COVID-19 requires special attention to the cardiovascular system aimed at better outcomes.

Aim: To study the status of cardiovascular disease in patients with arterial hypertension Covid-19 and its role in the treatment

Research materials and methods:

The Republican Clinical Hospital №1 and the Republican Scientific Center for Emergency Care in Uzbekistan will examine 60 patients with arterial hypertension conducted by COVID -19. All patients undergo clinical and laboratory-instrumental examinations. All data obtained are analyzed on the basis of statistical analysis: The following tests are performed on all patients

Collection of anamnesis, objective examination. Complex of laboratory tests. Results and discussion: The mean time of symptom onset is 5-6 days, and 97,8% of contaminated individuals will have symptoms in up to 11.5 days from exposure. Most patients (83%) have mild symptoms, the most common being fever (87%) and cough (66.7%). Although the predominant clinical manifestation of COVID-19 is viral pneumonia[1,2,3,4] .COVID-19 can also cause cardiovascular disorders such as myocardial injury, arrhythmias, ACS, Arterial hypertension and thromboembolism. Some patients who present without the typical symptoms of fever or cough have cardiac symptoms as the first clinical manifestation of COVID-19 [5,6]. Myocardial injury during the course of COVID-19 is independently associated with high mortality [7].

COVID-19 seems to follow a pattern seen with influenza and previous severe acute respiratory syndrome coronavirus (SARS-CoV) outbreaks: that the severity and mortality of the infection is higher in the elderly age group. As hypertension is strongly age related, the data could simply be confounded by age. However, an alternative explanation is end-organ damage in hypertensive patients. Hypertension results in a number of pathophysiological changes in the cardiovascular system such as left ventricular hypertrophy and fibrosis. This may make the hypertensive heart particularly susceptible to SARS-CoV-2. Researches that Wang et al. retrospectively reviewed 138 hospitalised patients with COVID-19, and showed 16.7% of patients developed dysrhythmia and 7.2% experienced acute cardiac injury, defined as serum levels of cardiac biomarkers (e.g. troponin I) above the 99th percentile upper reference limit or new changes on echocardiogram or electrocardiograph.[8] Ruan et al. noted similar findings in 150 patients from Wuhan, China, and noted 7% of the 68 deaths occurred due to myocardial damage, with a further 33% dying from both myocardial and respiratory failure. They concluded that COVID-19 could cause fulminant myocarditis.[9] This is supported by Huang et al.'s review of 41 patients with COVID-19, of whom 12% had acute cardiac injury with substantially increased hypersensitive troponin I.[10] Further data from Zhou et al. indicated that those who did not survive had significantly raised troponin I and lactate dehydrogenase through their clinical course compared to survivors.[11] A recent review of 187 patients in Wuhan showed that those with underlying cardiovascular disease and a raised troponin were at a higher risk of death than those with raised troponin and no underlying cardiovascular disease. Additonally, those patients with pre-existing cardiovascular disease were more at risk of developing a raised troponin, suggesting a causal link between underlying cardiovascular conditions (e.g. hypertension) and COVID-19 outcomes.[12] As the COVID-19 pandemic continues, there is an increasing risk of overwhelming healthcare infrastructures and jeopardizing patient care even in the most developed countries. As such, identification of reliable demographic, clinical and laboratory indicators are needed to distinguish which COVID-19 patients are at enhanced risk, thus needing more aggressive management through hospitalization or intensive care, from those who could be safely managed as outpatients. Some laboratory parameters which may predict worse progression have already been identified, including leukocytosis, lymphopenia, thrombocytopenia, along with increased values of D-dimer, procalcitonin, car-

diac biomarkers, pro-inflammatory cytokines and ferritin. [13] Notably, some clinical predictors of worse COVID-19 prognosis have also been reported in early studies, such as older age, male sex, as wells the presence of pre-existing cardiovascular diseases, diabetes, respiratory disorders, cancer and dementia.[14,15]. These findings are supported by observations in other respiratory and systemic illnesses, as the presence of one or more such comorbidities is now universally recognized as unfavourable prognostic factor in patients with many other pneumonias [16], ARDS25 and SIRS. [17] However, the strength of those comorbidities for increased risk of severe COIVID-19 has not been established. In this study, we observed that hypertension carries a nearly 2.5-fold higher risk of developing severe disease or dying from SARS-CoV-2 infection . Although this association seems weaker than that earlier reported for other co-morbidities, such as chronic obstructive pulmonary disease (COPD; over 5-fold higher risk)[18] or chronic kidney disease (CKD; over 3-fold higher risk),28 it still carries important clinical implications. As previously discussed, SARS-CoV-2 enters the cells by binding ACE2. Some interesting studies have previously shown that administration of some antihypertensive drugs such as ACE inhibitors (ACEis)29 and angiotensin receptor blockers (ARBs) [19] may be associated with enhanced ACE2 expression at the cell surface, thus ultimately supplying SARS-CoV-2 with a larger number of "anchors" for infecting cells.

While this is still the matter of contentious debate, it cannot be excluded that some hypertensive patients undergoing renin-angiotensinaldosterone system (RAAS) inhibition, especially those taking ACEis, may be more susceptible to SARS-CoV-2 infection, which would ultimately translate into a higher risk of developing local (i.e., ARDS) or systemic (i.e., SIRS/MOF) adverse COVID-19 consequences.[20] On the other hand, others have argued that hypertensives may experience a decreased ACE2 expression, which when bound by SARS-CoV-2 attenuates residual ACE2, leading to elevated angiotensin II levels driving development of ARDS.32 Moreover, evidence convincingly attest that both pulmonary and systemic hypertension is a risk factor for unfavourable progression in patients with pneumonia, [21] ARDS [22,23] and MOF. It is therefore plausible that coexistence of hypertension and SARS-CoV-2 infection would interplay to synergistically increase the risk of unfavourable prognosis compared to normotensive COVID-19 patients. The management of hypertensive patients is another important implication of our findings. [24] A limitation of the current analysed literature is the lack of age-adjusted data with respect to hypertension and disease severity. In our meta-regression by mean age of severe patients, significant odds of COVID-19 severity associated with hypertension was only seen in those over age 60. It is possible that the observed risk may be attributed to the higher overall severity and mortality in older patients, within whom the prevalence of hypertension increases in parallel with advancing age. We hypothesize that in older individuals, hypertension contributes to a compounding effect with other co-morbidities on mortality.

As such, in the coming weeks, we urgently need age-adjusted analyses for clinical predictors of severe and fatal COVID-19. Lastly, it is possible in the included studies that patients presenting without a history of hypertension, but presenting at admission with elevated blood pressure (potentially due to COVID-19), may be considered to have a history of hypertension, biasing results among individual studies.This view is supported by the European Medicines Agency, the Medicines and Healthcare products Regulatory Agency (MHRA), the European Society of Cardiology (ESC) and the ACC. This would allow for titration of medication through telemedicine clinics [25] and would encourage patient-initiated review when required rather than a timed review. We should advise patients to ensure that they have at least two weeks of antihypertensive medications, as there may be delays in procuring repeat prescriptions. We should be open with patients and inform them that we do not fully understand the relationship between COVID-19 and hypertension. More importantly, the duration of follow-up was short and some patients remained in the hospital at the time of publishing these studies, which means that real outcome was unknown. Obesity was not reported in available studies, and its influence could not be investigated. Furthermore, only one study reported basal values of systolic and diastolic blood pressure, which would help to estimate the percentage of uncontrolled hypertension. The same refers to prevalence of patients with uncontrolled diabetes. The most of studies included small number of patients, which is additional obstacle. Studies should consider all potential sources of bias and con-

founding, which is why additional investigations with improved design are warranted.

Conclusion: we still lack the definitive clues for establishing which comes first between the hypertension or the severe COVID-19, or even if these two conditions interplay in their pathophysiology. However, the results of this pooled analysis of the current scientific literature would suggest that hypertension may be associated with a up to 2.5- fold higher risk of severe and fatal COVID-19, especially among older individuals.

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Xulosa

COVID-19 BILAN OG'RIGAN BEMORLARNING YURAK QON TOMIR KASALLIKLARI HOLATI

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Toshkent Tibbiyot Akademiyasi

So'nggi tatqiqotlarga ko'ra arterial gipertenziya COVID-19 bilan og'rigan bemorlarda eng ko'p uchraydigan qo'shma kasalliklardan biri ekanligini ko'rsatdi. Ushbu tarqalish 10% dan 34% gacha ko'rsatgichni tashkil etgan. COVID-19 bilan og'rigan bemorlarda gipertoniyaning yuzaga kelishi,yoki oldin mavjud bo'lishi o'limning asosiy sabablaridan bo'lgan. Bu esa Covid-19 o'tkazgan arterial gipertenziyali bemorlarda yurak qon tomir kasalliklarini klinik funksional holatini o'rganish katta ahamiyat kasb etishini belgilaydi.

***Kalit so'zlar**. Arterial gipertenziya,COVID-19, AAF, yurak qon tomir sistemasi.*

Аннотация

СОСТОЯНИЕ СЕРДЕЧНО-СОСУДИСТЫХ ЗАБОЛЕВАНИЙ У ПАЦИЕНТОВ С COVID-19

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Ташкентская Медицинская Академия

Недавние исследования показали, что артериальная гипертензия - одно из самых распространенных заболеваний у пациентов с COVID-19. Этот разброс составлял от 10% до 34%. Возникновение или ранее существовавшая артериальная гипертензия у пациентов с COVID-19 была одной из основных причин смерти. Большое значение имеет обучение.

***Ключевые слова:** артериальная гипертензия, COVID-19, иАПФ, сердечно-сосудистая система.*