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Clinical aspects of COVID-19 on the background of HIV infection

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Abstract

Against the background of the COVID-19 pandemic, the number of patients with co-infection - HIV infection + COVID-19 - has increased critically. The features of the interaction of these two infections are of scientific, clinical and practical interest. On the one hand, the combination of two severe viral infections should aggravate the patient's health, on the other hand, people living with HIV infection receive antiviral therapy, which can have a positive effect on the course of COVID-19. This article is devoted to the study of the clinical aspects of the interaction of two dangerous viruses in the human body and the outcomes of this combined infection. A link was shown between the worsening of the course of the combined infection – HIV + COVID-19 infection and the rejection of antiretroviral therapy.

Objective of the study: The aim of this work was to study the prevalence of coronavirus infection among HIV-infected patients in Almaty and the clinical aspects of combined infection: HIV infection + COVID-19.

Materials and methods: During the period 2020-2021, we observed 74 outpatients and inpatients with HIV infection + COVID-19 in Almaty city. Indicators of immune status, HIV viral load, as well as PCR testing for SARS CoV2 were determined in all patients, in addition to general clinical laboratory examination methods. The lung tomography was performed in patients with severe COVID-19. The mutual influence of SARS-CoV-2 and HIV infection was considered within the framework of age, gender, stage of HIV infection, immune status, HIV viremia, conditions of specialized medical care, use of Antiretroviral Therapy (ART), severity of COVID-19 and the outcome of the disease.

Results: Indicators of immune status, HIV viral load, ART treatment, the stage of HIV infection, as well as the location of receiving medical care (inpatient or outpatient treatment) correlated with the severity of the course of COVID-19 + HIV co-infection and had prognostic significance. Adverse outcomes of HIV infection were associated with a decrease in CD4 lymphocyte count and an increase in HIV viral load.

Conclusion: Combined HIV infection + COVID-19 against the background of antiretroviral therapy do not worsen the outcome compared to mono COVID-19 infection. At the same time, a high level of HIV viral load and low - CD4 lymphocytes in the blood, infection with COVID-19 during stage 4 of HIV infection and/or adherence to antiretroviral therapy leads patients to severe COVID-19 and death.

Introduction

The World Health Organization declared the COVID-19 pandemic in March 2020. This pandemic has layered on the current HIV pandemic, which determined the relevance of the study [1].

COVID-19 is characterized by a local and systemic inflammatory response of the immune system of the macroorganism - a "cytokine storm", which leads to end otheliopathy of target organs, tissue edema and hyperactivation of the coagulation cascade, which can lead to the development of micro- and macro thrombosis, DIC and hypoxia [2-4].

One of the signs characterizing the severe course and bad clinical prognosis in COVID-19 is lymphopenia, which is often found in HIV patients, and may be associated with an increased mortality rate, especially in people with low levels of CD3, CD4 and CD8 T-lymphocytes. A risk factor contributing to generalization is immunosuppression (a decrease in the number of CD4 lymphocytes less than 200/ml) or an increase in the amount of HIV RNA in blood plasma more than 100,000 copies/ml, as a result of which there is a threat of joining a number of opportunistic diseases [5,6].

Currently, CDC and the International AIDS Society consider PLHIV with low CD4-lymphocyte count or without ART as potentially vulnerable to the more severe course of COVID-19.

There is no evidence that any other antiretroviral drugs are active against SARS-CoV-2, so there are no prerequisites for background protection of PLHIV [7].

WHO recommends that PLHIV take the same precautions as the general population. However, people living with HIV and receiving ARVs should be provided with a drug supply for a period of 30 days to 6 months, which leads to an increase in the cost of providing an adequate supply of medicines for the treatment of concomitant diseases [8].

The interaction of SARS-CoV-2 and HIV, pathogenetic features, clinical manifestations of combined infection remain an urgent topic for further research. The COVID-19 pandemic increases the number of patients with a combined infection - HIV infection + COVID-19.

The mechanisms of interaction of HIV with immunocompetent cells have been studied and well described in the literature, and for SARS-CoV-2, these studies have just begun. They are necessary for the development of clinical recommendations for the provision of medical care to HIV-infected patients with COVID-19. HIV infection is still one of the main global public health problems: more than 80 million people have been infected with HIV since its registration begun, more than 35 million have died. There are of the 40 million HIV-infected patients in the world, a significant part is alive thanks to Antiretroviral Therapy (ART) [9,10].

ART is the main tool for achieving viral suppression, reducing transmission of infection, preventing disease progression and death, and therefore adherence to ART is of particular importance. Increasing the coverage of people living with HIV, ART and their retention on ART for maximum effectiveness of treatment is a priority task for the healthcare of the Republic of Kazakhstan.

Various concomitant diseases aggravate the severity of the patients' condition and affect the prognosis and outcome of the disease. The simultaneous development of pandemics inevitably causes their negative interaction, and the immunodeficiency characteristic of HIV infection suggests more severe manifestations of comorbidity, especially against the background of a decrease in the medical care in conditions of quarantine [11,12].

In today's conditions, many questions arise about the mutual influence of infection with HIV and SARS-CoV-2. There are not many reports in the available scientific literature about the clinical course of combined pathology – HIV infection and COVID-19, and they are descriptive and sometimes contradictory [13].

Objective of the study

So, the objective of this work was to study the prevalence of coronavirus infection among HIV-infected patients in Almaty city and the clinical aspects of combined infection: HIV infection + COVID-19.

Materials and methods

During the period 2020-2021, we observed 74 out patients and in patients with HIV infection + COVID-19 in Almaty city. Indicators of immune status, HIV viral load, as well as PCR testing for SARS CoV 2 were determined in all patients, in addition to general clinical laboratory examination methods. The lung tomography was performed in patients with severe COVID-19.

The mutual influence of SARS-CoV-2 and HIV infection was considered within the framework of age, gender, stage of HIV infection, immune status, HIV viremia, conditions of specialized medical care, use of Antiretroviral Therapy (ART), severity of COVID-19 and the outcome of the disease.

Statistical processing of the primary material was carried out in the IBM SPSS Statistics v28.0.0.0 program with the calculation of the average rate in the group, standard error and confidence interval. The relative values were compared in the Epi-Info v7.2.4.0 program. To compare the data of the studied groups with a normal distribution, the Student's T-test for unrelated groups (t-test) was calculated, with further calculation of the significance level (p). For a distribution other than normal, nonparametric Mann-Whitney U test and Wilcoxon W testwere used for unpaired samples with the determination of the magnitude of Z and the significance level (p).

Results

HIV infection was the first disease in all 74 patients, all of them were registered at the city center for the Control and Prevention of AIDS in Almaty city.

According to the severity of COVID-19 and the outcomes, we divided the observed patients into two groups. 16 PLHIV with confirmed COVID-19 died in hospital (the first group).

58 PLHIV, suffered COVID-19, recovered and were discharged from the hospital for outpatient observation (the second group).

The duration of HIV infection in group 1 was 5.5 ± 1.21 years, and in group 2 - 6.1 ± 0.64 years. The difference was not statistically significant (p=0.37).

Table 1: Clinical symptoms and signs of COVID-19 on the background of HIV infection.

Clinical symptoms and signs	Mild course / recovery n=58		Severecourse / death n=16		p
	n	M ± m, %	N	M±m, %	
Fever	35	60,3 ± 6,48	11	68,8 ± 11,97	0,27
Fatigue	31	53,4 ± 6,61	12	75,0 ± 11,18	0,03
Pneumonia	26	44,8 ± 6,59	10	62,5 ± 12,50	0,09
Dyspnea	22	37,9 ± 6,43	12	62,5 ± 12,50	0,02
ARDS	12	20,7 ± 5,37	7	43,8 ± 12,81	0,02
Diarrhea	8	13,8 ± 4,57	6	37,5 ± 12,50	0,005
Heart failure	7	12,1 ± 4,31	5	31,3 ± 11,97	0,025
Arrhythmia	5	8,6 ± 3,72	2	12,5 ± 8,54	0,37
Tuberculosis	2	3,4 ± 2,42	3	18,8 ± 10,08	0,001
Pneumocystispneumonia	1	1,7 ± 1,72	2	15,5 ± 8,54	0,001
Total	58	100	16	100	

Table 2: HIV viral load and CD4 lymphocyte count in blood of COVID-19 + HIV infection patients.

Indicators value	Mild course / recovery n=58	Severecourse / death n=16	Manna-Whitney U	Wilcoxon W	Z	p
	IU	IU				
CD4 lymphocyte count/mkl	354,5	167,0	118,0	154,0	-2,058	0,04
HIV viral load/ml	50,0	9586,0	125,0	1665,0	-3,226	0,001

The average age in group 1 was 40.8 ± 2.1 years, in group 2 - 39.0 ± 1.3 years. The difference was statistically insignificant too (p=0.433).

When studying the gender composition of the groups, it was revealed that men significantly prevailed in group 1 (81.3 ± 10.08 - p<0.001).

COVID-19 on the background of HIV infection was severe and ended in the death of patients in the presence of concomitant infections such as tuberculosis and pneumocystis pneumonia (P < 0.001). The severe course of combined HIV infection + COVID-19 was characterized by the development of intestinal syndrome / diarrhea (P = 0.005). The severity of the course of combined HIV infection + COVID-19 manifested itself in the form of Acute Respiratory Distress Syndrome (ARDS), dyspnea (P = 0.02), as well as heart failure (P = 0.025) and severe weakness (P = 0.03) (Table 1).

Analysis of COVID-19 outcomes depending on the stage of HIV infection revealed a significant increase in the number of deaths at stage 4 (Odds ratio - 7,800, 95% Confidence interval (2,269-26,819), Pearson Xi-squared 10.258, (p=0.0012). At the same time, there were no differences in the outcomes of COVID-19 at stage 3 of HIV infection (p=0.380).

In the severe course of COVID-19 against the background of HIV infection, which ended in the death of the patient, there was a significantly higher HIV viral load (p=0.001) and a significantly lower CD4 lymphocyte count (p=0.04) in the blood (Table 2).

At the same time, in patients with severe and fatal COVID-19 + HIV infection, there was also a significant decrease in CD4 lymphocytes in the dynamics of treatment (p=0.001).

There was also a significantly more frequent mild course / recovery of COVID-19 against the background of HIV infection in people receiving antiretroviral therapy (73.0 ± 5.20%) compared to those who did not receive it (5.4 ± 2.65%), Pearson coefficient - 17.149 (p=0.0001), Fisher criterion - 0.00027.

It can be assumed that antiretroviral therapy has a positive effect not only in HIV infection, but also in COVID-19.

Of the 58 hospitalized patients with HIV + COVID-19 co-infection and receiving ART, none died and only 27.6 ± 5.92% of the disease was more or less severe. At the same time, mortality in hospitalized patients with COVID-19 reaches 4-5% or more.

Thus, it seems that the combined infection of HIV infection + COVID-19 in hospitalized patients on the background of antiretroviral therapy proceeds more easily than mono infection COVID-19.

Risk factors for severe course and death in situation of HIV infection + COVID-19 are, first of all, adherence to antiretroviral therapy, and infection with coronavirus against the background of stage 4 HIV infection.

Laboratory indicators of risk factors for severe course and death are high HIV viral load and low CD4 lymphocyte count in the blood.

Intestinal syndrome / diarrhea, Acute Respiratory Distress Syndrome (ARDS), dyspnea, heart failure and severe weaknessare clinical indicators of the severe course of COVID-19 against the background of HIV infection according to our data.

The combination of HIV infection + COVID-19 and tuberculosis or pneumocystis pneumonia is also an extremely negative factor.

Conclusion

The layering of COVID-19 on HIV infection against the background of antiretroviral therapy at least does not worsen the outcome compared to mono COVID-19 infection.

Severe course of combined HIV infection + COVID-19 is manifested by diarrhea, acute respiratory distress syndrome, heart failure.

The development of a combined HIV infection + COVID-19 against the background of tuberculosis or pneumocystis pneumonia usually leads to death.

Reliable risk factors for the fatal outcome of a combined HIV infection + COVID-19 are a HIV viral load and low CD4 lymphocyte count in the blood.

Infection with COVID-19 during stage 4 of HIV infection and/or adherence to antiretroviral therapy leads patients to death.

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