

# Superoxide Dismutase Activity in Male and Female Patients of Different Age with Moderate COVID-19

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The study involved 271 patients (132 men and 139 women) with moderate COVID-19. Superoxide dismutase (SOD) activity in erythrocytes was measured spectrophotometrically. In total group of patients (divided into age groups of 18-35, 36-45, 46-60, and 61-90 years), higher SOD activity was found in the 18-35 age group in comparison with the groups 46-60 years ( $p<0.01$ ) and 61-90 years ( $p<0.05$ ). Then, the groups were additionally divided by sex. In men, no differences in enzyme activity were found between the age groups. In women of early reproductive age, SOD activity was higher than in groups 36-45, 46-60, and 61-90 years. The sex differences consisted in higher SOD activity in women aged 18-35 years in comparison with men of this age. These data should be taken into account when choosing the tactics of therapy for patients with moderate COVID-19 course.

**Key Words:** *superoxide dismutase; COVID-19; sex and age standardization*

Superoxide dismutase (SOD) is a metal-containing antioxidant enzyme that acts as the first line of defense against ROS intensively generated during viral infections [1,2,11], including COVID-19 [7,9,12,14]. It has been shown that the intensity of oxidative stress does not differ in moderate and severe forms of COVID-19 [7]. Some studies showed a decrease in SOD activity in patients with severe and critically severe COVID-19 in comparison with mild COVID-19 [10], while in others, an increase in SOD activity was reported [12]. It should be noted that the studies did not take into account patient's sex and age, though these factors, according to some results, play a significant role in enzyme activity [3,8,15].

In this study, we assessed SOD activity in different age groups of male and female patients with moderate severity COVID-19 to obtain more sex- and age-standardized indicators.

## MATERIALS AND METHODS

The study was conducted at the Research Center for Family Health and Human Reproduction Problems in accordance with the ethical standards of the Declaration of Helsinki of the World Medical Association (revision 2013). The study included 132 men and 139 women aged from 18 to 90 years with a verified diagnosis of COVID-19, moderate severity, accompanied by pneumonia, admitted to the Irkutsk Regional Infectious Diseases Clinical Hospital during the period from June 2020 to March 2021. Each patient signed informed consent for participation in the study. The study protocol was approved by the Biomedical Ethics Committee of the Research Center for Family Health and Human Reproduction Problems (Protocol No. 6.1, June 19, 2020).

At admission, personal data were collected and medical records were analyzed, general clinical examination and CT were performed. The survey included information on the presence of positive PCR tests for SARS-CoV-2 RNA (laboratory verification of the infection at admission), data on the dynamic control of

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**TABLE 1.** Characteristics of Patients Participating in the Study ( $M\pm\sigma$ )

Parameters		Age 18-35 years (n=42)	Age 36-45 years (n=47)	Age 46-60 years (n=73)	Age 61-90 years (n=109)
Mean age, years	mixed group	28.00±5.34	41.00±2.81	53.0±4.4	70.0±8.7
	men	27.0±5.2	41.00±2.71	53.00±4.63	71.00±8.35
	women	29.00±5.24	41.00±2.67	53.00±4.23	69.00±8.77
BMI, kg/m <sup>2</sup>	mixed group	26.16±5.80	29.37±6.46	28.84±4.54	30.96±10.19
	men	27.74±5.78	28.93±6.67	28.29±3.39	30.67±13.36
	women	25.01±4.73	29.81±6.42	29.66±5.89	31.22±6.54

the presence of SARS-CoV-2 RNA by ELISA and PCR, course of the disease, epidemiological data on possible virus transmission route, general data about the patient, complications of the underlying disease, data on laboratory-confirmed viral or fungal co-infection, laboratory tests, *etc.*

The study participants were divided into 4 age groups (18-35, 36-45, 46-60, and 61-90 years) and then by sex within each group. The age and body mass index (BMI) of the patients are presented in Table 1.

The blood for measuring SOD activity was taken from the cubital vein early in the morning on an empty stomach. SOD activity was measured in erythrocytes on a BTS 350 spectrophotometer (Bio-Systems) [13].

The data obtained were processed in the Statistica 10 (StatSoft, Inc.). The samples were characterized by a predominantly normal distribution, so the differences between the groups were assessed by the parametric Student's *t* test. The results are presented as  $M\pm\sigma$ . The differences were significant at  $p<0.05$ .

## RESULTS

The results of comparative analysis of SOD activity in the mixed groups are shown in Figure 1. In the group 18-35 years, SOD activity was higher than in the groups 46-60 years ( $p<0.01$ ) and 61-90 years ( $p<0.05$ ).

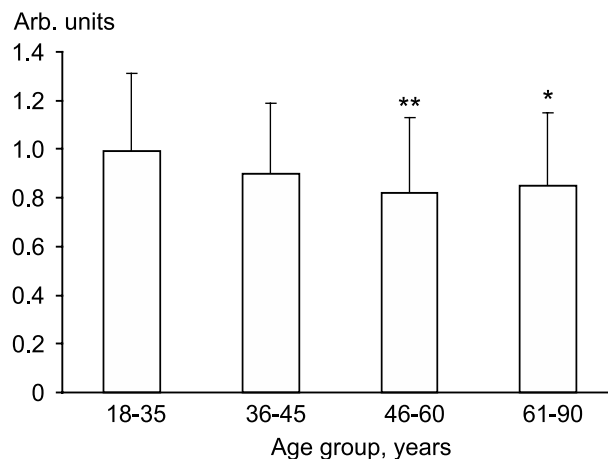
The division of groups by sex showed that 18-35-year-old women had higher SOD activity than 36-45- ( $p<0.05$ ), 46-60- ( $p<0.01$ ), and 61-90-year-olds ( $p<0.01$ ). This can be due to higher estrogen levels in the early reproductive period, because estrogens are known to have antioxidant properties and can influence activity of antioxidant enzymes, including SOD. Thus, in a study involving women with surgical menopause, along with a decrease in their estrogen level, reduced expression of SOD mRNA was found, while hormone replacement therapy increased this parameter [4].

When comparing the age groups of male and female patients separately, higher SOD activity was revealed in women only in the group 18-35 years ( $p<0.05$ ;

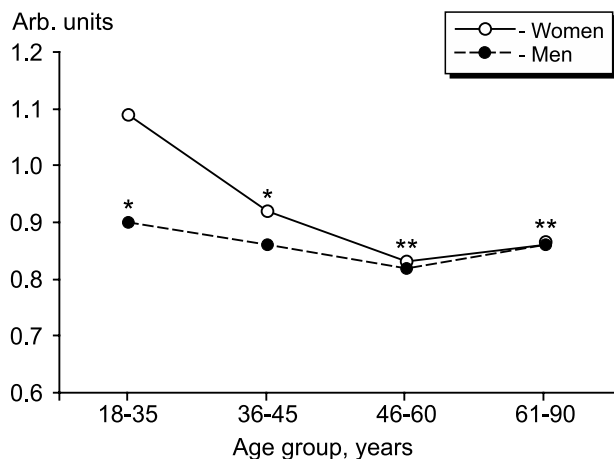
Fig. 2), which can also be determined by different estrogen levels in females and males. The absence of sex differences in other age groups is most likely due to gradual decrease in the level of sex hormones in women starting from the late reproductive period (36-45 years). Similar levels of enzyme activity across age groups in male patients with COVID-19 can also be due to the lack of regulatory effects of estrogen.

Previous studies of free radical processes in patients with COVID-19 showed both a decrease [10] and an increase in SOD activity [12] in the mixed groups (without division by sex and age). The study [10] compared patients with COVID-19 in severe and critical condition with patients with moderate COVID-19, while the study [12] included predominantly elderly patients, irrespective of the disease severity. The results obtained by us on standardized groups of patients showed the dependence of SOD activity on sex, as well as on age (in women). This should be taken into account when considering rationale for antioxidant therapy in COVID-19 patients, which is currently actively discussed [5,6].

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**Fig. 1.** SOD activity in patients with moderate COVID-19 in different age groups. \* $p<0.05$ , \*\* $p<0.01$  in comparison with the group 18-35 years.



**Fig. 2.** SOD activity in male and female patients with moderate COVID-19 in different age groups. \* $p < 0.05$ , \*\* $p < 0.01$  in comparison with 18-35-year-old women.

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