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Characteristics of Coagulation Hemostasis in Corona Virus Infection

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Abstract. Studying the activity of coagulation hemostasis in the main groups of coronavirus infection helps to prevent life-threatening complications . In the clinical study, 350 patients were examined, including 100 patients with mild, 150 moderate and 100 severe coronavirus infections. Coagulation hemostasis indicators did not reliably change in patients with mild coronavirus infection, but hypercoagulation was detected in moderate and severe coronavirus infection: active partial thromboplastin time decreased by 26 - 40%, INR decreased to 0.79 ± 0.05*, thrombin time 22, decreased by 3-45.2%, fibrinogen increased by 37.4 - 58.6%, D dimer increased by 69% and more.

Key words: Coronavirus infection, coagulation hemostasis, hypercoagulation.

Introduction.

During the initial period of the coronavirus infection, the disease suddenly worsened and led to high mortality even with optimal treatment. The conducted studies showed that the pathogenesis of the infection was associated not only with the development of viral pneumonia, severe respiratory failure, but also with the emergence of a strong hypercoagulable state. Molecular mechanisms of hypercoagulation in patients with COVID-19 have been found to be closely related to inflammation [6].

One of the factors that cause the activation of the blood clotting system is an increase in the amount of inflammatory cytokines, which leads to a "cytokine storm". The "cytokine storm" created as a result of inflammation leads to the formation of inflammatory thromboses-immunothrombosis [3].

Immunothrombosis of pulmonary microvessels is of great importance in the progression of respiratory failure in COVID-19 [7]. In addition, a sharp increase in the amount of antiphospholipid antibodies (anticardiolipin IgA, anti-β 2-glycoprotein 1, immunoglobulin A and G) in the blood of patients with multiple cerebral infarctions in severe COVID-19 can be a proof of a strong

inflammatory process. In a study by French scientists, 25 (45%) of 56 patients with COVID-19 had borax anticoagulants [9].

Coronavirus-induced coagulopathy initially leads to the development of hypercoagulation. D-dimer in this concentration increases sharply, prothrombintime (PV) decreases , fibrinogen increases. In rare cases , the concentration of antithrombin III (AT III) in the blood decreases by 80% , the concentration of protein C does not change [2]. At the same time, active partial thromboplastin time (APT) is reduced in COVID-19, and coagulation factor VIII is increased [8].

Monitoring of PV, AChTV, D-dimer, and fibrinogen levels is important in determining the prognosis of patients [3]. An increase in the concentration of D-dimer is a prognostic indicator of the severity of the patient's condition [10], indicating the need for intensive therapy [11].

According to ISTH recommendations, it is necessary to check D-dimer concentration, prothrombin time, platelet count in all patients with SARS-CoV-2 in order to determine the possibility of hospitalization [13].

Hyperfibrinogenemia is a marker of COVID-associated coagulopathy. N. Tang and co-authors found that all patients hospitalized with COVID-19 had an increased level of fibrinogen. They reported higher levels of fibrinogen in patients with COVID-19 compared to controls: 5.02 g/l in patients and 2.9 g/l in controls. An increase in D-dimer along with fibrinogen is considered a bad prognostic sign. When the amount of fibrinogen exceeds 5 g/l, a correlation with SRO was found, and in hypofibrinogenemia, a relationship between fibrinogen and INR was found [1]. M.Ranucci and co-authors found a correlation between hyperfibrinogenemia and increased interleukin-6 [4].

As a result of DTII-syndrome in patients infected with COVID-19, pulmonary microvessels are diffusely damaged, resulting in the development of acute respiratory distress syndrome (ARDS), which leads to death [14]. DTII syndrome occurred in 0.6% of patients who recovered, and 71.4% of patients who died [12].

In COVID-19, severe coagulopathy, arterial and venous thrombosis appeared to be the main causes of death [5]. Therefore, changes in coagulation hemostasis are an urgent problem.

Purpose of the study

Study of changes in coagulation hemostasis in patients with coronavirus infection (CI).

Materials and methods

Clinical studies were conducted at the 2nd Zangiota Infectious Disease Hospital during 2021. The study examined 350 patients, including 100 mild, 150 moderate, and 100 severe CI patients. The diagnosis was made using the diagnostic criteria presented in "Provisional recommendations for the

treatment of patients with coronavirus infection". CIvirus i markers in all patientsdetermined by enzyme immunoassay (IFA) and polymerase chain reaction (PCR) methods.

All examined patients were divided into 3 groups: group 1 consisted of 100 patients with mild CI, group 2 with 150 patients with medium-severe level, and group 3 with 100 patients with severe level of CI (Figure 1).

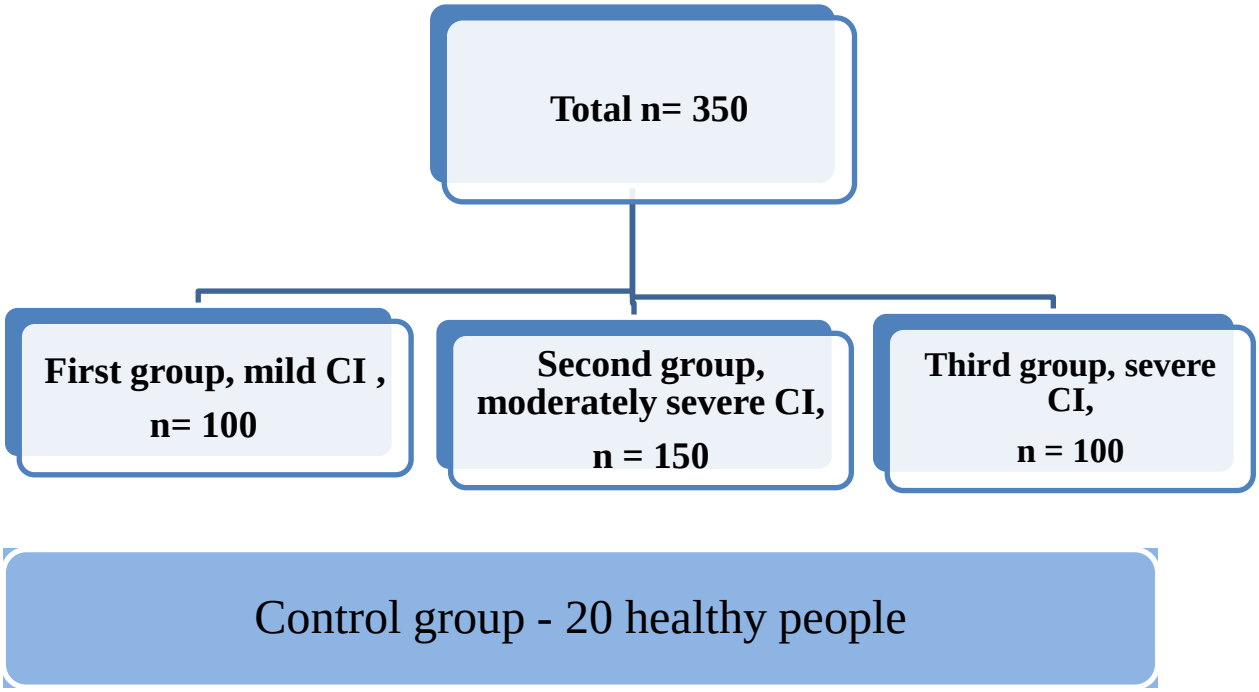

Figure 1. Research design

195 of 350 examined patients(55.7 %) were women and 155 (44.3 %) were men . The age of the patients in the study ranged from 18 to 74 years, and their average age was 48.2 ± 12.1 years .

In the main groups, there were 96 (27.4%) patients aged 18-44, 102 (29.1%) patients aged 45-59, and 152 (43.5%) patients aged 60-74 (table 1).

1 table
Distribution of patients by age

G groups	Patient age , years					
	18-44		45 – 5 9		60– 7 4	
	abc	%	abc	%	abc	%
First group, (n=100)	35	10.0	34	9.7	31	8.9
Second group, (n= 150)	33	9.4	36	10.3	81	23.1

Third group , (n= 100)	28	8.0	32	9.1	40	11.5
Total	96	27.4	102	29.1	152	43.5

From the above, it became clear that among the examined patients, women dominated and made up 195 (55.7%). Age distribution showed that among the selected patients, mainly patients aged 60-74 years prevailed.

Patients whose CI virus markers were not detected in IFA and PCR analyzes were not included in the study.

Active partial thromboplastin time (AQTV), prothrombin time (PV), prothrombin index (PTI), MNO (INR), thrombin time (TV), fibrinogen, D-dimer were examined to study the state of coagulation hemostasis.

AQTV, PV, PTI, INR, TV, fibrinogen, and D-dimer were tested on a Sysmex CA 660 automatic coagulometer (Japan), using Sysmex (Japan) reagents.

Research results

Determination of AQTV in the main groups of COVID-19 helped to determine the following changes: AQTV in group 127.5 ± 2.3 sec, in group 2 22.4 ± 1.9 sec*, in group 3 18.2 ± 1.5 sec ***, and in the control group, AQTV was 30.1 ± 2.8 sec. Reduction of QIV and AQTV indicates strong hypercoagulability in stage 1 of coagulation hemostasis (Fig. 2).

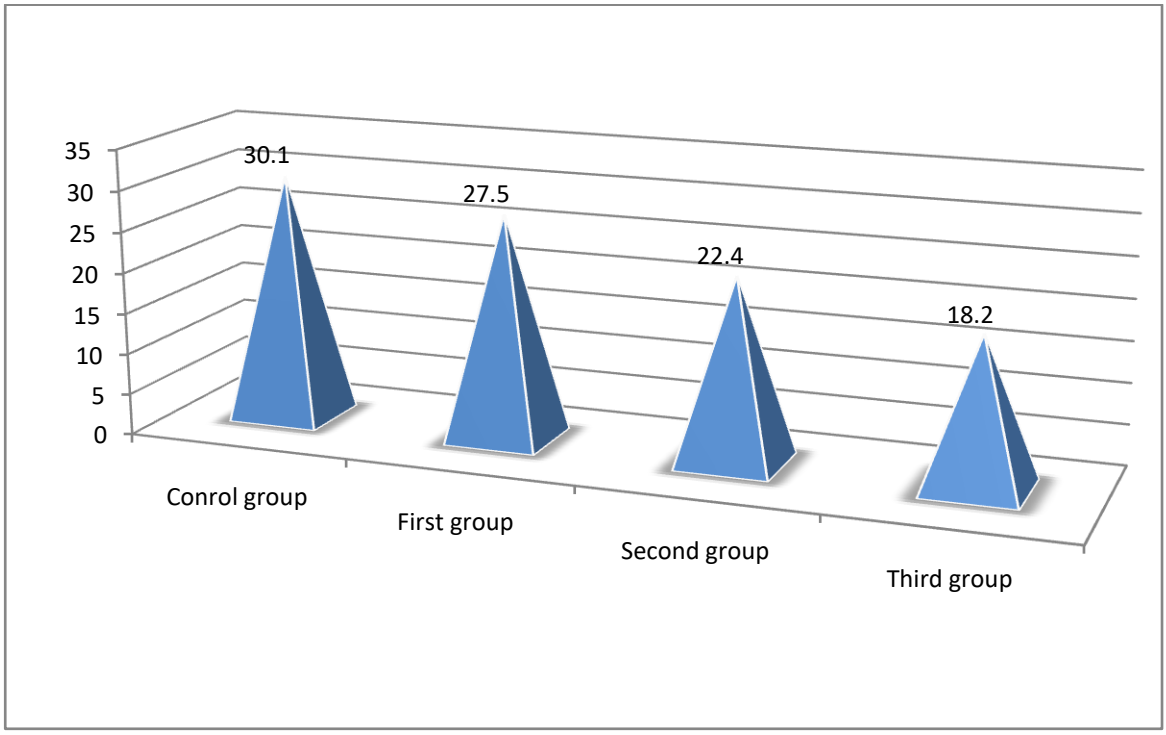

Figure 2. AQTV in coronavirus infection, sec.

In conclusion, it should be noted that AQTV did not reliably change in patients with mild CI, but in moderate and severe CI, AQTV was reduced by 26 - 40%, which indicates a hypercoagulable shift. Prothrombin time examination revealed that PV was 11.4 ± 0.7 sec in group 1, 10.2 ± 0.6 sec* in group 2, 9.5 ± 0.6 sec** in group 3, and 12 in the control group. It was 4 ± 1.1 seconds.
The prothrombin index was 105 ± 8.5% in group 1, 118 ± 7.5%* in group 2, 126 ± 10.1%* in group 3, and 97.0 ± 8.2% in the control group (2- table).

Table 2.

Evaluation of stage 2 coagulation in CI

G groups	**PV , s eq**	**PTI, %**	**INR**
Control group (n= 20)	12, 4 ±1.1	9 7 ± 8 .2	1.0 3 ±0.0 7
First group, (n=100)	1 1 , 4 ± 0.7	1 0 5± 8.5 _	0.95 ± _0.0 8
Second group, (n= 150)	10.2±0.6 *	118 ± 7.5 *	0.85±0.05*
Third group , (n= 100)	9.5 ± 0.6**	1 26 ± 10.1*	0.7 9±0.0 5 *

Note: * - the difference compared to the control group is reliable (*-R<0.05; **-R<0.01; *** - R<0.001)

As can be seen from the above data, the international normalized ratio did not change in mild CI, and INR decreased from 0.85 ± 0.05* to 0.79 ± 0.05* in moderate and severe CI. In the control group, INR was 1.03 ± 0.07.
Examination of thrombin time in CI revealed analogous changes. TV 14.6 in group 1±1.3sec, 12.3 ± 1.1 sec in group 2, 10.3 ± 0.9 sec in group 3, and 18.8 ± 1.0 sec in the control group. formed Analysis of VT showed that VT was normal in mild CI, and TV was reduced by 22.3-45.2% in moderate and severe CI compared to the control group, indicating gi percoagulation (Table 3).

Table 3. Thrombin time indicators in CI, sec.

Indicators	T rombin time
Control group , (n=20)	18.8 ± 1.0
First group, (n=100)	16.6±1.3
Second group, (n= 150)	15.3 ± 1.3*
Third group , (n= 100)	14.2 ± 1.2**

Note: * - controlgroupindicatorsrelatively the difference is reliable (*- R < 0.05; **- R < 0.01; *** - R < 0.001)

Fibrinogen is the factor 1 of blood coagulation, which was found to be increased in CI (see Table 3.5). Fibrinogen in group 1 was 3.55 ± 0.32 g/l, in group 2 4.85 ± 0.43 g/l, in group 3 5.60 ± 0.47 g/l , and in the control group 3.53 ± It was observed to be 0.20 g/l. In conclusion, it can be said that the amount of fibrinogen increased by 29.7% in mild CI compared to the control group, by 37.4% in moderate CI, and by 58.6% in severe CI (Table 4).

Table 4.Indicators of fibrinogen and D dimer in CI.

Indicators	**Fibrinogen , (mg/dl)**	**D dimer, ng/ml**
Control group, (n=20)	283 ± 22	154 ± 12
First group, (n=100)	355 ± 32	180 ± 22
Second group, (n= 150)	446 ± 43**	260 ± 28***
Third group , (n= 100)	510 ± 47***	350 ± 33***

Note: * - controlgroupindicatorsrelatively the difference is reliable (*- R < 0.05; **- R < 0.01; *** - R < 0.001)

D-dimer is a product of thrombus breakdown, and it has been observed to increase dramatically in patients with coronavirus infection. The amount of D dimer in group 1 was 180 ± 22 ng/ml, in group 2 it was 260 ± 28 ng/ml***, in group 3 it was 350 ± 33 ng/ml***, and in the control group it was 154 ± 12 ng/ml. did In group 1, the amount of D dimer was normal, in group 2 it was 69% higher than in the control group, and in group 3 it was more than 2 times higher.

Discussion of research results

In conclusion, it can be said that moderate and severe CI coagulation hemostasis in all joints has strong hypercoagulation compared to the control group.

In patients with mild CI, AQTV did not change reliably, but in moderate and severe CI there was a decrease in AQTV by 26 - 40%, which indicates a hypercoagulable shift.

Examination of the prothrombin time revealed that in group 1, it was reduced to 10.2 ± 0.6 sec* in moderate CI and 9.5 ± 0.6 s** in severe CI, compared to normal group 1. While the prothrombin index was normal in group 1, it increased by 21% in moderate CI and by 29% in severe CI. At the same time, the international normalized ratio did not change in mild CI, and INR decreased from 0.85 ± 0.05* to 0.79 ± 0.05* in moderate and severe CI.

Examination of thrombin time in CI revealed analogous changes. In mild CI, TV was normal, but in moderate and severe CI, TV was reduced by 22.3 - 45.2% compared to the control group, which indicates hypercoagulability.

Fibrinogen increased by 37.4% in moderate and 58.6% in severe CI. A sharp increase in D-dimer was observed in patients with coronavirus infection. In group 1, the amount of D dimer was normal, in group 2 it was 69% higher than in the control group, and in group 3 it was 2 times higher.

Conclusions

1. All indicators of coagulation hemostasis did not reliably change in patients with mild CI.
2. In moderate and severe CI, AQTV decreased by 26 - 40%, PV decreased from 10.2 ± 0.6 sec* to 9.5 ± 0.6 sec**, TV decreased by 22.3-45.2%, which indicates hypercoagulability.
3. The amount of fibrinogen increased by 37.4 - 58.6% in moderate and severe CI, while D dimer increased by 69% in group 2 and more than 2 times in group 3.
4. In conclusion, it can be said that moderate and severe CI coagulation hemostasis in all joints has strong hypercoagulation compared to the control group.

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