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#### **Research Article**

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#### Studying the Causes of Cavernous Sinus Thrombosis at COVID-19

M.M. Yakubova<sup>1</sup>, G.Q. Rakhmatullaeva<sup>2</sup>, K.S. Mirzaeva<sup>3</sup>, S.K. Said-Akhmedova<sup>4</sup>, M.A. Ikromova<sup>5</sup>

#### **ABSTRACT**

**Background.** Currently, complications developing in patients with COVID-19 are a serious health problem worldwide. Purpose of the study: to study the causes of thrombosis of cavernous sinus in patients with COVID-19

**Material and methods.** 147 patients with cavernous sinus thrombosis (TCS) and Covid-19 were investigated. Of these, 88 (61%) are men and 59 (39%) are women. Methods of Examination: clinical-neurological, general clinical and biochemical research, MRI/MSCT of the brain. Statistical analysis was carried out in Microsoft Excel 2010, descriptive statistics.

**Results.** The age of patients with TCS ranged from 22 to 81 years (average age 54.97±0.93), more often at the age of 40–70 years (80%). Men were more often ill between the ages of 41 and 60 years (59%) (average age 51.68±1.17), and women from 51 to 70 years (75%) (average age - 60.22±1,25). Before Covid-19, 73% of patients suffered from diabetes. The first clinical signs of COVID-19 were increasing body temperature (90%) and the violation of smell and taste (89%). The TCS developed in patients on average after 21.40±1.54 days after detection of COVID-19. However, in women, it begins earlier (an average of 18.56±2.12 days) than in men (an average of 23.37±2.13 days).

Conclusions. TCS at COVID-19 was more often observed (80%) aged 40–70 years (cf. age -  $54.97 \pm 0.93$ ). TCS is more often found in the average age group in men, however in women medium and elderly age group. Diabetes mellitus may be a risk factor for the development of TCS. The first clinical signs of COVID-19, in patients of the TCS, were increasing the body temperature (90%), and the violation of smell and taste (89%). TCS develop on average after  $21.40\pm1.54$  days, after the detection of COVID-19.

Keywords: COVID-19, cavernous sinus thrombosis, SARS-COV-2, coronavirus infection.

#### INTRODUCTION

urrently, there is no doubt that the complications that arise in patients who have passed the disease of COVID-19 are the main problem of the entire world health system. To determine the

causes, clinical course and prognostic factors of complications arising in patients with SARS-CoV-2, many works are being carried out by scientists from all over the world [2].

<sup>&</sup>lt;sup>1</sup> Professor, DSc, Department of Neurology and Medical Psychology, Tashkent Medical Academy, Tashkent, Uzbekistan, e-mail: <a href="marken:ma

<sup>&</sup>lt;sup>2</sup> Associate Professor, DSc, Department of Neurology and Medical Psychology, Tashkent Medical Academy, Tashkent, Uzbekistan, e-mail: gulnoramed@bk.ru

<sup>&</sup>lt;sup>3</sup> Associate professor, PhD, Department of Neurology and Medical Psychology, Tashkent Medical Academy, Tashkent, Uzbekistan, e-mail: kmirzaeva 1932@mail.ru

<sup>&</sup>lt;sup>4</sup> Independent researcher, Department of Neurology and Medical Psychology, Tashkent Medical Academy, Tashkent, Uzbekistan, e-mail: <a href="mailto:saodat-3352@yandex.ru">saodat-3352@yandex.ru</a>

<sup>&</sup>lt;sup>5</sup> Student of master's degree, Department of Neurology and Medical Psychology, Tashkent Medical Academy, Tashkent, Uzbekistan, e-mail: <a href="mailto:abdushukurovamufazzal95@gmail.com">abdushukurovamufazzal95@gmail.com</a>

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As research in this area increases, so does the number of identified risk factors for COVID-19 screening and complications. For the further development of the field of clinical medicine and public health, it is very important to pay special attention to those complications that pose a serious threat to human life [1].

Cavernous sinus thrombosis as a complication of the disease of COVID-19 is often reported in world scientific publications, including the reports that it is associated with various clinical neurological disorders as a result [3].

The connection between COVID-19 and cavernous sinus thrombosis (CST), the difference in survival in patients with gender, age, other somatic diseases, the correlation with the severity of the disease, the recovery time, and the extent to which it affects the quality of life of patients have not yet been sufficiently studied. Answering these questions and early detection of neurological changes after cavernous sinus thrombosis observed as a complication of COVID-19 is indeed an urgent task at present [4, 5].

The purpose of the study. To investigate the causes of cavernous sinus thrombosis in patients with COVID-19.

#### MATERIALS AND METHODS

147 patients with cavernous sinus thrombosis associated with coronavirus infection were studied. Their age ranged from 22 to 81 years (mean age 54.97±0.93). Of these, 88 (61%) were male (mean age 51.68±1.17), and 59 (39%) were female (mean age 60.22±1.25). Used examination methods: clinical-neurological, general clinical and biochemical analysis of blood and urine, MRI/MSCT of the brain. Statistical analysis was carried out in Microsoft Excel 2010, Descriptive statistics.

#### **RESULTS**

or the study, 147 patients with cavernous sinus thrombosis were studied. Of these, 88 (61%) were male and 59 (39%) were female (see table 1 and figure 1).

 $\label{eq:Table 1} \textbf{Table 1}$  Age and gender distribution of patients with cavernous sinus thrombosis

Age	Male	Male in %	Female	Female in %	Total number of patients
21-30 years old	2	2%	0	0%	2 (4%)
31-40 years old	11	13%	2	3%	13 (9%)
41-50 years old	28	32%	4	7%	32 (22%)
51-60 years old	24	27%	28	47%	52 (35%)
61-70 years old	18	20%	16	27%	34 (23%)
71-80 years old	5	6%	8	14%	13 (9%)
81-90 years old	0	0	1	2%	1 (0.7%)
Total number	88	61%	59	39%	147 patients

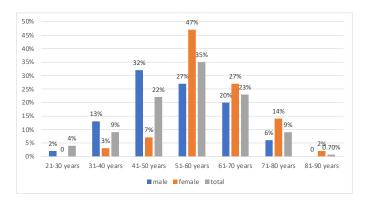


Figure 1. Distribution of patients with cavernous sinus thrombosis by age and sex

If we consider Table 1, the age of patients with CST varies widely. The youngest patient was 22 years old, and the oldest was 81 years old. There was also a difference in their average age. The mean age of the total patients was  $54.97\pm0.93$ , but the mean age of males  $(51.68\pm1.17)$  was lower than that of females  $(60.22\pm1.25)$  and the overall mean age.

Studies have shown that CST is more common (80%) among patients aged 40–70 years. When studied about gender, men with CST were more often affected in the middle age group (41-50 years - 32%, 51-60 years - 27%, total - 59%), and women in older age groups, that is, 51-60 years - 47%, 61-70 years old - 27%, total -75%.

Therefore, CST is generally more common in middle-aged patients. According to gender, it is more common in young and middle-aged men, and older women - middle-aged and elderly.

How many diseases did CST patients suffer from before the coronavirus infection? The results of the tests showed that the patients had the following diseases before the onset of COVID-19 (see Table 2 and Figure 2).

Gender	Diabetes mellitus type 2	Hyperten sion disease	Ischemi c heart disease	Diabetes mellitus diagnose d for the first time	Chronic renal failure	Anemia	Liver cirrhosis and hepatitis
Male	62 (58%)	21 (54%)	13 (48%)	10 (67%)	1 (33%)	4 (67%)	2 (67%)
Female	45 (42%)	18 (46%)	14 (52%)	5 (33%)	3 (67%)	2 (33%)	1 (33%)
Total	107 (73%)	39 (27%)	27 (18%)	15 (10%)	4 (3%)	6 (4%)	3 (2%)

The most common disease was type 2 diabetes (73%), 10% of which was diagnosed for the first time. 27% of patients had hypertension, 18% had ischemic heart disease, and less often - 2-4% had chronic kidney failure, anemia, liver cirrhosis and hepatitis.

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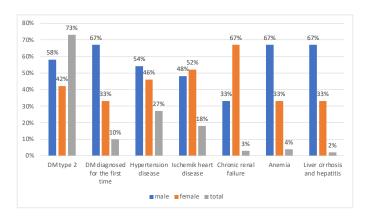


Figure 2. Distribution of comorbidities of patients who underwent CST

Therefore, the role of diabetes in the development of CST in the case of coronavirus infection is very important, and in some cases, diabetes is detected together with the disease for the first time.

During the study, the first clinical signs of coronavirus infection in patients who underwent CST were found as follows (see Table 3 and Figure 3).

Table 3
Early clinical signs of coronavirus infection in patients who underwent CST.

Initial manifestations of COVID-19	Male N=88	%	Female, N=59	%	Total N=147	%
Increased body temperature	81	92	53	90	134	91
Panting and breath failure	33	37	10	17	43	29
Chest pain	7	8	3	5	10	7
Rhinitis	13	15	6	10	19	13
Impaired sense of smell and taste	79	90	52	88	131	89
Cough	40	45	18	30	58	39

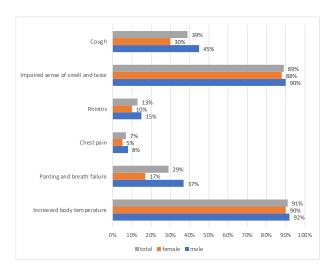


Figure 3. Early clinical signs of coronavirus infection in patients who underwent CST

Patients were primarily bothered by increased body temperature (90%) and impaired sense of smell and taste (89%). Cough (39%), panting and shortness of breath (29%), rhinitis (13%) and chest pain (7%) were observed in a small number of cases. When comparing the sexes, no significant difference was found, except that respiratory failure was twice as common in men than in women (men-37%, women-17%).

The first symptoms of CST developed in patients on average 21.40±1.54 days after detection of COVID-19. However, it starts earlier in women (mean 18.56±2.12 days) than in men (mean 23.37±2.13 days) (see table 4 and figure 4).

 $\label{thm:constraints} Table~4~$  Days after the onset of COVID-19 when the first symptoms of CST appear

CST initial marks period	Days of average	Reliability criterion		
Male	23,37±2,13	P≤0,05		
Female	18,56±2,12	P≤0,05		
Total	21,40±1,54	P≤0,05		

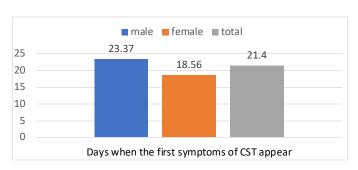


Figure 4. Days after the onset of COVID-19 when the first symptoms of CST appear

When the duration of the initial symptoms of CST is studied by gender, in days and percentages, the disease mainly falls.

#### DISCUSSION

ccording to literary data, due to COVID-19, the cause of thrombosis of the cavernous sinus was usually the spread of bacteria from the places of infection in the face (including the skin of the nose) or sinuses. It was believed that thrombosis of the cavernous sinus was an extremely rare complication of infectious diseases of the maxillofacial region, most often boils of the nasal vestibule (50%), sphenoid or ethmoid sinusitis (30%) and odontogenic infections (10%) [11,12]. The most common pathogens are Staphylococcus aureus (70%) and Streptococcus generation bacteria. In the case of infection of one of the sinuses of the nose or dental infection, anaerobes are a more common source [6-9].

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Among the predisposing factors, the most frequent are hereditary and acquired thrombophilia - pathological conditions, characterized by an increased tendency to develop blood vessel thrombosis, which is based on disturbances in various links in the hemostasis and hemorheology system [10]. But, from the advent of the coronavirus infection, the TKS began to meet more often leading to death or severe disability [3,13]. In affordable literature, there is very little data about TCCs during COVID-19. We hope that our article will help to learn about some causal factors for the development of TKS during COVID-19.

#### **CONCLUSION**

o, what conclusions have we reached because of studying the causes of cavernous sinus thrombosis developed against the background of COVID-19? When cavernous sinus thrombosis was studied about age, the age of patients varied widely (from 22 to 81 years). The average age is 54.97±0.93 and it is more common among patients aged 40–70 years (80%). But when studied about gender, it is more common in young and middle-aged men, and older women - middle-aged and elderly.

In a study of the causes of cavernous sinus thrombosis, it was found that most patients had diabetes before the onset of COVID-19 (73%), and in some cases, diabetes was detected for the first time with the disease (10%).

The first clinical signs of coronavirus infection in patients undergoing CST were increased body temperature (90%) and impaired sense of smell and taste (89%). Relatively fewer patients were bothered by cough (39%), shortness of breath and shortness of breath (29%). However, shortness of breath is twice as common in men as in women (men-37%, women-17%).

The first symptoms of CST develop in patients on average 21.40±1.54 days after detection of COVID-19. When the duration of the initial symptoms of CST is studied about gender, in days and percentages, the disease mainly corresponds to the first 30 days after the infection of COVID-19 (87%). In women, it was detected more often in the first 20 days (71%), and in men in the first 30 days (86%).

**Conflict of interest:** the authors declare that there is no conflict of interest.

**Financing source.** The authors declare that no funding was received for this study.

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#### KOVID-19 DA KAVERNOZ SINUSI TROMBOZIN-ING KELIB CHIQISH SABABLARINI O'RGAN-ISH

## M.M. Yakubova, G.Q. Rakhmatullaeva, K.S. Mirzaeva, S.K. Said-Akhmedova, M.A. Ikromova Toshkent Tibbiyot Akademiyasi Abstrakt

**Dolzarbligi.** COVID-19 bilan kasallangan bemorlarda yuzaga keladigan asoratlar bugungi kunda butun jahon sog'liqni saqlash tizimi uchun jiddiy muammo bo'lib qolmoqda.

**Tadqiqot maqsadi.** COVID-19 boʻlgan bemorlarda kavernoz sinusi trombozi (KST) kelib chiqishini sabablarini oʻrganish.

**Tadqiqot materiali.** COVID-19 boʻlgan KST bor 147 ta bemor oʻrganildi. Ularning yoshi 22 dan 81 yoshgacha boʻlgan (oʻrtacha yoshi - 54,97±0,93). Bulardan 88 nafari (61%) erkak va 59 nafari (39%) ayol jinsiga mansubdir.

**Tadqiqot uslublari.** Klinik-nevrologik, umumklinik va biokimyoviy tahlillar, bosh miya MRT/MSKTsi. Statistik tahlil «Microsoft Excel 2010, Opisatelnaya statistika» dasturida oʻtkazildi.

Tadqiqot natijasi. Kasallik 40–70 yoshli bemorlar o'rtasida ko'p uchragan (80%), o'rtacha yoshi 54,97±0,93 boʻlgan. Erkaklar KST bilan koʻproq oʻrta yosh guruhida (41-60 yoshda, jami - 59%, oʻrtacha yoshi -51,68±1,17), ayollar esa yoshi kattaroq guruhlarda (51-70 yoshda, jami -75 %, oʻrtacha yoshi 60,22±1,25) kasallangan. COVID-19 boʻlishdan avval 73% bemorlarda qandli diabetning 2-tipi boʻlgan. COVID-19 ning ilk klinik belgilari tana haroratini oshishi (90%) va xid va ta'm sezgisini buzilishi (89%) bo'lgan. KST ning birinchi belgilari bemorlarda COVID-19 aniqlangandan keyin o'rtacha 21,40±1,54 kunda rivojlangan. KST koʻproq ayollarda birinchi 20 kunlikda (71%), erkaklarda esa, birinchi 30 kunlikda aniqlangan (86%).

**Xulosa.** COVID-19 da KST 40–70 yoshli bemorlar oʻrtasida koʻp (80%) uchraydi, (oʻrtacha yosh - 54,97±0,93). Qandli diabet KST keltirib chikaruvchi omil boʻlishi mumkin.

KST boʻlgan bemorlarda COVID-19 ning ilk klinik belgilari tana haroratini oshishi (90%) va xid va ta'm sezgisini buzilishi (89%) boʻlgan. KST ning birinchi belgilari, COVID-19 aniqlangandan keyin, oʻrtacha 21,40±1,54 kunda rivojlangan.

**Kalit so'zlar:** COVID-19, kavernöz sinus trombozi, SARS – CoV-2, koronavirus infeksiyasi.

#### ИЗУЧЕНИЕ ПРИЧИН ТРОМБОЗА КАВЕРНОЗНОГО СИНУСА ПРИ COVID-19

М.М. Якубова, Г.К.Рахматуллаева, К.С.Мирзаева, С.К.Саид-Ахмедова, М.А.Икромова Ташкентская Медицинская Академия АБСТРАКТ

**Актуальность.** Осложнения, возникающие у больных COVID-19, в настоящее время являются серьезной проблемой здравоохранения во всем мире.

**Цель исследования:** Изучить причины возникновения тромбоза кавернозного синуса у пациентов с COVID-19

**Материал исследования.** Исследованы 147 пациентов с тромбозом кавернозного синуса (ТКС) с COVID-19. Из них 88 (61%) - мужчины и 59 (39%) -женщины.

Методы обследования: клиниконеврологический, общеклинический и биохимический исследования, MPT/MCKT головного мозга. Статистический анализ проводился в Microsoft Excel 2010, описательная статистика.

Результаты исследования: Возраст больных ТКС колебался от 22 до 81 года (ср. возраст  $54,97\pm0,93$ г.), чаще в возрасте 40-70 лет (80%). Мужчины чаще болели в возрасте от 41 до 60 лет (59%) (ср. возраст  $51,68\pm1,17$ г.), а женщины от 51 до 70 лет (75%) (ср. возраст -  $60,22\pm1,25$ г.). До COVID-19 73% больных страдали сахарным диабетом. Первые клинические признаки COVID-19 были повышение температуры тела (90%) и нарушение обоняния и вкуса (89%). ТКС развивался у пациентов в среднем через  $21,40\pm1,54$  дня после выявления COVID-19. Однако, у женщин оно начинается раньше (в среднем на  $18,56\pm2,12$  день), чем у мужчин (в среднем на  $23,37\pm2,13$  день).

**Выводы.** ТКС при COVID-19 чаще наблюдался (80%) в возрасте 40–70 лет (ср. возраст -  $54,97\pm0,93$  г.) У мужчин ТКС чаще встречается в средней

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возрастной группе, а у женщин – средней и пожилой. Сахарный диабет может быть фактором риска развития ТКС. Первыми клиническими признаками COVID-19, у пациентов перенесших ТКС, были повышение температуры тела (90%), нарушение

обоняния и вкуса (89%). ТКС развиваются в среднем через  $21,40\pm1,54$  дня, после выявления COVID-19.

**Ключевые слова:** COVID-19, тромбоз кавернозного синуса, SARS-CoV-2, коронавирусная инфекция.