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Medical and Socio-Psychological Consequences of the COVID-19 Pandemic on People with Congenital Bleeding Disorders and Their Caregivers

Haluk Zülfikar[1], Başak Koç[2], Gülnihal Gözüdok[3], Bülent Züfikar[2]

[1]Istanbul University, Faculty of Economics, Istanbul, Turkiye
[2]Istanbul University, Oncology Institute, Inherited Bleeding Disorders Center, Istanbul, Turkiye
[3]Abant Izzet Baysal University, Faculty of Medicine, Bolu, Turkiye

ORCID ID: H.Z. 0000-0002-9712-5373; B.K. 0000-0002-0978-7992; G.G. 0000-0001-9207-0767; B.Z. 0000-0002-7586-6939

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ABSTRACT

Objective: This study aimed to reveal the effects of the COVID-19 pandemic on congenital bleeding disorders (CBDs) patients and the hematology specialists following them.
Material and Methods: CBDs patients with and without a history of COVID-19 being followed up at the oncology institute of a university hospital were considered one study group (71 patients), and hematology specialists from Turkey were considered a separate study group (35 physicians). Data were collected using two questionnaires during face-to-face interviews.
Results: During the pandemic, it was found that 29.3% of COVID-19-positive patients and 50% of COVID-19-negative patients had various degrees of bleeding (p=0.023). It was observed that the data on increase in bleeding, switching to treatment when bleeding, and decrease in mobilization were more negative in patients who were not diagnosed with COVID-19 compared to those who were diagnosed with COVID-19. No difference was found between the two groups in terms of having problems accessing the product used in treatment. More than half of the patients with CBDs expressed high levels of pandemic-related anxiety for themselves and their relatives.
Of the physicians, 34.3% stated they were highly concerned about the patients they followed during the pandemic. Physicians with more professional experience also had higher levels of anxiety about COVID-19.
Conclusion: Our study shows that the COVID-19 pandemic has caused mental health problems not only among patients with chronic health problems but also among healthcare workers who are fighting the pandemic on the frontlines.
Keywords: COVID-19, hemophilia, blood coagulation disorders, patient health questionnaire

INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARSCoV-2), which emerged in Wuhan, China in late 2019, has spread rapidly, leading to the Coronavirus Disease 2019 (COVID-19) pandemic. While the most common clinical findings are influenza-like symptoms, 15% to 20% of patients, in particular those with advanced age and comorbidities, develop severe interstitial pneumonia and respiratory failure, which may result in death and require intensive care and mechanical ventilation (1,2).

For the past two years, an unprecedented global health crisis has been ongoing, affecting patients, doctors, and other health professionals, causing changes in attitudes and behaviors. In addition, many countries are resorting to social isolation as a precautionary measure to combat the pandemic, and there are concerns that these measures may limit access to the usual standard of medical care and create problems with the management of chronic diseases (1,3).

As in other chronic diseases, there are some concerns about the sustainability of treatment management for patients with congenital bleeding disorders (CBDs). These concerns are related

Corresponding Author: Haluk Zulfikar **E-mail:** halukzul@gmail.com
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to therapeutic product supply chains as well as potential negative impacts on patients' medical care and mental health (4,5). The impact of the pandemic and the measures taken on patients with CBDs has yet to be fully established. Recommending healthy practices to patients with congenital bleeding disorders is particularly important to prevent the serious consequences of the COVID-19 pandemic. Similarly, the impact of the pandemic on the physicians who treat patients with CBDs is also an important issue that needs to be addressed.

In this study, we aimed to reveal the effects of the COVID-19 pandemic on patients with CBDs and the adult and/or pediatric hematology specialists who follow them and the resulting changes in attitudes and behaviors.

MATERIAL AND METHODS

This study was planned as a non-interventional, cross-sectional type and was conducted on two different target groups. CBDs patients with and without a history of COVID-19 who were being followed up at the oncology institute of a university hospital were considered as one study group, and adult and/or pediatric hematology specialists from a total of 27 different centers from all 12 regions of Turkey within the scope of NUTS1 were considered as a separate study group. All participants gave informed consent and the study was approved by the by the clinical research ethics committee of a university (18.02.2022-approval no: 750500) in accordance with the Declaration of Helsinki.

Data were collected using two questionnaires for participating patients and physicians during face-to-face interviews. The patient questionnaire included demographic information as well as measurement items (questions) that assessed changes in clinical findings, treatment compliance and practices, and anxiety levels during the COVID-19 pandemic. The questionnaire for physicians included demographic information and items measuring the extent to which they had been affected by the COVID-19 pandemic.

Statistical Analysis

Statistical Package for Social Science; version 21 (SPSS) program was used for data analysis. In descriptive statistics, numerical data were presented as mean and standard deviation, whereas categorical variables were expressed as frequencies and percentages. Differences between subgroups were analyzed by Student's t-test for numerical variables and Chi-square (χ^2) test for categorical variables. Correlation analyses were performed using Spearman (r_s) test. The significance value was considered as $p<0.05$.

RESULTS

Between April 2020 and May 2021, 71 people completed the questionnaires, among whom 41 patients with CBDs, including 40 patients diagnosed with COVID-19 and one exposed, and 30 CBD cases without a diagnosis of COVID-19 (Table 1). The diagnosis was made by PCR test in 31 patients, by clinical findings in nine patients, and by computerized thoracic tomography (CT) in one patient. Patients diagnosed with COVID-19 accounted for 6.3% of the 648 patients with CBDs admitted to our institution. The number of COVID-19 positive people in the data of the Ministry of Health on the same dates was 163.942 and the ratio of this number in the population of Turkey was 0.19% (163.942/85.04 million) (6).

The mean age of patients who were COVID-19 positive was 33.5±15 years and 7.32% of them were female, while the mean age of COVID-19 negative patients was 31.5±9.9 years and all of them were male. Of these patients, 82.5%(n=33) were on clotting factor concentrates (16 for prophylaxis, 17 when bleeding), 7.5%(n=3) were on bypass-acting clotting concentrates (two for prophylaxis, 17 when bleeding) and (n=4) were on fitusiran, which is currently under clinical investigation. Twelve patients with COVID-19 had comorbid conditions. These were diabetes, hypertension, and thyroid disease in three patients each, and obesity, asthma, Familial Mediterranean Fever, intracranial shunt, basal cell carcinoma, heart valve insufficiency, and celiac disease in one patient each. Among COVID-19-negative patients, one had comorbidity (autoimmune thyroiditis).

During the pandemic, it was found that 29.3% of COVID-19-positive patients and 50% of COVID-19-negative patients had various degrees of bleeding due to hemophilia and other CBDs (Table 2). This difference was found to be statistically significant ($p=0.023$; $p<0.05$).

Table 1: Baseline characteristics of COVID-19 positive and negative cases enrolled in the study.

	COVID-19 Positive (+)	COVID-19 Negative (-)	Total
Hemophilia A	21	27	48
• Severe (with inhibitor)	19 (5)	26	45 (5)
• Moderate	2	1	3
Hemophilia B	11	3	14
• Severe	4	3	7
• Moderate	5	-	5
• Mild	2	-	2
vWD	7	-	7
FXI Deficiency	1	-	1
EXPOSED	1	-	1
TOTAL	41	30	71

Table 2: Bleeding status of Congenital Bleeding Disorder cases during the pandemic.

	n	%	n	%
None	29	70.7	15	50.0
Mild bleeding*	4	9.8	3	10.0
Moderate bleeding**	6	14.6	11	36.7
Severe bleeding***	2	4.9	1	3.3
Total	41	100.0	30	100.0

* Severe bleeding with major trauma or surgery; rare spontaneous bleeding; ** Occasional spontaneous bleeding; prolonged bleeding with minor trauma or surgery; *** Mainly spontaneous bleeding into joints or muscles without identifiable hemostatic strain (trauma, surgery, etc.) (19).

Changes in clinical signs and treatment were evaluated and it was observed that the data on increase in bleeding, switching to treatment when bleeding, and decrease in mobilization were more negative in patients who were not diagnosed with COVID-19 compared to those who were diagnosed with COVID-19 ($p \leq 0.05$) (Table 3). No difference was found between the two groups in terms of having problems accessing the product used in treatment ($p \geq 0.05$). Only four of the cases (5.6%) reported having difficulty accessing the product (Table 3).

More than half (54.9%) of the patients with congenital bleeding disorders expressed high levels of pandemic-related anxiety for themselves and their relatives. The rate of high anxiety was 43.9% in the group with COVID-19 and 70% in the group without COVID-19 (p=0.096, Table 4).

Of the hematology specialists included in the study, 77% (n=27) were pediatricians and eight 23% (n=8) were internal medicine specialists, all of whom were treating patients with congenital bleeding disorders. Among the physicians, most of whom (30/35; 86%) worked in a university hospital, 34% were women, 20% had less than 5 years of experience and 31% had more than 15 years of experience.

Eighty percent of the hematologists reported mild or moderate bleeding in their patients.

Of the physicians, 34.3% stated that they were highly concerned about the patients they followed during the pandemic. A significant relationship was found between the gender of the physicians and their level of concern in favor of the female gender (r_s=0.39 (39%); p=0.021) (Table 5). Physicians with more professional experience also had higher levels of anxiety about COVID-19 (Figure 1). No difference was found between pediatric and adult hematology specialists' levels of concern about the COVID-19 risk of the patients they followed during the pandemic (p=0.766>0.05; rs=-0.102).

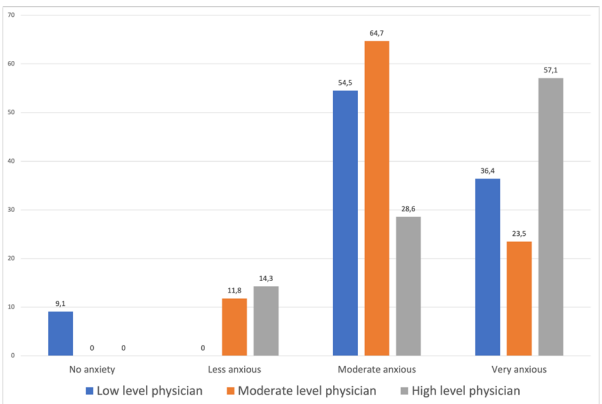


Figure 1: Physician's anxiety levels

DISCUSSION

The pandemic has led to psycho-social problems as well as medical problems with the suspicion that those with comorbidities in addition to signs of systemic disease

Table 3: Selected behaviors of cases with congenital bleeding disorders who are COVID-19 positive and negative.

	COVID-19 negative		COVID-19 positive		Difference Values (Positive-Negative)	
	n	%	n	%	n	%
Decreased frequency of infusions	8	26.7	11	26.8	3	- 0.2
Switch from prophylaxis regimen to infusion as bleeding occurs	12	40.0	11	26.8	1	+13.2
Postponement of scheduled surgeries	7	23.3	10	24.4	3	- 1.06
Forced switch due to product supply problems	1	3.3	3	7.3	3	- 3.98
Decreased communication due to the requirement to visit the hospital	13	43.3	15	36.6	2	+ 6.8
Obligation to learn how to use infusion at home	4	13.3	7	17.1	3	-3.7
TOTAL (CBD = 71)	30	100.0	41	100.0	11	

Table 4: Anxiety levels of cases with congenital bleeding disorders who are COVID-19 positive and negative

	Level of Anxiety				
	None	Low	Moderate	High	Total
COVID-19 negative	1 (3.3%)	3 (10.0%)	5 (16.7%)	21 (70.0%)	30 (100.0%)
COVID-19 positive	5 (12.2%)	3 (7.3%)	15 (36.6%)	18 (43.9%)	41 (100.0%)
Total	6 (8.5%)	6 (8.5%)	20 (28.2%)	39 (54.9%)	71 (100.0%)

*p= 0.096

Table 5: Anxiety levels of hematology specialists by gender

	Women		Men		Total	
	n	%	n	%	n	%
Low	0	0.0	4	16.7	4	11.4
Middle	5	45.5	14	58.3	19	54.3
High	6	54.5	6	25.0	12	34.3
TOTAL	11	100.0	24	100.0	35	100.0

related to the sars cov-2 virus were more affected (5). The suspicion of over-exposure in the elderly, as well as those with immunodeficiency, chemotherapy, or biological product users, was questionable in all those with CBDs, especially hemophiliacs (3,4).

Many scientific organizations such as the World Federation of Hemophilia (WFH) consider that patients with hemophilia are not at high risk for COVID-19 infection (7,8). However, there are also studies suggesting that patients with CBDs had a higher incidence of COVID-19 during this period (7). In addition, since most patients with CBDs show a general state of hypocoagulability, a study has also been published stating that this creates a protective effect against hypercoagulability in COVID-19 (9).

Based on the results of the questionnaire completed by 71 cases of CBD in our study, 26.8% of 41 patients who were COVID-19 positive or exposed during the pandemic, and 53.3% of 30 patients who were COVID-19 negative experienced various degrees of bleeding. The difference was statistically significant. During the pandemic, a greater increase in bleeding, a higher rate of switching to treatment due to bleeding, and a greater decrease in mobilization were observed in those who did not have COVID-19. In addition, pandemic-related concerns about themselves and their relatives were higher in this group, although not statistically significant.

The presence of chronic disease was a prominent source of concern during the pandemic. In patients with a life-long bleeding disorder, the sources of concern vary considerably. Failure to maintain the supply chains of the factor concentrates they use continuously, reduced donations of blood and plasma, reduced access to healthcare facilities and/or hemophilia treatment centers, postponement of elective surgeries they need, and the potential cessation of clinical trials in which they are involved are the main concerns (3-5,7,10-12).

Dorgalaleh et al. observed that in 25 COVID-19 patients with CBD, the main concern was the infection and death of their loved ones and the economic burden resulting from the infection of themselves or their relatives. During the pandemic, 6 patients had depression, and all but one of them missed replacement therapies. Of the four patients who received prophylaxis, only one received full treatment during the stay-at-home period, while the others discontinued prophylaxis. The authors stressed that COVID-19 infection had significant consequences on the lives of patients with CBD and caused some of them to engage in dangerous actions such as discontinuing treatment (12). In our study, 30% of our patients with COVID-19 and 37% of our patients without COVID-19 discontinued prophylaxis and switched to treatment when bleeding.

It was emphasized that the treatment, nutrition, and mental health of patients with hemophilia may be affected during the COVID-19 pandemic (1,7). The World Federation of Hemophilia (WFH) has published specific recommendations for these patients, however, it is known that interruption in the supply of replacement products due to problems in air transportation and other restrictions may be a problem for patients living in low- and middle-income countries where the rate of exposure to the virus is high and access to treatment is inadequate (1). In our study, only 8% of 71 patients with CBD reported difficulties in product procurement.

Apart from the logistical effects of the pandemic on patients' treatment, changes in patients' thoughts, behaviors, and emotions about their medical care cause them to worry and

have negative effects on their mental health (4,5).

In a systematic review of 16 quantitative studies conducted with 40,076 participants between 2019 and 2021 during the pandemic, high rates of anxiety, depression, and stress due to the pandemic were observed in adolescents with different backgrounds. It was also demonstrated that the frequency of alcohol and cannabis use by adolescents increased during the COVID-19 pandemic (13).

Moreover, it is known that insomnia has been quite common during the pandemic, and psychological reactions and poor sleep hygiene have also been reported in individuals without COVID-19 infection. It has been reported that prominent anxiety and depressive symptoms during the pandemic are associated with the fear of being infected in an environment with a rapidly increasing number of cases. In addition, economic stress, social distancing rules, and travel restrictions have also been found to be effective (14,15). In addition, suspected/confirmed cases, living in the most affected areas, and longer exposure to media during the day have been associated with a higher likelihood of anxiety and depression (15).

A review of 24 articles on the psychological impact of quarantine found that effective causes of stress included prolonged quarantine, fear of infection, frustration, boredom, inadequate supplies, inadequate information, financial losses, and stigmatization (16). In another study conducted in the USA to understand the psychological problems of the COVID-19 pandemic and its impact on the general fear associated with the virus, it was reported that the pandemic was associated with high levels of psychological stress and led to mental health disorders such as depression, anxiety and substance use (17). In this study, it was also found that age, male gender, and physical health were protective factors for stress (17). In our study, no statistically significant relationship was found between age and level of anxiety ($p>0.05$).

In the COVID-19 pandemic, healthcare workers mobilized all their resources to provide emergency and widespread healthcare services in an environment of general uncertainty. This situation has increased the concerns of healthcare professionals treating and caring for COVID-19 patients about mental health, psychological adjustment, and patient recovery. The factors affecting this situation are diverse. They include the number of individuals infected with the virus, lack of information about the course of the disease, deaths among health professionals, depletion of personal protective equipment, concerns about not being able to provide competent care when placed in a new area, lack of specific medications, increasing number of critically ill patients, lack of full-fledged care and treatment units, significant changes in social and family life, the feeling of inadequate support, concerns about their own health, fear of transmitting their infection to family members or others. There is also consensus that healthcare workers are at high risk of high levels of stress, anxiety, depression, burnout, addiction, and post-traumatic stress disorder, which may have long-term psychological effects (18).

In conclusion, our study shows that the COVID-19 pandemic has caused mental health problems not only among patients with chronic health problems but also among healthcare workers who are fighting the pandemic on the frontlines. Similar studies are important to show that health worker protection measures are also an important component of future health strategies. Therefore, we believe that it is necessary to develop strategies such as psychological support and training on crisis management for healthcare workers exposed to similar pandemic processes.

Ethics Committee Approval: This study was approved by Istanbul University Istanbul Faculty of Medicine Clinical Research Ethics Committee (18.02.2022-approval no: 750500)

Informed Consent: Written consent was obtained from the participants.

Peer Review: Externally peer-reviewed.

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