

ORIGINAL ARTICLE

Clinical haemophilia

Impact of first COVID-19 lockdown on paediatric and adult haemophilia patients treated in a French Haemophilia Comprehensive Care Centre

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Abstract

Introduction: The coronavirus disease 2019 (COVID-19) pandemic has created an unprecedented global health crisis.

Aim: To investigate the impact of the 1st COVID-19 lockdown on haemophilia patients in terms of symptoms, management, medication adherence, mental health and lifestyle behaviours.

Methods: A prospective cross-sectional phone survey using a two-part questionnaire was conducted in haemophilia patients (adults and children) followed-up in a French Haemophilia Comprehensive Care Centre between May 5, 2020 and June 2, 2020 (CLEO CD study: NCT04390126).

Results: Among 284 haemophilia A or B patients with FVIII or FIX < 40% contacted for the study, 239 (84%) including 183 adults and 56 children participated to the survey. In 81% of children and 78% of adults, bleeding episodes remained unchanged or decreased. Medication adherence was 82.0% in adults and 98.2% in children. Non-adherence concerned haemostatic agents in six patients and analgesics in three. Overall, 67% of adults and 71% of children felt as good as before lockdown. In both adults and children, the three major changes in lifestyle behaviours were: increase in screen time (49% and 57%), decrease in physical activity (43% and 48%), and weight gain (32% and 27%), respectively.

Conclusions: Encouraging results were observed in terms of haemophilia symptoms, medication adherence, and mental health. Conversely, a negative impact was observed on lifestyle behaviours in a cohort of French haemophilia patients during the 1st lockdown.

KEYWORDS

COVID-19, haemophilia, lifestyle behaviours, lockdown, medication adherence, symptoms

1 | INTRODUCTION

On May 14, 2021, the number of deaths due to the coronavirus disease 2019 (COVID-19) worldwide exceeded 3.3 million, with 107,000

in France.¹ Following the COVID-19 outbreak in Wuhan, China, the disease spread rapidly throughout the world. Therefore, governments were forced to impose nationwide lockdowns. Lockdowns likely exert a devastating impact on patients suffering from chronic diseases.²⁻⁴

Although such effects have already been partly investigated in the general population,⁵ among healthcare professionals,⁶ and in patients suffering from cancer,⁷ little is known on their global impact in haemophilia patients.⁸⁻¹⁵ Concerns have rapidly emerged regarding the pandemic's impact of and its deleterious consequences on healthcare access and global management of haemophilia patients. Moreover, the COVID-19 pandemic may also encourage adverse changes in health behaviours, such as decrease in physical activity¹⁶ and sleep times, or increase in alcohol consumption, thereby altering the patients' general health and well-being.¹⁷ We thus hypothesised that younger and older haemophilia patients might experience further discomfort, unusual anxieties, and peculiar fears during this pandemic. Therefore, we aimed to investigate the impact of the 1st COVID-19 lockdown on haemophilia symptoms and management, as well as mental health and lifestyle behaviours.

2 | PATIENTS AND METHODS

2.1 | Haemophilia management during 1st lockdown

The Haemophilia Comprehensive Care Centre at Dijon University Hospital offers 24h/24 dedicated care, every day of the year, to haemophilia patients, involving a multidisciplinary team with three haematologists, one nurse, and two medical secretaries.

Since the beginning of the first French COVID-19 lockdown, local protocols in accordance with the recommendations established by the World Federation of Haemophilia (WFH) for optimal management and follow-up of haemophilia patients were adopted in our centre.¹⁸⁻²² In a first step, all of our 40 patients suffering from severe haemophilia A or B were contacted by phone. Calls primarily sought to reassure patients on the continuity of care during lockdown period. Patients were informed that the hospital pharmacy would continue to supply them with haemostatic treatments based on regular appointments. They were also informed that they had to attend the centre only in case of emergency (overt bleeding or haemarthrosis). Non-urgent face-to-face visits were performed by phone or reported after June 2020. Non-urgent surgeries were reported. Physical presence of the multidisciplinary team was limited to the strict necessary, with one full-time haematologist in the centre and another one in the haemostasis laboratory. Finally, all members of the multidisciplinary team could be contacted by phone at any time, if necessary.

2.2 | Study population

The COVID-19 Lockdown Effects On Chronic Diseases (CLEO-CD) phone survey was a cross-sectional study involving stay-at-home patients of all ages from eight different chronic disease cohorts or registries located in the Burgundy region, one of the main epicentres of the 1st COVID-19 outbreak in France. The CLEO-CD study was reg-

ESSENTIALS

- The Haemophilia Comprehensive Care Centre of Dijon University Hospital provides dedicated care to patients with haemophilia and other bleeding disorders.
- Since the beginning of the 1st COVID-19 lockdown, local protocols in accordance with the recommendations established by the World Federation of Haemophilia (WFH) for optimal management and follow-up of haemophilia patients have been adopted.
- The CLEO-CD cross-sectional study (NCT04390126) aimed to investigate the impact of COVID-19 lockdown on haemophilia symptoms and management, as well as mental health and lifestyle behaviours.
- Encouraging results were observed in terms of haemophilia symptoms, medication adherence, and mental health. Conversely, a negative impact was observed on lifestyle behaviours in a cohort of French haemophilia patients during the 1st lockdown.

istered on ClinicalTrials.gov (identifier: NCT04390126). Oral consent was obtained for each patient before enrolment.

The recruitment to the CLEO-CD study was previously described.²³⁻²⁶ The entire haemophilia patient population followed-up in our centre was invited to participate to the study. Inclusion criteria were: haemophilia A or B or haemophilia A or B carriers, with factors (F) VIII or IX activities < 40%; children aged between 1 and 18 years or adults over 18 years. Exclusion criteria were: non-response to three phone calls at different times of the day and different days of the week, impossibility to communicate orally due to language barrier or cognitive impairment, refusal to participate, and death.

2.3 | Study design

The phone survey was based on a structured two-part questionnaire, with a general and specific part. General and specific parts were slightly different for adults and for children. All questionnaires were tested and slightly modified before the beginning of the study. In the general questionnaire, patients were mainly asked about sociodemographic, global and mental health data, as well as lifestyle behaviours during lockdown. Specific questionnaires focused on symptomatic or therapeutic (haemostatic and analgesics) changes, health care, and psychosocial aspects for children.

The 30-min interviews were conducted by different members of the multidisciplinary team of our centre (two haematologists, one nurse, and one medical secretary) with the help of two medicine/pharmacy students specifically recruited for the study. All interviewers were trained to CLEO-CD questionnaires before they started phone calls.

Phone calls were performed between May 5 and June 2, 2020 (i.e., between the end of the 1st lockdown period and the beginning of the 1st post-lockdown period). For children aged < 10 years, parents were invited to answer.

Medication non-adherence was defined if the patient spaced out, discontinued, or changed the dosage of at least one of his/her current medicines him/herself without any healthcare professional advice (physician; pharmacist).

Psychological distress was assessed based on the Kessler Psychological Distress Scale K6 score.²⁷ The K6 scale has been widely used, evidencing reliability and validity across a wide variety of mental health surveys.^{27,28} The scale includes six items associated with psychological distress during the previous 4 weeks. It is based on six questions, which were used in our survey as follows: How often have you been feeling (a) nervous, (b) restless or fidgety, (c) so sad nothing could cheer you up, (d) hopeless, (e) everything was an effort, and (f) worthless? The answer to each question was given via a 5-point Likert scale ranging from 0 'never' to 4 'very often'. A K6 result of 5 or above indicates psychological distress.²⁷

2.4 | Statistical analysis

Data were described for the entire population or specifically for adults and children. In adults and children (< 10 [parents responders] and ≥ 10 years [children responders]), haemophilia symptoms, haemostatic treatment adherence, mental health variables were also described and compared depending on severity (severe, moderate and minor), type of the disease (A and B) and haemostatic treatment (on demand and prophylactic) using chi-square or Fisher exact test. P values < .05 were considered significant. Categorical variables were expressed as counts and percentages. Continuous variables were summarised as means \pm standard deviations, or medians and ranges, depending on their distribution. Statistical analyses were performed using SAS statistical software, Version 9.1 (SAS Institute, Cary, NC, USA).

3 | RESULTS

3.1 | Baseline patient characteristics

Sociodemographic and clinical characteristics of the study population are summarised in Table 1. Among 284 patients contacted by phone, 239 (84%) agreed to participate to the study. There were 56 (23%) children and 183 (77%) adults, with a mean age of 9.5 ± 4.8 years and 47.6 ± 18.1 years, respectively. For children aged < 10 years, only parents ($n = 29$) responded to the phone calls. There were 175 (73%) haemophilia A (HA) and 64 (27%) haemophilia B (HB) patients, most of them suffering from mild disease. An inhibitor was present in seven (3%) cases. Haemostatic treatments were on-demand in 203 (85%) and prophylactic in 36 (15%) patients. Only four (2%) patients were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

using polymerase chain reaction during the period, with all found to be negative.

Of the 239 patients, 221 (92%) were living in a house or an apartment with terrace or garden, and only 18 (8%) in an apartment without terrace nor garden. Overall, 144 (60%) patients lived in a rural area. Only 29 (16%) adults were living alone.

3.2 | Haemophilia management

During the 1st lockdown period, 21 scheduled face-to-face visits were performed by phone, nine were reported, and two were cancelled. Of the 27 scheduled interventions/surgeries, 11 were carried out with two of them in severe HB patients (one anal fistula and one coronarography). Sixteen non-urgent interventions/surgeries were reported or cancelled in one child (circumcision) and 15 adults (dental, $n = 7$; orthopaedic, $n = 3$; digestive, $n = 3$, gynaecologic, $n = 1$, varicose veins, $n = 1$).

3.3 | Haemophilia symptoms, medication adherence and mental health

Haemophilia symptoms, haemostatic treatment adherence and mental health during the 1st lockdown period are presented in Table 2 for adults and in Table 3 for children (< 10 and ≥ 10 years). During the period, there were 74 bleeding episodes in 70 (29%) patients. Forty nine adults presented 52 bleeding episodes (out of which six haemarthroses) and 21 children presented 22 bleeding episodes (out of which two haemarthroses); 74% of all bleeding episodes were self-treated with or without haematologist advice. No severe consequences were observed in these patients. In patients with haemorrhagic signs before lockdown, 78% of adults and 81% of children had stable or decreased bleeding frequencies. A similar observation was made for joint pain, with no changes observed in a majority of patients.

Overall medication adherence (haemostatic and other medicines) was 82.0% in adults and 98.2% in children. Non-adherence concerned haemostatic agents in six patients and analgesics in three. Among the 36 patients receiving a prophylactic haemostatic treatment, six (17%; one child, five adults) spaced out intervals between injections due to reduced physical activity ($n = 4$), reduced professional activities ($n = 1$), or fear of drug shortage ($n = 1$). All of them were receiving extended half-life agents. Among the 181 patients taking analgesics, three (2%; three adults) decreased intakes because of fear of adverse events/developing a more severe form of COVID-19 in the event of infection.

Overall, 67% of adults and 71% of children felt as good as before lockdown. At the time of the survey, 74% of adults and 70% of children declared they felt good or very good. Approximately 84% of adults were not considered as suffering from any psychological distress (i.e., K6 score < 5). No changes were observed in 71% of children behaviours according to their parents or the children themselves

TABLE 1 Sociodemographic and clinical characteristics of the study population

Variables	Overall population (n = 239)	%	Paediatric patients (n = 56)	%	Adult patients (n = 183)	%
<i>Gender</i>						
Female	51	21	14	25	37	20
Male	188	79	42	75	146	80
<i>Age</i>						
Mean \pm SD	38.7 \pm 22.7	-	9.5 \pm 4.8	-	47.6 \pm 18.1	-
Median [Q1;Q3]	37.8 [19.4;59.0]		8.9 [5.7;13.3]		44.1 [33.0;63.3]	
<i>Residence during lockdown</i>						
House, apartment with terrace/garden	221	93	54	96	167	91
Apartment without terrace/garden	18	7	2	4	16	9
<i>Residence area during lockdown</i>						
Rural (< 2000 inhabitants)	144	60	30	54	114	62
Urban (\geq 2000 inhabitants)	95	40	26	46	69	38
<i>Family environment during lockdown</i>						
Living alone	-	-	-	-	29	16
Living with other people	-	-	-	-	154	84
Living with both parents	-	-	42	75	-	-
Living with one parent	-	-	10	18	-	-
Unknown	-	-	4	7	-	-
<i>Type of haemophilia</i>						
A	175	73	43	77	132	72
B	64	27	13	23	51	28
<i>AHF level</i>						
Mean \pm SD	15.6 \pm 13.6	-	14.0 \pm 15.3	-	16.1 \pm 13.0	-
Median [Q1;Q3]	13.0 [3.0;29.0]		6.0 [0.0;31.0]		14.0 [4.0;28.0]	
<i>Severity</i>						
Severe (AHF < 1%)	40	17	20	36	20	11
Moderate (AHF [1;6]%)	45	19	7	13	38	21
Mild (AHF [6;40]%)	154	64	29	52	125	68
<i>Inhibitor</i>						
No	232	97	54	96	178	92
Yes	7	3	2	4	5	8
<i>Type of treatment</i>						
On demand	203	85	36	64	167	91
Prophylaxis	36	15	20	36	16	9
<i>Comorbidities</i>						
Cardiovascular diseases	49	21	1	2	48	26
Pulmonary diseases	23	10	8	14	15	8
Digestive diseases	9	4	0	-	9	5
Cancer \pm treatment	5	2	0	-	5	3
Venous thromboembolism	2	1	0	-	2	1
Other disorders	17	7	4	7	13	7

(Continues)

TABLE 1 (Continued)

Variables	Overall population (n = 239)		Paediatric patients (n = 56)		Adult patients (n = 183)	
		%		%		%
COVID-19 screening						
No	235	98	56	100	179	98
Yes	4	2	0	-	4	2
COVID-19 screening result						
Negative	4	2	0	-	4	2

Abbreviations: AHF, anti-haemophilic factor.; Q, quartile; SD, standard deviation.

TABLE 2 Haemophilia symptoms, haemostatic treatment adherence and mental health in adults by type and severity

Haemophilia type	A (n = 132)			B (n = 51)		
	Severe (n = 14, 11%)	Moderate (n = 12, 9%)	Minor (n = 106, 80%)	Severe (n = 6, 12%)	Moderate (n = 26, 51%)	Minor (n = 19, 37%)
Haemostatic treatment, n (%)						
On demand	2 (14)	12 (100)	106 (100)	2 (33)	26 (100)	19 (100)
Prophylactic	12 (86)	-	-	4 (67)	-	-
Haemophilia symptoms						
Bleeding episodes, n (%)						
No	8 (57)*	7 (58)*	83 (78)*	2 (33)	18 (69)	16 (84)
Yes	6 (43)*	5 (42)*	23 (22)*	4 (67)	8 (31)	3 (16)
Overt bleeding	5 (83)	5 (100)	23 (100)	2 (50)	8 (100)	3 (100)
Haemarthrosis	2 (33)	-	1 (4)	3 (75)	-	-
Haemorrhagic signs before/during lockdown, n (%)						
No	7 (50)	7 (58)	83 (78)	2 (33)	17 (65)	16 (84)
No change	5 (36)	4 (33)	17 (16)	2 (33)	7 (27)	2 (11)
Decrease	1 (7)	-	1 (1)	-	1 (4)	-
Increase	1 (7)	1 (8)	5 (5)	2 (33)	1 (4)	1 (5)
Joint pain before/during lockdown, n (%)						
No	4 (26)	8 (67)	52 (49)	-	18 (69)	11 (58)
No change	6 (43)	3 (25)	42 (40)	2 (33)	7 (27)	4 (21)
Decrease	2 (14)	-	2 (2)	1 (17)	-	-
Increase	2 (14)	1 (8)	10 (9)	3 (50)	1 (4)	4 (21)
Haemostatic treatment adherence						
No spacing	8 (67)	NA	NA	3 (75)	NA	NA
Spacing	4 (33)	NA	NA	1 (25)	NA	NA
Mental health						
Worse feeling than before lockdown, n (%)						
No	8 (57)	8 (67)	71 (67)	6 (100)	17 (65)	11 (58)
Yes	6 (43)	4 (33)	35 (33)	-	9 (35)	8 (42)
K6 score, n (%)						
<5	11 (79)	10 (83)	90 (85)	4 (67)	22 (85)	16 (84)
≥5	3 (21)	2 (17)	16 (15)	2 (33)	4 (15)	3 (16)

*p = .045 (Fisher exact test); no other significant differences were observed.

Abbreviations: K6, Kessler psychological distress scale-6 items; NA, not applicable.

TABLE 3 Haemophilia symptoms, haemostatic treatment adherence and mental health in children by type and severity

Age category	<10 years (parents responders ; n = 29)					≥10 years (children responders ; n = 27)					
Haemophilia type	A (n = 23)*		B (n = 6)			A (n = 20)			B (n = 7)		
Severity	Severe (n = 12, 52%)	Minor (n = 11, 48%)	Severe (n = 2, 33%)	Moderate (n = 3, 50%)	Minor (n = 1, 17%)	Severe (n = 4, 20%)	Moderate (n = 2, 10%)	Minor (n = 14, 70%)	Severe (n = 2, 29%)	Moderate (n = 2, 29%)	Minor (n = 3, 42%)
<i>Haemostatic treatment, n (%)</i>											
On demand	-	11 (100)	-	3 (100)	1 (100)	-	2 (100)	14 (100)	-	2 (100)	3 (100)
Prophylactic	12 (100)	-	2 (100)			4 (100)	-	-	2 (100)	-	-
<i>Haemophilia symptoms</i>											
<i>Bleeding episodes, n (%)</i>											
No	8 (67)	5 (45)	1 (50)	2 (67)	1 (100)	3 (75)	2 (100)	9 (64)	-	2 (100)	2 (67)
Yes	4 (33)	6 (55)	1 (50)	1 (33)	-	1 (25)	-	5 (36)	2 (100)	-	1 (33)
Overt bleeding	4 (100)	6 (100)	1 (100)	1 (100)	-	1 (100)	-	5 (100)	1 (50)	-	1 (100)
Haemarthrosis	-	1 (17)	-	-	-	-	-	-	1 (50)	-	-
<i>Haemorrhagic signs before/during lockdown, n (%)</i>											
No	7 (59)	5 (45)	-	2 (67)	1 (100)	3 (75)	1 (50)	7 (50)	-	2 (100)	1 (33)
No change	4 (33)	3 (27)	1 (50)	-	-	1 (25)	-	4 (29)	2 (100)	-	1 (33)
Decrease	1 (8)	-	-	-	-	-	1 (50)	3 (21)	-	-	1 (33)
Increase	-	3 (27)	1 (50)	1 (33)	-	-	-	-	-	-	-
<i>Joint pain before/during lockdown, n (%)</i>											
No	11 (92)	10 (91)	2 (100)	3 (100)	1 (100)	2 (50)	2 (100)	10 (71)	1 (50)	2 (100)	3 (100)
No change	1 (8)	-	-	-	-	1 (25)	-	3 (21)	-	-	-
Decrease	-	-	-	-	-	-	-	-	-	-	-
Increase	-	1 (9)	-	-	-	1 (25)	-	1 (8)	1 (50)	-	-
<i>Haemostatic treatment adherence</i>											
No spacing	12 (100)	NA	2 (100)	NA	NA	3 (75)	NA	NA	2 (100)	NA	NA
Spacing	-	NA	-	NA	NA	1 (25)	NA	NA	-	NA	NA
<i>Mental health</i>											
<i>Worse feeling than before lockdown, n (%)</i>											
No	10 (83)	5 (45)	2 (100)	2 (67)	1 (100)	2 (50)	1 (50)	11 (79)	1 (50)	2 (100)	3 (100)
Yes	2 (17)	6 (55)	-	1 (33)	-	2 (50)	1 (50)	3 (21)	1 (50)	-	-
<i>Child feeling towards the pandemics (multiple possible options)</i>											
Serene**	8 (67)	5 (45)	1 (50)	2 (67)	1 (100)	2 (50)	2 (100)	6 (43)	2 (100)	2 (100)	3 (100)
Sad	-	2 (18)	1 (50)	-	-	1 (25)	-	1 (7)	-	-	-
Worried	3 (25)	5 (45)	-	-	-	1 (25)	-	6 (43)	-	-	-
Anxious	-	2 (18)	-	-	-	-	-	1 (7)	-	-	-
Nervous/irritable	-	3 (27)	1 (50)	1 (33)	-	-	-	1 (7)	-	-	-
Angry	2 (17)	3 (27)	-	-	-	-	-	3 (21)	-	-	-
Isolated	1 (8)	1 (9)	-	-	-	-	-	3 (21)	1 (50)	-	-

(Continues)

TABLE 3 (Continued)

Age category	<10 years (parents responders ; n = 29)					≥10 years (children responders ; n = 27)					
	A (n = 23)*		B (n = 6)			A (n = 20)			B (n = 7)		
Haemophilia type	Severe (n = 12, 52%)	Minor (n = 11, 48%)	Severe (n = 2, 33%)	Moderate (n = 3, 50%)	Minor (n = 1, 17%)	Severe (n = 4, 20%)	Moderate (n = 2, 10%)	Minor (n = 14, 70%)	Severe (n = 2, 29%)	Moderate (n = 2, 29%)	Minor (n = 3, 42%)
Lack of appetite	1 (8)	1 (9)	-	-	-	-	-	1 (7)	-	-	-
Sleeping disorders	4 (33)	2 (18)	-	-	-	-	-	4 (29)	-	-	-
Others	-	2 (18)***	-	-	-	-	-	1 (7)****	-	-	-

*No child < 10 years had a moderate HA.

** HA children were significantly less serene than HB children (53% vs. 84%; $p = .02$); no other significant differences were observed.

*** Need of "kisses"; **** "Sick and tired".

Abbreviations: K6, Kessler psychological distress scale-6 items; NA, not applicable.

but 38% of children declared they presented difficulties at studying. Table 4 summarises children and parents daily life perceptions during the 1st lockdown.

In adults and in children (< 10 and ≥10 years), only two significant differences in terms of haemophilia symptoms, haemostatic treatment adherence and mental health depending on type and severity of the disease were observed (Tables 2 and 3). In HA adults, bleeding episodes were significantly different in severe, moderate and minor patients (43%, 42% and 22%, respectively; $p = .04$; Table 2); HA children were significantly less serene than HB children (53% vs. 84%; $p = .02$; Table 3). Only slight differences were observed for other criteria. As examples, severe HB adults presented a higher percentage of haemorrhagic signs increase (33%), joint pain increase (50%) and psychological distress (33% with a K6 score ≥5) (Table 2); in children, increase in haemorrhagic signs and/or joint pain were not only observed in case of severe A or B disease (Table 3).

3.4 | Lifestyle behaviours

In both adults and children, the three major changes in lifestyle behaviours included increase in screen time (49% and 57%), decrease in physical activity (43% and 48%), and weight gain (32% and 27%), respectively. In adults, a 16%-decrease in alcohol consumption was reported, as well as a 12%-increase in smoking/vaping (12%) (Table 5).

4 | DISCUSSION

Limited data are currently available concerning the impact of COVID-19 on haemophilia patients and their management.¹³ In particular, the major strength of our study is to bring about information on the whole population of haemophilia patients including children, providing a global evaluation on medical and pharmaceutical but also mental and lifestyle aspects.

Of the 284 patients followed-up in the Haemophilia Comprehensive Care Centre of our French administrative area, 239 patients including 56 children and 183 adults took part in the survey, resulting in an 84%

rate of participation. None of them was infected by the virus during the study period. The 84%-rate of participation compares favourably with most health-related surveys, highlighting the implication of patients or their parents in regard to the subject.²⁸

Due to the strict application of patient supply protocols between the hospital pharmacy and the centre, no haemostatic treatment shortage occurred. Of the 36 patients undergoing prophylactic treatment, only 17% of them were considered non-adherent because they spaced out their injections. No increase in the number of breakthrough bleedings was observed for these five adults and one child with extended half-life factors. Finally, after pharmacokinetic assessments, haematologists decided to prolong their dosing intervals, taking account of their reduced physical or work activities. Data from the Community of Madrid suggested that the main reasons for spacing out factor infusions were also fear of being left untreated when bleeding, becoming infected when attending the hospital pharmacy, and because of lower physical activity.¹³

No significant changes in frequencies of haemorrhagic signs occurred in most adults or children. The same finding was observed for joint pain and analgesic use. Even if we logically observed more bleeding episodes in severe and moderate HA adults and a trend towards higher frequencies of haemorrhagic signs and joint pain in severe HB adults, caution is needed regarding the small sample size. Globally, we only observed slight differences in terms of haemophilia symptoms or haemostatic prophylaxis adherence whatever the type and the severity of the disease. Of the 27 scheduled interventions during the study period, 16 interventions were postponed, while 11 were carried out. Nearly half of them were dental interventions that could easily be reported. Face-to-face consultations were mostly replaced by phone calls or postponed whenever possible. Physical visits were done in case of emergencies explaining the non-increase in haemophilia symptoms/complications. Finally, the low percentage of overall medication non-adherence (haemostatic agents and analgesics), in particular in children, is another positive indicator that may be explained by the rapid onset of management protocols in accordance with the recommendations established by the World Federation of Haemophilia (WFH) for optimal management and follow-up of haemophilia patients.¹⁸⁻²²

TABLE 4 Children and parents perceptions

Variables	Paediatric patients N = 56	%
<i>Parents behavioural change towards their child's haemophilia</i>		
No	42	75.0
Yes	14	25.0
<i>Reason for change</i>		
<i>Fear of COVID-19</i>	4	7.1
<i>Fear of bleedings during the lockdown/ "Not the moment to attend the emergency department"</i>	10	17.9
<i>Child behavioural change towards his/her family</i>		
No	40	71.4
Yes	16	28.6
<i>Nature of the behavioural change</i>		
<i>Opposition</i>	12	21.4
<i>Jealousy, possessiveness</i>	1	1.8
<i>More respectful</i>	1	1.8
<i>Dependence</i>	1	1.8
<i>Fear for COVID-19</i>	1	1.8
<i>Difficulties in studying and doing his/her homework</i>		
MD	7	12.5
No	28	50.0
Yes	21	37.5
<i>The child is missing ... (multiple options possible)</i>		
Family	44	78.6
Friends	41	73.2
Vacations/trips	35	62.5
Physical activity/sports	26	46.4
School	25	44.6

Abbreviation: MD, missing data.

We have reported encouraging results in terms of patient mental health. To date, only one German multicentric cross-sectional study focused on mental health in inherited bleeding disorders patients, showing particular thoughts and worries regarding COVID-19 with significant differences between caregivers and patients.¹² We did not observe any significant differences in mental health data reported by children ≥ 10 years old or their parents when they were < 10 years old. More than two-thirds of adults and children felt good or very good at the time of our survey, in accordance with a low 16%-percentage among adults considered as suffering from psychological distress (*i.e.*, K6 score > 5). Moreover, for more than two-thirds of children, behaviours towards their parents and family were unchanged. We only observed that HA children were less serene than HB children. Our positive mental health findings contrast with those of other surveys conducted during the same period. A British survey targeting healthcare professionals (HCPs) from 47 countries²⁸ reported that most of them changed their clinical practice to more virtual communication, as we did. However, 80% of HCPs declared mental health

of their patients worsened during COVID-19, despite overall satisfactory (48%) to good (26%) management of chronic diseases.²⁶ According to the authors, many patients with chronic diseases still prefer physical visits. Another limit of the development of telehealth, in particular in low- and middle-income countries, is the lack of technology, tools, and money. The preserved health status observed in a majority of our patients is probably explained by the fact that 62% of adults and 54% of children lived in the countryside, with a large majority living in a house with garden or an apartment with terrace.

On a more negative note, the 1st lockdown period was associated with a deterioration of lifestyle behaviours in almost half of our adult (43%) and paediatric (48%) population. As reported in patients with heart failure,²³ idiopathic interstitial pneumonia,²⁴ chronic coronary syndromes,²⁵ and giant cell arthritis,²⁶ the main changes concerning lifestyle behaviours were: increase in screen time, decrease in physical activity, as well as weight gain. This result is worrying, as it was already observed just a few weeks after lockdown beginning.

TABLE 5 Lifestyle behaviours

Variables	Overall population N = 239	%	Paediatric patients N = 56	%	Adult patients N = 183	%
<i>Physical activity</i>						
MD	1	0	1	2	0	-
Increase	33	14	11	20	22	12
No change	100	42	17	30	83	45
Decrease	105	44	27	48	78	43
<i>Smoking status/vaping</i>						
Other (no change, non-smoker/vaper, missing)	NA	-	NA	-	154	84
Increase	NA	-	NA	-	22	12
Decrease	NA	-	NA	-	7	4
<i>Decrease in sleep quantity/quality</i>						
MD	1	0	1	2	0	-
No	166	70	42	75	124	68
Yes	72	30	13	23	59	32
<i>Increase in screen time</i>						
No	117	49	24	43	93	51
Yes	122	51	32	57	90	49
<i>Change in body weight (self-declaration)</i>						
MD	9	4	4	7	5	3
Increase	74	31	15	27	59	32
Decrease	32	13	5	9	27	15
No change	124	52	32	57	92	50
<i>Alcohol consumption</i>						
Other (no change, non-consumer, missing)	NA	-	NA	-	135	74
Increase	NA	-	NA	-	19	10
Decrease	NA	-	NA	-	29	16

Abbreviation: MD, missing data.

We strongly believe that, in order to prevent negative lockdown-related consequences in haemophilia patients, a strong hospital-centred follow-up should be maintained. This is exactly the way our patients are being cared for by our dedicated staff. For more than 10 years, our reference centre has been involved with patients, seeking to develop therapeutic education through numerous individual and collective sessions. Despite the study's encouraging results, face-to-face visits were reimplemented in our centre, along with the concomitant development of telemedicine tools, in order to ensure maximum benefits for all of our patients.

4.1 | Study limitations

Due to practical reasons, the major limitation of our study is the lack of follow-up of the patients over a longer time period, in particular over the second and third lockdowns. Therefore, our results cannot be generalized to a longer timeframe. A second limitation is that the analysis was restricted to a single French centre. A third limitation is

the absence of patient electronic diaries to verify in particular data on bleeding episodes and medication adherence as the e-diary is not yet available in France.

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AUTHOR CONTRIBUTION

Fabienne Volot, Anamaria Callegarin, Stephanie Delienne, Mathieu Boulin performed the research. Fabienne Volot, Agnes Soudry-Faure, Eléa Ksiazek, Yves Cottin, Marc Maynadié, Mathieu Boulin designed the research study. Fabienne Volot, Yves Cottin, Marc Maynadié, Mathieu Boulin contributed essential reagents or tools. Fabienne Volot, Agnes Soudry-Faure, Anamaria Callegarin, Eléa Ksiazek, Stephanie Delienne, Yves Cottin, Marc Maynadié, Mathieu Boulin analysed the data. All authors wrote the paper.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

DISCLOSURES

The authors stated that they had no interests which might be perceived as posing a conflict or bias.

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