

Impact of Covid-19 pandemic on Hemophilia prophylaxis in children: experience of a hemophilia treatment center in West Bengal, India

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Abstract:

The World Health Organization lockdown declared COVID 19 a global pandemic; it has reduced the access to treatment centers and has challenged the management of hemophiliacs requiring regular and frequent in-person visits. In the present study, we retrospectively analyzed the impact of COVID 19 on hemophiliac children who were on regular prophylaxis earlier. The mean annualized bleed rate before lockdown was 2.4, whereas it significantly increased to 8.2 during the lockdown. Among various reasons cited by them for not attending Hemophilia treatment centre, the important reasons were non availability of transport (97.5%), fear of corona virus infection (95%) and high cost of alternate transport (90%). During such crisis period telemedicine plays an important role to overcome some of the issues related to hemophilia care. The best possible alternative option to continue regular prophylaxis in this crisis situation is implementation and practice of 'home therapy'.

Key Words: COVID-19 pandemic, hemophilia prophylaxis, unprecedented challenges, telemedicine, home therapy

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I. Introduction

Hemophilia is a rare X-linked congenital bleeding disorder characterized by a deficiency of coagulation factor-VIII called hemophilia A (HA) or factor-IX called hemophilia B (HB); severity of bleeding manifestations generally correlates with the degree of the clotting factor deficiency¹. Hemophilia A is much more common than hemophilia B and is estimated to account for 80%-85% of all hemophilia cases whereas hemophilia B is estimated to account for 15%-20% of all hemophilia cases². The aim of prophylaxis in hemophilia is to maintain hemostasis to prevent bleeding, especially in joints and other internal organs and to enable people with hemophilia (PWH) to lead a healthy and active life similar to the non-hemophilic population³. COVID-19, a disease caused by a novel corona virus (SARS -CoV -2), was declared a pandemic by World Health Organization (WHO) on 11 March, 2020⁴. This novel virus that spreads from person -to -person via respiratory droplets has resulted in morbidity and mortality throughout the world. It mainly results in respiratory tract infections and potentially fatal pneumonia in frailer patients⁵. Current available data suggest that the mortality due to COVID 19 is low in younger and fit patients (<20 years) but much higher, even up to 20 %, in older patients specially presenting with co morbidities. However, exceptions are always there.

Complete nationwide lockdown was enforced in India from 25th March 2020 (phase 1) passed through the phase 4 (18-31 May) in view of containing the further spread of COVID 19 infections with ban on people from stepping out of their homes and many others^{6,7}. Although, the nationwide lockdown helped the nation to fight corona virus infection, however it did impact the healthcare system and had many social and economical effects. The stepwise unlock process started on 1st June (unlock 1.0) and now in the phase of unlock 3.0 (1-31 August)⁸. Announcing 'Unlock 3' guidelines, the Ministry of Home Affairs, Govt. of India removed restrictions on many different issues; however strict enforcement of lockdown in containment zones has been extended till August 31⁹. The measures which were taken to contain the COVID-19 pandemic during the lockdown and unlock phases reduced the access to treatment centers, laboratories and pharmacies and challenged the management of patients with chronic diseases (including hemophilia) or requiring regular follow up¹⁰. Thus, in the present study we have analyzed the impact of COVID-19 pandemic on people with hemophilia who were on regular prophylaxis prior to the announcement of lockdown in India.

II. Material and Methods

Retrospective analysis of data of PWH who were on regular prophylaxis (twice in week on Tuesday and Friday) was done for a period of 4 months before lockdown (25/11/2019 to 24/03/2020) and during lockdown/unlock period of 4 months (25/3/2020 to 24/7/2020). Patients who were on regular prophylaxis and used to follow up (with minimal absenteeism for some definite reasons) before lockdown were selected. Four patients who were irregular with prophylaxis even before lockdown were excluded from the study. Data based on the reasons cited by PWH and/or their family members (legal guardians) related to absenteeism for prophylaxis during lockdown/unlock phase was analyzed. Annualized bleed rate (ABR) before lockdown was compared with that of during lockdown/unlock period. Sites of bleeding before and after lockdown were also noted. Z test was applied to compare ABR and to analyze the data; p value of <0.05 was taken as statistically significant.

III. Result

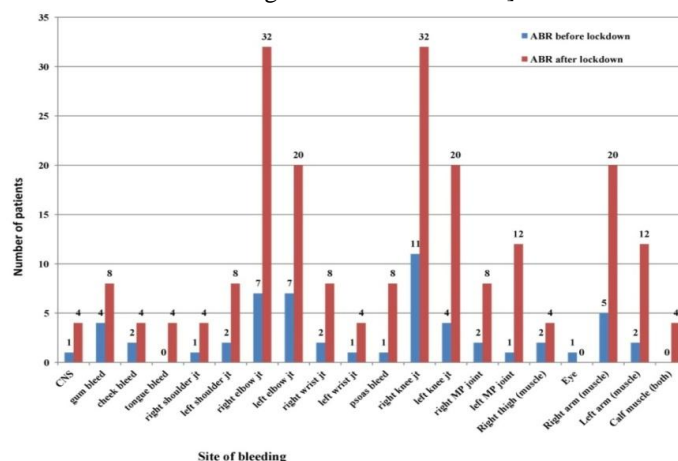
Out of total 40 PWH children who participated in the study, 22 patients had severe HA and 7 had moderate HA whereas only 6 patients had severe HB and the remaining 5 patients had moderate HB. The median age of the patients was 8.5 years (range, 3-12). The median days of attendance of all the patients before lockdown was 31 (30-34) whereas it was 11 (0-20) during lockdown/unlock phases. The mean ABR for all the patients before lockdown was 2.4, whereas it was 8.2 during the lockdown; the Z score among these was statistically significant ($p = 0.00001$). Similarly the Z score of ABR before and after lockdown in each subgroup of moderate and severe HA and HB respectively was also statistically significant (table 1). Out of these 40 patients, one (2.5%) patient had required hospitalization due to psoas bleed during the 4 month period before lockdown. However, during lockdown/unlock phase 5 patients (12.5%) had required hospitalization out of which 2 patients had CNS bleed and 3 patients had psoas bleed.

Table 1: Comparison of different parameters studied before and after lockdown (n=40)

Parameters studied	Before lockdown (4 months)	Lockdown/unlock phase (4 months)	Remarks
Days of attendance for prophylaxis; median (range)	31 (30-34)	11 (0-20)	-
Mean ABR:			p-value
Total:- 40 cases	2.4	8.2	0.00001
Hemophilia A:-			
• moderate (7 cases)	2.57	9.68	0.04006
• severe (22 cases)	2.86	8.16	0.00012
Hemophilia B:-			
• moderate (5 cases)	1.63	6.44	0.05602
• severe (6 cases)	1.71	8.56	0.00748
Hospitalizations:	<u>n (%)</u>	<u>n (%)</u>	
Yes:-			
• CNS bleed	0 (0)	2 (5.0)	-
• Psoas bleed	1 (2.5)	3 (7.5)	
No:-	39 (97.5)	35 (87.5)	

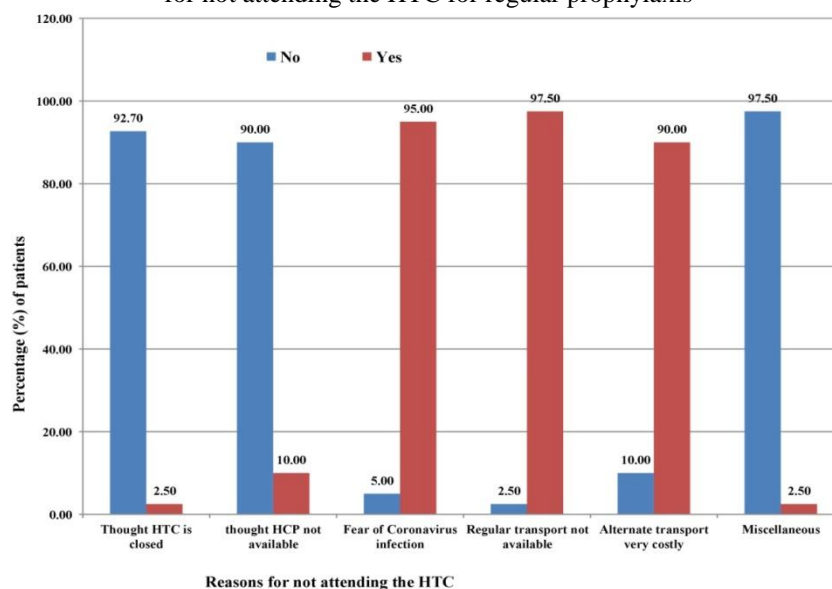
Figure 1 shows the number of bleeds at different sites including joints before and after lockdown. There were 1 episode of CNS bleed before lockdown and 4 episodes during lockdown. There were 8 episodes of psoas bleed after lockdown whereas only 1 episode before lockdown.

Figure 1: Detailed account of sites of bleeding before and after lockdown (n=40) [in many cases there was bleeding at more than one site]



The various reasons cited by the PWH and or their family members for not attending Hemophilia treatment centre (HTC) were analyzed (Figure 2). The main reason for not attending HTC was non availability of transport (97.5%) followed by fear of corona virus infection (95%) and high cost of alternate transport (90%). Though the HTC service facility was open for the PWH in the lockdown phase as before, 2.5 % thought that HTC was closed whereas 10% thought that Health care professionals (HCP) were not available. Few others had also cited the reasons of illness of either parent, sudden joblessness of only earning member in the family etc – represented as miscellaneous cause in figure 2.

Figure 2: Various reasons cited by the persons with hemophilia and/or their family members (legal guardians) for not attending the HTC for regular prophylaxis



IV. Discussion

COVID-19 pandemic has resulted in many unprecedented effects on chronic diseases that require regular follow up. Many of the consequences, direct or indirect, immediate or delayed, are also affecting the management of hemophilia worldwide. Under such situations, it is essential to identify these likely consequences. This could help in better management of the current challenges and difficulties that could be faced in the longer term. Due to lockdown, the journey of patients to hospital has also become a challenge. The major concern at present is to ensure access to hemophilia treatment; the deliveries of replacement therapies through HTC's or home delivery programs have been impacted^{10, 11}. As shown in the present study, COVID 19 pandemic has resulted in major impact on hemophilia management. The patients, who used to attend HTC regularly before lockdown, did not attend HTC regularly after lockdown. The main reasons cited by them were non-availability and very high cost of alternate transport during lockdown, but fear of getting infected with corona virus was another major concern for them. It is evident from the study (Table 1 and Figure 2) that majority of the patients on prophylaxis were not able to attend the HTC during lockdown for some or other reasons that directly resulted in significant increase in ABR during lockdown; hospitalization due to serious/internal bleeds also increased. Lockdown has impacted hemophilia care in other countries also due to lack of access to HTC among many others. As stated by Agnes Kisakye from Uganda – "The care delivery has been severely affected due to the lockdown. All forms of transport were banned and the patients cannot access health facilities"¹¹. In our study also, as already discussed, the main reasons for patients not been able to attend HTC during lockdown was non availability of transport. Christopher Davis from South Africa very rightly pointed about the socio-economic impact of COVID 19 pandemic on hemophilia care and stated that "As the result of COVID-19 we have a number of hemophilia families that are suffering financially who have lost their jobs or are at home for more than 50 days without any income"¹¹. The similar kind of socio-economical impact witnessed in our study also as one of the main reasons cited by them for not being able to attend the HTC was high cost of alternate transport.

Here comes the role of telemedicine during such crisis times. With the invent of smart phones and new technologies, the concept of telemedicine had started before COVID 19, however, the real benefit of this concept has been seen during this pandemic times only. Telemedicine provides the ability to healthcare professionals (HCPs) to directly interact with patients in different and remote locations¹². Originally it was used to contact with patients in remote areas distant from the HCP. But today, during times of crisis, telemedicine has

evolved as a necessary way of delivering healthcare to all but the sickest. It brings medical care to patients at their home and at the same time helps to reduce the transmission of COVID-19 among patients, families, and clinicians by avoiding direct contact¹³. These technologies offer several possible advantages including the ability to quickly ask and receive answers to questions; can be used in such crisis times to overcome some problems which are faced by patients by providing a direct interacting platform for patients. Another alternative and best possible option (as practiced by many developing countries) to continue regular prophylaxis is 'home based therapy'; that is rarely practiced in India. While talking about 'home treatment' in hemophilia, Rajesh Neelayya, President of Haemophilia Association of Mauritius has stated that "This was in process well before COVID-19 but the procedures were accelerated with the pandemic."¹¹.

Prophylaxis with extended half-life (EHL) factor VIII (FVIII) and factor IX (FIX) concentrates can also be an alternative during such crisis situations. It allows prolonged intervals between intravenous infusions (thus minimizing the number of in-person visits) and higher protection from bleeding due to increased factor trough levels. The FVIII-mimetic bispecific monoclonal antibody emicizumab also provides highly effective prophylaxis in HA with and without inhibitors. Therefore, PWH and HCP can benefit from the advantages of these treatment choices, which are even more very important and relevant under the lockdown restrictions¹⁴. Though these treatment choices benefit and reduce the burden on medical care, economical consideration is an important cause of concern. Due to such reasons, this perspective might not be realistic however can hold some good future promises.

COVID-19 is a new disease still invading the world; a lot still needs to be explored about it. Many more studies will be needed to further analyze the impact of this pandemic on healthcare delivery. HTC'S should explore for more other alternatives for continuation of hemophilia prophylaxis on a regular basis in this crisis situation.

V. Conclusion

The ongoing COVID 19 pandemic has resulted in many unprecedented effects in the management of PWH that require regular follow up. During such crisis period telemedicine plays an important role to overcome some of the issues related to hemophilia care that provides the ability to healthcare professionals to directly interact with PWH in different and remote locations and vice versa. The alternative and best possible option to continue regular prophylaxis in this crisis situation implementation and practice of 'home based therapy'; the stakeholders have to realize it in time.

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References

- [1]. WFH Guidelines for the Management of Hemophilia, 3rd edition - Srivastava - - Haemophilia - Wiley Online Library [Internet]. [cited 2020 Aug 19]. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/hae.14046>
- [2]. Iorio A, S. Stonebraker J, Chambost H, Makris M, Coffin D, Herr C, et al. Establishing the Prevalence and Prevalence at Birth of Hemophilia in Males: Establishing the male prevalence and prevalence at birth of hemophilia: A meta-analytic approach using national registries. *Ann Intern Med.* 10 September 2019 [Epub ahead of print]. doi:10.7326/M19-1208.
- [3]. Blanchette VS, Key NS, Ljung LR, Manco- Johnson MJ, Berg HM van den, Srivastava A. Definitions in hemophilia: communication from the SSC of the ISTH. *J Thromb Haemost.* 2014;12(11):1935-1939. doi:10.1111/jth.12672
- [4]. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med.* 2020; 382(8): 727-733. doi:10.1056/NEJMoa2001017
- [5]. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med.* 2020; 382(18): 1708–20. DOI: 10.1056/NEJMoa2002032
- [6]. Singh KD, Goel V, Kumar H, Gittleman J. India, Day 1: World's Largest Coronavirus Lockdown Begins. 25 March 2020). *The New York Times.* ISSN 0362-4331.
- [7]. COVID-19 pandemic lockdown in India. https://en.wikipedia.org/wiki/COVID19_pandemic_lockdown_in_India#cite_note-IElockdown5-66
- [8]. oronavirus India lockdown Day 150 updates | August 21, 2020 [Internet]. Link: <https://www.thehindu.com/news/national/coronavirus-india-lockdown-august-21-2020-live-updates/article32409874.ece>
- [9]. Unlock 3.0 guidelines: Here is what's allowed, what's not. *The Indian Express.* 30 July 2020. Retrieved 1 August 2020.
- [10]. Hermans C, Weill A, Pierce GF. The COVID-19 pandemic: New global challenges for the haemophilia community. *Haemophilia.* 2020; 26(3): 371–2. <https://doi.org/10.1111/hae.14001>
- [11]. Covid-19: Unprecedented challenges led to unprecedented initiatives in the haemophilia community [Internet]. *Novo Nordisk Haemophilia Foundation (NNHF).* 2020 [cited 2020 Aug 21]. Available from: <https://nnhf.org/covid-19-unprecedented-challenges-unprecedented-initiatives-in-the-haemophilia-community>

- [12]. Valentino LA, Skinner MW, Pipe SW. The role of telemedicine in the delivery of health care in the COVID-19 pandemic. Haemophilia [Internet]. [cited 2020 Aug 19];n/a(n/a). Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1111/hae.14044>
- [13]. . Ohannessian R, Duong TA, Odone A. Global Telemedicine Implementation and Integration Within Health Systems to Fight the COVID-19 Pandemic: A Call to Action. JMIR Public Health Surveill [Internet]. 2020 Apr 2 [cited 2020 Aug 19];6(2). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7124951/>
- [14]. Hermans C, Lambert C. Impact of the COVID-19 pandemic on therapeutic choices in thrombosis-hemostasis. J Thromb Haemost [Internet]. 2020 May 11 [cited 2020 Aug 19]; Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7262403/>

Dr Prakas Kumar Mandal, et. al. "Impact of Covid-19 pandemic on Hemophilia prophylaxis in children: experience of a hemophilia treatment center in West Bengal, India." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(8), 2020, pp. 01-05.