



ISSN : 2350-0743



RESEARCH ARTICLE

THE INTERFERENCE OF COVID-19 DURING THE HEMATOLOGICAL TREATMENT OF HEMOPHILIAC PATIENTS

Jady Moreira Oliveira¹, Lavine Pamella Lima Silva², Maria Gabriella de Souza Coelho Salles³ and Ana Carolina Santana de Oliveira⁴

^{1,2,3}Graduanda em Biomedicina na Unidade de Ensino Superior de Feira de Santana; ⁴Doutora em Medicina Tropical e Infectologia e Docente do curso de Biomedicina na Unidade de Ensino Superior de Feira de Santana

ARTICLE INFO

Article History

Received 25th July, 2025
Received in revised form
29th August, 2025
Accepted 19th September, 2025
Published online 30th October, 2025

Keywords:

Hemophilia A, Hemophilia B, Blood Coagulation Disorders, COVID-19.

*Corresponding author:

Jady Moreira Oliveira

ABSTRACT

Introduction: During COVID-19 infection in hemophilic patients, several laboratory parameters associated with coagulation are affected. A significant increase in D-dimer levels is one of the main indicators of a hypercoagulable state, often related to greater disease severity and thrombotic complications. **Objective:** To analyze how the pathophysiology of SARS-CoV-2 infection interferes with the management of therapeutic processes in patients with hemophilia in its various forms. **Methodology:** This work is a bibliographic study of an exploratory-descriptive type with a qualitative approach. The literature review was conducted from 2019 to 2024. The literature search was carried out in the databases of the Virtual Health Library (VHL), PubMed, and Science Direct. The descriptors were: Hemophilia A, Hemophilia B, Blood Coagulation Disorders, and COVID-19. **Results and Discussion:** SARS-CoV-2 infection can worsen the clinical manifestations of hemophilia after treatment. The exacerbated inflammatory response associated with the infection, along with the formation of microthrombi, can compromise the effectiveness of standard treatment with clotting factors. In some cases, this condition may require adjustments in replacement factor dosages or the introduction of adjunct therapies such as anticoagulants, which is a challenge, as it may increase the risk of bleeding, creating a therapeutic dilemma. **Conclusion:** Thus, SARS-CoV-2 infection can significantly worsen coagulation in hemophilic patients, affecting both disease severity and treatment response.

Copyright©2025, Jady Moreira Oliveira et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Citation: Jady Moreira Oliveira, Lavine Pamella Lima Silva, Maria Gabriella de Souza Coelho Salles and Ana Carolina Santana de Oliveira, 2025. "The interference of covid-19 during the hematological treatment of hemophilic patients", *International Journal of Recent Advances in Multidisciplinary Research*, 12,(10), 11860-11863.

INTRODUCTION

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has posed significant challenges to global healthcare systems, both due to the direct impact of the infection and the indirect consequences on the treatment of chronic conditions. Among these conditions are congenital bleeding disorders, such as hemophilia. COVID-19 has stood out not only for its high transmissibility but also for its ability to trigger severe hematological complications, such as sepsis-associated coagulopathy and thromboembolic events. These factors highlight the complexity of managing patients who already have a predisposition to coagulation disorders amid the pandemic (1, 2). The specific theme of this study refers to the interaction between the pathophysiology of COVID-19 and the therapeutic management of patients with hemophilia. This condition, characterized by a congenital deficiency of clotting factors VIII or IX, requires highly individualized therapeutic strategies to prevent severe bleeding. During the pandemic, limited access to treatment centers, logistical difficulties in the distribution of clotting factors, and the risk of complications associated with SARS-CoV-2 infection worsened the situation for these patients. Furthermore, the presence of COVID-19-associated coagulopathy could further complicate the management of already challenging cases (3, 4).

Epidemiological data emphasize that, although COVID-19 has affected the global population, some groups—such as the elderly and individuals with comorbidities—have suffered greater impact in terms of mortality and morbidity. However, studies on patients with hemophilia are still limited. Reports suggest that these patients are not more susceptible to SARS-CoV-2 infection than the general population, but they do face challenges in therapeutic management, including difficulties accessing treatment and being underrepresented in clinical studies and experimental therapies (3). In patients with hemophilia infected with SARS-CoV-2, the characteristic coagulopathy of COVID-19 adds complexity to clinical management. Data show that elevated D-dimer levels, often observed in severe infections, also occur in hemophilic patients, potentially increasing the risk of thrombotic events and requiring adjustments in antithrombotic strategies and clotting factor regimens (1, 2). The general objective of this article is to analyze how the pathophysiology of SARS-CoV-2 infection interferes with the management of therapeutic processes in patients with hemophilia in its various forms. The rationale for this investigation is based on the need to understand the interactions between these conditions in order to provide guidelines that assist in decision-making, minimizing clinical complications and optimizing outcomes for this vulnerable patient group. This study is particularly relevant for the development of

protocols that integrate the specificities of hemophilia with those of SARS-CoV-2 infection.

METHODOLOGY

This is a bibliographic study of an exploratory-descriptive type with a qualitative approach, developed based on data obtained from scientific literature. Bibliographic research is carried out using previously developed material, mainly composed of books and scientific articles. This type of research seeks to gather theoretical insights on a given subject by collecting information on what different authors report about the topic. In addition, exploratory studies involve literature review and the analysis of examples that may clarify concepts and develop new approaches for future investigations. Within this context, the present study aimed to deepen the understanding of the interaction between COVID-19 and coagulation disorders, specifically in patients with Hemophilia A and B. The descriptive research was conducted with the objective of recording, classifying, and interpreting observed facts, establishing relationships between them. The qualitative approach employed in this study was directed toward the informational value of the data, correlating specifications and variables to thoroughly understand the experiences of the patients in question. This approach was essential for building scenarios and new perspectives within the investigated reality. Data collection was carried out through a literature review conducted in major scientific databases. Articles published in the last five years (2018–2023) and available in Portuguese, English, and Spanish were included, following inclusion criteria that covered full and relevant content related to the proposed theme. Exclusion criteria included irrelevant, duplicate, incomplete articles, debates, reviews, abstracts, and materials not available in full. The databases consulted were PubMed, Virtual Health Library (VHL), SciELO, and ScienceDirect. The search used Health Sciences Descriptors (DeCS): Hemophilia A, Hemophilia B, Blood Coagulation Disorders, and COVID-19, with the aid of Boolean operators “AND” and “OR.”

The methodology began with the careful selection of keywords in DeCS, followed by searches in indexed databases. Screening was carried out in two stages: elimination of duplicate articles and initial selection based on title relevance. Then, the abstracts of the selected articles were read, and those meeting the inclusion criteria were submitted to an in-depth reading for detailed analysis. For the critical analysis of the articles, three discussion axes aligned with the study's objectives were defined and transformed into guiding questions. These questions structured the data analysis, providing a theoretical framework for the interpretation of the results. The meticulous approach used allowed for the systematic organization of information, reinforcing the validity and consistency of the conclusions.

RESULTS AND DISCUSSION

LABORATORY PARAMETERS ASSOCIATED WITH COAGULATION: The treatment of patients with Hemophilia A or B using FVIII and FIX concentrates can be complicated by the development of neutralizing antibodies (inhibitors) against the infused clotting factors. Patients with low inhibitor titers (<2 Bethesda units) may still respond to higher doses of FVIII, allowing treatment with conventional concentrates (5). In addition, recombinant FVIII concentrates with extended half-life offer benefits such as less frequent injections and the maintenance of higher plasma levels. These advances are particularly important in contexts like COVID-19, which can complicate the management of patients with coagulopathies due to the exacerbated inflammation that increases FVIII and von Willebrand factor (vWF) levels, potentially masking conditions such as Hemophilia A and von Willebrand disease (3). During the COVID-19 pandemic, a significant increase in FVIII and vWF levels was observed in infected patients, which may lead to a hypercoagulable state. In non-hemophilic patients, FVIII levels can exceed 369%, whereas in hemophilic patients receiving monitored FVIII administration, levels do not surpass 196% (6). Some studies

suggest that this FVIII elevation may mitigate the pro-thrombotic state of COVID-19, raising the hypothesis that hemophilic patients could have a relatively better prognosis regarding thrombotic events. However, further research is necessary to validate this observation and to understand any protective factors related to coagulopathies in the context of SARS-CoV-2 infection. Clinical case reports illustrate the challenges of managing hemophilia and COVID-19 simultaneously. For example, a patient with Hemophilia A and high inhibitor levels responded effectively to emicizumab, a prophylactic therapy that significantly prevented bleeding episodes (7). In another case, the combination of continuous FVIII concentrate infusion and intensified antithrombotic prophylaxis using low molecular weight heparin (LMWH) successfully prevented both bleeding and thrombotic complications (8). These reports highlight the importance of collaboration between hematologists and multidisciplinary teams in managing complications associated with coagulopathies and COVID-19. Additionally, the inflammatory response in infected patients, marked by elevated interleukin-6 (IL-6), C-reactive protein (CRP), and ferritin levels, can further complicate clinical management (9). This inflammatory profile, often associated with elevated D-dimer levels, demands constant monitoring and therapeutic adjustments to balance the risks of thrombosis and bleeding. The use of LMWH at therapeutic doses, combined with FVIII infusions, has proven to be an effective approach to stabilize critically ill patients, despite laboratory challenges with the reliability of activated partial thromboplastin time (aPTT)-based tests.

Moreover, mild Hemophilia A cases in COVID-19 patients have shown marked increases in FVIII and vWF during infection, with levels remaining elevated even post-recovery. The coexistence of normal coagulation profiles, as evidenced by tests like thromboelastometry, alongside high immunological markers, reinforces the need for individualized treatment strategies (10). Prophylactic strategies such as continuous emicizumab use have proven effective in reducing joint bleeds and improving joint health in long-term studies (7). Managing hemophilia in patients infected with SARS-CoV-2 requires rigorous monitoring of hematological and inflammatory parameters, as well as integrated treatment strategies to prevent hemorrhagic and thrombotic complications. These challenges emphasize the need for ongoing research to better understand the interaction between hereditary coagulopathies and acute infections such as COVID-19, and to develop guidelines that ensure safety and efficacy in the care of these patients.

IMPACTS THAT THE VIRAL INFECTION MAY HAVE ON THE CLINICAL PRESENTATION OF HEMOPHILIA AFTER TREATMENT: Managing coagulopathies in COVID-19 patients—especially in those with congenital bleeding disorders (CBDs)—presents significant challenges. Prophylaxis and antithrombotic treatment require careful adjustments due to the risk of bleeding induced by the disease or its treatment. The selection of clotting factors, including maintaining adequate protective levels, is essential to minimize risks, particularly in invasive procedures such as arterial blood gas monitoring and mechanical ventilation. For hospitalized patients, it is important to inform medical teams about the CBD history, provide contact information for the Hemophilia Treatment Center (HTC), and continue or implement prophylactic regimens as needed to avoid hemorrhagic complications (3).

Case reports suggest that COVID-19 may not significantly worsen hemorrhagic events in hemophilic patients. For instance, a patient with severe Hemophilia A and COVID-19 showed no hemorrhagic complications when treated with FVIII replacement therapy and home-based care. This approach, which included antiviral and antibiotic medications, proved effective, and the patient recovered completely without further bleeding events (2, 11). Furthermore, early administration of FVIII at the onset of SARS-CoV-2 infection may prevent bleeding events, suggesting that home management may be suitable for mild COVID-19 cases in patients with hemophilia (11). However, broader studies have revealed that hemophilic patients experience higher hospitalization rates compared to the general population, possibly due to the risk of bleeding or medical

complications. The incidence of venous thromboembolism (VTE) was similar between hemophilic patients and controls, although non-CNS-related bleeding rates were significantly higher in the hemophilia cohort. These findings underscore the importance of prophylactic factor replacement and anticoagulation strategies in selected patients (12). In regard to COVID-19-associated coagulopathy (CAC), the hypercoagulable state characterized by elevated FVIII, vWF, and D-dimer levels is a common feature of the infection. Patients with severe hemophilia may be less susceptible to this hypercoagulability due to impaired thrombin generation. However, endothelial damage associated with SARS-CoV-2 infection may activate alternative pro-thrombotic pathways, increasing the risk of thrombotic complications in cases of severe infection (6, 13). Nevertheless, routine prophylaxis with emicizumab or FVIII appears to improve baseline hemostasis and reduce bleeding events in patients with Hemophilia A, although these individuals may be at greater risk of thrombotic complications in severe infections. The use of thromboprophylaxis in combination with FVIII replacement may be considered in severe cases or as a precaution during invasive procedures, although its application remains debated (13, 14).

COVID-19 cases in pediatric patients with hemophilia showed fewer bleeding events, likely due to reduced physical activity during the infection period. Data suggest that the hypercoagulable state associated with COVID-19 may contribute to a decrease in bleeding events in these patients, although further studies are needed to validate this hypothesis (15). On the other hand, the pandemic has highlighted gaps in the management of hemophilic patients, especially in regions with limited access to home therapy. Delays in on-demand treatment result in secondary complications and increased costs, underscoring the need to expand access to prophylaxis and home therapies to reduce morbidity and the burden associated with hospital-based care (16). Although case reports and retrospective studies offer important insights, the understanding of the interactions between hemophilia and COVID-19 remains incomplete. There is a clear need for further research aimed at developing management strategies that balance bleeding and thrombosis risks in hemophilic patients during pandemics and other critical scenarios.

CONCLUSION

The findings of this study highlight that the management of patients with hemophilia in the context of COVID-19 infection requires careful monitoring, considering both the potential for hypercoagulability and the risk of bleeding. Current therapeutic protocols, such as recombinant FVIII concentrates and the use of emicizumab, show significant advances in preventing complications, but do not eliminate the need for continuous clinical and laboratory vigilance. Therefore, an integrated and individualized approach, led by multidisciplinary teams, is essential to ensure greater effectiveness and safety in treatment. Furthermore, the lack of more comprehensive analyses reinforces the importance of future research capable of establishing clear and specific guidelines to inform the care of patients with coagulopathies in the context of systemic viral infections.

REFERENCES

- McBane, R. D., 2nd, Torres Roldan, V. D., Niven, A. S., Pruthi, R. K., Franco, P. M., Linderbaum, J. A., Casanegra, A. I., Oyen, L. J., Houghton, D. E., Marshall, A. L., Ou, N. N., Siegel, J. L., Wysokinski, W. E., Padrnos, L. J., Rivera, C. E., Flo, G. L., Shamoun, F. E., Silvers, S. M., Nayfeh, T., ... Murad, M. H. (2020). Anticoagulation in COVID-19: A systematic review, meta-analysis, and rapid guidance from Mayo Clinic. *Mayo Clinic Proceedings*, *95*(11), 2467–2486. <https://doi.org/10.1016/j.mayocp.2020.08.030>
- Ornelas-Ricardo, D., & Jaloma-Cruz, A. R. (2020). Coronavirus disease 2019: Hematological anomalies and antithrombotic therapy. *The Tohoku Journal of Experimental Medicine*, *251*(4), 327–336. <https://doi.org/10.1620/tjem.251.327>
- Coppola, A., Tagliaferri, A., Rivolta, G. F., Quintavalle, G., & Franchini, M. (2020). Confronting COVID-19: Issues in hemophilia and congenital bleeding disorders. *Seminars in Thrombosis and Hemostasis*, *46*(7), 819–822. <https://doi.org/10.1055/s-0040-1712961>
- Hermans, C., Lambert, C., Sogorb, A., Wittebole, X., Belkhir, L., & Yombi, J. C. (2020). In-hospital management of persons with haemophilia and COVID-19: Practical guidance. *Haemophilia: The Official Journal of the World Federation of Hemophilia*, *26*(5), 768–772. <https://doi.org/10.1111/hae.14045>
- Srivastava, A., Santagostino, E., Dougall, A., Kitchen, S., Sutherland, M., Pipe, S. W., Carcao, M., Mahlangu, J., Ragni, M. V., Windyga, J., Llinás, A., Goddard, N. J., Mohan, R., Poonnoose, P. M., Feldman, B. M., Lewis, S. Z., van den Berg, H. M., Pierce, G. F., & WFH Guidelines for the Management of Hemophilia panelists and co-authors. (2020). WFH Guidelines for the Management of Hemophilia, 3rd edition. *Haemophilia: The Official Journal of the World Federation of Hemophilia*, *26 Suppl 6*(S6), 1–158. <https://doi.org/10.1111/hae.14046>
- Taranchenko, Y. L., Martinez Garcia, F., Benitez-Hidalgo, O., Aguilar, M., Massons, J., & Nuñez, J. H. (2020). COVID-19 infection after a total knee arthroplasty in a patient with hemophilia A: A case report: A case report. *JBJS Case Connector*, *10*(3), e20.00537. <https://doi.org/10.2106/JBJS.CC.20.00537>
- Callaghan, M. U., Negrier, C., Paz-Priel, I., Chang, T., Chebon, S., Lehle, M., Mahlangu, J., Young, G., Kruse-Jarres, R., Mancuso, M. E., Niggli, M., Howard, M., Bienz, N. S., Shima, M., Jiménez-Yuste, V., Schmitt, C., Asikanius, E., Levy, G. G., Pipe, S. W., & Oldenburg, J. (2021). Long-term outcomes with emicizumab prophylaxis for hemophilia A with or without FVIII inhibitors from the HAVEN 1-4 studies. *Blood*, *137*(16), 2231–2242. <https://doi.org/10.1182/blood.2020009217>
- Pinto Pereira, J., Hantson, P., Gerard, L., Wittebole, X., Laterre, P.-F., Lambert, C., & Hermans, C. (2021). Management of COVID-19 coagulopathy in a patient with severe haemophilia A. *Acta Haematologica*, *144*(3), 319–321. <https://doi.org/10.1159/000510591>
- Fernández-Oliveira, C., Rotea-Salvo, S., Fernández-Docampo, M., González-Piñeiro, S., & Martín-Herranz, I. (2023). Treatment of high-risk bleeding with susoctocog alfa in a patient with acquired haemophilia A and a nosocomial severe acute respiratory syndrome coronavirus 2 infection. *European Journal of Hospital Pharmacy. Science and Practice*, *30*(3), 177–179. <https://doi.org/10.1136/ejhpharm-2021-002805>
- Zanon, E., Pasca, S., Campello, E., Spiezia, L., Vettor, R., & Simioni, P. (2020). How haemophilia A impacts severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) treatment: a case report. *Journal of Thrombosis and Thrombolysis*, *50*(4), 795–798. <https://doi.org/10.1007/s11239-020-02227-z>
- Cui, D., Zhang, A., Liu, A., & Hu, Q. (2020). Clinical findings in a patient with haemophilia A affected by COVID-19. *Haemophilia: The Official Journal of the World Federation of Hemophilia*, *26*(4), e214–e216. <https://doi.org/10.1111/hae.14000>
- Sharathkumar, A., Wendt, L., Ortman, C., Srinivasan, R., Chute, C. G., Chrischilles, E., Takemoto, C. M., & National COVID Cohort Collaborative Consortium. (2024). COVID-19 outcomes in persons with hemophilia: results from a US-based national COVID-19 surveillance registry. *Journal of Thrombosis and Haemostasis*: *JTH*, *22*(1), 61–75. <https://doi.org/10.1016/j.jth.2023.04.040>
- Urbaniak-Kujda, D., Biernat, M. M., Skalec, T., Jacków-Nowicka, J., Windyga, J., & Wróbel, T. (2021). Successful treatment of COVID-19 in a patient with severe haemophilia A on emicizumab prophylaxis in the intensive care unit. *Haemophilia: The Official Journal of the World Federation of Hemophilia*, *27*(4), e567–e570. <https://doi.org/10.1111/hae.14326>
- Pipe, S. W., Kaczmarek, R., Srivastava, A., Pierce, G. F., Makris, M., Hermans, C., Interim Guidance, & Coagulation Products Safety, Supply and Access (CPSSA) Committee of the World Federation of Hemophilia. (2021). Management of COVID-19-associated coagulopathy in persons with haemophilia. *Haemophilia: The*

- Official Journal of the World Federation of Hemophilia*, 27(1), 41–48. <https://doi.org/10.1111/hae.14191>
- Zhang, S., Xie, B., Lin, Y., Chen, C., Yang, S., Xu, S., Chen, J., Li, X., Yang, F., & Huang, M. (2024). Impacts of the COVID-19 pandemic on pediatric and adult patients with hemophilia. *Annals of Hematology*. <https://doi.org/10.1007/s00277-024-05992-6>
- Sait, H., Sajjan, S. M., & Phadke, S. R. (2022). Haemophilia management programme: Transformation during COVID-19: Transformation during COVID-19. *The Indian Journal of Medical Research*, 155(5 & 6), 472–477. https://doi.org/10.4103/ijmr.ijmr_1941_21
