

chromosome with a mutation in the FVIII gene. In addition, it is estimated that there are 1.6 female carriers for every male HA patient. HA Carriers are classified into five categories based on residual plasma FVIII level (FVIII:C) and phenotype: (i) FVIII:C > 40% with bleeding phenotypes are classified as symptomatic; (ii) FVIII:C > 40% without bleeding phenotypes are classified as asymptomatic; (iii) FVIII:C > 5% to 40% are classified as mild HA; (iv) FVIII:C 1% to 5% are classified as moderate HA; and (v) FVIII:C < 1% are classified as severe HA. The aim of this study was to analyze the clinical and hemorrhagic profiles of female relatives of patients with severe HA with intron-22 inversion treated at Fundação Hemominas and older than 12 years. To date, sixteen participants have been enrolled in the study after signing an informed consent form. Participants answered two questionnaires: 1) evaluation of bleeding - ISTH (BAT-ISTH); and 2) evaluation of arthralgia. Peripheral blood samples were collected in a citrate tube and processed for DNA extraction. Genotyping to identify intron 22 inversion was performed by inverse PCR. Of the 16 participants, seven (44%) were identified as carriers of the mutation. Among the carriers, the median (MED) age was 35 years (IQR 34 - 35.5) and the bleeding score MED was 6 (IQR 4.8 - 9). In addition, carriers reported pain in the joints of the shoulders (3 - 42.9%), hips (2 - 28.6%), knees (2 - 28.6%), and ankles (2 - 28.6%). For participants who were not carriers, the age MED was 36 years (IQR 30 - 56) and the bleeding score MED was 4 (IQR 1 - 7). In addition, participants who were not carriers had pain in all joints studied, i.e., shoulders (3 - 33.33%), elbows (1 - 11.11%), hips (2 - 22.22%), knees (4 - 44.44%), and ankles (2 - 22.22%). Molecular diagnosis was important to identify family members with intron-22 inversion and to provide appropriate genetic counseling for family planning. A significant statistical difference ($p=0.019$) was found between carriers and non-carriers in bleeding score. This is an ongoing study and the number of participants needs to be increased in order to draw conclusions. We thank all participants, Fapemig, Fundação Hemominas, and the CGSH of the Ministry of Health.

<https://doi.org/10.1016/j.htct.2022.09.475>

QUALITY OF LIFE OF PATIENTS WITH VON WILLEBRAND DISEASE

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von Willebrand disease (VWD) is the most common bleeding disorder due to a qualitative or quantitative disorder of von Willebrand Factor (VWF). There are three main types of the disease (types 1, 2, and 3) and a total of 6 subgroups. Type 1 patients present low levels of VWF; type 2 patients present low activity of VWF, and type 3 patients have a virtual absence of this VWF. VWD is the most common coagulopathy in the human population, but is the least diagnosed. Undiagnosed individuals may present symptoms that are often neglected. The aim of this study was to analyze the quality of

life of patients with VWD who are treated at Fundação Hemominas. Patients were invited to participate in consultations and examinations. The 30 patients included (17 women and 13 men) answered a 36-item brief health questionnaire (SF-36). The analysis of quality of life in women showed that the concept of physical functioning received a median (MED) of 82.5% (IQR 73.8%-95%); the concept of role limitations due to physical health received a MED of 100% (IQR 18.8%-100%); the concept of pain received MED of 61% (IQR 61%-84%); the concept of general health received MED of 77% (IQR 60.8%-88.3%); the concept of energy/fatigue received MED of 57.5% (IQR 33.8%-80%); the concept of social functioning received MED of 81.5% (IQR 25%-100%); the concept of emotional well-being received MED of 83.5% (IQR 33%-100%); and the concept of mental health received MED of 76% (IQR 34%-80%). In men, on the other hand, the analysis of quality of life showed that the concept of physical functioning received a MED of 90% (IQR 70%-100%); concept of role limitations due to physical health received a MED of 25% (IQR 0%-75%); the concept of pain received MED of 72% (IQR 50%-84%); the concept of general health received MED of 67% (IQR 47%-85%); the concept of energy/fatigue received MED of (IQR 50%-80%); the concept of social functioning received MED of 75% (IQR 38%-75%); the concept of emotional well-being received MED of 100% (IQR 67%-100%); and the concept of mental health received MED of 80% (IQR 68%-84%). After analyzing these data, it was not possible to find a significant difference between male and female patients. In conclusion, our study is important to better understand which aspects of quality of life are most impaired in patients with VWD. This study has some limitations because patients were not subdivided by VWD type, and no participants were genotyped yet. This is an ongoing study and the number of participants needs to be increased to draw conclusions. We thank all participants, Fapemig, Fundação Hemominas, and the CGSH of the Ministry of Health.

<https://doi.org/10.1016/j.htct.2022.09.476>

RECLASSIFICATION OF PATIENTS WITH HEMOPHILIA A BY MOLECULAR DIAGNOSIS

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The state of Minas Gerais has the third largest population of hemophilia A (HA) patients in Brazil. Fundação Hemominas is the treatment center of reference in the state for clinical and laboratory care of HA patients. Patients are classified according to residual plasma FVIII activity (FVIII:C): Patients with FVIII:C 5%-40% are classified as mild HA; FVIII:C of 1%-5% are classified as moderate HA; and patients with FVIII:C <1% are classified as severe HA. Patients with severe HA often have inversions of introns 1 and 22 in the FVIII gene. The aim of this study was to diagnose inversions of introns 1 and 22 patients with severe and moderate HA. For this purpose, peripheral blood samples were collected from 39 male patients, median (MED) age was 31 years (IQR 19 -42 years),

classified as severe (27 patients) or moderate (12 patients) with FVIII:C dosage <3%. After collection, samples were processed for genomic DNA extraction. First, patients were genotyped for intron 22 inversion by inverse PCR. Patients who were negative for intron 22 inversion were genotyped for intron 1 inversion. Samples negative for both inversions will be full-length NGS sequencing. Among 39 patients, 21 (54%) were diagnosed with intron 22 inversion and one (2%) with intron 1 inversion. In addition, among 12 patients previously diagnosed with moderate HA, seven (58%) patients were reclassified as severe HA because they presented intron 22 inversion. The molecular diagnosis proved to be important for the correct classification of the severity of HA patients. Due to the diagnosis normally based only on residual activity of plasmatic FVIII, the disease severity classification may be incorrect. It is believed that the high variability of coagulometric techniques and the treatment of patients prior to laboratory diagnosis may affect the correct classification of HA patient severity. This is an ongoing study and the number of participants needs to be increased in order to draw conclusions. We thank all participants, Fapemig, Hemominas, and the CGSH of the Ministry of Health.

<https://doi.org/10.1016/j.htct.2022.09.477>

QUALITY OF LIFE OF HEMOPHILIA A FEMALE CARRIERS OF INTRON 22 INVERSION

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Assessing the quality of life of family members of patients with hemophilia A (HA) is necessary given the emotional overload and dedicated care of their family members. The 36-item Short Form Health Survey (SF-36) measure quality of life related to health using eight health concepts: physical functioning (PF), limitations due to physical health (PH), pain (P), general health (GH), energy/fatigue (EF), social functioning (SF), limitations due to emotional problems (EP), and emotional well-being (EW). The aim of this study was to analyze the quality of life profile of family members of patients with severe hemophilia A with intron 22 inversion mutation treated at Fundação Hemominas. To date, sixteen participants have been enrolled in the study after signing an informed consent form. Participants answered a 36-item short health questionnaire and collected peripheral blood samples in citrate tubes. Samples were processed for DNA extraction and genotyping. Participants were divided into two groups: Carriers of the intron 22 inversion and participants who were not carriers of the intron 22 inversion mutation. Among carriers the median (MED) scores were: 88% (IQR 77.5%-96%) for PF; 100% (IQR 56.3%-100%) for PH; 61% (IQR 61%-72%) for P; 87% (IQR 77%-92%) for GH; 60% (IQR 38.8% - 66.3%) for EF; 69% (IQR 47% - 75%) for SF; 100% (IQR 24.8% - 100%) for EP; and 70% (IQR 59% - 76%) for EW. Among participants who were not carriers, 93% (IQR 81.3% - 95%) for PF; 88% (IQR 18.8% - 100%) for PH; 72% (IQR 58.3% - 88%) for P; 67% (IQR

47%-80.3%) for GH; 58% (IQR 41.3%-70%) for EF; 69% (IQR 52.8%-91%) for SF; 84% (IQR 0%-100%) for EP; and 68% (IQR 54%-78%) for EW. Interestingly, carriers presented a significant higher score in general health domain ($p=0.03$). In conclusion, this study is important to assess the quality of life in relatives (carriers and non-carriers) of HA patients. This is an ongoing project and the number of participants needs to be increased in order to draw conclusions. We thank all participants, Fapemig, Fundação Hemominas, and the CGSH of the Ministry of Health.

<https://doi.org/10.1016/j.htct.2022.09.478>

INVESTIGATION OF INHERITANCE BY MOLECULAR DIAGNOSIS IN A FAMILY WITH NO FAMILY HISTORY OF HEMOPHILIA A: CASE REPORT

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Hemophilia A (HA) is classified according to residual circulating FVIII (FVIII:C). Patients with FVIII:C 5%-40% are classified as mild HA; patients with FVIII:C 1%-5% are considered moderate; and patients with FVIII:C <1% are classified as severe HA. Patients with severe HA have two common mutations: Inversions of introns 1 and 22 of the F8 gene. The aim of this study is to report the case of a patient diagnosed with HA without any family history of the disease and treated in Fundação Hemominas in 2022. Male patient, NB, presented an extensive hematoma on the back after 24 hours of delivery. A blood count was performed, which reveals a hemoglobin value of 5 g/dL (reference value approximately 16 g/dL). Patient is admitted to the ICU where a blood transfusion and coagulometric tests are performed, indicating HA. The patient is referred to the pediatric hematology unit of Fundação Hemominas. Coagulation tests confirmed the diagnosis of severe HA. The patient was referred for molecular diagnosis of the disease. In addition, three members of the patient's family agreed to participate in the molecular diagnosis. The family members answered two questionnaires: 1) bleeding assessment score - ISTH (BAT-ISTH); and 2) arthralgia assessment. Peripheral blood was drawn from all participants in a citrate tube, and samples were processed for genomic DNA extraction. Genotyping of the intron 22 inversion mutation was performed by inverse PCR. The patient was positive for intron-22 inversion, confirming the diagnosis of severe hemophilia A. The patient's mother (34 years old), with a bleeding score of 3, without joint pain, was diagnosed with the same inversion and received genetic counseling when the report was handed over. The patient's aunt (30 years old), with a bleeding score of 0, without joint pain, had a negative result for intron inversion 22. The patient's grandmother, 59 years old, with a bleeding score of 1, who presented right knee pain, also had a negative result. Evaluation of the patient's three-generation pedigree suggests that the patient inherited the de