NAME OF PROJECT: International Registry on the Symptomatic Hemophilia A/B Carriers: The Pink Color of Hemophilia

Subcommittee: Women's Health Issues in Thrombosis and Haemostasis

Person responsible (Chair / Principal Investigator):

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Collaborators from the women’s SSC: Robert Sidonio, Elvira Grandone

Chair: Maha Othman

Description Abstract

Although the first reports concerning women with hemophilia date back to the 1950s, not much is known about the true incidence of symptomatic women and their treatment.

We often speak about the women carriers of hemophilia only as mothers, sisters or daughters of hemophiliac patients, but this is not enough. The recognition of the status of hemophilia carrier occurs almost only in these cases, while the identification of a hemophiliac woman based only on her hemorrhagic history are rare, but not impossible.

The diagnosis of the true disease behind bleeding can therefore be very late. Hemarthroses in women are infrequent, their presence depends on the level of deficient coagulation factor, but the diagnostic delay may favor the onset of hemophiliac arthropathy that even requires substitutive and also invasive treatments. Some women may therefore present the same problems that afflict hemophilic males, depending on their level of plasmatic factor.

Design and methodology (Data expected to collect, sample size and statistical analysis):

The first objective of our Registry is therefore to establish how many women with hemophilia A and B are actually followed in the different Hemophilia Centers around the world and how many of these are symptomatic. It is also important to define what are the types of bleeding (traumatic, spontaneous), which are the most affected sites (joints, soft tissues, etc.) to better understand how hemophilic pathology occurs in the female sex and what are the consequences of these bleeding (e.g. arthropathy). Among the secondary objectives, it is
essential to understand which treatments are used on demand or in prophylaxis in this group of patients and how they can be managed differently in the different Countries. What is the quality of life of these women, who in many cases are simultaneously patients and caregivers, is undoubtedly interesting to try to understand how to act both pharmacologically and psychologically.

In order to be able to answer these questions, it is therefore necessary to make a simple and easy to complete Survey, accessible to all, which allows to underline all the aspects that we want to investigate and which can then be subject to accurate statistical analysis. The study carried out in two distinct and successive phases: 1) Creation of the online Registry; 2) Analysis of Registry data. A first CRF is present on the RedCap platform, but it is necessary to promote this study worldwide and to improve this data capture.

Descriptive statistical analyzes will be performed using the Windows 7 SAS version 9.2 (SAS, Cary, NC) statistical program. Given the non-interventional nature of this study, all patients will be included in the analysis, no particular statistical strategy will be adopted. All the collected variables will be subsequently summarized in tables that will use appropriate descriptive statistics: mean, standard deviation (SD), mean, range, percentage. More detailed statistical analyzes (e.g. multivariate, univariate analyzes, etc.) will subsequently be carried out with the support of the Statistics Department of the University of Padua (Italy).

Study population (Inclusion, exclusion, eligibility) (patient population; recruitment of participating institutions/physicians and subjects; minimum number needed; expected number):

All hemophilia A and B carriers of any age can be included in the Registry through the e-CRF reported in the specific RedCap platform.

- Definition of hemophilia carriers: all females with proven low level of FVIII or FIX and with proven mutation in the FVIII or FIX gene: 6-50% mild, 1-5% moderate, <1% severe, >50% with bleeding normal.

- Definition of symptomatic hemophiliac women: all women with hemophilia who have or have experienced major or minor traumatic or spontaneous bleeding at different sites, requiring medical treatment (consultation only, treatment with FVIII/FIX, antifibrinolytics, etc.)

- Bleeding severity was defined based on the European Network of Rare Bleeding Disorders (EN-RBD) Classification (7). 1) asymptomatic: no documented bleeding episodes; 2) Grade I bleeding: bleeding that occurred after trauma or drug ingestion (antiplatelet or anticoagulant therapy); 3) Grade II bleeding; spontaneous minor bleeding as bruising, ecchymosis, minor wounds, oral cavity bleeding, epistaxis and menorrhagia; 4) Grade III bleeding: spontaneous major bleeding as large haematomas, haemarthrosis, intracranial haemorrhage, gastrointestinal and umbilical cord bleeding.
All Hemophilia Centers who treat or have treated hemophiliac women are encouraged to participate at our Registry.

The e-CRF will be divided into different sections: 1. Demographic; 2. Laboratory; 3. Genetics; 4. Medical history (not related to hemophilia); 5. Clinic (related to hemophilia); 6. Pharmacological (related to hemophilia); 7. Quality of life. Each of the sections will also be divided into several sub-sections.

All data will be collected both in retrospective terms (without time limitation) and in prospective terms (from the study start date to the closing date of the data collection).

Expected timeline:

- Project stage/set up: Ongoing
- Launch: July, 2020 (ISTH Congress – Milan)
- Duration: 2 years
- Finalization/analysis: July 2022
- Reporting: first report ISTH 2021 (Philadelphia, USA); second report ISTH 2022 (London, UK); final report ISTH 2023 (Montreal, Canada) and results publication.

Expected outcomes (ie. publications):

We expect to answer the questions formulated and listed in the previous paragraphs regarding the real burden of this pathology in the female sex. The results will be made public initially through oral communications and / or posters at the next congresses and subsequently through complete publication of the data obtained.

Publication type (SSC Communication, Guidance document or original article):
Based on the collected data, Original Article and/or SSC Communication

Description of project set/up and management, needed infrastructure and resources (summary):

The Survey should be managed by the RedCap Platform. No other infrastructure or resources are needed.

Possible references:


