REVIEW ARTICLE

Screening Of Patients With Fabry Disease In Low-Resource Settings – Establishing Diagnostic And Therapeutic Modalities – The Example Of Bosnia And Herzegovina

Goran Topic[1], Edin Begic[2], Nejra Prohic[3], Ada Djozic[2], Damir Rebic[4], Mirna Aleckovic-Halilovic[5], Tamara Kovacevic-Preradovic[6], Ivica Brizic[7], Mensuda Hasanhodzic[8]

[1] Clinic for Nephrology, University Clinical Centre of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina
[2] Department of Cardiology, General hospital "Prim.dr. Abdulah Nakas", Sarajevo, Bosnia and Herzegovina
[3] Department of Internal medicine, General hospital "Prim.dr. Abdulah Nakas", Sarajevo, Bosnia and Herzegovina
[4] Clinic for Nephrology, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina
[5] Department of Nephrology, Clinic for Internal Medicine, University Clinical Centre Tuzla, Tuzla, Bosnia and Herzegovina
[6] Clinic for Cardiology, University Clinical Centre of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina
[7] Clinic for Cardiology, University Clinical Centre Mostar, Bosnia and Herzegovina
[8] Center for rare diseases, University Clinical Centre Tuzla, Tuzla, Bosnia and Herzegovina

Corresponding Author: Goran Topic MSc., Clinic for Nephrology, University Clinical Centre of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina; E-mail: goran.topic@kc-bl.com; Phone: +387 51 342-100; ORCID ID: 0009-0003-0290-7909

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Abstract

Fabry disease (FD) is a multisystem disorder, an X-linked lysosomal storage disease caused by decreased activity of alpha-galactosidase A, resulting in lysosomal accumulation of neutral glycosphingolipids and globotriaosylceramide (GL-3). Rare diseases represent conditions that are likely underdiagnosed, and the number of patients is certainly higher than what is reported. In the conditions found in Bosnia and Herzegovina, or generally in low-sesource settings, the diagnosis and treatment of rare diseases is challenging. There is no screening for rare diseases, no registry for them exists, and therapeutic or pharmacological options are not available. All of this represents challenges in the daily work of clinicians. The aim of this paper is to present the situation regarding the diagnosis and treatment of patients with FD in Bosnia and Herzegovina.

Keywords: rare diseases, Fabry disease, screening.

INTRODUCTION

Fabry disease (FD) is a multisystem disorder, an X-linked lysosomal storage disease caused by decreased activity of alpha-galactosidase A, resulting in lysosomal accumulation of neutral glycosphingolipids and globotriaosylceramide (GL-3) (1). The clinical presentation of the disease, including its most common features, is shown in Figure 1

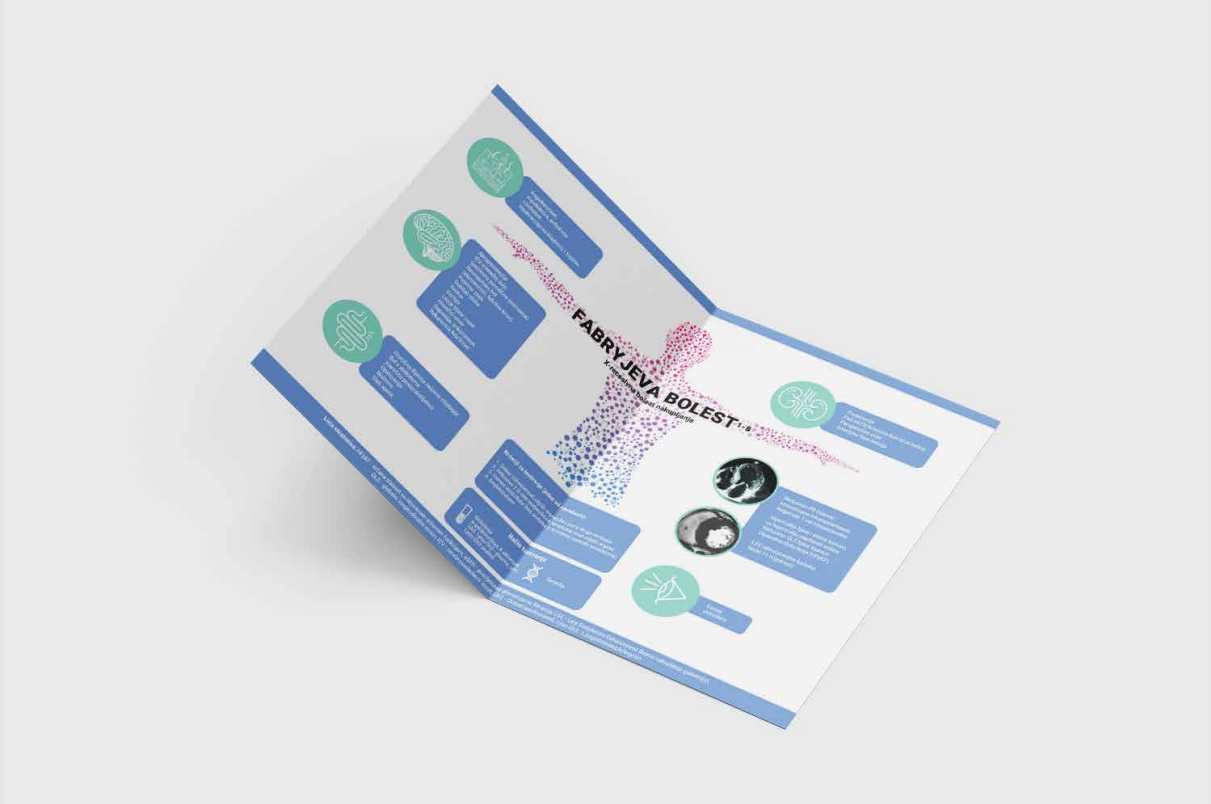

Figure 1. Clinical presentation of Fabry disease - The authors present a leaflet that was prepared for physicians throughout the entire healthcare system; the leaflet is written in the language used in Bosnia and Herzegovina, and as such, its aim was to raise awareness about the existence of the disease.

It is believed that FD is an underdiagnosed condition (prevalence of FD varies from 1 in 40.000 to 1 in 117.000), and awareness of its existence, especially in low-resource settings remains low. A potential awareness-raising project would likely need to be developed through the engagement of specialists in pediatrics, dermatology, nephrology, cardiology, neurology, ophthalmology, and gastroenterology. A collaborative, multidisciplinary approach, supported by professional associations, is imperative. The presence of symptoms such as angiokeratomas, unexplained hearing loss, stroke in younger individuals, cornea verticillata, or unexplained proteinuria should serve as key indicators prompting consideration of FD. Cardiological evaluation of young patients with a history of stroke should also include an assessment of myocardial longitudinal strain (2). Cardiac magnetic resonance imaging, which is not easily accessible, would be very helpful, primarily in the evaluation of left ventricular hypertrophy.

LOW-RESOURCE SETTINGS - EXAMPLE OF BOSNIA AND HERZEGOVINA

Finding patients in low-resource settings is likely a significant challenge. The first step is raising awareness about the disease, establishing dedicated hospital units to address this condition (and rare diseases in general; recognizing that internal medicine and the broad expertise of internists are key elements), and leveraging support from pharmaceutical companies to enable enzyme activity testing as well as genetic analysis. Additionally, the establishment of a central genetic counseling center and a laboratory capable of analyzing and interpreting results emerges as an important step. Creating national patient registries is also essential, as this would provide a clearer picture of the number of patients, enabling better planning for diagnosis, monitoring, and treatment—which currently remains largely unavailable.

The belief that the disease cannot be treated is likely widespread, but it is essential to

promote the message that treating the disease is both meaningful and effective (3–5).

The treatment of FD involves early initiation of enzyme replacement therapy (ERT) with alpha-galactosidase (alpha or beta) as soon as the diagnosis is confirmed, or migalastat (chaperone therapy), regardless of the presence of clinical symptoms in affected males or whether the patient is receiving renal replacement therapy. Pegunigalsidase-α is also available in Bosnia and Herzegovina (B&H).

Enzyme replacement should be considered for female carriers and affected males with reduced Alpha-Gal A activity only when clinical signs involving the kidneys, heart, or nervous system are present. In case of classical Fabry disease, all male patients are treated, while female patients are treated if symptomatic or with signs of early organ involvement. In non-classical or late-onset Fabry disease, patients are treated if early signs of organ damage (kidney, heart, nervous system) are present. Patients undergoing long-term dialysis are also candidates for ERT (3-5). In cases of end-stage renal disease, renal transplantation can be performed safely, with ERT continued after transplantation.

DETECTED PATIENTS IN BOSNIA AND HERZEGOVINA - WHAT TO DO WITH THEM

As of June 17, 2025, five patients have been diagnosed with Fabry disease in Bosnia and Herzegovina through multidisciplinary collaboration and pharma-industry support. A family pedigree including four of these patients is shown on Figure 2.

The question of pharmacological modalities also requires a multidisciplinary understanding of the disease. Figure 3 shows a patient whose left ventricular longitudinal strain was analyzed (strain abnormalities in the basal and mid inferoseptal segments are characteristic of Fabry disease). The patient's electrocardiogram shows ST segment depression up to 1 mm, accompanied by clinical symptoms of dyspnea. A previously performed coronary computer tomography (CT) angiography confirmed a calcium score of 0 and ruled out obstructive coronary artery disease. Angiokeratomas were previously verified on the left thoracic area, scapular region, and left lumbar region. Testing showed Lyso-Gb3: 5.8 ng/mL; GLA gene mutation: c.334C>G p.(Arg112Gly) – heterozygous.

Additional genetic testing needs to be acknowledged and actively supported by the governing health authorities. The development of this sector is essential not only for Fabry disease but for all rare diseases. Progress in this area is also a hallmark of the overall advancement of the healthcare system (6). Bosnia and Herzegovina's territorial division into the Federation of B&H, the Republic of Srpska, and the Brcko District, along with its complex organizational struc-

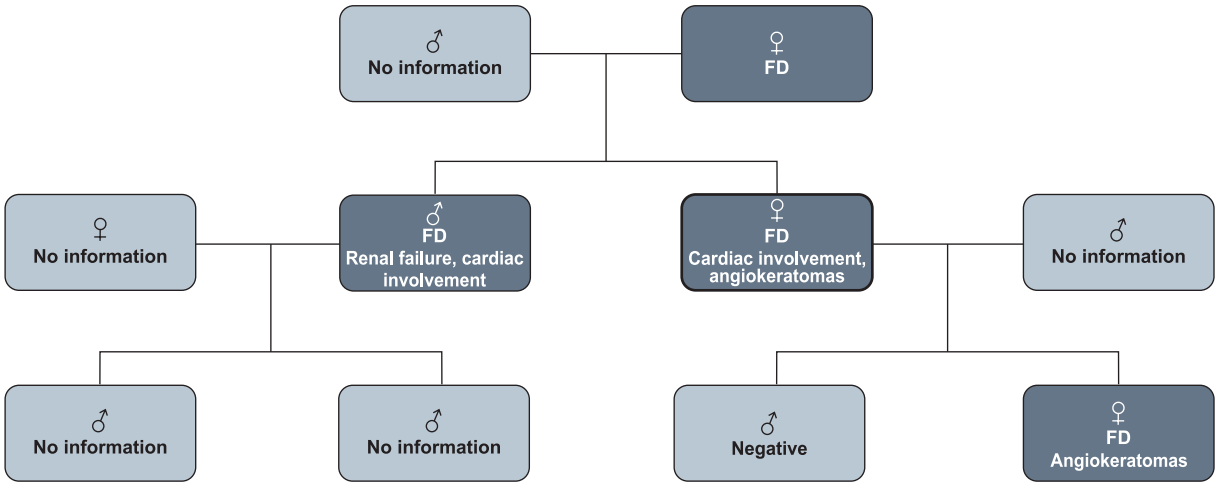

Figure 2. Pedigree of the identified family

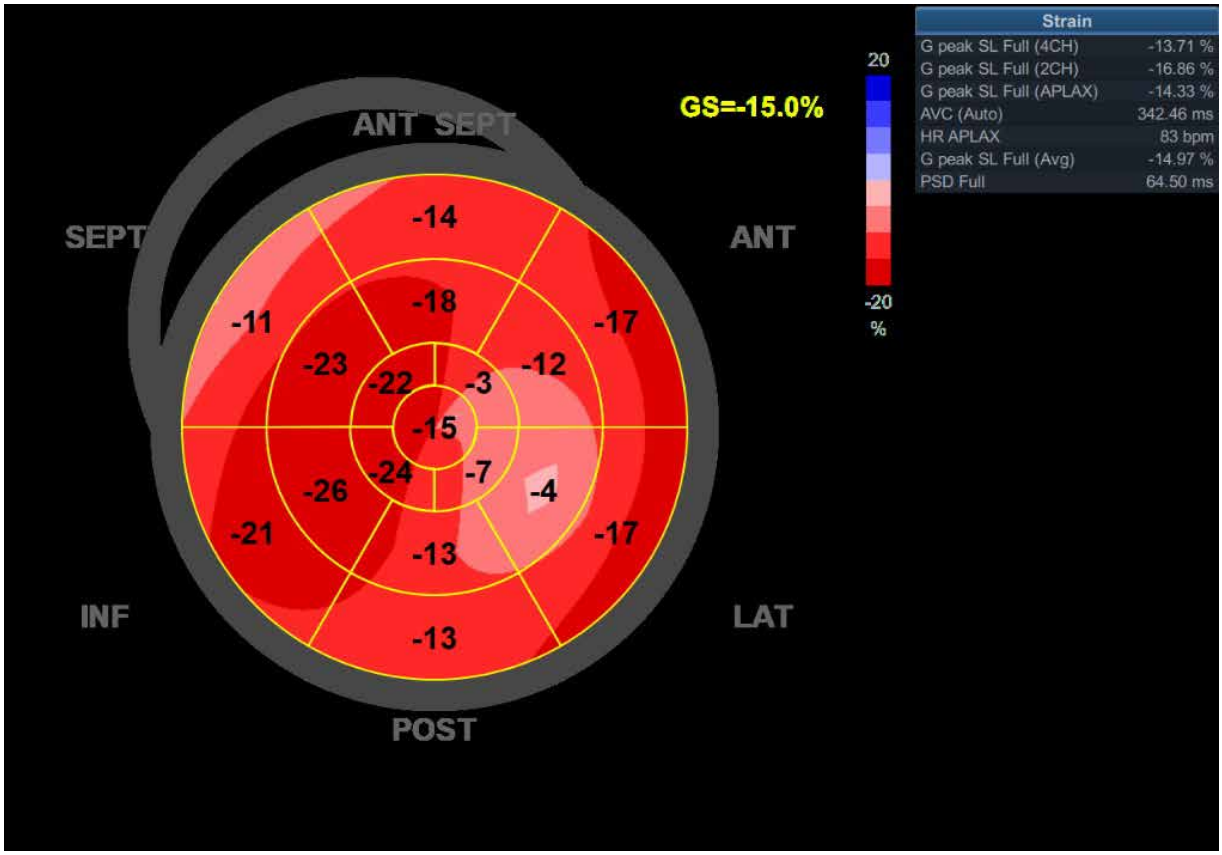

Figure 3. A 55-year-old female patient with cardiac involvement, previously verified angiokeratoma on the left thoracic area, in the scapular region, as well as in the left lumbar region; Lyso-Gb3: 5.8 ng/mL, GLA gene: c.334C>G p.(Arg112Gly) – heterozygous

ture, 13 ministries of health without the state level one (in Federation of B&H), poses a significant challenge to the effective implementation of crucial services such as organ transplantation and the treatment of rare diseases (6) that should be a national projects.

Currently, Funds have limited resources for the treatment of rare diseases, but with an increasing number of diagnosed patients and greater awareness of the disease including healthcare decision makers, this issue will likely need to be addressed. It is imperative to start the patient on the pharmacological treatment as soon as possible.

CONCLUSION

Raising awareness about the existence of rare diseases is essential, and it will also contribute to the development of specific segments of clinical practice related to particular rare conditions. Registries for rare diseases, referral centers, the identification of dedicated professionals who will focus on these conditions, and the establishment of Funds that will finance diagnostics and treatment must already be integral parts of today's healthcare system in Bosnia and Herzegovina.

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