



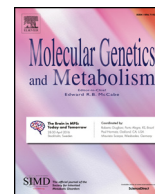
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Brief communication

## Impact of COVID-19 pandemic on patients with Fabry disease: An Italian experience

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## ABSTRACT

We conducted an observational study to assess the impact of COVID-19 emergency on management and outcomes of patients with Fabry disease referring to our Center in Naples, Italy.

No patient of the 129 included reported suspected symptoms; 3 isolated themselves in auto-quarantine for flu-like symptoms. All treated patients regularly continued their therapies; 8 missed one infusion: 3 for self-isolation with 2 relatives, and 3 refused to receive nurse at home.

All elective procedures were deferred and telemedicine was adopted.

## 1. Text

Coronavirus disease 2019 (COVID-19), a severe acute respiratory syndrome with a high mortality rate caused by the SARS-CoV-2, was labelled as a global pandemic by the World Health Organization in March 2020. Italy is one of the most severely affected countries: from the beginning of the emergency until 11th May 2020, the Italian Ministry of Health have reported 220,000 confirmed cases and 30,000 deaths [[www.salute.gov.it](http://www.salute.gov.it)]; therefore, the landscape of the Italy's healthcare system has been rapidly and dramatically altered. In particular, a main challenges in this pandemic is represented by balancing patient care needs with limited resources. Therefore, to face the changing resource allocation during the COVID-19 pandemic, several strategies have been implemented to minimize interruption of care and treatment.

Patients with underlying chronic multisystemic disorders, like Fabry disease (FD), are considered at greater risk of COVID-19 infection and more likely to have higher morbidity and mortality [1]. FD is an X-linked disorder caused by lysosomal  $\alpha$ -galactosidase A ( $\alpha$ -Gal) deficiency, with subsequent deposition of undegraded glycosphingolipid products, mainly globotriaosylceramide (Gb3) and globotriaosylsphingosine (lyso-Gb3), in multiple organs, with significant morbidity and premature death [2]. To date, the treatment options for this genetic disease include intravenous (i.v.) infusion of enzyme replacement therapy (ERT) with agalsidase alfa or agalsidase beta every other week, and oral therapy with the pharmacological chaperone migalastat [3].

Moreover, clinical trials to evaluate the efficacy of pegunigalsidase alfa, a pegylated dimerized version of agalsidase alfa, infused at two different doses either every other week or monthly, are currently ongoing [3].

The Fabry Center of Federico II University of Naples is one of the main referral centers for FD in Italy, with more than 150 patients, performing about 500 annual outpatient clinic visits. The rapid spread of COVID-19 combined with the consequent complete global lockdown, required a number of changes in our FD center organization to avoid unnecessary exposure of staff and patients to infection, while still continuing to provide care and support to our patients. Therefore, we conducted an observational study with the aim to assess the impact of COVID-19 emergency on clinical management and outcomes of patients with FD.

All FD patients referring to our center were contacted by phone by physicians, to collect data about their health status and to organize their follow-up.

A total of 129 patients were included, 60 males (46.5%) and 69 females (53.5%), mean age  $47.5 \pm 15.9$  years. No patient reported either symptoms suspected for COVID-19, or a direct contact with a known positive case; therefore, no patients was specifically tested with nasal swab. Only 3 patients presenting fever  $< 37.5$  °C and flu-like symptoms, isolated themselves in auto-quarantine for 14 days, with no further investigation.

At the beginning of the emergency, 36 patients (27.9%) were not treated, 71 patients (55%) were receiving i.v. ERT (agalsidase alfa or

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beta), and 16 (12.4%) were on oral treatment with migalastat. Six patients (4.7%), enrolled in the clinical trials for the evaluation of pegunigalsidase alfa efficacy, were receiving infusions at hospital: 3 of them received i.v. pegunigalsidase monthly, and the other 3 received blinded therapy with i.v. pegunigalsidase alfa or agalsidase beta every other week.

Regular drug supply or delivery were ensured for all patients. In particular, Italian Medicine Agency (AIFA) extended the deadline for prescriptions of treatments for rare diseases by three months [[https://www.aifa.gov.it/documents/20142/1124329/comunicato\\_proroga\\_PT\\_AIFA\\_11-03-2020.pdf/4362b271-212c-7c9f-657f-979f6c34ad9a](https://www.aifa.gov.it/documents/20142/1124329/comunicato_proroga_PT_AIFA_11-03-2020.pdf/4362b271-212c-7c9f-657f-979f6c34ad9a)].

No interruption or modification occurred for patients receiving oral therapy. All patients receiving intravenous treatments were on home-therapy; therefore, they continued their infusions regularly, except for 8 patients (11%), who missed one infusion: 3 because of self-isolation for like-flu symptoms, 2 for flu-like symptoms occurring in their relatives, and 3 for patient's personal decision (fear of infection), to not receive the nurse at home.

New enrolment into clinical trials has been paused during the COVID-19 crisis, but FD patients enrolled in therapeutic clinical trials continued the study drug. Specifically, for these patients, we organized home therapy services to maintain necessary infusion schedule while minimizing social contact.

Psychological support services were proposed to all patients, and 3 patients (2.3%) contacted the psychologist.

Moreover, to promote physical distancing and in anticipation of increased workload due to a pandemic, elective treatments and procedures, routine laboratory testing and non-urgent outpatient clinics were deferred. Telemedicine, including both video and telephone-only contacts, is emerging as an important tool for maintaining outpatient care while limiting direct patient contact [4]. When clinically appropriate, telemedicine was adopted to care for ambulatory patients. No programmed visit resulted undeferrable, so each patient with a scheduled visit was contacted 24 to 48 h before their appointment by a clinic coordinator to confirm their visit date and time and to explain that it would be conducted in the comfort of their own homes with the use of our telehealth facilities. Then, medical staff called patients on the day and time of their clinic appointments. Patients were asked to take their temperature, pulse, weight and blood pressure. If necessary, visual examinations were performed, including evaluation for respiratory

distress and oedema, using platforms such as FaceTime, WhatsApp, and Zoom to expedite this process. For patients needing laboratory surveillance, we limited it focusing on laboratory tests easily drawn at not a hospital-based laboratory. Moreover, we suggested the use of urine dipsticks for home monitoring of proteinuria. Finally, patients' medications and prescriptions were evaluated and adjusted.

Specific recommendations have been provided to our staff office to respond to patient questions about a possible COVID-19 exposure.

From our survey data, among 129 interviewed patients, no one was infected. However, since no specific tests (oropharyngeal swab or serum antibodies) were performed, asymptomatic or pre-symptomatic cases cannot be excluded among our cohort. The reason of the absence of infection in our FD population could be the particular attention of this category of patients in respecting measures of hygiene and infection prevention. A further explanation could be the safe organization of home-therapy, that seems to be the most efficient way to maintain therapy access during a pandemic, obviously monitoring the involved personal and guaranteeing the correct use of personal protective equipment. In fact, the only experience reported in the literature on the impact of COVID-19 on therapies for lysosomal storage disorders (LSD), showed that 49% of patients receiving ERT in the hospital experienced treatment disruption [5].

At present, no official indication exist on the management of FD patients during emergency and post-emergency period. Therefore, the analysis of the COVID-19 pandemic effects on medical care and health status of patients with FD will be useful to delineate consensus guidance.

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