INVESTIGATING PATIENTS WITH FABRY DISEASE
(2018)

EXECUTIVE SUMMARY OF MAIN RESULTS[1]

Summary of the Investigation

The data presented in this executive summary are the main results of a survey administered across Italy and promoted by the Italian Anderson Fabry Association (AIAF). It was carried out by the Centre for Applied Economic Research in Health (CREA Sanità) in autumn 2018. The questionnaire was aimed at people living with Fabry disease and was shared across the Association's network. It was compiled online by a total of 106 respondents, 91% of whom were people with Fabry disease and 9% of whom were the patients' parents. Based on the estimates of the prevalence rate of Fabry disease across the Italian population, the coverage rate of the survey is within the range of 6.6% - 15.1%. The analyses of the main results were carried out by Sinodè in the first few months of 2021.

1. People with Fabry Disease

59% of people with Fabry disease who responded to the questionnaire were female; half of the respondents were between the age of 35 and 54 years, just over 1 in 5 were over 55 years old while 17% were between 18 and 34 years. Out of all respondents, only 12% were under 18 years old. Almost 90% of patients with Fabry disease live with other people; just over 1 out of 10 lives alone (11%); 1 out of 3 patients is single. 44.3% have graduated from secondary school, 20.8% have a degree or a doctorate. 54% are in work (as an employee or self-employed). In 16% of cases, fewer than 3 years have elapsed since their diagnosis; for 28%, 3 - 5 years have elapsed; for 19%, 5 - 10 years have elapsed; and for 37%, over 10 years have elapsed since their diagnosis.

2. Diagnosis and Specialists following Patients with Fabry Disease

In 35% of cases, a diagnosis of Fabry disease comes after the age of 40 (range: min = 0; max = 66 years) while in 1 in 4 cases (26%), their diagnosis occurred while they were still children, mainly as a result of another family member having the illness (and/or, to a lesser extent, due to screening): in fact, 3 out of 4 minors were diagnosed in this way (globally 1 out of 2 patients, due to a delay in diagnosis where there is no family history of the illness). For those who have no previous cases within the family or were not screened as new-borns or later, the time elapsed between the patient's first symptoms and their diagnosis was over 3 years in over 2 out of 3 cases (around 30% higher than cases diagnosed through family history and/or screening). 1 out of 5 patients was diagnosed outside the region where they reside, which is in line with global data for rare diseases at a national level[2]. In almost 8 out of 10 cases, the first suspicion of their diagnosis came from a single specialist, mainly a nephrologist, cardiologist, geneticist or neurologist. In just under 4 in 10 cases, a final diagnosis was given by a group of specialists, especially in the most severe cases. Medical specialists that are most commonly involved in the care of people with Fabry disease are nephrologists (1 in 2 cases), cardiologists (1 in 3 cases) and neurologists (1 in 4 cases). Other medical professionals are less frequently involved: in 1 out of 10 cases, the patient is followed by their General Practitioner, and in the same number of cases, the patient

[1] This document was written by Romano Astolfo, Paola Bragagnolo and Marco Stocco, Sinodè srl.

[2] Source: UNIAMO Italian Federation for Rare Diseases ("*Federazione Italiana Malattie Rare*") "MonitoRare – report on the situation of people with rare diseases, 2017", in reference to rare diseases pursuant to Ministerial Decree 279/2001.

is followed by their primary care paediatrician, a geneticist, an internal medicine physician and an ophthalmologist

3. Access to Financial Support

Almost 8 out of 10 people with Fabry disease (79%) are exempt from paying the health service fee ("ticket") due to illness, an additional 6% are exempt due to low wage and illness, and a further 1% is exempt for low wages: therefore, 14% of people are not currently exempt from paying the health service fee. This is a situation that is shown to improve the more time elapses since the patient's diagnosis: this is made clear by the fact that almost 30% of those who had had their diagnosis for less than 2 years were still not exempt from paying the health service fee, while for those who had received their diagnosis over 5 years ago, that dropped to less than 10%. The acknowledgement of civilian invalidity also rises as the number of years since diagnosis increases (in 7 out of 10 cases that were diagnosed over 10 years previously, civilian invalidity had been recognised to the patient, dropping to 3 out of 10 of those diagnosed within the last 5 years). Overall, civilian invalidity has been acknowledged to around 1 in every 2 cases (46%): however, it is noteworthy that fewer than 1 in 10 people were not aware that they were eligible to apply for it. 33% of people have been recognised as having a handicap pursuant to article 3 of Law 104/1992 (46% of whom are recognised as having a serious disability, pursuant to article 3 para. 3). Finally, 2% of cases have been able to access a carers' allowance. 8% of minors in the study have received a monthly school attendance benefit. Patients who were diagnosed with Fabry disease later in life tend to have more severe forms of the illness, due to the delay in intervention: this is shown by the higher rates of recognition for civilian invalidity and disability (almost half of those diagnosed at over 35 years old, compared to less than 1 in 4 of those diagnosed at under 35 years). It is important to note that 12% of people with Fabry disease also have a private health insurance policy.

4. Relationship with Organisations and Associations dealing with Illness

Almost 6 out of 10 people with Fabry disease (59%) are in contact with an organisation or association dealing with disease: once again, the time elapsed since the patients' diagnosis plays an important role, as shown by the fact that the number of people who are in contact with an association that deals with these illnesses is lower for those who were diagnosed less than 5 years ago (at 51%). These organisations provide a wide range of support services for people with Fabry disease: they constitute a place where, for 79.4% of cases, patients can meet other people living with the illness and share experiences, for 66.7%, can receive updates on scientific innovations about the disease and, for 63.5%, receive updates on treatment. For many patients, a less significant yet still present reason to contact these associations is to receive information and advice on specialist medical professionals (34.9%) and to get information on specialised centres within their region (17.5%). In 1 out of 4 cases, organisations dealing with Fabry disease can help patients to access financial support, in particular information on applying for the civilian invalidity allowance (25.4%) or on resolving bureaucratic problems at their local health authority (22.2%). Finally, in 1 out of 5 cases (20.6%), these organisations provide psychological support. These two aspects represent the most common enquiries by patients with Fabry disease to these organisations: more than 4 in 10 (41.3%) people have asked for more guidance on the information needed to apply for the civilian invalidity allowance; fewer people (34.9%) would like more support in resolving bureaucratic issues with their local health authority and psychological support in managing their needs, not to mention the aforementioned "traditional" aeras of action which these associations deal with, requested by more than a quarter of patients.

5. Employment Status of Patients with Fabry Disease

54% of people with Fabry disease are in employment (45.3% work as an employee and 8.5% are self-employed) while 9.4% are unemployed and around 11% are still in full-time education. Among those in employment, 48% have had to reduce their number of hours due to their illness. In almost 1 case in 5 (23.8%), the patient had to quit their job and in 16.7% of cases, the patient had to change their role. Further comparison with data from the European Health Interview Survey (EHIS3, 2015) highlights the huge impact of Fabry disease on the lives of patients: in the last twelve months, 62.4% of people with Fabry disease have missed at least one week or work or study due to their illness, as opposed to just 23.4% of the larger population of people with chronic illnesses. In almost 4 cases in 10 (38.6%), people with Fabry disease must use their holiday leave to manage their treatment-related absences from work. This illness clearly limits job opportunities and managing and treating their disorder uses up resources for the patient, both in terms of time and money. This leads to a higher level of dissatisfaction of the patient's financial situation compared to the wider population: 11.3% of people with Fabry disease report being completely dissatisfied with their own financial situation compared to 3.8% of the general population (Source: ISTAT, *Aspects of daily life*, 2019).

6. Relationship with Health Services

91% of people with Fabry disease is followed by a specialised centre, but only 1 out of 5 general practitioners/primary care paediatrician is in contact with the specialised centre that follows their patient. In 72% of cases, follow up visits and medical tests ordered by specialists are carried out across multiple, non-consecutive days, which forces patients to patients to travel (and consequently pay) more and also to miss more days of work. In just 2 in 5 cases (21%), medical tests ordered by a specialist will take place on the same day as a periodic follow up visit. Satisfaction with these specialised centres is fairly high, especially when considering clinical management (average: 7.0 on a scale of 1 - 10, where 1 = completely dissatisfied and 10 = completely satisfied) rather than organisation (average: 6.7) and communication with staff members (average: 6.6).

Respondents report that mental health support services are provided in 17% of specialised centres, although knowledge of these services is not consistently shared by all patients frequenting the centre (most people answered "I don't know" to this specific question): in this respect, 72% of respondents would like to see a mental health professional among the staff members in support centres; this solution is preferable to an online or telephone service for mental health services, although this is still seen as positive by 49% of respondents. 4% of people with Fabry disease went to therapy sessions to support their mental health in the last 12 months. More than 84% of people with Fabry disease reported to have attended consultations or medical visits with a specialist in the last year and in 9 out of 10 cases (91%), this referred to a consultation with a cardiologist, in 6 out of 10 cases (62.9%) with a nephrologist, in 5 out of 10 cases (53.9%) with a neurologist and an ophthalmologist and in 4 out of 10 cases (43.8%), with an otolaryngologist. 70% of patients have had diagnostic tests and analyses for problems related to Fabry disease linked to the specialist that followed their illness in the last 12 months.

[3] European Health Interview Survey (EHIS) was conducted from 2013 and 2015 in all Member States of the European Union, plus Iceland and Norway. It investigated the key aspects of health of the population and their health service usage.

7. Treatment

8 out of 10 patients with Fabry disease (82%) receive pharmacological treatment: 74% of cases receive intravenous enzyme replacement therapy with AGALSIDASE ALFA (48% of the total number of cases of patients with Fabry disease) or with AGALSIDASE BETA (26%), while the rest take MIGALASTAT (oral route) (8%). Just 13.8% of people undergoing pharmacological treatment are "not very" or "not at all" satisfied with their treatment, although this dissatisfaction is more pronounced for those taking medication orally. In 4 out of 10 cases (40.2%), the patient has perceived some improvement in their health status since beginning their course of treatment and in the same number again (39.1%), they see substantial stability: in just over 1 in 10 cases (11.5%) patients report a slight worsening in their health status, and almost the same number (9.2%) see a more significant deterioration. 51% of people with Fabry disease undergo intravenous enzyme replacement therapy at home (in 3 out of 4 cases with nursing staff from the pharmaceutical company) with high levels of satisfaction (97.5% of patients say they are satisfied with the way of administering the medication at home and 95% of people have had no problems with the nursing staff who administer this infusion). Among those who do not undergo intravenous enzyme replacement therapy at home, around half (48.7%) only do so as it is impossible to do otherwise (this way of administering medication is not foreseen by law in the region where they reside), while a further quarter (28.2%) do so due to their choice of clinic and for 15.6% it is a personal choice: just 2.1% do so explicitly because they perceive a higher level of safety. 64% of patients who are currently treated in hospital or in an outpatient clinic report that being treated at home would improve their quality of life; at the same time, none of the patients who currently undergo at home treatment state that they would go back to receiving their treatment in hospital. The place in which patients are treated has a major impact on the number of days of work/school that the patient misses: for those who have to travel to a regional specialised centre, 8 out of 10 patients have missed at least a week of work/school across the past year, as opposed to 6 out of 10 patients who undergo treatment at home. Due to the varying amount of time necessary for the administration of different medication, specific treatment can impact on the number of days of work/school missed by patients (in 80% of cases, patients who are treated with AGALSIDASE BETA have missed at least 10 days of work/school in the last 12 months, compared to 60.4% of patients who are treated with AGALSIDASE ALFA and 33.3% of those treated with MIGALASTAT, a medication which is generally used for less severe cases of Fabry disease).

8. Health Status and Degree of Acceptance of Illness

1 in 5 people with Fabry disease (20.7%) reports problems in accepting this illness, which substantially affects their perceived health status: further evidence of the need to provide psychological support for people with Fabry disease. Among those who fail to take action regarding their illness, their perceived health status corresponds to an average score of 3 on a 0 - 10 scale (where 0 = extremely compromised and 10 = not at all compromised by their illness) while those alternate between accepting and rejecting their illness report an average score of 5.1, compared to an overall average of 6.4 (and of 7.0 for those who accept their illness and try to live their lives as they had done in the past). Further evidence to this is demonstrated by the fact that just 38.5% of those who report their own health status to be "poor" (that is, in the 3 out of 4 cases that reported a deterioration in their condition in the last 12 months) express that they live their lives in acceptance of their illness, compared to 76.7% of those who report their health status as fair and 94.3% of those who report their health status as good. Fabry disease strongly affects the everyday life of those living with the illness: the issues that most affect patients' quality of life are anxiety (46% of cases, which is the sum of the "a lot" and "quite a lot" responses on the questionnaire) and the decision to have children (40%) which just fewer than 1 in 4 people (22.6%) report as very important (it is the issue that is reported as being the most problematic). Other issues included relationship difficulties, loneliness and isolation, fear of judgment

from others – these were more limited, with respondents reporting them as “highly critical” in 5 out of 100 cases, the same rate as depression. Almost 2 out of 3 patients with Fabry disease (63.2%) indicated problems with fatigue (highly significant for 22.6%), while 4 out of 10 people (39.6%) report complaints of chronic/persistent pain and almost 3 out of 10 (27.4%) report having mobility difficulties.