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CHANGES IN THE CARE OF PATIENTS WITH LYSOSOMAL STORAGE DISEASES IN THE POST-COVID-19 ERA

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***ABSTRACT* – Objective:** The aim of this study is to assess the extent of changes in the care of patients with lysosomal storage disorders (LSDs) during the COVID-19 pandemic and to determine which of these changes have been maintained in the post-COVID-19 era.

Patients And Methods: Data were analyzed from a single large Reference Center for Lysosomal Storage Diseases (the Regional Coordinating Center for Rare Diseases in Udine, Italy). Changes in patient care were assessed by comparing the pre-pandemic period (December 2019) with the post-pandemic period (December 2023), focusing on the proportion of patients who transitioned to home therapy and the use of telemedicine consultations.

Results: A total of 102 patients with LSDs followed at the Regional Coordinating Center for Rare Diseases were included in the analysis. Before the pandemic, 71 patients were receiving enzyme replacement therapy (ERT), with 55 treated in the hospital and 16 at home. During the pandemic, an additional 15 patients transitioned to home-based ERT, and only 2 later resumed hospital-based infusions. No adverse events were reported in the home setting. Telemedicine services were utilized by 53 out of 102 patients during the pandemic and by 47 out of 102 patients in the post-pandemic period.

Conclusions: The COVID-19 pandemic led to changes in the management of patients with LSDs, including an increase in home therapy and the implementation of telemedicine services. These changes have persisted in the post-COVID-19 era.

Keywords: LSD, ERT, Home therapy, Telehealth, COVID-19.

List of abbreviations: AIFA – Italian Medicines Agency; CCRMR – Regional Coordinating Center for Rare Diseases; CCRMR-FVG – Regional Coordinating Center for Rare Diseases of Friuli Venezia Giulia; COVID-19 – Coronavirus Disease 2019; ERT – Enzyme Replacement Therapy; HomeERT – Home-based Enzyme Replacement Therapy; LSD – Lysosomal Storage Disease; LSDs – Lysosomal Storage Diseases; WHO – World Health Organization.

INTRODUCTION

Lysosomal storage diseases (LSDs) are a heterogeneous group of inherited metabolic disorders that affect multiple organs and systems, with an estimated overall prevalence of approximately 1 in 5,000 live births[1]. These rare genetic disorders are characterized by the accumulation of toxic substances within lysosomes due to the absence or dysfunction of specific enzymes responsible for their degradation. This accumulation can lead to systemic involvement and, in some cases, premature death[2]. Although LSDs are rare, their clinical and social implications are significant, particularly due to the need for highly specialized, multidisciplinary medical care and regular monitoring. For some LSDs, targeted therapies

are available, requiring consistent administration to ensure their effectiveness. These include enzyme replacement therapy (ERT), administered intravenously, as well as oral treatments such as substrate reduction therapy and chaperone drugs[3].

In 2020, the global health emergency caused by the coronavirus (COVID-19) pandemic, driven by the SARS-CoV-2 virus, had a profound impact on healthcare systems worldwide. This was particularly evident during the early stages of the pandemic, as it disrupted healthcare delivery models and posed unprecedented challenges for patients with chronic diseases, including LSDs[4]. For these patients, the transition from hospital-based ERT to home therapy, along with the implementation of telemedicine, served as crucial strategies to ensure continuity of care while simultaneously reducing the risk of infection in healthcare settings[5,6].

The shift in healthcare services toward telemedicine and home therapy may persist in the post-COVID-19 era[7]. However, to date, no studies have analyzed which changes in the management of LSDs induced by the COVID-19 pandemic have been maintained in the post-pandemic period.

The aim of this study was to assess the extent of these changes from the pre-COVID-19 to the post-COVID-19 period by analyzing data from a large Reference Center for LSDs.

PATIENTS AND METHODS

A retrospective analysis was conducted on the care processes at the Regional Coordinating Center for Rare Diseases of Friuli Venezia Giulia (CCRMR-FVG) in Udine, Italy, covering the period from December 2019 to December 2023. The analysis included all adult patients with a confirmed diagnosis of LSD who were continuously followed at the center and were on a specific treatment, excluding those on clinical trials.

The pre-pandemic reference period was defined as December 2019. Changes occurring during the pandemic were considered from March 11, 2020, to May 5, 2023, in accordance with the World Health Organization's definition of the COVID-19 pandemic period[8]. The post-pandemic period was defined as December 2023.

The analysis aimed to address the following questions:

1. Which proportion of patients experienced modifications to their usual enzyme replacement therapy (ERT) regimen, specifically transitioning to home therapy during the pandemic?
2. Which proportion of patients resumed hospital-based infusions after the pandemic?
3. Which proportion of patients utilized telemedicine services, including medical or psychological consultations, before, during, and after the pandemic?

Data were extracted from the hospital's electronic clinical system with prior patient consent. The study was conducted in accordance with the principles of the Declaration of Helsinki. This study has been approved by the Local Ethical Committee – CEUR FVG Prot. N. 860.

Statistical analysis

A descriptive statistical analysis was performed. Data were reported as absolute numbers and percentages.

RESULTS

A total of 102 patients with LSDs followed at the Regional Coordinating Center for Rare Diseases were included in the analysis. The distribution of diseases was as follows: Gaucher disease (44 patients; 39 with type I, 5 with type III), Pompe disease (16 patients), Fabry disease (15 patients), mucopolysaccharidoses (12 patients; 3 with type I, 5 with type II, 1 with type IV, 3 with type VI), Niemann-Pick disease type C (10 patients), and cystinosis (5 patients). More details on general characteristics of patients have been included in Table 1.

In December 2019, 71 patients (69.6%) were receiving ERT with imiglucerase, velaglucerase, laronidase, galsulfase, idursulfase, elosulfase alpha, alglucosidase alpha, or alpha and beta galactosidase. Among these, 55 patients (77.5%) received treatment in the hospital, while 16 (22.5%) underwent home therapy.

Table 1. General characteristics of patients.

	Frequency	Percentage
Sex		
• Female	49	48.04%
• Male	53	51.96%
Disease		
• Cystinosis	5	4.90%
• Fabry	15	14.71%
• Gaucher I	39	38.24%
• Gaucher III	5	4.90%
• MPS I	3	2.94%
• MPS II	5	4.90%
• MPS IV	1	0.98%
• MPS VI	3	2.94%
• Niemann Pick C	10	9.80%
• Pompe	16	15.69%
Age (years)		
• *n*=102 patients	Range: 18–87 years	Mean ± SD: 38.8 ± 18.6

During the pandemic years, no patients transitioned from home therapy to hospital-based treatment, whereas 15 patients (27.3% of those previously receiving ERT in the hospital) switched to home-based ERT. Consequently, the number of patients on home therapy nearly doubled (+93%).

By December 2023, only two of these patients had resumed hospital-based infusions in the post-pandemic period, both due to logistical issues related to the unavailability of home-care nurses in their respective areas. As a result, home-based ERT was maintained in 86.6% of cases (Figure 1). No adverse events were reported in the home setting.

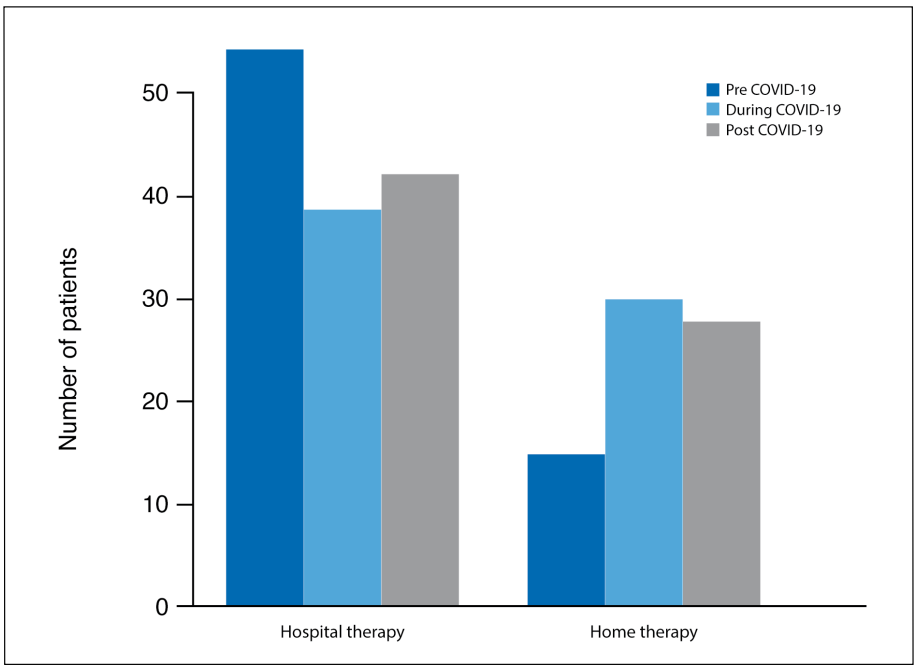

Figure 1. Changes in the administration setting of enzyme replacement therapy from the pre-pandemic to the post-pandemic period.

Regarding telemedicine, no patients utilized teleconsultation services before the pandemic, as this service was not available at the Regional Coordinating Center for Rare Diseases. During the pandemic years, 53 patients (52% of the total LSD cohort) accessed telemedicine services. In the post-pandemic period, 47 patients continued to use telemedicine (Figure 2).

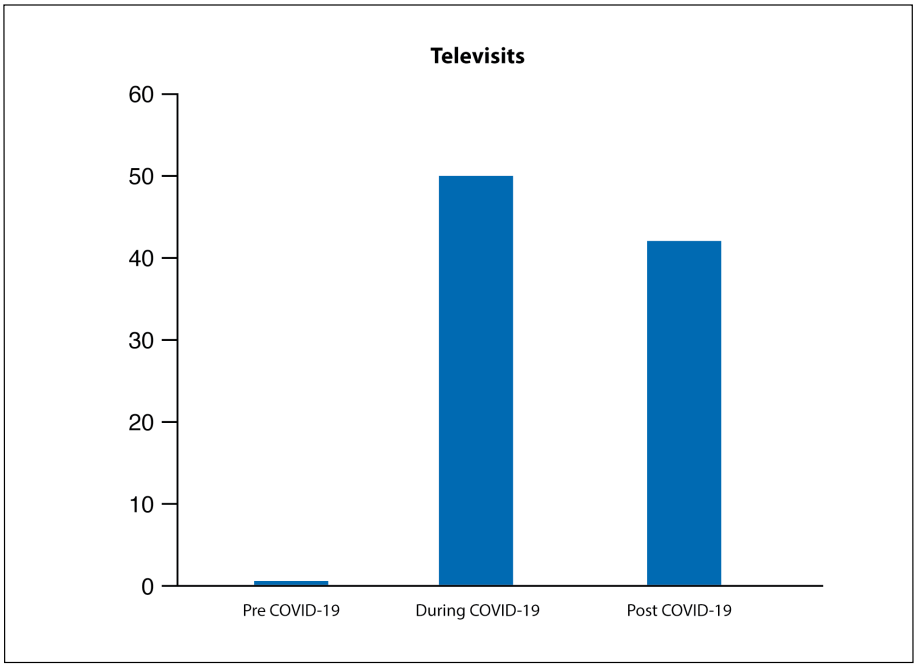

Figure 2. Number of patients who utilized telemedicine services from the pre-pandemic to the post-pandemic period.

DISCUSSION

The COVID-19 pandemic placed significant strain on healthcare systems worldwide. During this period, social distancing measures, temporary closures of healthcare facilities, and the reallocation of resources affected medical care and patient management to varying degrees. For patients with LSDs, the necessity of attending hospitals for essential treatments conflicted with concerns – shared by both patients and healthcare professionals – about the risk of COVID-19 infection[9].

ERT, which delivers the deficient enzyme through regular infusions, is often the only specific treatment available for LSDs. Missing multiple infusions can lead to complications, including symptom exacerbation, disease progression, and an increased risk of adverse drug reactions upon resumption of treatment. With the spread of COVID-19, hospitals became potential hotspots for infection, posing a particular risk to vulnerable patients, such as those with LSDs[10]. As a result, many patients initially chose to forgo scheduled hospital infusions, even at the expense of their health. This highlighted the need for more flexible therapeutic strategies, including alternative routes and settings for drug administration. Consequently, changes in treatment management were implemented, such as transitioning to home therapy or switching from intravenous to oral therapy where available and clinically appropriate[5]. In the early stages of the pandemic (April 2020), the Regional Coordinating Center for Rare Diseases of Friuli Venezia Giulia (CCRMR-FVG) conducted a survey among its LSD patients, revealing that 49% of those receiving hospital-based ERT experienced treatment interruptions. The primary reasons were fear of infection (62.9%), and logistical challenges related to the reorganization of infusion centers (37%). In contrast, only 6% of patients on home therapy experienced treatment interruptions[5]. In March 2020, the Italian Medicines Agency (AIFA) issued Resolution 341/2020, allowing a broader implementation of home therapy for LSD patients. This resolution also enabled home-based ERT for patients with Pompe disease, a treatment option that had previously not been permitted in Italy.

Our data indicate a 93% increase in the number of patients receiving home-based ERT during the pandemic, with 86.6% of these patients continuing home therapy in the post-pandemic period. No adverse events were reported in the home setting, a finding consistent with previous studies on home

therapy[11-13]. Despite its numerous advantages for patients – including reduced impact on daily activities, decreased travel time, and lower perceived stress[14] – home therapy remains unavailable in many countries. Even within Italy, access to home-based ERT varies across different regions.

The implementation of telemedicine emerged as a key resilience strategy during the COVID-19 pandemic. By enabling remote consultations, patients with chronic diseases, including LSDs, were able to receive prescriptions, medical advice, and follow-up care without the need to visit healthcare facilities, thereby reducing the risk of infection[15].

Although telemedicine was not a new concept, its use expanded significantly during the pandemic, profoundly transforming healthcare delivery. This approach not only allowed patients and physicians to interact safely and effectively during the COVID-19 crisis[16] but also facilitated continued patient-provider communication in the post-pandemic period.

Studies on LSD patients during the COVID-19 pandemic highlighted the negative impact of the pandemic on mental health[17]. In response, the Regional Coordinating Center for Rare Diseases (CCRMR) expanded its telemedicine services to include psychological consultations.

CCRMR data indicate that while telemedicine utilization surged during the pandemic, it has been retained in the post-COVID-19 era, not as a replacement for in-person visits but as an integrated component of patient care. This hybrid approach allows for more frequent and flexible interactions between patients and healthcare providers, even remotely.

Limitations

The primary limitation of this analysis is that it was conducted at a single center. While the Regional Coordinating Center for Rare Diseases (CCRMR) serves as a valuable model due to its large cohort of LSD patients, certain center-specific characteristics may have influenced the findings. Notably, approximately 80% of patients followed at the CCRMR reside outside the region. This may have contributed to the high proportion of patients who continued using telemedicine in the post-COVID-19 period. Additionally, the CCRMR was one of the first centers in Italy to implement clinically and institutionally recognized teleconsultations, including both medical and psychological visits, with formal documentation. The large number of out-of-region patients may have also impacted the transition to home-based ERT, as the feasibility of home therapy depended on regional healthcare policies, which varied based on the patient's place of residence. Another major limitation of this study is its reliance on purely numerical data, lacking qualitative patient feedback. Consequently, it remains unclear whether patients perceived these changes positively and whether they had a meaningful impact on their disease experience and quality of life.

A patient-reported outcome questionnaire assessing the qualitative aspects of HomeERT and telemedicine is currently being validated, which may support future multicenter studies. Other indicators of efficacy of home-infusion and telemedicine can be subject of these future studies, including numbers of missed infusions at home compared to hospital, number of contacts for telemedicine, type of interventions, and eventual coordination with general practitioners.

CONCLUSIONS

The COVID-19 pandemic led to potentially beneficial changes in the management of patients with LSDs, including the transition to home-based ERT and the integration of traditional healthcare with telemedicine. These changes have been maintained in the post-COVID-19 era. Further studies involving a larger number of centers and incorporating patient perspectives are needed to better assess the actual impact of these changes on clinical practice and patient quality of life.

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Availability of data and material:

The datasets generated or analyzed during the current study are not publicly available due to the nature of the analysis but are available from the corresponding author on reasonable request.

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The authors declare that they have no conflict of interest to disclose.

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