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Humanistic Burden of Neurodegenerative Lysosomal Disorders in the US: Insights from Caregivers of Patients Living with GM1 and GM2 Gangliosidoses

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BACKGROUND

- GM1 and GM2 (Tay-Sachs and Sandhoff diseases) gangliosidoses are rare, autosomal recessive, potentially life-threatening, disabling disorders characterized by progressive neurodegeneration and caused by reduced activity of β-galactosidase and β-hexosaminidase A or A/B, respectively.[1]
- Currently, there are no disease-modifying therapies to directly treat these conditions, and progression of symptoms/functional limitations can impact daily activities and life expectancy of patients, thereby increasing disease burden.[2]
- There is limited evidence on the burden of caregivers in GM1 and GM2 gangliosidoses; one study reported high caregiver burden and decline in caregivers' quality of life for patients with GM1 gangliosidosis.[3]

OBJECTIVES

- To **understand the humanistic burden of GM1 and GM2 gangliosidoses from caregivers' perspective**:
  - To expand knowledge on the day-to-day responsibilities of primary caregivers while providing care and support to the overall life course of patients with GM1/GM2 gangliosidoses.
  - To identify physical, emotional, financial, and social impacts experienced by caregivers of patients living with GM1 and GM2 gangliosidoses at different ages.

METHODS

- Primary caregivers* of patients with GM1/GM2 gangliosidoses (≥6 years) were recruited through their membership of National Tay-Sachs & Allied Diseases Association (NTSAD) and Cure GM1 Foundation. Caregivers residing in the United States who could participate in a 90-minute group interview were eligible for inclusion.
- Six 90-minute focus group interviews were conducted with caregivers based on the age of patients under their care (children [6–11 years], adolescents [12–17 years], adults [≥18 years]) with GM1/GM2 gangliosidoses in two phases:
  - Phase 1: In-person group interviews with those attending the 44th Annual NTSAD Family Conference in Denver, Colorado during July, 2022.
  - Phase 2: Online group interviews with those having access to a device for online conferencing platform during November–December, 2022.
- The focus group interviews were recorded and subsequently transcribed; interview transcripts were iteratively coded in MAXQDA qualitative data analysis software; saturation analysis was used to determine whether any new concept emerged in the final interviews.

*A primary caregiver (≥18 years) was identified either by self or by the patient as the key person providing care, support, and assistance for daily activities to their loved ones with GM1/GM2 gangliosidoses.

RESULTS

- A total of 29 caregivers of patients with GM1/GM2 gangliosidoses participated in the study. The characteristics of patients and caregivers are presented in **Figure 1**.

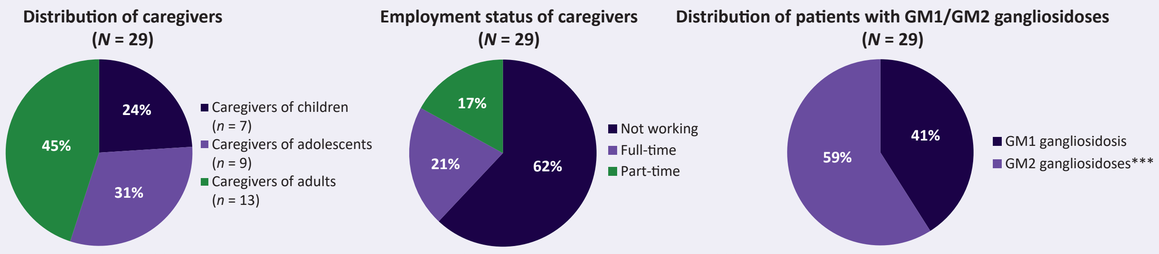
Figure 1: Characteristics of caregivers and patients with GM1/GM2 gangliosidoses

Caregivers

Age (mean [range], years; *N* = 27*)	Gender (*N* = 29)	
	Female	Male
49 [37–75]	79%	21%

Patients with GM1/GM2 gangliosidoses

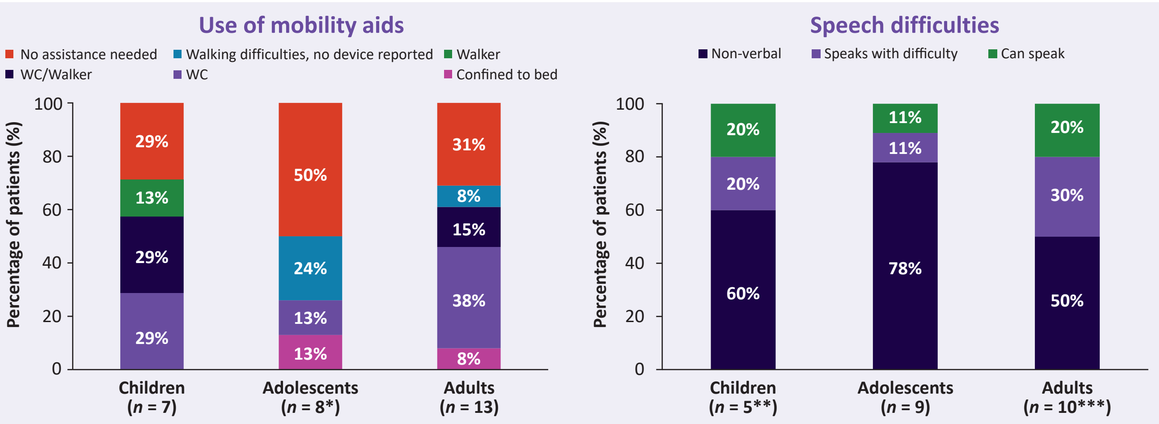
Age (mean, years; *N* = 28**)			Gender (*N* = 29)	
Children	Adolescents	Adults	Female	Male
8	14	36**	72%	28%



Unreported: *n = 2, **n = 1, one caregiver did not report age of one adult living with the disease. ***76% Tay-Sachs, 18% Sandhoff, 6% not reported.
N, total number of individuals with available data; *n*, number of individuals

- **Figure 2** illustrates disease severity of patients with GM1/GM2 gangliosidoses based on difficulties in mobility and speech, as reported by caregivers.

Figure 2: Mobility and speech difficulties of patients with GM1/GM2 gangliosidoses reported by caregivers



Percentage based on number of caregivers reporting; questions related to these data were not directly asked to all caregivers.
Unreported: *n = 1, **n = 2, ***n = 3.
n, number of patients; WC, wheelchair

- Caregivers described their caregiving responsibilities as non-stop, pervasive, increasing with disease progression, and often completed alone (without additional support), regardless of the disease type (GM1/GM2 gangliosidoses) or patient age.
- The most reported responsibility was "providing assistance with activities of daily living" across caregivers of children (100%), adolescents (78%), and adults (92%), followed by "symptom care and management" and "maintaining quality of life" across all caregivers irrespective of age of the patient with disease (69% and 45%, respectively). Some of their responses are illustrated in **Figure 3**.

Figure 3: Caregivers' perspectives in understanding their responsibilities towards their loved ones

Activities of Daily Living

> *So when they were full-time in a wheelchair, **I was a lot more responsible for getting them from Point A to Point B**, getting them transferred, **getting them dressed**. When they **lost their ability to use the restroom**, that was then my responsibility. When they **lost their ability to eat**, that was my responsibility. **So as milestones started to regress, my responsibilities became greater**.*
> -Caregiver of an adult with GM1 gangliosidosis

> ***Laundry, making the bed, changing the bed**. Making sure she has meals. **It's like having a baby without having a baby**.*
> -Caregiver of an adult with GM2 gangliosidosis

Symptom Care and Management

> *I think as a parent I **care for my daughter in regular ways** and even **above and beyond** ways, however, there are some things like my daughter **has motility issues and is chronically constipated**. Every single day **I have to give her an enema**… That **I look at as more of a caretaker**. I do it because I'm her parent, but I look at that…that's like an **above and beyond caretaker responsibility**.*
> -Caregiver of a child with GM1 gangliosidosis

> We have to ***make sure she doesn't choke*** on the foods that we do give her. It has to be blended foods or soft foods.
> -Caregiver of a child with GM2 gangliosidosis

> *Because every morning you're **planning for a different circumstance**. Which **doctor** to take him to. Which **therapy**, you have to take him to. Which **medications**…*
> -Caregiver of an adolescent with GM2 gangliosidosis

Maintaining Quality of Life

> *In [REDACTED]'s case, **she never had friends**. So as an adolescent, I was **trying to make her friends**. I made friends with mothers who had daughters and said, **"Would you please play with my daughter?** If you're having a party, would you please have them invite [REDACTED]?" **I was her advocate for a social life [and now] I'm her social life.***
> -Caregiver of an adult with GM2 gangliosidosis

> *My **job** is to **get her to whatever** I think she **would want to do to enjoy the day**.*
> -Caregiver of an adult with GM1 gangliosidosis

> *We talk to him as normal people and say hi, good morning, I'm here. And then **during the day all the time I try to give him my love**. And then, okay, **I turn the song for him…the song that he had memorized when he was okay**. And then, okay, **I sing for you**, and **you can dance with me**.*
> -Caregiver of an adolescent with GM2 gangliosidosis

Physical Health

> *The **stretching I do with my daughter** I stretch her on an exercise ball. I also **bounce her on an exercise ball to help her relax**. It helps her relax, and relax her muscles, but **I also do basically it's like PT** on an exercise ball with my daughter.*
> -Caregiver of a child with GM1 gangliosidosis

Emotional Health

> *I oftentimes **dream of finding something** that I could just **give her that would make her happy and content. Because seeing your child in pain hour after hour after hour destroys her...** That's the most unbearable thing for me.*
> -Caregiver of an adolescent with GM1 gangliosidosis

- Overall, 25 different impacts were reported by caregivers. The most reported impacts included constant psychological burden (*n* = 24), physical ailments/strain (*n* = 18), anxiety/fear/worry (*n* = 17), financial difficulties (*n* = 17), limited time for other family members (*n* = 16), and limitations on relationships outside family (*n* = 15) **(Figure 4).**

Figure 4: Bothersome impacts of caregiving reported by caregivers

Emotional: Depression, anxiety, fear, sadness, worry, and frustration

> *You start getting **depressed** because you're so **stressed** and **angry**. You're angry because the **disease is taking away your child and you can't really do anything about it**.*
> -Caregiver of an adolescent with GM2 gangliosidosis

> *So **every time they regress you** end up somewhere on that grief cycle where it's like all over again emotionally…..*
> -Caregivers of children with GM1 and GM2 gangliosidoses

Physical: Physical strain on body due to lifting, assisting individual with disease

> *I have **shoulder** issues. I've got **back** issues. I've got knee issues. My husband's also dealing with back issues.*
> -Caregiver of an adult with GM1 gangliosidosis

Leisure: Unable to participate in activities, no opportunity to enjoy, and pursue hobbies

> *We don't get it. That's not a part of our lives. **Having leisure with this diagnosis is not part of our lives.***
> -Caregiver of a child (unknown diagnosis)

Family Life: Less time to spend with other children, strain on relationships

> *I mean, ultimately, **I got divorced** mostly because of her diagnosis. No fault to [him], just we handled things differently. He shut down and I didn't, so we got divorced.*
> -Caregiver of an adult with GM1 gangliosidosis

Financial: Loss of income, insurance challenges, and cost of medications and equipment

> *I have to work. I mean in general, **in order to support her lifestyle and my lifestyle. I am 73 years old and I work full-time**.*
> -Caregiver of an adult with GM2 gangliosidosis

Work/Career: Leaving career

> *I've had a job since I was like 16 years old, so **I've always loved working**. I've always found I've been very fulfilled by that. **It's hard [to give it up]**.*
> -Caregiver of a child with GM1 gangliosidosis

Personal Goals and Plans: Unable to pursueretirement plans, cannot travel or live the life they imagined with their children

> *When I retire at 65, **I'm not going to have that typical retired life** where it's time for me and my wife to go and travel and do.*
> -Caregiver of an adult with GM2 gangliosidosis

Social Life: No time for friends

> *I feel completely **cut off from society**. It's near impossible for us to participate in anything that goes on in our community. Or to go to a restaurant or to meet with friends or to have vacations.*
> -Caregiver of an adult with GM1 gangliosidosis

- While providing care and support deleteriously impacted caregivers' lives, there were positive impacts on relationship building, personal development, family cohesion, community support, and life outlook.
- Caregivers reported relying primarily on patient advocacy groups for resources and assistance. Although a few received support from their clinicians, they expressed the need for more information about disease management.
- Additionally, caregivers stated the need for resources, broader disease awareness, and disease-modifying treatments that would help reduce their caregiving burden (**Figure 5**).

Figure 5: Resources/public awareness/disease-modifying treatments needed to reduce caregivers' burden

Treatment

> ***[Hoping]** there might be something that **would stop** this disease and **improve it a little bit**…///…**Yeah, prolong the progression**…///…**Stop the progress and improve it and I would feel then my life was not lived for nothing**.*
> -Caregivers of adults with GM2 gangliosidoses

Financial

> *It'd be really great if I could get paid for my service staking care of the girls because we've lost the income of my employment.*
> -Caregiver of an adult with GM1 gangliosidosis

Government Support

> *We went about 2 years ago to the city and back to get the approval to have ramp and special…**we had problems with the city, that they said no, you can't do it [put ramp and addition and other things]**.*
> -Caregiver of an adolescent with GM2 gangliosidosis

Respite

> *It's also just finding \ those **people that are skilled that are quality that you can trust** and that truly will do the things that are difficult to do for your child, and learn your child, and then keep them…those people.*
> -Caregiver of a child with GM1 gangliosidosis

Medical Education

> *Doctors that understood where we were coming from, that **understood the disease better**, that had a clue what they were talking about.*
> -Caregiver of an adult with GM1 gangliosidosis

Equipment

> *It would be really nice to not have to jump through hoops to get **medical equipment**. That would be phenomenal.*
> -Caregiver of an adult with GM1 gangliosidosis

Emotional Support

> *Because every single day I'm overwhelming. **I need to look at a psychologist therapy**.*
> -Caregiver of an adolescent with GM1 gangliosidosis

Community Awareness/Services

> *I guess the community **being more understanding of the physically challenged** and taken more serious.*
> -Caregiver of an adult with GM2 gangliosidosis

LIMITATIONS

- Recruitment through patient advocacy groups may limit the generalizability of the findings.
- Because of the dynamic nature of the discussion during interviews, not all concepts were consistently probed for each caregiver; this might have led to an underestimation of the number of impacts reported and/or the number of caregivers acknowledging certain impacts.
- Relatively small sample sizes of caregivers of children and adolescents may limit the representativeness of the findings for these sub-populations.

CONCLUSIONS

- **This study showed substantial humanistic burden related to GM1 and GM2 gangliosidoses with long-term impacts.**
- **These findings provide important insights to enhance clinical care and help assess the value of novel therapies while advocating for the resources needed to alleviate the burden and improve lives of caregivers and patients with GM1 and GM2 gangliosidoses under their care.**

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CONFLICTS OF INTEREST:
MBR: Sanofi — employee, may hold stock and/or stock options in the company. **KH, RK,** and **NGP**: IQVIA — salaried employees; IQVIA received professional service fees from Sanofi for conducting this research. **RK**: Principal Investigator of the study. **CW**: Cure GM1 Foundation — a non-salaried volunteer, which receives sponsorships from Sanofi for their annual conference. **DJ**: National Tay-Sachs & Allied Diseases Association (NTSAD) — a salaried employee. NTSAD receives support from Sanofi in the form of educational and programmatic grants.

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