Concept Elicitation Interviews to Understand the Patient Experience of Limb Girdle Muscular Dystrophy

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BACKGROUND

- Limb girdle muscular dystrophies (LGMDs) are a group of rare, genetically and phenotypically heterogeneous disorders involving progressive shoulder and pelvic girdle musculature weakness and wasting.[1]
- Estimated prevalence of LGMD is 0.9 to 2.3/100,000.[2]
- Sarcoglycanopathy subtypes, a group of LGMDs caused by genetic defects in the sarcoglycan proteins, represent about 15% of LGMDs in the United States (US).[3]
- To date, only a handful of qualitative studies have identified and described symptoms and impacts that matter most to patients with LGMD and their caregivers.[4, 5, 6, 7]
- This study provides qualitative evidence about patients' experience of living with sarcoglycanopathy subtypes 2C, 2D, and 2E (recently renamed R3-R5)[8] and their perceptions of overall health, disease course, and treatment expectations and goals.

METHODS

- This cross-sectional, qualitative interview study was conducted with individuals with LGMD subtypes 2C, 2D, or 2E with or without their caregiver in the US.
- Participants were recruited by Schlesinger Group, from their profiled panel members; recruitment was supplemented with outreach via patient advocacy groups, a sponsor-provided registry list, and a genetic counseling database. Schlesinger screened interested parties.
- Eligible, consenting individuals participated in one 60-minute semi-structured video interview between February 8 and May 4, 2021.
- Interviews were recorded and professionally transcribed for analysis.

RESULTS

- Conceptual saturation was achieved within 18 of the 23 interviews.
- Fourteen ambulatory and 9 non-ambulatory individuals participated in the study.
- The majority of individuals with LGMD were adult (n=18 out of 23; 78%). Other participant characteristics are shown in Table 1.

Table 1: Demographics and Clinical Characteristics of Participants with LGMD

Characteristics	Adults (n=18)	Children (n=5)	Total (N=23)
Age, mean (SD) [range][1]	40.9 (12.14) [18,63]	12.6 (2.97) [8,16]	34.8 (16.08)[8,63]
Gender identity, n (%)			
Male	9 (50.0)	1 (20.0)	10 (43.5)
Female	8 (44.4)	4 (80.0)	12 (52.2)
Transgender female	1 (5.6)	0 (0.0)	1 (4.4)
Race, n (%)			
White	14 (77.8)	5 (100.0)	19 (82.6)
Asian	1 (5.6)	0 (0.0)	1 (4.4)
Black or African American	2 (11.1)	0 (0.0)	2 (8.7)
Prefer not to answer	1 (5.6)	0 (0.0)	1 (4.4)
Hispanic, n (%)	2 (11.1)	0 (0.0)	2 (8.7)
Age of symptom onset, mean (SD) [range][1]	11.9 (10.26) [0,41]	6.5 (3.08) [2,10]	10.5 (9.21) [0,41]
Age of diagnosis, mean (SD) [range][1]	28.0 (12.37) [6,49]	8.2 (1.92) [6,11]	23.5 (13.76) [6,49]
LGMD Subtype, n (%)			
2C/R5	2 (11.1)	2 (40.0)	4 (17.4)
2D/R3	11 (61.1)	1 (20.0)	12 (52.2)
2E/R4	5 (27.8)	2 (40.0)	7 (30 .4)
Ambulation Status, n (%)			
Ambulatory	10 (55.6)	4 (80.0)	14 (60.9)
Non-Ambulatory	8 (44.4)	1 (20.0)	9 (39.1)

Main Symptoms and Impacts

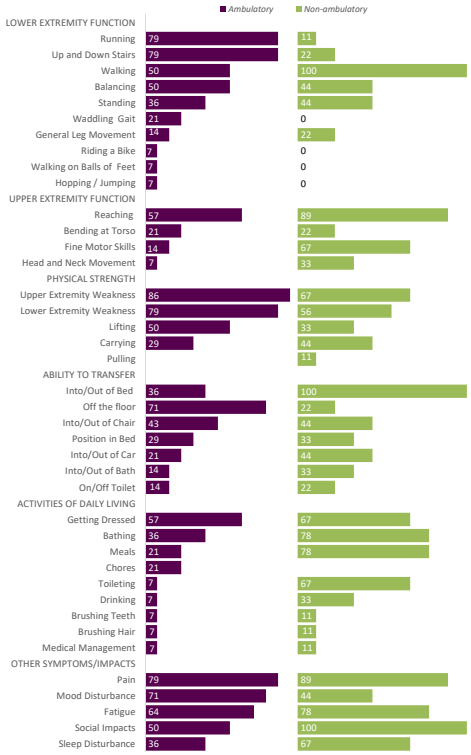
- Differences in symptoms and impacts emerged by **ambulation status** (Figure 1).
- No differences were found by LGMD subtype or adult vs. child participants.

- **Ambulatory participants** identified **difficulty with complex physical activities** (e.g. running, climbing stairs; n=11, 78.6%), **upper and lower extremity weakness** (n=12, 85.7% and n=11, 78.6% respectively), and **difficulty getting off the floor** (n=10, 71.4%)
  - *"Now I prefer not to use stairs. If I have the opportunity not to, I don't. Because, it's like literally every – I have to do one step and then my other foot has to come up and then one – literally one step at a time and that's – I'm worn out by the time I get wherever I need to go."* [SAR010]

- All **non-ambulatory participants** discussed **difficulty with transfers** (e.g. getting in/out of bed), **problems with activities of daily living** (ADLs),and **upper extremity mobility** (n=9, 100.0%), particularly reaching (n=8, 88.9%) and **fine motor skills** (n=6, 66.7%)
  - *"Well, yeah now there's no muscle there in my arms. It's a little bit but I can now I can…I'm not able to use a screwdriver or anything like that. Yeah, not so much pain it's just I can't do it."* [SAR003]
  - *"Yeah, I get up, well, I wake up, I have my attendant help me with getting dressed and help me wipe my eyes and get my respirator ready and my wheelchair ready for the day."* [SAR008]

- **Pain was the most common symptom** reported by both **ambulatory** and **non-ambulatory** participants (n=19, 82.6%)
  - *"But with, like, the past few years when I started getting the hip pain, the buttock pain, the foot pain, like it's eye-opening, it's like oh, crap, is this that pivot point where you just never know how the disease will progress, could this be, I'm only 35, and there's still so much we want to do."* [SAR015]

Figure 1: Percentage of Participants Reporting LGMD Symptoms and Impacts by Ambulation Status



"Worst" or Most Bothersome Symptoms

When asked about their "worst" current symptoms…

- **Ambulatory participants** (n=14) most commonly reported **lack of physical strength**, including lower extremity weakness (n=7, 50.0%) and upper extremity weakness (n=4, 28.6%), followed by pain (n=7, 50%).
- **Non-ambulatory participants** (n=9) most commonly reported **upper extremity weakness** (n=3, 33.3%) and lower extremity mobility and function, including difficulty walking (n=3, 33.3%).

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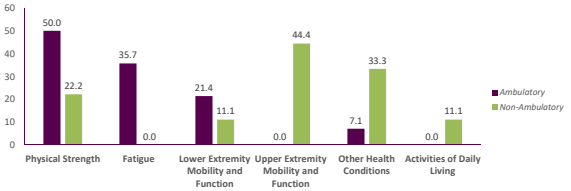
Treatment Expectations

- All of the participants (N=23; 100.0%) reported that a LGMD treatment which maintained their current functioning would be beneficial.
- The majority of participants (n=20; 87.0%) reported that a treatment which slowed the worsening of their symptoms would be beneficial.
- When asked which symptoms they would like to improve first when considering a new LGMD treatment, **ambulatory participants desired improvement in physical strength and fatigue**, while **non-ambulatory participants** were **interested in improved upper extremity mobility and function** and other health conditions (Figure 3).

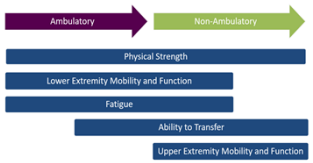
Figure 3. Symptoms of LGMD to Improve First



Conceptual Model of LGMD

- Difficulty with physical strength is experienced throughout all phases of disease progression.
- Fatigue and difficulty with lower extremity mobility and function are important throughout the ambulatory and early non-ambulatory phases.
- The ability to transfer becomes important as ambulation wanes and is important throughout the non-ambulatory phase.
- Upper extremity mobility and function becomes important in the non-ambulatory phase.
- Although pain was commonly reported, pain reduction was infrequently reported as a treatment goal. The concept of pain warrants further investigation to better understand its pathophysiology, origin, and type among patients with LGMD.

Figure 2. LGMD Conceptual Model



CONCLUSIONS

- This study provides qualitative evidence of the core signs, symptoms, and impacts of LGMD across the ambulatory spectrum of disease progression.
- These findings are vital to informing patient-centered measurement strategies in clinical studies by highlighting disease concepts most relevant and important to individuals with LGMD.

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