Global Characterization of GM1 Gangliosidosis: Insights from a Patient-Powered Registry

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ABSTRACT

GM1 Gangliosidoses

- ULTRA-RARE: *1 in 100,000–200,000 live births*
- AUTOSOMAL RECESSIVE INHERITANCE
- LYSOSOMAL STORAGE DISORDER

Cure GM1 Registry

- INPUTS FROM CAREGIVERS & PATIENTS
- INTERNATIONAL: *Respondents (n=175) from 36 Countries*
- LONGITUDINAL: *Data collected since June 2019*

Study Results

n=165	74% DELAYED DIAGNOSIS	US v. ROW
55% ♀	55% HYPOTONIA AT ONSET	1:1.7 TYPE 1 INFANTILE
33%	52% SPEECH, MOTOR DETERIORATION AT ONSET	1:0.6 TYPE 2b JUVENILE

Study Summary

CURE GM1 REGISTRY REVEALS:

- Diagnostic delays are common
- GM1 subtype variation by geography
- Heterogeneity in symptoms at onset

BACKGROUND

GM1 gangliosidosis is a rare autosomal recessive lysosomal storage disorder (1 in 100,000–200,000 live births) caused by pathogenic GLB1 variants, leading to progressive neurodegeneration and multisystem involvement. Limited epidemiological data and global dispersion hinder research and delay the development of evidence-based care. With no approved treatments and few active trials, a patient-powered registry was established to generate a centralized, research-ready community. Here, we provide an initial characterization of the registry to advance understanding of the global GM1 population and support future research and care strategies.

METHODS

The Cure GM1 Patient Insights Network is a web-based platform collecting demographic, genotypic, phenotypic (motor, language, eating, visual, breathing), care, and pharmacological data longitudinally from caregivers to GM1 gangliosidosis via IRB-approved surveys and online informed consent. Categorical comparisons used chi-square or Fisher's exact tests; proportions were assessed by Z-test. Survey data were collected from June 2019 to July 2025.

RESULTS

- Of 174 participants, data for 165 (study population) were included in this study. [FIGURE 1]
- Majority GM1 type 1 Infantile (87, 53%), female (89/163, 55%), white (113/139, 81%), delayed diagnosis (74% (52/70). [TABLE 1]
- Country of Residence: 36 countries across six continents, with highest representation from the US (55) and Brazil (22). [FIGURE 2]
- GM1 type distribution differed significantly between the US and rest of world (ROW) [FIGURE 3]; other country by country differences did not reach significance. [DATA NOT SHOWN]
- In the subset recording at least one symptom at onset (n=73), the most common initial symptoms were hypotonia (55%) and deterioration in speech or motor function (52%). [FIGURE 4]

DISCUSSION

This registry offers foundational insight into the global GM1 population, revealing diagnostic delays, geographic variation in subtype distribution, and symptom heterogeneity. Findings underscore the need for coordinated data collection to inform clinical endpoints, accelerate therapeutic development, and guide future care strategies.

FIGURE 1. Participant Disposition

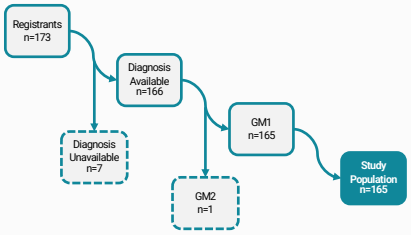


TABLE 1. Study Population Characteristics

Characteristic	Type 1 infantile (n=87)	Type 2a late infantile (n=31)	Type 2b juvenile (n=43)	Type 3 adult (n=4)	Total (n=165)
Gender					
Female	45/85 (53%)	16/31 (52%)	26/43 (60%)	2/4 (50%)	89/163 (55%)
Male	40/85 (47%)	15/31 (48%)	17/43 (40%)	2/4 (50%)	74/163 (45%)
Race					
American Indian or Alaska Native	1/70 (1%)	/27 (0%)	2/38 (5%)	/4 (0%)	3/139 (2%)
Asian	11/70 (16%)	2/27 (7%)	1/38 (3%)	/4 (0%)	14/139 (10%)
Black or African American	5/70 (7%)	/27 (0%)	/38 (0%)	/4 (0%)	5/139 (4%)
Multi	/70 (0%)	1/27 (4%)	2/38 (5%)	/4 (0%)	3/139 (2%)
Native Hawaiian or Other Pacific Islander	1/70 (1%)	/27 (0%)	/38 (0%)	/4 (0%)	1/139 (1%)
White	52/70 (74%)	24/27 (89%)	33/38 (87%)	4/4 (100%)	113/139 (81%)
Delayed Diagnosis*	23/34 (68%)	13/16 (81%)	16/19 (84%)	/1 (0%)	52/70 (74%)

*Limited to those with responses for both age at onset and age at diagnosis.

FIGURE 2. Study Population by Country of Residence

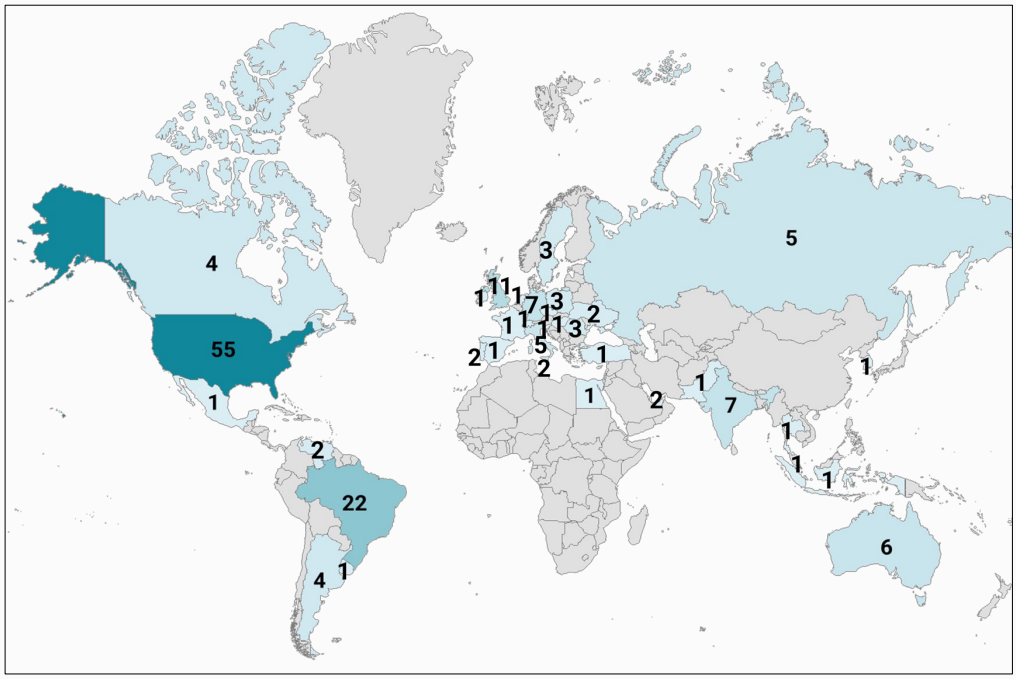


FIGURE 3. GM1 Type Distribution: US (n=55) vs. ROW (n=110)

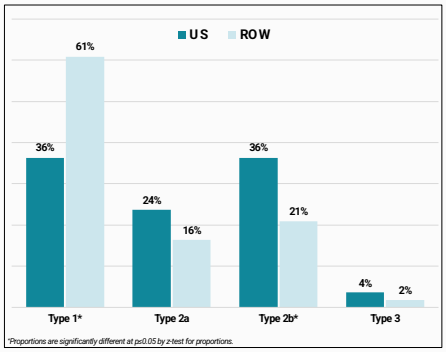
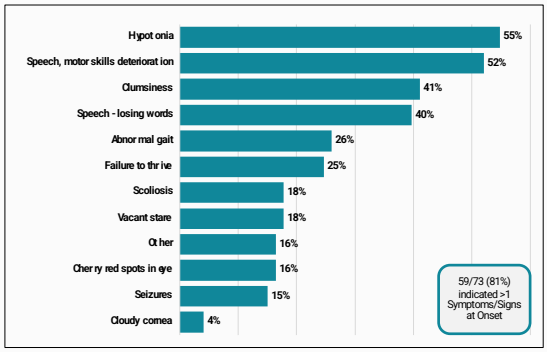


FIGURE 4. Study Population Symptoms/Signs at Onset (n=73)



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