Fragile X Syndrome Diagnosis and Patient Journey: The Caregiver's Perspective

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BACKGROUND

- Fragile X syndrome (FXS) is a rare genetic condition characterized by a range of developmental, neuropsychiatric, and behavioral symptoms[1,2]
  - Core FXS clinical symptoms include social avoidance/withdrawal, anxiety, irritability, deficits in learning and cognition, and sleep difficulties[1,3,4]
- FXS symptoms are frequently compounded by comorbid conditions, with autism and attention-deficit/hyperactivity disorder occurring in an estimated 35% and 54%-59% of male patients with FXS, respectively[5,6]
- Initial symptoms and developmental delays are often first recognized by parents, and subsequent clinical diagnosis of FXS is based on genetic testing for mutations in the *FMR1* gene[7-9]
- Early diagnosis of FXS is important to facilitate treatment and coordinate the multidisciplinary supportive care and educational interventions required to manage the symptoms of FXS[9]
- Diagnosis of FXS is often delayed, with a 2008 study reporting a delay of 24-26 months between initial symptoms and diagnosis, and mean age at diagnosis has remained delayed over time (31.9 months in 2018 vs 37.9 months in 2008)[7,8]
- A greater understanding of the patient journey surrounding initial presentation and diagnosis is needed to support effective screening and reduce diagnostic delay

OBJECTIVE

- To characterize the patient journey in FXS surrounding diagnosis and clinical experiences through an online caregiver survey

METHODS

- A 30-minute, anonymized, quantitative online survey was conducted in the United States from May 3-June 12, 2019
  - Participants were identified via recruiter panels, Facebook groups, and advocacy groups
- Caregivers completed initial screening questions and were required to meet the following criteria before advancing to the full survey:
  - Primary caregiver of a child with FXS who is aged 3-17 years, has a full *FMR1* mutation, and experiences social avoidance
  - Not paid for caregiving services
  - Assists with activities of daily living (ADLs), participates in doctors' appointments, and is involved in treatment decisions and management
- Additional topics addressed by questions in the screener and full survey included the following:
  - Caregiver and patient demographics
  - Patient health and medical history
  - FXS symptoms and severity
  - Diagnosis

RESULTS

PARTICIPANTS

- The survey was completed by 35 caregivers of children with FXS
  - Caregivers were predominantly female (80%), and most respondents were parents of children with FXS (**Table 1a**, **Figure 1**)
- The mean age of the children with FXS at the time of the survey was 9.1 years, and 74.3% were male (**Table 1b**)

Table 1a. Caregiver Demographics

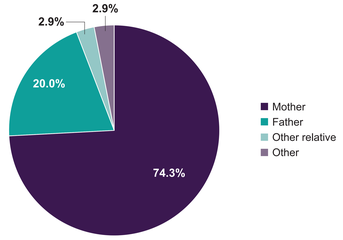
Demographic	Caregiver Respondents N = 35
Age, years	
Mean (SD)	42.6 (7.89)
Sex, n (%)	
Female	28 (80.0)
Male	7 (20.0)

Table 1b. Patient Demographics

Demographic	Child With FXS N = 35
Age, years	
Mean (SD)	9.1 (4.11)
Sex, n (%)	
Female	9 (25.7)
Male	26 (74.3)

FXS, fragile X syndrome.

Figure 1. Caregiver relationship to child with FXS.

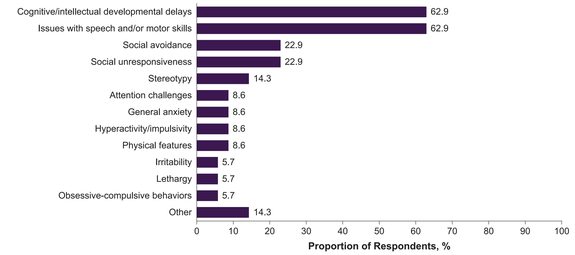


FXS, fragile X syndrome.

PATH TO DIAGNOSIS

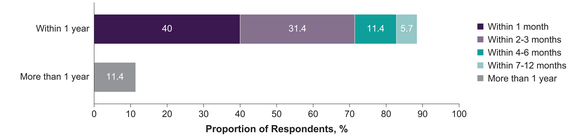
- The mean age of children with FXS at the time of diagnosis was 3.0 years (SD, 2.52 years)
- When asked to rate the top 3 factors prompting caregivers to schedule an initial visit with a physician, the most common were: cognitive/intellectual developmental delays, issues with speech and/or motor skills, and social avoidance/social unresponsiveness (**Figure 2**)

Figure 2. Most common factors prompting initial physician visit.



- Most caregivers scheduled an initial visit with a physician within 6 months of noticing symptoms (82.9%; **Figure 3**)

Figure 3. Length of time between noticing symptoms and initial physician visit.



- The first physician seen was most frequently a primary care physician (family doctor or general pediatrician, 71.4%) (**Figure 4**)
- Formal diagnosis of FXS was most often made by a specialist (80.0%) (**Figure 5**)

Figure 4. First physician consulted.

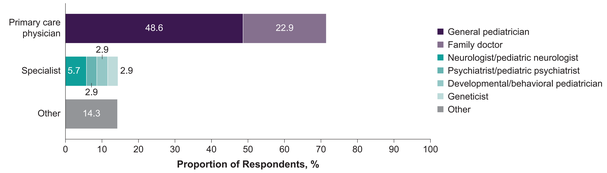
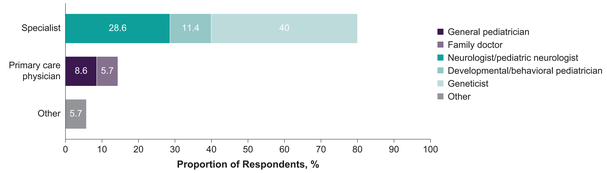


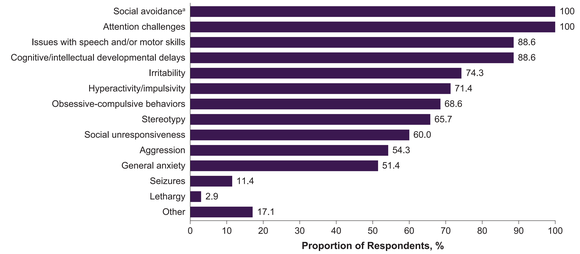
Figure 5. Diagnosing physician.



CURRENT EXPERIENCE OF FXS

- The most frequently experienced current symptoms of FXS were social avoidance and attention challenges, which were each reported by 100% of caregivers (**Figure 6**)
- Most caregivers (85.7%) rated the severity of FXS at the time of the survey as severe (45.7%) or moderate (40.0%)

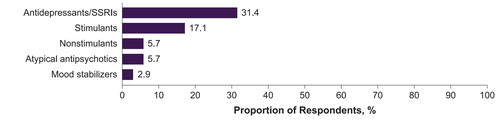
Figure 6. Current FXS symptoms.



FXS, fragile X syndrome.
*Social avoidance was a requirement for participation in the survey.

- The mean number of treatments children were currently receiving was 1.94
- 77.1% of children were currently receiving counseling/therapy, 45.7% were currently receiving traditional prescription treatment, and 31.4% were currently receiving nonprescription treatment/supplements
- The most commonly received traditional prescription medications were antidepressants/selective serotonin reuptake inhibitors and stimulants (**Figure 7**)

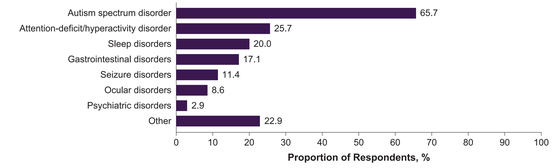
Figure 7. Current prescription medication received for FXS.



FXS, fragile X syndrome; SSRI, selective serotonin reuptake inhibitor.

- 77.1% of the children were reported to have comorbid conditions, the most common being autism spectrum disorder (65.7%) and attention-deficit/hyperactivity disorder (25.7%, **Figure 8**)

Figure 8. Comorbid conditions.



CONCLUSIONS

- This survey supports and expands upon existing knowledge of the initial presentation/diagnosis and experience of FXS, finding an average age of 3 years at initial diagnosis, a high prevalence of comorbid conditions, and standard of care consisting primarily of counseling/therapy and traditional prescription medications
- While caregivers of children with FXS often notice a variety of initial symptoms early and seek help from a health care professional, it is not until subsequent physician visits, often involving a specialist, that a formal diagnosis is made
- Further research and education are needed to help support early recognition of FXS by various stakeholders throughout the patient journey

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