

BACKGROUND

- Fragile X syndrome (FXS) is caused by an expansion of the CGG trinucleotide repeat on the X chromosome, with a normal range between 6-35 repeats. 

- FXS is the leading inherited cause of intellectual disability, with impact on behavior and functional abilities (e.g., daily living skills, communication, and social-emotional skills).

OBJECTIVE

- A targeted literature review was conducted to characterize the clinical unmet needs and burden associated with FXS.

METHODS

- Searches were conducted using predefined criteria, including titles, abstracts, and keywords. 

- Articles were included if they met the inclusion criteria and were relevant to the topic of FXS.

RESULTS

Prevalence and Diagnostic Procedures

- No large-scale, population-based screening studies have been conducted to determine the prevalence of FXS, so rates vary dramatically across studies. 

- Early studies found prevalence rates of 1-4,000 for males and 1-8,000 for females. 

- Recent meta-analyses reported a rate of 1:7,143 for males and 1:11,111 for females.

- FXS is typically diagnosed around 36 months, with concerns by parents starting around 12 months and a developmental delay confirmed by a professional at approximately 20 months.

Clinical Presentation

- The impact of FXS on functioning and behavior over an individual's life span is presented in Figure 2.

Table 1: Clinical Unmet Needs and Burden in Fragile X Syndrome: Results of a Targeted Literature Review

<table>
<thead>
<tr>
<th>Description</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intellectual Disability</td>
<td>77%</td>
<td>87%</td>
</tr>
<tr>
<td>Functional Abilities</td>
<td>87%</td>
<td>77%</td>
</tr>
<tr>
<td>Socio-emotional Skills</td>
<td>77%</td>
<td>87%</td>
</tr>
<tr>
<td>Behavior</td>
<td>87%</td>
<td>77%</td>
</tr>
<tr>
<td>Quality of Life</td>
<td>87%</td>
<td>77%</td>
</tr>
</tbody>
</table>

Infancy/early childhood

- Parents typically express concerns about their child's development before 12 months of age.

- Males with FXS have expressive language impairments that begin with delayed first words.

- Delays in all motor milestones reported for boys—including sitting, crawling, and walking.

Middle childhood/adolescence

- More than 90% of males and 50% of females with FXS meet the criteria for intellectual disability by age 9.

- Majority of males 6 or older have co-diagnosis of development delay (96%), attention problems (84%), hyperactivity (66%), and anxiety (70%).

- Between 15% and 52% receive a co-diagnosis of autism, which results in a more severe phenotype.

- About 18% experience seizures with the first occurring between 4 and 10 years of age.

Adulthood

- Approximately 95% of adult males with FXS have an IQ below 70.

- 70% of women with FXS have some degree of cognitive impairment.

- Most adult males and females are verbal and independently use the toilet, bathe, dress themselves, and eat.

- As males age, the hyperactivity, irritability, impulsiveness diminish, shy behavior and poor eye contact, however, remain constant throughout the lifespan.

- Irritability in females with FXS decreases with increasing age.

SYMPTOMS AND DISEASE MANAGEMENT

- FXS impacts several clinical domains; however, behavioral symptoms have the most profound impact on the individual. Although limited, the data suggest behavioral symptoms can be a mediating factor on family and caregiver quality of life.

- Several pharmacological interventions are available to address the various behavioral symptoms, but they are not helpful in all cases and the level of functional improvement or efficacy is not well characterized.

- There is a need for new treatment options to address the unmet clinical need and help minimize the impact on quality of life for patients, caregivers, and families.

REFERENCES

- Raquel Cabo, Jeannie Visootsak, Melissa Raspa, PhD, RTI International, Research Triangle Park, NC, United States; Donald B. Bailey, Jr., RTI Health Solutions, Research Triangle Park, NC, United States; Patrice Sacco, RTI International, Research Triangle Park, NC, United States; Raquel Cabo, RTI International, Research Triangle Park, NC, United States; Patricia Sacco, RTI Health Solutions, Research Triangle Park, NC, United States; Melissa Raspa, PhD, RTI Health Solutions, Research Triangle Park, NC, United States; Jeannie Visootsak, RTI International, Research Triangle Park, NC, United States; Raquel Cabo, RTI International, Research Triangle Park, NC, United States.

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CONCLUSIONS

- FXS impacts several clinical domains; however, behavioral symptoms have the most profound impact on the individual.

- Caregivers typically express concerns about their child's development before 12 months of age.

- Males with FXS have expressive language impairments that begin with delayed first words.

- Delays in all motor milestones reported for boys— including sitting, crawling, and walking.

- Approximately 95% of adult males with FXS have an IQ below 70.

- 70% of women with FXS have some degree of cognitive impairment.

- Most adult males and females are verbal and independently use the toilet, bathe, dress themselves, and eat.

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The authors do not have any information to disclose or any conflict of interest.

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