Review

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Prevalence of fragile X syndrome in South Asia, and importance of diagnosis

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Abstract: Fragile X syndrome (FXS) is a genetic disorder caused by a mutation in the *FMR1* gene on the X chromosome, leading to a range of developmental and intellectual disabilities. FXS is characterized by intellectual disability, behavior challenges, and distinct physical features such as an elongated face, large ears, and hyperflexible joints; FXS remains the most common inherited cause of intellectual disability. Behavioral manifestations often include attention deficits, hyperactivity, anxiety, and features of autism spectrum disorder. The prevalence of FXS in the South Asian population is not well-documented, but existing studies suggest it may be comparable to global prevalence rates, which are approximately 1 in 4,000 males and 1 in 8,000 females. Accurate diagnosis of FXS in South Asians is crucial due to the implications for early intervention and treatment, which can significantly improve the quality of life and developmental outcomes for affected individuals. Early diagnosis also facilitates genetic counselling and family planning, helping to reduce the risk of recurrence in families. Increased awareness and screening in South Asian communities are essential to address the diagnostic gap and ensure timely support for individuals with FXS or disorders associated with the premutation of *FMR1.*

Keywords: *FMR1* gene; fragile X syndrome; fragile X premutation; South Asian prevalence; neurodevelopmental disorders

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Introduction

Fragile X syndrome (FXS) is the most common inherited cause of intellectual disability and autism spectrum disorder [1]. FXS is caused by an expansion of the CGG repeat number to greater than 200 on the 5′ end of *FMR1* on the X chromosome. This mutation leads to a deficiency or absence of the *FMR1* protein (FMRP), which is crucial for normal cognitive development and synaptic function [2]. Individuals with FXS typically exhibit a range of cognitive impairments, behavior challenges, and distinctive physical features, such as an elongated face, large ears, and hyperflexible joints [3]. The impact of FXS on individuals and their families is profound, necessitating early and accurate diagnosis to enable timely intervention and support.

Mutation in the *FMR1* gene are expansions of the CGG trinucleotide repeat within the *FMR1* gene. When the number of CGG repeats exceeds 200 (the full mutation), the gene becomes methylated and silenced, leading to a deficiency or absence of FMRP, which is essential for normal neural development and synaptic functioning [2].

The *FMR1* gene has a higher prevalence of premutations (55–200 CGG repeats) than full mutations. Reliable prevalence estimates for the premutation range from 1 in 130–250 for females and 1 in 250–800 for males, and this has been obtained from a number of demographic surveys [4–6].

The *FMR1* premutation in carriers typically produces normal levels of FMRP although those with >120 repeats may have slightly lower levels of FMRP [7]. If FMRP levels are lower than normal, then carriers may have some features of FXS such as prominent ears or hyperextensible finger joints but typically not intellectual disabilities. However, carriers run the risk of developing other health conditions, such as fragile X-associated primary ovarian insufficiency (FXPOI) in females characterized by early menopause before age 40. The premutation can also cause fragile X-associated tremor/ataxia syndrome (FXTAS) in older males and females which is a neurodegenerative disorder associated with tremor, balance problems, ataxia and cognitive decline [8].

FXS is inherited in an X-linked dominant pattern. This means that the mutation is located on the X chromosome and males (who have only one X chromosome) with the full

mutation will exhibit symptoms of FXS because they lack a second X chromosome to potentially compensate for the mutation. Females (who have two X chromosomes) but only one has the full mutation, may have milder symptoms due to the presence of a second, typically functioning, X chromosome [9].

Premutation female carriers have a risk of passing an expanded CGG repeat to their offspring. During the process of oogenesis (egg formation), the CGG repeat can expand, leading to the possibility of a full mutation in the child, thereby causing FXS [10]. The risk of expansion to a full mutation increases with the number of CGG repeats in the mother's premutation.

Globally, the prevalence of FXS is estimated to be approximately 1 in 4,000 males and 1 in 8,000 females [11]. However, specific prevalence data for South Asian populations are limited. Existing studies suggest that the prevalence in South Asians may be comparable to global figures, but there is a significant gap in comprehensive epidemiological data [12]. This lack of data is concerning, given the size and diversity of the South Asian population, which includes people from India, Pakistan, Sri Lanka, Bangladesh, Bhutan, and the Maldives.

The importance of diagnosing FXS in South Asians cannot be overstated. Early and accurate diagnosis allows for interventions that can significantly improve cognitive, behavioral, and adaptive outcomes for affected individuals. Early intervention programs, such as behavioral interventions, speech therapy and occupational therapy, are most effective when started early in a child's development [4]. Additionally, genetic counselling provided upon diagnosis helps families understand the hereditary nature of the condition and make informed reproductive choices, thereby reducing the risk of recurrence in future generations.

Despite the clear benefits of early diagnosis, several barriers hinder the timely identification of FXS in South Asian communities. Cultural, social, and infrastructural barriers often delay or prevent diagnosis. For instance, the stigma associated with intellectual and developmental disabilities can lead to reluctance in seeking medical advice and support [13]. Furthermore, limited access to specialized healthcare services and a lack of awareness about FXS among healthcare providers and the general public contribute to underdiagnosis and delayed intervention.

Current studies on FXS provide valuable insights into the genetic, clinical, and psychosocial aspects of the disorder. Research has highlighted the variability in clinical presentation and the importance of tailored interventions [2]. However, there is a notable paucity of research focused specifically on South Asian populations. This gap underscores the need for more comprehensive prevalence studies and the development of culturally sensitive diagnostic and intervention strategies.

Understanding the prevalence of FXS in South Asians and the associated diagnostic challenges is critical for several reasons. First, it can inform public health policies and resource allocation to support affected individuals and their families. Second, it can enhance awareness and understanding of FXS within the community, thereby reducing stigma and encouraging early help-seeking behavior. Third, it can guide the development of targeted screening programs and intervention services that are culturally and contextually appropriate.

The prevalence of FXS in Asians is an under-researched area [14], with significant implications for public health and individual well-being. Addressing this gap through comprehensive prevalence studies and improving diagnostic and intervention strategies is essential. Doing so will not only enhance our understanding of FXS in this population but also ensure that affected individuals receive the timely and appropriate care they need to achieve their full potential.

This paper aimed to review the prevalence of FXS in South Asians and underscore the critical need for increased diagnostic efforts within this demographic. Enhancing awareness and implementing systematic screening programs are essential steps toward mitigating the impact of FXS and improving the quality of life for affected individuals and their families (Tables 1 and 2).

Overview of global prevalence of fragile X syndrome

There are regional and population-based variations in the prevalence of FXS worldwide [15]. Understanding these prevalence rates is crucial for informing public health strategies and resources allocation for affected individuals and their families.

Globally, FXS is estimated to affect approximately 1 in 4,000 males and 1 in 8,000 females [11]. These figures reflect the sex-linked nature of the disorder, where males typically present with more severe symptoms due to having only one X chromosome [16]. Females, having two X chromosomes, often exhibit milder symptoms or may be asymptomatic carriers due to the potential compensatory effect of their second, unaffected X chromosome and the degree of involvement relates to the X activation ratio (AR; the percentage of cells with the normal X as the active X) [17].

In the United States, previous studies demonstrate a prevalence of 1 in 2,454 to 1 in 3,717 in the general population

Table 1: Reported prevalence estimate of FXS among those with ID or general population in India.

Territory	Population	Sample size	Frequency	Reference
Tamil Nadu, South India	GP	705 (F)	0.3 %	Indhumathi et al. 2012 [41]
South India, Calcutta	CR	98	7.14 %	Baskaran et al. 1998 [31], Saha et al. 2001 [30]
Delhi	CR	360 (M)	5.27 %	Jain et al. 1998 [32]
New Delhi	CR	93 (M) & 37 (F)	7.7 %	Sharma et al. 2001 (33)
Uttar Pradesh	CR	146	2.54 %	Pandey et al. 2002 [34]
Uttar Pradesh	CR	59	10 %	Muthuswamy et al. 2016 [35]
Karnataka	CR	25 (M)	4 %	Karunasagar et al. 2005 [36]
North India	CR	294 (271 M & 10 F)	12.24 %	Kabra et al. 2006 [37]
Calcutta	CR	157 (112 M & 45 F)	3.178 %	Bhowmik et al., 2009 [38]
Andhra Pradesh	CR	337 (316 M & 21 F)	3.6 %	Katikala et al. 2011 [39]
Lucknow, Chandigarh, Jodhpur, Pondicherry	CR	233 (218 M & 15 F)	7.7 %	Dean DD et al., 2019 [40]
Tamil Nadu	CR	36 (29 M & 7 F)	10.34 %	Indhumathi et al., 2021 [42]

GP, general population; CR, clinical referral for individuals with intellectual disability.

Table 2: Reported prevalence estimate of the fragile X syndrome among Pakistani populations.

Country	Population	Sample size	Frequency	Reference
Pakistan	GP	808 (F)	0.7 %	Neelam et al., 2022 [43]
Pakistan	CR	395 (287 M, 108 F)	3.3 %	Madiha Kanwal et al. 2015 [44]

GP, general population; CR, clinical referral for individuals with intellectual disability.

and the figures have increased to 0.3–1.6 % in those with intellectual disability [18, 19]. Similar rates have been reported in European countries, with some variability due to differences in study methodologies and population demographics [20].

There is a significant variation in FXS prevalence within Europe. For instance, the Netherlands has a general population prevalence of 1 in 6,045, whereas the United Kingdom exhibits a range from 1 in 1,818 to 1 in 3,553, depending on the study [21].

Studies in African populations are limited, but available data suggests a lower prevalence compared to Western countries. For instance, a study in South Africa finds a prevalence of about 1 in 5,000 males [22].

In Australia, the prevalence is like that of North America and Europe, with estimates around 1 in 4,000 males in a general population, however, in a special need population with intellectual disability the prevalence increases to 10/472 (2.1 %).

Population-based carrier screening and prenatal diagnosis of FXS in East Asian populations (South Korea, mainland of China and Taiwan, China) involving over 44,000 pregnant women showed the prevalence of a fetus with premutation was estimated to be 1/581 and full mutation is 1/3,124 [23].

Studies conducted in Iran have revealed a concerning prevalence of FXS among intellectually disabled individuals, with a rate of 1 in 360, leading to an alarmingly high frequency of 3.4–15.3 % within this group. This underscores the critical need for focused diagnostic efforts and early intervention strategies [24].

Turkey also shows a significant prevalence, with 11.7 % of a tested group of 120 special need individuals found to have FXS, indicating a notable impact of the syndrome in this population [25]. Similarly, in Spain, 8.7 % of a group of 92 individuals with ID tested positive for FXS, highlighting the importance of continuous research and awareness to effectively address the challenges posed by this genetic disorder across different regions [26].

In Croatia, two separate studies have highlighted the variability in FXS prevalence. One study found a rate of 17.3 % (n=14) out of 81 individuals tested, while another reported a lower prevalence range of 0.9–2.6 % in 114 individuals with ID. These contrasting figures suggest regional differences and the need for more comprehensive studies [27].

The available studies in Southeast Asia region involve a cohort study done on Indonesian intellectually disabled population. This study reveals the prevalence of FXS is 9/527 (1.7 %), where males and females are 1.5 % (5/329) and 2 % (4/198), respectively [28].

The available studies in Southeast Asia region involve a cohort study done on Indonesian intellectually disabled population. This study revealed the prevalence of FXS is 9/527 (1.7 %), where males and females are 1.5 % (5/329) and 2 % (4/198), respectively [28]. In Malaysia, with 2,108 children with developmental disabilities from mixed ethnicities, the

FXS full mutation was reported as 70 (3.6 %) in males and 3 (2.4 %) in females [29]. However, data from South Asia is sparse and often limited to small-scale studies, highlighting the need for more comprehensive research in this region.

Regional prevalence of fragile X syndrome and available studies in South Asian countries

FXS is a significant genetic disorder globally, therefore, understanding the regional prevalence of FXS in South Asian countries is important for effective healthcare planning and resource allocation. Additionally, awareness and health education initiatives can be more effectively tailored, helping to ensure that early diagnosis and adequate support is provided in a timely manner. Furthermore, local research and development efforts benefit from regional data, fostering the creation of region-specific treatments and support programs.

India

In India, the prevalence of FXS has been explored in several studies in intellectually disabled individuals, highlighting the need for broader screening program. Such studies include one done in Calcutta with prevalence of 7.14 % [30, 31], Delhi with prevalence of 5.27 % [32], New Delhi with prevalence of 7.7 % [33], Uttar Pradesh with two studies in which one has prevalence of 2.54 % [34] and another one with 10 % [35], Karnataka with prevalence of 4 % [36], North India with prevalence of 12.24 % [37], Calcutta with prevalence of 3.178 % [38], Andhra Pradesh with prevalence of 3.6 % [39], Lucknow, Chandigarh, Jodhpur and Pondicherry with prevalence of 7.7 % [40] and Tamil Nadu with prevalence of 10.34 %. One study in the general population in South India (Tamil Nadu) including 705 women found that one in 353 women carried the premutation and none had the full mutation [41]. Despite these studies, there remains a substantial gap in comprehensive data, necessitating nationwide prevalence studies.

Pakistan

Research on FXS in Pakistan is limited, with only a few studies addressing its prevalence and genetic characteristics. A premutation carrier screening performed in a total of 808 pregnant women in Khyber Pakhtunkhwa region of Pakistan showed 0.7 % prevalence rate [43]. In another molecular diagnostic study involving 395 intellectual disabled individuals identified *FMR1* gene full mutations in 3.3 % individuals, where most of them did not have typical FXS features [44]. This indicates that FXS is present but likely underdiagnosed in the Pakistani population. The sociocultural stigma surrounding intellectual disabilities and limited access to specialized healthcare services are significant barriers to accurate diagnosis and reporting in Pakistan.

Sri Lanka

Sri Lanka has also seen limited research on FXS prevalence. A study assessing FXS among children with ID attending special education in Sri Lanka was studied by evaluating 850 (540 male and 310 female) students with age distribution 5–18 years. This study gave a prevalence figure of 2.2 % for CGG repeat expansions and the prevalence of FXS full mutation was 1.3 % [45]. The country's healthcare infrastructure and awareness about genetic disorders are improving, but more extensive studies are needed to understand the full impact of FXS.

Nepal, Bangladesh, Bhutan, and Maldives

Research on FXS in Nepal, Bangladesh, Bhutan, and Maldives is virtually non-existent. The lack of prevalence studies on FXS in countries like Nepal, Bangladesh, Bhutan, and Maldives can be attributed to several factors. These include limited healthcare Infrastructure and genetic testing facilities and resource constraints. Lack of awareness among both healthcare providers and the general population about genetic disorders, can lead to underdiagnosis and a lack of demand for genetic testing and research. Without accessible diagnostic tools, it is challenging to conduct prevalence studies or provide accurate diagnoses. Efforts to address these challenges include increasing investment in healthcare infrastructure, raising awareness about genetic disorders, improving access to genetic testing, and fostering international collaborations to support local research initiatives.

Methodology

This paper employs a narrative review approach to synthesize and analyze existing literature on the prevalence FXS in South Asia and the importance of accurate diagnosis. The

review involved a comprehensive search of medical journals, publications, and relevant databases, including PubMed, Scopus, and Google Scholar, to identify studies pertinent to the topic. A systematic search was conducted across various medical databases and search engines to gather studies published on FXS within the South Asian context. Keywords such as "Fragile X Syndrome," "prevalence," "South Asia," and "diagnosis" were used to locate relevant articles. The search was limited to studies published in English.

Inclusion and exclusion criteria

The selection criteria focused on studies that specifically addressed the prevalence of FXS in South Asian countries, including India, Pakistan, Bangladesh, Sri Lanka, Nepal, Bhutan, and Maldives. Only peer-reviewed articles, systematic reviews, and epidemiological studies were included. Studies that did not focus on South Asia or did not provide explicit data on FXS prevalence were excluded from the review.

Data categorization and analysis

Relevant studies were categorized based on the country of origin within South Asia. The data extracted from these studies were then summarized and organized into tables, allowing for a clear presentation of prevalence rates and diagnostic practices across different regions.

Potential biases and limitations

The primary limitation of this methodology is the restricted number of studies available on FXS within South Asia. This limitation may introduce potential biases, as the findings may not fully represent the actual prevalence and diagnostic practices across the entire region. Additionally, the reliance on published studies may omit unpublished data or studies in non-English languages, further affecting the comprehensiveness of the review.

Challenges in current diagnostic practices

Early diagnosis of FXS is crucial as it allows for timely interventions that significantly improve cognitive, behavioral, and adaptive outcomes. Early interventions, such as speech therapy, occupational therapy, and behavioral programs, are most effective when initiated during the early developmental stages [46]. Early diagnosis also facilitates better educational planning and genetic counselling, helping families understand the hereditary nature of FXS and make informed reproductive choices [4].

Current diagnostic practices in South Asia face several challenges, including limited availability of genetic testing facilities and trained specialists. The high cost of genetic tests and lack of standardized screening protocols further hinder effective diagnosis. Many regions lack the necessary infrastructure, leading to significant delays or missed diagnoses.

The availability and accessibility of healthcare services, particularly specialized genetic testing, vary widely across South Asian countries. Limited access to genetic testing facilities and specialists trained in diagnosing FXS contributes to the underdiagnosis of the condition. In many rural and underserved areas, healthcare providers may lack the resources and knowledge to recognize and diagnose FXS, leading to significant gaps in prevalence data.

Awareness and education about FXS among healthcare providers and the public are crucial for improving diagnosis rates. In South Asia, there is often a lack of awareness about FXS, its symptoms, and the importance of early intervention. Educational programs and training for healthcare providers can help improve the recognition and diagnosis of FXS, leading to more accurate prevalence estimates.

In addition, socio-cultural factors also have a significant impact on the diagnosis and reporting of FXS in South Asia. Cultural stigma associated with intellectual disabilities often leads to reluctance in seeking medical evaluation and support. This stigma can result in underreporting and misdiagnosis of FXS, as families may avoid seeking help due to fear of social ostracism [47].

Diagnostic methods

Comprehensive screening involves a combination of diagnostic tests, genetic testing, neurodevelopmental assessments, the active role of healthcare professionals, and community awareness and education. Screening for FXS can be conducted through various methods, including genetic testing and neurodevelopmental assessments, both of which play essential roles in early detection and diagnosis.

Genetic testing

Genetic Testing (e.g., *FMR1* DNA Testing) Is the gold standard for diagnosing FXS. The most common method is *FMR1* DNA

testing, which detects the number of CGG repeats in the *FMR1* gene. Individuals with over 200 repeats are diagnosed with FXS, while those with 55–200 repeats are considered premutation carriers. Techniques such as polymerase chain reaction (PCR) and Southern blot analysis are used to quantify CGG repeats and identify methylation status [2, 48].

Recent advancements in molecular diagnostics have led to the development of more sensitive and accurate techniques. For instance, triplet-primed PCR (TP-PCR) has emerged as a powerful tool for detecting FMR1 repeat expansions, offering greater sensitivity and the ability to detect mosaic patterns that may be missed by traditional methods [49]. Additionally, Next-Generation Sequencing (NGS) has been explored as a method to provide comprehensive coverage of the *FMR1* gene, including identifying sequence variants that could contribute to the clinical presentation of FXS [50].

Southern blot analysis

This technique involves fragmenting DNA and hybridizing it with a probe to detect large expansions and methylation patterns. It is often used to confirm results from PCR and to identify full mutations and to calculate the AR ratio in females.

Neurodevelopmental Assessments are crucial for evaluating cognitive, behavioral, and developmental milestones in children suspected of having FXS. These assessments help identify areas of delay or impairment that may warrant further genetic testing.

Individuals for whom fragile X diagnostic testing should be considered

According to American College of Medical Genetics (ACMG) Professional Practice and Guidelines Committee, testing is recommended for the following groups [51].

Fragile X syndrome:

- Individuals of either sex with intellectual disability, developmental delay, or autism, especially if they have
  (a) any physical or behavioral characteristics of FXS
  (b) a family history of FXS
  (c) male or female relatives with undiagnosed intellectual disability.
- Individuals seeking reproductive counselling who have
  (a) a family history of FXS
  (b) a family history of undiagnosed intellectual disability.
- Fetuses of known carrier mothers.
- Affected individuals or their relatives in the context of a positive cytogenetic fragile X test result who are seeking further counselling related to the risk of carrier status among themselves or their relatives. The cytogenetic test was used prior to the identification of the *FMR1* gene and is significantly less accurate than the current DNA test. DNA testing on such individuals is warranted to accurately identify premutation carriers and to distinguish premutation from full mutation carrier women.

Ovarian dysfunction:

- Women who are experiencing reproductive or fertility problems associated with elevated follicle stimulating hormone (FSH) levels, especially if they have
  (a) a family history of premature ovarian failure
  (b) a family history of FXS
  (c) male or female relatives with undiagnosed intellectual disability.

Tremor/ataxia syndrome:

- Men and women who are experiencing late onset intention tremor and cerebellar ataxia of unknown origin, especially if they have
  (a) a family history of movement disorders
  (b) a family history of FXS
  (c) male or female relatives with undiagnosed intellectual disability.

Healthcare professionals play a critical role in the screening and diagnosis of FXS. Their responsibilities include early identification. Paediatricians, geneticists, neurologists, and developmental specialists are often the first to notice developmental delays or behavior issues that may suggest FXS. Effective screening and management of FXS require collaboration among various healthcare professionals, including therapists, educators, and medical specialists, to provide comprehensive care.

Current available treatments for fragile X syndrome

Although there is no cure for FXS, but there are treatments that help minimize the symptoms of the condition. Many individuals with FXS exhibit delays in development and can also have challenging behaviors, both of which can impact academic and daily functioning. Certain medications assist people to develop the best possible life skills and enable them to integrate more easily into adult, social, and educational settings.

Pharmacological treatments

Pharmacological interventions for FXS aim to manage behavior symptoms and address underlying molecular mechanisms [52]. Common medications include:

- Stimulants: Stimulant medications such as methylphenidate (Ritalin) or amphetamines (Adderall) may be prescribed to manage symptoms of hyperactivity and attention deficit hyperactivity disorder (ADHD) in individuals with FXS and it works best if the child is 5 years or older [52, 53].
- Antidepressants: Selective serotonin reuptake inhibitors (SSRIs) sertraline or fluoxetine may be used to alleviate symptoms of anxiety commonly seen in individuals with FXS [53, 54].
- Antipsychotics: Atypical antipsychotics like risperidone or aripiprazole may be prescribed to manage aggressive behavior or mood instability in some individuals with FXS [52].

Non-pharmacological treatments

Non-pharmacological interventions play a crucial role in managing FXS symptoms and promoting overall well-being. These include:

- Behavioral Intervention: Behavioral interventions such as applied behavior analysis (ABA), and social skills training can help individuals with FXS improve social interactions and manage challenging behaviors [55].
- Speech and language therapy: To develop communication skills [56].
- Occupational and Physical therapy: To improve developmental delays, motor abilities, hypotonia and develop daily living skills.
- Individualized educational support: Special education programs, individualized education plans (IEPs), and classroom accommodations are essential for supporting academic success and addressing learning challenges in individuals with FXS [57].

Genetic and molecular approaches and new targeted treatments

Emerging treatments targeting the underlying genetic mechanisms of FXS, such as drugs that modulate the activity of the GABA receptor or modulate the BK ionic channel or gene therapy approaches, are currently under investigation and hold promise for future treatment options [2, 58]. Recent studies that inhibit the phosphordiesterase 4D enzyme with zatolmilast, which upregulates cAMP have shown improvements in cognition in adults with FXS [59] so further studies are taking place in children who are 9 years and older. In addition, topical cannabidiol (CBD) ointment made by Zynerba can be helpful for behavior in those with FXS [59]. More recently several case studies and open label trials have found metformin which lowers the mTOR pathway that is elevated in FXS to be beneficial for behavior and language abilities [60, 61]. While these treatments can improve the quality of life for individuals with FXS, a comprehensive, multidisciplinary approach that combines pharmacological and non-pharmacological interventions is often necessary to address the complex needs of individuals with the condition.

Benefit of identification of fragile X syndrome patients and premutation carriers

Identifying FXS offers several benefits for affected individuals and their families. Early identification allows for prompt intervention, including speech therapy, occupational therapy, and behavioral interventions, which can significantly improve outcomes for individuals with FXS [4]. Diagnosed individuals and their families can access support services, such as educational resources, support groups, and counselling, to help navigate the challenges associated with FXS.

Identification of premutation carriers allows for genetic counselling, where families receive information about the risk of passing on FXS to future generations. Genetic counsellors provide guidance on family planning options, reproductive choices, and the likelihood of recurrence based on the carrier's CGG repeat size [3]. This will enable families to make informed decisions to reduce the risk of FXS recurrence and to further investigate premutation involvement. With proper guidance, carriers can opt for pre-implantation genetic diagnosis (PGD), prenatal testing, or adoption to avoid passing on the condition to their children [4].

Early identification enables proactive monitoring of premutation carriers for potential health issues associated with the premutation. Carriers are at risk of developing FXTAS [62], fragile X-associated neuropsychiatric disorders (FXAND) including anxiety, depression, and insomnia [63] or FXPOI [64]. Understanding the genetic basis of the condition can alleviate guilt and uncertainty, allowing families to access support groups, resources, and counselling services. It also fosters a sense of community and solidarity among families facing similar challenges.

Late or missed diagnosis of FXS has profound implications. Without early identification, children may not receive timely interventions, leading to more severe developmental delays and behavior challenges. Families face prolonged uncertainty and stress, and without genetic counselling, they may be unaware of the risk of recurrence in subsequent pregnancies and in future generations. Delayed diagnosis also increases healthcare costs due to the need for more intensive support services later in life [4, 46].

Implications for public health policy

Policymakers should prioritize the integration of Fragile X screening into public health programs and policies. This includes advocating for universal newborn screening for Fragile X and ensuring access to genetic testing and counselling services for at-risk populations [46].

It is necessary to try to fortify and broaden the diagnostic framework for FXS. This includes increasing the availability of genetic testing facilities, training healthcare professionals in Fragile X screening and diagnosis, and reducing barriers to access, such as cost and geographical location. It is also important to train health care providers in treatments that are available for FXS and for premutation disorders [65].

Public awareness campaigns and educational initiatives are essential for increasing awareness about FXS among healthcare providers, policymakers, and the general population. Increasing public knowledge of the warning signs and symptoms of fragile X, the value of an early diagnosis and treatment, and the resources for support should be the main goals of these initiatives.

Genetic services should be integrated into primary healthcare settings to facilitate early identification and referral of individuals with FXS. This includes providing training to primary care providers on Fragile X screening guidelines, genetic counselling, and treatment strategies [65].

Summary and future directions

FXS is a genetic condition characterized by intellectual disabilities and behavior challenges, affecting individuals worldwide. However, there is limited data on its prevalence in South Asia region. Comprehensive prevalence studies are crucial for understanding the true burden of FXS and informing healthcare policies and interventions.

Despite the limited studies, the importance of conducting comprehensive prevalence studies cannot be overstated. Such studies would provide valuable insights into the prevalence of FXS in different populations, facilitating early diagnosis, intervention, and support services for affected individuals and their families.

Moving forward, future research and practice should focus on expanding prevalence studies in underserved regions, improving diagnostic infrastructure, and increasing awareness and education about FXS. By addressing these gaps, healthcare professionals, policymakers, and researchers can better meet the needs of individuals with FXS and improve their quality of life.

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