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Knowledge and perceptions about fragile X syndrome and fragile X-premutation-associated conditions among medical doctors in Nigeria

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Abstract

Fragile X syndrome (FXS) is a significant cause of intellectual disability and autism, while Fragile X Premutation -Associated Conditions (FXPAC) are a significant cause of morbidity and mortality globally. This study assessed the level of knowledge and perceptions about FXS and FXPAC among doctors in Nigeria. It was a web-based, cross-sectional study conducted among a cohort of doctors in Nigeria. Socio-demographic profile, knowledge of FXS, perceptions about FXS, knowledge of FXPAC, experience of doctors, and suggested ways of improving knowledge and management of FXS were obtained. Data were analyzed using STATA 16.0. Chi-square and Fisher's exact tests of association were used to determine the association between variables, with the significance level set at $p < 0.05$. A total of 274 doctors participated in the study. A significant proportion of respondents had limited knowledge about the clinical features of FXS. Nine of ten (90.0%) participants with good knowledge of FXS had good perceptions of FXS management. This was statistically significant ($p < 0.001$). There was a high nonresponse rate to what FXPAC is (164/274, 59.9%) among the respondents because of insufficient knowledge.

Suboptimal knowledge of FXS which influenced perception was noted among doctors. More strategies should be considered to improve doctors' knowledge and management of FXS and FXPAC in Nigeria.

KEYWORDS

doctors, experience, fragile X knowledge, FXS and FXPAC, Nigeria, perception

1 | INTRODUCTION

Fragile X Syndrome (FXS) is an X-linked dominant genetic disorder known to be the leading cause of inherited intellectual disability and autism.[1,2]

The molecular pathologic mechanism of FXS is linked to the expansion of the cytosine-guanine-guanine (CGG) repeats in the 5′ region of the Fragile X messenger ribonucleoprotein 1 (*FMR1*) gene, leading to the silencing of the gene and a decrease in the production of the *FMR1* Protein (FMRP).[3–5] FMRP is essential for normal brain development and other bodily functions.[1,2,6,7] FXS occurs when there is a full mutation (>200 CGG repeats) in the *FMR1* gene.[8] FXS affects 1 in 4000 males and 1 in 8000 females and is typically diagnosed in early childhood based on clinical symptoms and genetic testing.[1,5]

An additional group of disorders called Fragile X Premutation Associated Conditions (FXPAC) is in the family of Fragile X-associated disorders, but occurs when the *FMR1* gene has a smaller mutation; trinucleotide expansion in the *FMR1* gene (from 55 to 200 CGG repeats) but still allows for some production of the FMRP protein, albeit sometimes at lower levels when repeats are over 120.[9,10] FXPAC can lead to a variety of physical and mental health issues, including neurological problems like tremors, balance issues, infertility, memory loss, anxiety, depression, chronic fatigue, chronic pain, and sleep problems.[10–13] FXPAC includes some disorders like the Fragile X-associated Tremor Ataxia syndrome (FXTAS), Fragile X-associated primary ovarian insufficiency (FXPOI), and Fragile X-associated neuropsychiatric disorders (FXAND).[1,10] These individual disorders have varied symptoms which increase morbidity and mortality for the individual and their families. For example, FXTAS develops in later adulthood, usually after 50 years of age, and is a progressive neurological disorder that affects balance, coordination, and cognitive function.[10,14–17] FXPOI, on the other hand, is associated with infertility and premature menopause in women and should be considered in those being evaluated for infertility.[10,12] FXAND presents with symptoms of neuropsychiatric illness like anxiety, depression, sleep disorders, chronic pain, and chronic fatigue.[1,10,12,18]

Several clinical checklists have however been proposed to aid diagnosis in affected persons.[19–23]

Understanding the knowledge and perceptions about FXS and FXPAC among medical practitioners is vital for ensuring timely diagnosis, appropriate treatment, and support for individuals and families impacted by these conditions.

Some authors have reported that many practitioners were unfamiliar with FXS and premutation disorders (55–200 CGG repeats), and lacked confidence in their ability to diagnose and manage these conditions.[24,25] Additionally, a survey of physicians by Budimirovic et al[25] reported low levels of awareness and knowledge about FXS and FXPAC, suggesting a need for increased education and resources for medical practitioners to effectively recognize and manage these conditions.

The lack of knowledge about FXS and FXPAC among medical doctors can significantly negatively impact affected individuals and their families, resulting in delays in accessing appropriate care and support. Discrimination and stigmatization of individuals with FXS and FXPAC can further worsen the challenges they face in their daily lives.

To mitigate the possible negative outcomes resulting from medical doctors' inadequate understanding of FXS, it is crucial to rectify these knowledge deficiencies and improve awareness of these disorders within the healthcare community. This study not only highlights the need for healthcare providers to have a better understanding of these conditions to support individuals and families affected by FXS and FXPAC effectively,[24,26] but also aimed to evaluate the knowledge and perceptions about FXS and FXPAC among medical doctors in Nigeria, the most populous country in Africa.[27] By improving medical doctors' knowledge and perceptions about FXS and FXPAC, there may be effective management and improved quality of life for affected individuals and their families.

2 | MATERIALS AND METHODS

The study was a web-based, cross-sectional survey of consenting medical doctors, resident in Nigeria, conducted from 9th March 2024 to 4th May 2024.–

2.1 | Sample size

The sample size was calculated using the formula[28] $n = Z^2P(1-P)/d^2$, where n is the minimum sample size, Z is the normal standard deviate corresponding to a significance level. For a significance level/precision of %, $Z = 1.96$, P is the estimated proportion (of healthcare providers with correct knowledge of FXS) from a previous study set at 20%.[26] This gave a minimum sample size of 246. An additional 10% attrition was added for incorrectly filled questionnaires, giving a calculated sample size of 273.

2.2 | Study instrument and data collection

An online, semi-structured, self-administered questionnaire was adapted and modified from Protic et al.[26] Content validity of the

questionnaire was done by experts before the eventual distribution of the questionnaires. It was shared using a link (Google form link) shared by the researchers (medical doctors), using WhatsApp Messenger (Facebook, Inc., California, Menlo Park, USA), and electronic mails (emails) to various doctors' social media fora and personal mobile phones. Only consenting medical doctors in Nigeria were eligible for this study. Google Form was opted for because of its instant messaging, cloud storage, and easy accessibility, retrieval, and analysis of data obtained. The questionnaire was divided into three sections; sociodemographic profile of participants; Knowledge of FXS (9 semi-structured items), Factual knowledge of FXPAC (4 items, 2 structured and 2 unstructured), and perceptions about FXS (3 semi-structured items). It also asked 1 question on suggestions for improving knowledge and management of FXS and FXPAC among doctors in Nigeria. Questions asked under the sociodemographic characteristics were age at last birthday, gender, marital status, presence of relative or family member with an intellectual or behavioral disorder, duration of practice, specialty, location of practice, type of institution of practice, and prior genetic training. The questions asked for Knowledge of FXS included awareness of the disorder, what the disorder is (open-ended), its cause, physical features, behavioral features, percentage of FXS who have autism, FXS as the most common cause of inherited intellectual disability, diagnosis, and management. For Knowledge of FXS, each correct answer was given 1 point, while an incorrect response, "don't know" or "maybe" was given 0 points. The total score for knowledge was 9, classified using Bloom's scoring for Knowledge, Attitude and Practice (KAP) studies as Good (80%–100% or >7 correct answers), fair (60%–79% or 5–7 correct answers), poor (<60% or 0–4 correct answers). Each correct item was given 1 point, while an incorrect or 'don't know' response was given 0 points. Similarly, questions asked for Knowledge of FXPAC were about what FXPAC is, clinical features (6 correct items), investigation to confirm FXPAC, and treatment of FXPAC. Each correct item was given 1 point, while an incorrect or "don't know" response was given 0 points. The total response for knowledge of FXPAC was 9. This was also classified using Bloom's scoring for KAP studies.

Questions asked under perception were "When I see a patient who has an intellectual disability, I will recommend screening for FXS"; "When I see a patient who has autism, I will recommend screening for FXS"; and "I am willing to recommend gene therapy for FXS." This section was scored as good (3 correct answers), average (2 correct answers) or poor (0–1 correct answer). Questions on Factual knowledge of FXS and doctors' experiences with people living with FXS were also obtained. Questions on knowledge and perceptions were coded in Microsoft Excel before they were entered into STATA 16.0 for data analysis.

The Google form was turned off to stop receiving responses after the required sample size had been obtained. Then, data downloaded from the Google form were cleaned up in Microsoft Excel before analysis. Incorrectly filled forms were excluded from the data analysis (Nigerian physicians practicing outside Nigeria who filled out the questionnaires). Nonresponse answers were classified as "don't know." The study followed the guidelines according to the Declaration of Helsinki. Ethical approval for the study was obtained from the Ethics and Research Committee of Chukwuemeka Odumegwu Ojukwu University Teaching Hospital, Anambra State (COOUTH/CMAC/ETH.C/VOL.1/FN:04/321). Informed consent was obtained before the study and there was no financial inducement.

TABLE 1 Sociodemographic characteristics of participants.

	Variable	Frequency ($N = 274$)	Percentage (%)
Gender	Male	133	48.5
	Female	141	51.5
Age	21–30	44	16.1
	31–40	139	50.7
	41–50	75	27.4
	51–60	12	4.4
	61–70	4	1.6
	Mean ± STD	38.1 ± 7.6	
Marital status	Single	62	22.6
	Married	209	76.3
	Widowed	3	1.1
Years of practice	<5 years	47	17.2
	5–10 years	78	28.5
	10 years and above	149	54.4
Geopolitical zone where you practice	South east	108	39.4
	South–south	55	20.1
	Southwest	54	19.7
	North	57	20.8
Type of practice	Tertiary facility	204	74.5
	Secondary facility	23	8.4
	Primary healthcare	47	17.1
Specialty	Pediatrics	82	29.9
	Obstetrics and Gynecology	43	15.7
	Other physicians	114	41.6
	Surgery	35	12.8
Relative/family member has intellectual or behavioral disorder	Yes	57	20.8
	No	217	79.2

3 | DATA ANALYSIS

Data were analyzed using STATA 16.0 software (Stata Corp College Station, Texas, USA). Numerical variables in the dataset

TABLE 2 Knowledge of fragile X syndrome among participants.

		Frequency ($N = 274$)	Percent (100.0%)
Heard about FXS	**Yes**[a]	**239**	**87.2**
	No	35	12.8
	Total	274	100.0
What is Fragile X Syndrome?	Don't know/can't recall	66	24.1
	It's a genetic disorder (no further detail)	57	20.8
	Deletion of chromosome 22	1	0.4
	Genetic disease characterized by reduced intellectual ability.	111	40.5
	A genetic disorder affecting the Fragile X ribonucleic acid 1[a]	**13**	**4.7**
	It is a genetic disorder that is associated with mental retardation/menstrual disorders/subfertility	2	0.7
	Fragile X syndrome, also termed Martin-Bell syndrome or marker X syndrome, is the most common cause of inherited mental retardation, intellectual disability, and autism[a]	**21**	**7.7**
	It is a genetic condition that leads to certain physical body anomalies	3	1.1
	Total	274	100.0
What is the cause of FXS	**Genetic mutation**[a]	**254**	**92.7**
	Infectious agents	1	0.4
	Unknown	19	6.9
	Total	274	100.0
Characteristic physical features of FXS	I don't know	60	21.9
	Large testicles, large ears, long face, soft skin, hyperextensible joints[a]	**122**	**44.5**
	Microcephaly, prominent jaw, coarse skin, prominent ears	69	25.2
	Micrognathia, microcephaly, protuberant abdomen, macroorchidism	23	8.4
	Total	274	100.0
Common behavioral features	I don't know	69	25.2
	Gaze aversion	12	4.4
	Hand flapping	36	13.1
	Hand biting	6	2.2
	b and c only	20	7.3
	All of the options[a]	**131**	**47.8**
	Total	274	100.0
Percentage of FXS cases have autism spectrum disorders?	5%	16	5.8
	10%	28	10.2
	60%[a]	**17**	**6.2**
	80%	5	1.8
	No response (don't know)	208	75.9
	Total	274	100.0
Diagnosis of FXS is by	I don't know	26	9.5
	Physical examination	10	3.6
	Blood tests	9	3.3
	Genetic testing[a]	**227**	**82.8**
	X-ray imaging	2	0.7
	Total	274	100.0
FXS is the most common inherited cause of intellectual disability	**True**[a]	**97**	**35.4**

(Continues)

TABLE 2 (Continued)

		Frequency ($N = 274$)	Percent (100.0%)
	False	79	28.8
	Maybe	91	33.2
	No response	7	2.6
	Total	274	100.0
FXS is managed by	I don't know	71	25.9
	Psychopharmacological therapy[a]	**179**	**65.3**
	Behavioral treatment only	21	7.7
	Pharmacological	3	1.1
	Total	274	100.0

Note: Correct responses were written in bold characters.
[a]Correct response.

(age) were summarized using mean and standard deviation. Further categorization of age, type of practice, location of practice, and specialty was done during the analysis. Categorical variables like gender, marital status, close relative or friend with intellectual disability, duration of practice, area of specialization, location of practice, type of practice (classified into tertiary, secondary, and primary centres), prior genetic training, knowledge of FXS and perceptions about FXS were summarized using frequency and percentage. Factual knowledge of FXS and doctors' experiences with people living with FXS were determined, categorized into themes, and summarized using frequency and percentages.

Cross tabulation was used to evaluate the relationship between socio-demographic variables (age category, gender, marital status, close relative/family member with intellectual disability, duration of practice, area of specialization, type of practice, and location of practice) and knowledge, and perceptions using Chi-square. Fisher's exact test was applied where necessary. The level of significance for tests of the association was set at a p-value of less than 0.05. Cross-tabulation was also used to assess the association between knowledge and perception.

4 | RESULTS

Two hundred and seventy-four doctors participated in this study, with 133/274 (48.5%) respondents being males, giving a male-to-female ratio of 0.9: 1. The age range of participants was 25–70 years, with a mean age of 38.1 ± 7.6 years. More than half of the participants ($n = 149/274$, 54.4%) had practiced medicine for 10 or more years. One hundred and eight respondents (39.4%) were from the southeastern region, while 82/274 (29.9%) worked in the Pediatric specialty. Fifty-seven participants (20.8%) had a relative or family member who had intellectual disability (Table 1).

5 | KNOWLEDGE OF FXS AMONG DOCTORS IN NIGERIA

Among the doctors interviewed, only 10/274 (3.6%) of them had a good knowledge of FXS. Less than half of the respondents (134/274, 48.9%) had a good perception of FXS management. Although 239/274 (87.2%) had heard about FXS, 66/274 (24.1%) of them could not recall or didn't know the definition of FXS. Twenty-one of them associated Fragile X with mental retardation, intellectual disability, and autism, while when asked the cause of FXS, 254/274 (92.7%) rightly attributed it to genetic mutation while as much as 19/274 (6.4%) attributed it to unknown causes. As many as 60/274 (21.8%) of them didn't know the characteristic clinical features of FXS, with only 122/274 (44.5%) citing large testicles, large ears, long faces, soft skin, and hyperextensible joints as characteristic physical features of FXS. When asked about the percentage of FXS cases with autism spectrum disorders, only 17/274 (6.2%) respondents correctly answered the percentage as 60%. In terms of the management modality, 71/274 (25.9%) did not know how FXS is managed. Only 4 out of the 9 questions on knowledge of FXS were positively/correctly answered by 50.0% of the respondents. The questions with very poor correct scores were those on the definition of FXS ($n = 34$, 12.4%), characteristic physical features ($n = 122$, 44.5%), and percentage of FXS cases with autism spectrum disorders ($n = 17$, 6.2%). See Table 2 and Supplementary material.

5.1 | Relationship between sociodemographic profile and knowledge and perceptions of FXS among participants

One hundred and three participants (37.6%) had a poor knowledge of FXS, 161/274 (58.8%) had a fair knowledge,10/274 (3.6%) had good knowledge. One hundred and thirty-four participants (48.9%) had a good perception, 48 (17.5%) had a fair perception, while about a third

TABLE 3 Relationship between knowledge of fragile X syndrome and sociodemographic factors.

Variable	Poor (%)	Fair (%)	Good (%)	Total (100%)	*p*-Value
Age range					0.304*
21–30	22 (50.0)	20 (45.5)	2 (4.5)	44.0	
31–40	49 (35.3)	84 (60.4)	6 (4.3)	139	
41–50	28 (37.3)	46 (61.3)	1 (1.3)	75	
51–60	4 (33.3)	7 (58.3)	1 (8.3)	12	
61–70	0 (0.0)	4 (100.0)	0 (0.0)	4	
Total	103	161	10	274	
Gender					0.604
Male	47 (35.3)	82 (61.7)	4 (3.0)	133	
Female	56 (39.7)	79 (56.0)	6 (4.3)	141	
Total	103	161	10	274	
Marital status					
Single	27 (43.6)	33 (53.2)	2 (3.2)	62	0.793
Married	75 (35.9)	126 (60.3)	8 (3.8)	209	
Widowed	1 (33.3)	2 (66.7)	0 (0)	3	
Total	103	161	10	274	
Relative has intellectual/behavioral disorder					
Yes	22 (38.6)	32 (56.1)	3 (5.3)	57	0.735
No	81 (37.3)	129 (59.5)	7 (3.2)	217	
Total	103	161	10	274	
Years of practice					
<5 years	22 (46.8)	23 (48.9)	2 (4.3)	47	0.402
5–10 years	24 (30.8)	52 (66.7)	2 (2.5)	78	
10 years and above	57 (38.3)	86 (57.7)	6 (4.0)	149	
Total	103	161	10	274	
Geopolitical zone					
Southeast	34 (31.5)	69 (63.9)	5 (4.6)	108	0.727*
South–south	23 (41.8)	31 (56.4)	1 (1.8)	55	
Southwest	21 (38.9)	31 (57.4)	2 (3.7)	54	
North	25 (43.9)	30 (52.6)	2 (3.5)	57	
Total	103	161	10	274	
Specialty					
Pediatrics	27 (32.9)	52 (63.4)	3 (3.7)	82	0.895*
Obstetrics and Gynecology	18 (41.9)	24 (55.8)	1 (2.3)	43	
Other physicians	42 (36.8)	67 (58.8)	5 (4.4)	114	
Surgery	16 (45.7)	18 (51.4)	1 (2.9)	35	
Total	103	161	10	274	
Type of practice					
Tertiary facility	73 (35.8)	125 (61.3)	6 (2.9)	204	0.160
Secondary facility	12 (52.2)	11 (47.8)	0 (0.0)	23	
Primary facility	18 (38.3)	25 (53.2)	4 (8.5)	47	
Total	103	161	10	274	
Had training in genetics					
Yes	40 (36.4)	65 (59.1)	5 (4.5)	110	0.786
No	63 (38.4)	96 (58.5)	5 (3.1)	164	
Total	103 (37.6)	161(58.8)	10 (3.6)	274	

*Fisher's exact value.

(33.6%) had a poor perception of FXS. There was no significant difference in the level of knowledge of FXS and the sex, age category, or type of practice of participants respectively ($p > 0.05$) (Table 3).

5.1.1 | Doctors' perception of FXS and experience with people living with FXS

Over half of the doctors (61.3%) responded that they would recommend screening for FXS if a patient had an intellectual disability, while most participants ($n = 233$, 85.0%) were willing to recommend gene therapy for FXS. Most participants ($n = 266$, 97.1%) had never diagnosed or treated a patient with FXS. More than two-thirds of respondents ($n = 190$, 69.3%) did not know how a diagnosis of FXS is made (Table 4).

5.1.2 | Relationship between participants' Knowledge and perception of FXS

Most participants with a good knowledge of FXS had a significantly good perception of FXS management (See Table 5).

5.1.3 | Knowledge and experience with FXPAC

All participants ($n = 274$, 100.0%) had a poor knowledge of FXPAC. A few participants ($n = 21$, 7.7%) identified FXTAS as a disorder constituting FXPAC, while 11 participants (4.0%) felt it was the same as FXS. See Table 6.

5.1.4 | Improving the knowledge and management of FXS and FXPAC in Nigeria

More than two-thirds of the participants ($n = 192$, 70.1%) suggested incorporating FXS/FXPAC into the curriculum of medical education, while about 166/274 (60.6%) gave suggestions on how to improve the knowledge and management of FXS in Nigeria (Table 7).

6 | DISCUSSION

Our findings showed that most doctors' (96.4%) had a suboptimal (poor or average) knowledge of FXS, more than half of participants studied (51.1%) had a poor perception of FXS, while all participants had a poor knowledge of FXPAC. In another study by Protic et al.[26] among senior medical students in Serbia, Georgia and Colombia, overall, they observed poor knowledge in about 80% of participants. They explored knowledge of FXS from the perspective of onset of FXS symptoms, early treatment in FXS, onset, frequency and types of pharmacotherapy for FXS in contrast to our study that assessed knowledge of what the condition is, etiology, clinical features, diagnosis and management. Budimirovic et al.[25] in their survey of physicians and medical students knowledge, attitudes and practice of FXS and FXPAC in Serbia found low knowledge levels among both groups of participants, with knowledge of FXPAC being higher among medical students (53.5%) compared to physicians (41.2%). Our study was conducted among only physicians and found that all participants ($n = 274$100.0%) had poor knowledge of FXPAC although there

TABLE 4 Doctors' Perception of fragile X syndrome (FXS) and experience with people living with FXS.

		Frequency	Percent (%)
Have you ever treated or diagnosed a patient with Fragile X syndrome?	Yes	8	2.9
	No	266	97.1
How often do you see cases of FXS in your practice?	Never	248	90.5
	1/year	18	6.6
	1/6 months	7	2.6
	1/month	1	0.4
How is the diagnosis of FXS made in your practice?	Don't know/ never seen one	190	69.3
	Clinical/ physical exam	30	10.9
	Genetic	45	16.4
	Clinical and genetic	8	2.9
	Imaging	1	0.4
What happens to cases of FXS in your practice?	Case is referred	143	52.2
	Case is managed or treatment given	27	9.9
	No response	104	38.0
When I see a patient who has an intellectual disability, I will recommend screening for Fragile X syndrome[a]	=		=
When I see a patient who has autism, I will recommend screening for Fragile X syndrome[a]			
	Neutral	84	30.6
I am willing to recommend gene therapy for Fragile X syndrome if it becomes available[a]	Yes	233	85.0
	No	4	1.5
	Neutral	37	13.5
	Total	**274**	**100.0**

[a]Participants' perception of FXS.

TABLE 5 Relationship between participants' knowledge of fragile X syndrome (FXS) and perception of FXS management.

	Perception(%)				
	Poor	Fair	Good	Total	*p*-Value
Knowledge					
Poor	56 (54.4)	18 (17.5)	29 (28.2)	103 (100.0)	<0.001*
Fair	36 (22.4)	29 (18.0)	96 (59.6)	161 (100.0)	
Good	0 (0.0)	1 (10.0)	9 (90.0)	10 (100.0)	
Total	**92(33.6)**	**48 (17.5)**	**134 (48.9)**	**274 (100.0)**	

*Significant *p*-value.

TABLE 6 Knowledge and experience with fragile X premutation-associated conditions.

		Frequency	Percentage
What are Fragile X premutation-associated conditions and disorders that constitute it?	Autism	33	12.0
	Fragile X-associated tremor/ataxia syndrome (FXTAS)	21	7.7
	Fragile X-associated primary ovarian insufficiency (FXPOI)	16	5.8
	Fragile X-syndrome	11	4.0
	Intellectual disability	5	1.8
	These are conditions with genetic mutations similar to but not as encompassing as fragile X.*	6	2.2
	Angelman syndrome	1	0.4
	Conditions associated with the fragile X genetic changes*	17	6.2
	No response (don't know)	164	59.9
Enumerate the clinical features of FXPAC:	Tremors/ataxia*	26	9.5
	Intellectual disability	43	15.7
	Autism/abnormal behaviors	29	10.6
	Delay in developmental milestones	12	4.4
	Large ears	12	4.4
	Gonadal failure*	17	6.2
	Long faces	12	4.4
	Anxiety/depression/sleep disorder/fatigue*	13	4.7
	Chronic pain*	4	1.5
	Hyperthyroidism/autoimmune diseases	4	1.5
	Microcephaly	8	2.9
	Hypermobile joint	5	1.8
	No response (don't know)	89	32.4
What investigations are specific for FXPAC?	Physical Examination	1	0.4
	Genetic testing*	79	28.8
	Sex hormone assay	3	1.1
	Imaging	3	1.1
	Urine testing	1	0.4
	No response (don't know)	187	68.2
What happens to cases of FXPAC in your practice?	Case is referred	143	52.2
	Case is managed or treatment given	21	7.7
	No answer	110	40.1
	Total	274	100.0

*Connotes participants' are most correct responses.

were differences in the methods of assessment among the studies. From our literature search, no study has been done exclusively to assess physicians' knowledge of FXPAC. A possible explanation for the low level of knowledge of FXS could be that these countries are developing nations with limited resources for diagnosis, with more focus on other diseases and conditions that have facilities for testing.

TABLE 7 Improving knowledge and management of fragile X syndrome and fragile X premutation-associated conditions in Nigeria.

		Frequency ($n = 274$)	Percentage (%)
FXS/FXPAC should be part of our curriculum in medical education	Yes	192	70.1
	No	6	2.2
	Neutral	76	27.7
Enumerate your suggestions for improving knowledge and management of FXS/FXPAC among doctors in Nigeria	Part of curriculum and health education	81	29.6
	Awareness programs	51	18.6
	Provision of diagnostic tools	14	5.1
	Provision of treatment facility including counseling	10	3.6
	Screening for disease	5	1.8
	Research and publication	3	1.1
	Not important because it's rare	2	0.7
	No response	108	39.4

The poor knowledge of FXPAC is not surprising because FXPAC is still an evolving condition that is not widely known even among experts in developed countries. More than half of the study participants could not correctly identify characteristic clinical features or define FXS/FXPAC, highlighting the need to create more awareness among physicians who are usually the leaders of the health team in Nigeria. This can be achieved by introducing genetic disorders like FXS/FXPAC in the curriculum of the undergraduate medical education, conducting more conferences and webinars on FXS/FXPAC, and providing resources for physicians. None of the sociodemographic factors had a significant relationship with the level of knowledge of FXS. This suggests that sociodemographic background may not influence Nigerian doctors' knowledge of an unexplored disorder like FXS thereby reiterating the need for refresher courses and specific training to create awareness.

From the doctors' experience with people with FXS/FXPAC, we found that most participating doctors had never seen a person with FXS (90.1%), nor diagnosed and treated any affected person (97.1%). More than half of the participants (52.2%) referred cases suspected to be FXPAC. FXS is seen as a rare disorder in Nigeria, but the question remains, is it really rare? Doctors who may have responded that they had never seen a patient with FXS may have seen but been unable to identify their clinical and behavioral characteristics, in addition to the scarcity of screening and testing facilities in the country. The estimated prevalence of FXS in Africa is thought to be like that in other parts of the world at 1:4000–8000 persons.[1,5] This implies that for a populous country like Nigeria with over 200 million inhabitants, over 50,000 people have FXS. The poor perception of FXS among participants is surprising since one would have expected doctors to champion the cause to identify people affected by FXS who would benefit from early intervention and management. Less than two-thirds of the participants were willing to recommend screening for FXS in people with ID, or autism also evident in their responses to the questions assessing knowledge of FXS, further suggesting their low level of knowledge of the relationship between FXS, ID, and autism. There is a high burden of intellectual disability and neurodevelopmental disorders like autism in Nigeria.[29] It is possible that some of these disorders may be associated with FXS, stressing the urgent need to improve Nigerian doctors' knowledge and perceptions of this disorder. However, the participants' level of knowledge significantly influenced their perceptions of FXS. This further stresses the importance of improving knowledge of participants as this would enable them manage patients better. It is important to note that most participants (85.0%) were willing to recommend gene therapy for FXS when it becomes available. This highlights doctors' inherent need to seek cures for any medical condition that may affect their patients.

Participants suggested ways of improving the knowledge and management of FXS/FXPAC among doctors in Nigeria including incorporating FXS/FXPAC into the curriculum of medical education. The need to strengthen the medical curriculum in Nigeria by introducing topics on genetic disorders and neurodevelopmental disorders has been highlighted in a previous study. In a study on the knowledge of autism among a cohort of Nigerian doctors, the introduction of autism in the medical curriculum was identified as a strong modality for bridging the identified knowledge gap.[30] Other suggestions by participants were awareness campaign strategies, screening and treatment facilities, and more research and publications on FXS/FXPAC. These suggested strategies are helpful in the improvement of knowledge of several disease conditions.[31–34]

7 | CONCLUSION

Our study showed a suboptimal level of knowledge of FXS and FXPAC, and suboptimal perception about FXS among participating Nigerian doctors, and that having a higher level of knowledge of FXS significantly influenced doctors' perception of FXS. However, most participants were willing to suggest ways to improve doctors' knowledge and management of FXS/FXPAC. Thus, there is a need to consider these proven available strategies to improve the knowledge and management of FXS/FXPAC in Nigeria.

8 | LIMITATIONS

This study was a web-based one and so, it was difficult to access doctors who did not have mobile phones, or those in remote areas that

lacked internet access or power supply. The high nonresponse rate could also be a limitation of this study.

AUTHOR CONTRIBUTIONS

The manuscript was conceived by Chioma N. P. Mbachu, Ikechukwu Mbachu and Randi Hagerman. Study design was by Chioma N. P. Mbachu, Edwin Eseigbe, Randi Hagerman, Amalachukwu Odita, Chizalu Ndukwu, and Malachy Echezona. Data acquisition was done by Chioma N.P. Mbachu, Ikechukwu Mbachu, Samuel Ilikanu, Amalachukwu Odita, Kasarachi Akowundu, Onyedikachi Okereke, Sylvia Echendu, Ifeoma Udigwe while data analysis was done by Chioma N. P. Mbachu and Malachy Echezona. The initial draft was produced by Chioma N. P. Mbachu, Onyedikachi Okereke, Chizalu Ndukwu, Samuel Ilikanu; and reviewed by Randi Hagerman, Edwin Eseigbe, Ikechukwu Mbachu, Kasarachi Akowundu and Ifeoma Udigwe. All authors agree with the final edited manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/cge.14619.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in Mendeley at https://data.mendeley.com/datasets/mr9n5bzpxw/2, reference number 10.17632/mr9n5bzpxw.2.

ETHICS STATEMENT

Ethical approval for the study was obtained from the Ethics and Research Committee of Chukwuemeka Odumegwu Ojukwu University Teaching Hospital, Anambra State (COOUTH/CMAC/ETH.C/VOL.1/FN:04/321).

INFORMED CONSENT STATEMENT

Informed consent was obtained from all participants before the commencement of the study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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