June 2023

DPT

DEVELOPMENTAL PEDIATRICS TODAY

Monthly e-Newsletter of IAP Chapter of Neurodevelopmental Pediatrics

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Editorial

Respected seniors and dear friends,

Greetings from the Neurodevelopmental Chapter of IAP!

June marks the observance of PTSD (Post-Traumatic Stress Disorder) Awareness Month, a crucial time to raise awareness about this debilitating mental health condition. PTSD can affect anyone, regardless of age, gender, or background.

In an effort to increase awareness about mental disorders, PTSD Awareness Day is observed all over the world on 27 June every year.

PTSD triggers typically fall into one of two categories: internal triggers and external triggers. Internal triggers encompass what you experience inside your body, including thoughts, emotions, memories, and bodily sensations.

There are different types of PTSD?

- Delayed-onset PTSD. If your symptoms emerge more than six months after experiencing trauma, this might be described as 'delayed PTSD' or 'delayed-onset PTSD'.
- Complex PTSD
- Birth trauma.

Symptoms of PTSD are intrusive and can impact someone's life significantly. PTSD is not limited to one presentation, as PTSD comes in other types, including uncomplicated, complex, dissociative, and comorbid PTSD.

3rd June is "Telehealth awareness day ".As we all are aware , during the Pandemic screen time has increased for everybody including kids. There has been an increase in the number of kids presenting to us with delay in speech , ASD ,ADHD , Poor scholastic performance etc. So we need to increase awareness about the adverse impact of increased screen time on child development. IAP has come up with screen time guidelines for children which is in sync with AAP guidelines We should disseminate this knowledge to parents.

Long live IAP!

Dr. Lata Bhat
Chief Editor

Chairperson's Message

Dear Readers,

Greetings from NDP Chapter.

The sweltering heat of summer is keeping us happily indoors in our airconditioned rooms but have we paused to realise the amount of chloro flurocarbons (CFCs) emitted which is damaging the ozone layer and we are entering a viscous cycle of global warming and health hazard, and so are the adverse effects onplants and marine organisms.
The effects of climate change is already evident globally with freak bizarre climatic conditions, lurking infections in the air and of course not to forget the epigenetic role in subtle developmental deviations.

It is time to think of getting back to Khus khus tatties and each one play our individual responsibility.

During COVID period brought in a massive dip in socialization and high use of mobile devices being used as nannies got many a children out of gear in language development. The effects of digital use is becoming evident .

The month of June is Telehealth Awareness month. To commemorate the day this issue of the Newsletter has an article on screentime. I hope you enjoy reading and do your part to in counselling parents and spreading the news.

Happy reading and looking forward to meet you in the upcoming conference in Guwahati.

Regards

Dr. Shabina Ahmed MD, FIAP
National Chairperson
Neurodevelopmental Pediatrics Chapter of IAP

Snippets from the Secretary

Respected Seniors and dear friends,

Seasons greetings from the IAP Chapter of Neurodevelopmental Pediatrics.

The chapter is having its 20th national conference at Guwahati this year in the first week of October in association with IAP Assam branch and we look forward to having a great academic and cultural feast in natures lap at Guwahati. I urge the chapter members to register and participate in large numbers to make the conference to make it a big success.

Fellowship program of the chapter under the aegis of IAP has been flourishing well and we are entering into the ninth year this year. We are hoping to add few more centres for fellowship this year. With increasing recognition of neurodevelopmental disorders in the community, there is a strong need to increase the number of trained personnel working in the field and the chapter is striving hard in this direction.

The chapter's quarterly journal of developmental and behavioral pediatrics is now out with second issue and is being appreciated by all. Members can submit their scientific papers and case reports to the journal for publication.

Chapter elections for the post of office bearers for 2024-2025 will be held this year and the announcement will happen soon on the website and by email.

June month has many important health days - World Environment Day, World Brain Tumour Day, International Yoga Day to name a few. We have some interesting articles in the journal from our past fellowship students.

Jai Hind! Jai IAP !

Long live IAP!

Wg Cdr (Dr) KS Multani
National Secretary
IAP Chapter of Neurodevelopmental Paediatrics

Case Report

Screen time among children in the post-pandemic era - The elephant in the room

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Abstract: Like the famous idiom says "The elephant in the room" screentime has been now an important issue that everyone knows but that happens to be unavoidable after the pandemic situation. Various researches highlight the serious effects of screentime on overall development, physical and psychological wellbeing of children and adolescents. This article emphasizes on factors influencing screentime and parental perceptions, current guidelines on screentime recommendations and effects of screentime on children with neurodevelopmental disorders.

Introduction: Screentime has been on the rise in the last decade and screen time exposure has increased more in recent times due to the COVID pandemic. Smartphones have become essential in life as they are handy and can be carried everywhere. They have made the internet easily accessible. Nevertheless, the advent of smartphone and tablet devices has resulted in increased screen time which poses risk for language delay in younger children. Unregulated screen time and exposure to inappropriate content in late childhood and adolescence is associated with far-reaching physical and psychological consequences.

Definition for screen time: The amount of time that a child spends in front of a screen device, e.g., a computer, a television, an iPad, a mobile phone, or a tablet, is screen time. [1,2]

- "Active" screen time is the time spent by the child on devices that allow interaction and engagement, e.g., parents actively interacting while co-viewing with the child or video games involving physical movements.
- "Passive" screen time is the time spent by the child watching shows, movies or clips without interaction.

The magnitude of the problem: Despite the various consensus guidelines for parents on screen time put forth by various Paediatrics organizations [3,4,] studies show that screen time starts before 18 months of age in 99.7% of children in urban North India with a median age of introduction at ten months (as early as from 2 months of age).[5] The study also showed that more than 96% had been exposed to smartphones and 89% to television viewing. Furthermore, around 72% of the parents were not concerned about their children's screen time and only 0.5%

of the parents were aware of the screen time recommendations. Another Indian study conducted among children of the 2-5 years age group showed that 59.5% of the children exceeded the recommended screen time. Time spent on screen by the kids had a significant positive association with the caretaker's screen time and a negative association with the mother's educational status.[6] A study that compared media use in pre-pandemic and the pandemic era among children aged 3 to 7 years from six countries showed an overall increase in screen time after the onset of the pandemic.[7]

Why screentime??

Even though parents are concerned about the risks of emedia, parents find it as an easy calming tool in their busy schedules to manage their work and household chores and also, the nuclear family style and limited options in view of safety concerns when both parents were working.

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Factors influencing screentime and Parental perceptions towards factors influencing screentime:

Screentime is significantly associated with educational status and occupation of the parents, screentime of the family members, socioeconomic status of the family, number of devices at home including bedroom devices, parental view on the purpose and timings (meal time or leisure activities) of screentime.[5,6] Few qualitative studies representing multi-cultural and multi-geographic parental perceptions regarding pre-schooler's screentime reported screentime is mainly used for educational purposes.[8–10] Apart from being used as a baby-sitter, screentime is considered as a safer option when parents are late home from work and few consider it as a common timepass to be spent as a family together and some want their kids to enjoy their weekends as they like. Few parents were concerned about the sedentary time spent in front of the television and the content of programmes kids watch. Barriers to limiting screentime reported were parents' failure to limit their own screentime, involvement of whole family dynamics and failure to see TV as a problem. Parents in these studies reported allowing screentime as a reward, setting time limits and engaging in non-screen activities like involving kids in sports or other physical activities were the alternative approaches tried by them to limit screentime in their kids.

On the contrary, a survey among low-income Latino population attending special nutrition supplement program, considering people belonging to low socioeconomic status were at risk of excessive screentime showed half of the children (53%) met AAP guidelines on screentime

limits, 56% had no media in their bedrooms. It was also found that among those who met the AAP guidelines had less than 2 devices at home, parents had restricted their screen time and set a few rules like screen-free dinner times. [11]

How does parental screen time impact a child's development?

Children learn from face-to-face interactions and parental screen time can reduce their meaningful interactive time even when physically available. This negative parent-child relationship can lead to developmental and behavioural issues. Moreover, children look to parents as their role models in learning behaviour.

Pros and cons of screen time: In the digital era, screen devices cannot be considered totally as non-essential. There are a few advantages of using digital technology apart from the disadvantages. The balance between healthy and unhealthy screen habits makes the difference

Pros of screentime:

1. Social interaction: Helps in connecting with people around the world. Especially in this pandemic, digital technology has helped people to stay connected with family members and friends around and has prevented psychological consequences.

2. Educational: Helps in developing early language skills through phonics, vocabulary-building apps, listening to stories and reading eBooks. Educational apps help in understanding difficult concepts in the subjects such as science experiments, and geographical concepts. Apps that promote creativity can be a great alternative. There are open-ended apps that allow children to make decisions and learn throughout the game or task. These interactive apps let children create content on their own rather than just sitting and watching. Apart from this, children can also learn music, dance, and art and crafts of different regions of the world through videos.

3. Health awareness: Smartphone apps can help encourage kids to adopt healthy behaviours, such as regular exercise, healthier food choices, and sex education. Video games that involve physical activity can be a better option than passive viewing even though they cannot replace active outdoor physical activity.

4. Entertainment: Family time can be spent together

for a restricted time to relax in weekends and fitness activities (yoga and dance) can be done together

Cons of screentime:

Screentime has developmental, physical and psychological consequences. [2,12,13]

1. Developmental: Even though kids acquire some vocabulary skills, and learn preschool concepts from videos, it cannot be replaced by learning from real-life experiences. Unengaged passive screentime has been linked with language delays and deficits in problem-solving skills, memory and social communication deficits. A study that was done to explore the association between screen time exposure and the integrity of brain white matter tracts supporting language and literacy skills among 47 healthy preschool children had shown a negative association between screen time and expressive vocabulary, phonological processing speed and literacy skills.[14] Touch screen use hinders fine motor skills and eye-hand coordination as it does not require any complex actions compared to handling a toy, scribbling or writing with hands, or handling buttons. A study by Lin et al, comparing the fine motor skills of users of touch screen and non-users in typically developing preschool children had shown that those using the touch screen over a period of 24 weeks have less fine motor precision, fine motor integrity and manual dexterity.[15] Excess screen time also leads to poor attention skills.

2. Physical:

o Obesity: Sedentary screentime along with poor eating habits and advertisements promoting unhealthy foods has led to the pandemic of obesity among children.

o Sleep: TV or mobile viewing in the late evening or night cause melatonin suppression and this results in delayed sleep initiation, and reduced sleep hours as children have to get up early for school the next day. Even the presence of an electronic device suppresses melatonin secretion affecting sleep. The fast-paced or violent content viewed can cause nightmares and frequent awakenings. This effect on the quantity and quality of sleep results in poor scholastic performance.

o Vision: excessive screen use results in digital eye strain and myopia, dry eyes

o Postural problems: Screentime associated with poor posture (improper positioning and viewing) can result in neck pain and back pain, headaches.

3. Psychological: Increased screen time along with watching fast-paced content and associated poor sleep quality and quantity causes poor scholastic performance, inattention and difficulty in completing a task. Adolescents are at higher risk of addictions to social media as they are attracted towards short-term gratifications when

they get rewarded in online gaming activities. The failure to obtain those immediate gratifications in real life leads to inattention and intolerance to accept even small failures can result in low self-esteem, depression and suicidal tendency. The violent content they watch along with peer pressure can take them to anti-social activities. Also, advertisements portraying perfect body images can lead to reduced self-esteem among teens and eating disorders. Alcohol and drug abuse are other major risk associated with social media exposure. Adolescents are exposed to inappropriate and unsafe content that can lead them to the risk of cyberbullying and abuse. A meta-analysis review on the effects of excess screentime on neurodevelopment, learning, memory, mental health and neurodegeneration has reported overall increased screen time is associated with negative outcomes such as lowered self-esteem, increased incidence and severity of mental health issues and addictions, slowed learning and acquisition, and an increased risk of premature cognitive decline.[16]

Question remains??

Having discussed the advantages and disadvantages of screen time, the question remains whether to allow

or not to allow screen time and if allowed, how much is considered excessive? The answer to the question is it depends on how appropriately the media is used by the parents and the children together rather than the time of exposure alone.

IAP Guidelines for screentime, physical activity and sleep[3]

For children less than 2 years, zero screen time except for occasional video calls. Digital devices should not be used to feed the baby or to calm the baby. Active parental involvement insisted on playing, storytelling, music, movement and age-appropriate toys to promote early childhood development.

For children between 2-5 years of age, supervised screen time to maximum of 1 hour (per day with each session not more than 20-30 min); the lesser the better, provided the content should be educational, age-appropriate, non-violent, healthy, and preferably interactive. Screentime should not be used during meals, within one hour before sleep, or during surface travel. A minimum of 3 hours of physical activities and 10–14 hours of good quality sleep should be insisted.

For children between 5-10 years of age: Screentime should be limited to less than 2 hrs per day, inclusive of educational and extra-curricular assignments and the lesser the better.

Co-view and monitor the use of digital media by children to ensure appropriateness of the content, and children's safety and security. Adequate time should be insisted for homework, play, sleep, hobbies and family time or 'me' time. A minimum of 9-12 hours of sleep and at least one hour per day of physical activity is recommended.

Adolescents (10-18 years of age): Preference for one hour of outdoor physical activity, 8-9 hours of night sleep, and time for schoolwork, meals, hobbies, peer interaction and family time should be given rather than screentime. If those activities are compromised, then screen time should be reduced. Parents should be aware of the content of digital media watched by their children.

Excessive screen time: If any of the essential activities such as sleep, physical activity, study, family, meal, and hobby times are displaced due to screen time, then it is called excessive screen time and it should be reduced.

Green time Vs Screentime??

Green time is the time spent outdoors, which may be a simple unstructured play or a walk in the park, that may naturally cut down the screen time. Play enhances their physical strength, promotes quality sleep, improves attention, promotes creativity and problem-solving skills, helps in cognitive development and builds resilience. Studies have shown an association between better psychological outcomes in those who spend more outdoor time than those who had excess screen time. [17] This stresses that nature and outdoor activities have to be included in regular academics and as a preventive point of view in promoting the positive mental health of adolescents and children in this digital era.

How to effectively manage screen time?

• Parents have to monitor the age appropriate content through devices or program settings provided by the cable service providers. Co-viewing and interacting will help to generalise the content to real life. Inappropriate content can be taught as social stories and discussed to promote developing healthy behaviour. As the child grows few rules can be changed accordingly depending on their academic and non-academic needs.

• Digital Rules for the whole family with regard to screen timings and observing a screen-free day should be insisted on.

• Structuring the day - planning adequate time to meet the required time for physical activity, academic and extracurricular activities, meals and adequate sleep time and screentime can be used as rewards.

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• Alternatives to screentime to be considered: Family time by joining in daily routines and helping them, e.g., cooking meals, cleaning the house, doing the groceries together, etc. or reading books together.

• Install software or apps that block access to violent, pornographic sites. Google family app keeps parents informed about the social media activity of their child.

• Educate about the need for safe and healthy use of media, risks of cyberbullying/ sexting, to inform parents in case of inappropriate content or cyberbullying or any threat.

• No access to inappropriate content/ no social media/ games / payment gateway access and not to share personal information.

• Follow online etiquette and safety.

Electronic screen monitors: In considering the restriction of screentime, electronic screen monitors that restrict screentime are under trial in a few countries. Studies implementing electronic TV time monitors along with measures to reduce obesity have shown a reduction in weekly screen time to 40-50% with a decrease in sedentary behaviour. [18,19] A pilot study in New Zealand to monitor the effect of electronic screen monitors in restricting screen time has reported Television viewing had reduced by 4.2 hrs and there was a reduction in intake of snacks compared to the control group. [20]

Screentime in children with Neurodevelopmental disorders (NDD):

Children with NDDs are exposed to more screen time compared to typically developing children. Caregivers use it as a calming tool which in turn has a negative effect on their sleep, behaviour and emotional regulation and this further makes it difficult to detach the screen from them. Children with NDD have coexisting sleep problems which are further aggravated when their sleep time is replaced by screentime. Poor sleep quality and quantity in turn exacerbate their behavioural and emotional difficulties. A study associating the role of sleep and emotional and behavioural difficulties with screentime has reported more than 94% had exceeded the recommended screentime allowances.[21] Number of bedroom devices and exposure below 18 months were significantly associated with sleep problems and emotional and behavioural difficulties.

Screen Time and Children with Autism Spectrum Disorder (ASD):

The role of environmental factors in ASD is a well-known association. Evidence has shown that 40-50% accounts for environmental factors, of which screentime is considered as one potential factor. A developmental model for the causation of autism has been proposed in which screen device exposure in a genetically susceptible individual leads to the maturation of non-social audio-visual processing areas through neuroplasticity which in turn has a negative effect on the development of social pathways. [22] This abnormal neural maturation leads to atypical facial processing, speech, auditory and visual processing, responsible for social and communication deficits in ASD. This deficit in socialisation and communication skills together with atypical speech processing (preference over artificial speech than human) leads to poor language development.

Advantages of digital media in ASD:

Through digital media, ASD kids can be taught social stories with their favourite characters to promote the development of appropriate behaviours. Social and communication skills can be developed. Sometimes these kids may become anxious when encountering a new place or person. In such situations, priming can diminish anxiety. Emotions, life skills and concepts can be learnt from screen devices. Autistic kids have learning needs and media helps them to learn at their own pace, understand concepts better and reduce their stress amidst the other kids. Augmentative and alternative communication (AAC) helps ASD kids to augment functional communication skills and increases their vocabulary by linking sounds with pictures or real-life objects.

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Disadvantages of digital media in ASD:

Screentime inhibits learning from facial cues among children with autism, and it inhibits their socialisation and communication skills and delays language development. As in the case of typically developing children, children with ASD also develop screen addiction which makes it difficult to take off the screen from them because of behavioural problems. Prolonged screen time affects their sleep and causes behavioural problems like inattention, anxiety and mood disorders and tics.

Points to consider while using digital media in ASD:

Taking account of the few advantages of digital media autistic children, what needs to be considered when allowing screen time in ASD? Westby proposed a 3-factor model that

includes the child as a whole, the content the child is exposed and the context or environment in which the child is learning.[23] The caregiver co-viewing with the child should be actively interacting with them and help them to relate the experiences to real life so that actual learning occurs. Regarding the content, it should be meaningful, age-appropriate, meaningful and imitate social reciprocations and should convey what purpose it was meant to and not with distractions.

Conclusion:

Considering the physical and mental health impacts of screen time in children, primary care paediatricians should raise awareness among parents regarding the duration of media exposure, most importantly the content, age appropriateness, learning together and parents' role in guiding the adolescents. Adequate green time and time for physical activity, sleep, family time, personal time and options for screen-free alternatives should be discussed with the parents.

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Case Report

Fragile X Family with Maternal Inheritance

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Abstract:

Fragile X syndrome (FXS) is one of the common causes of Intellectual disability (ID) in males, next to Down syndrome.1 FXS should be suspected in any male child with unexplained ID, autistic features and dysmorphic facies, though the characteristic craniofacial features and macro-orchidism may not be evident until puberty .1,2 It is now considered as a spectrum as the disorder manifests with different phenotypes both in premutation and full mutation state.3 Here, we report a family from north India with FXS, girl child with early onset of fragile X features and proven maternal inheritance.

Case report:

A 9-y-old boy first born to non-consanguineous parents from northern state of India was brought for the evaluation of developmental delay, behavioral issues and poor socialization. Maternal and birth history unremarkable. Examination showed tall stature and head circumference just above 50th centile. On examination, long elongated facies with pointed chin, broad forehead, large prominent ears, high arched palate, hyperextensible joints, autistic traits and hypotonia were noted. Mild hearing loss was detected on hearing assessment. Neurodevelopmental assessment by Binet Kamet test revealed severe ID (IQ=30.6) and severe deficits in communication and activities of daily living domains and moderate deficits in social skills (Vineland Adaptive Behavioral Scales).

His 2.5y old sister had global developmental delay and behavioral concerns. Anthropometry was normal and facial features were like the proband. Detailed family history revealed that one of the maternal cousins aged 4year has global developmental delay, autistic traits and self-injurious behavior. During infancy he had seizures and has shuddering attacks now. His examination revealed normal anthropometric measurements and frontal bossing, high forehead, pointed chin, prominent ears, nystagmus, sparse eyebrows, prognathism, prominent upper lip vermillion border, broad nasal tip and poor dentition.

With a high index of clinical suspicion of FXS, fragment analysis by polymerase chain reaction was carried out in proband, sibling, first cousin, mother and maternal grandmother. PCR analysis in proband, sibling and maternal cousin showed CGG expansion repeats more than

200 (281±1), suggestive of Fragile X syndrome and repeat expansion in premutation range (77±1) in mother and (65±1) in maternal grandmother, confirming the carrier status. However, the mother and maternal grandmother were asymptomatic. The proband's mother has two brothers and sisters who are asymptomatic and a sister with infertility, but testing has not been done in them.

Fig 1: Capillary electrophoresis of PCR for CGG repeats of the family: A, B and C: bold arrow shows peak in full mutation zone. The two peaks in C, D and E are due to repeat expansion from normal X chromosome (line arrow). D and E shows extra peak corresponding to the premutation zone.

Discussion:

Fragile X syndrome, known as "Martin Bell syndrome" was first described by J. Purdon Martin and Julia Bell.1 The Fragile X Mental Retardation gene (FMR1) is located on the exon 27 of long arm of chromosome X. Mutations in the FMR1 gene occurs due to expansion of triple nucleotide cytosine-guanine-guanine (CGG)

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bases in 5′ untranslated (5′ UTR) region in most patients thereby resulting in hypermethylation of the FMR1 promoter region and inactivation of the gene with absent FMRP.3 FMRP is highly expressed in neurons, connective tissue and spermatogonia of testis. FMRP plays a role in maturation of the dendritic spines and pruning, and synaptic plasticity, the deficiency of which is responsible for varying degrees of cognitive deficits and learning disabilities.4

The clinical manifestations depend on the number of trinucleotides repeat expansions. Based on number of repeat expansions, four allele forms have been described, Normal (5-45), Intermediate (45-54), Premutation (55-200), Full mutation (>200). Expansion to full mutation from premutation state occurs when mother transmits the X chromosome to her offspring which depends on the size of repeats in the mother and a high risk has been identified if repeat numbers are more than 100 and associated with family history of FXS (54%) compared to 18% without a family history.5–7 Compared to full mutation state, premutation state results in abnormally elevated unmethylated FMR1 mRNA.1 In this family, expansion of the repeats can be seen from grandmother (65) to mother (77) to her children (>200), explaining the phenomena of anticipation.

As a rule of X-linked disorders, FXS is reported to be more common in males. But the interesting fact is that even though it is a X linked disorder, FXS does not follow typical mendelian inheritance pattern where females can manifest symptoms when CGG repeat expansions are more than 200 and males remain unaffected if repeats are in premutation range. As females carry two X chromosomes, severity of clinical manifestation depends on the ratio between inactive and active X chromosome expressing FMRP and 25% female patients with FXS may have even normal IQ.1,3,4,8 Female sibling of our proband was manifesting with a clinical phenotype similar to proband and may be possibly due to skewed X-inactivation.

The typical phenotypic features and degree of cognitive deficits depend on the number of repeat expansions and methylation status of FMR1 gene.1,3,4 In contrast, the severity of FXS cannot be ascertained by number of repeats as more than 200 repeats results in absent FMRP in general. The characteristic facial features are long narrow face (83%), large prominent ears

(75-78%), prominent jaws (80%), high arched palate and head circumference more than 50th percentile. Macro-orchidism is reported in 95% of the cases at pubertal age but fertility remains normal. Recurrent otitis media due to collapsed eustachian tube is also commonly observed in children. Connective tissue abnormalities result in hyperextensible joints, hernias and mitral valve prolapse due to floppy mitral valve and have associated pes planus, pectus excavatum, scoliosis. Seizures occur in 20% of the population. They can also have strabismus, nystagmus and refractive errors and dental malformations. Feeding difficulties may occur in early infancy and later may develop hyperphagia and obesity. Since most of phenotypic features start appearing as child reaches adolescence and 25% may not even have typical phenotype, FXS is suspected based on behavioral phenotype with subtle dysmorphic features. In our scenario, all three had typical facial features as described in most of FXS.

Global developmental delay is reported in 100% of the children with FXS. Initially they may have hypotonia with predominant motor delay and later may manifest with predominant language delay. Both males (75-90%) and females (25%) develop moderate to severe ID due to impairment in the executive functions, working memory, visuo-spatial perception and adaptive skills. The average IQ is around 40% in most of the males. As mentioned earlier, 25% of the females may have normal IQ because of the presence of some amount of FMRP from normal X chromosome. The IQ assessment of our proband was in severe range (30.6) as reported in many studies.3,4 Complete assessment could not be done on his sibling and his cousin as they were not cooperative.

Case Report

Attention deficit hyperactivity disorder (ADHD) is the most common behavioral abnormality in FXS.3,4,9 Though hyperactivity has been reported to improve with age, inattention may persists in to adulthood with impulsivity and aggressiveness. The risk of autism in FXS is around 30-60% and these patients manifest with impairments in social interaction characterized by social anxiety, extreme shyness, eye gaze avoidance. These symptoms may increase with an advancing age. Autism in children with FXS usually exhibit more self-injurious behavior, aggression, stereotypes and perseverative speech. They may insist on repeating same phrases or actions. Obsessive compulsive disorder is another commonly reported behavior in FXS. Compared to boys, hyperactivity is reported less in girls with FXS, but may have inattention, anxiety and shyness. Our proband had the typical perseverative speech, aggressive and self-injurious behavior, as reported in autistic kids with FXS. During assessments, his sibling's behavior was manageable than the proband and his cousin which may imply mild phenotype in the females.

Though individuals with premutation state remain asymptomatic and hold clinical importance for transmitting expanded alleles to their offspring, recent evidence shows these individuals also develop some cognitive and emotional difficulties and medical comorbidities.6,10–12 This depends on the number of repeats and the amount of abnormal FMR1 mRNA production. Females with premutation carrier state are at risk of developing immune mediated diseases, anxiety and emotional problems, depression, primary amenorrhea, infertility and premature ovarian insufficiency syndrome (FXPOI).1,4,8 Carriers with premutation alleles in both genders may develop late onset Fragile X associated Tremor/Ataxia syndrome (FXTAS), though it is more common in males.11 Proband's mother need to be screened for behavioral problems and followed up for FXPOI later. One of the maternal aunts had primary infertility which may be attributed to premutation state. Maternal uncle, though asymptomatic now should be tested and followed up for FXTAS during late adulthood if found positive.

Diagnosis is established by polymerase chain reaction (PCR) to measure the number of repeats and Southern blot test to look approximate size of the repeats, methylation status. Even though chromosomal microarray (CMA) is the first tier of genetic test for individuals with ID with dysmorphism, repeat expansions cannot be detected by CMA and needs PCR/ Southern blot test to diagnose FXS.

Conclusion:

FXS should be suspected in a male child manifesting with developmental delay, behavioral abnormalities and facial dysmorphism. IAP has proposed a consensus on interventions and management of comorbidities of FXS from infancy to early adulthood.8 Multidisciplinary management includes speech therapy, occupational therapy, behavioral therapy and genetic counselling.

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