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Pedigree of fragile X syndrome – An option for reproductive planning

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Abstract

Background*:** Five percentage of the public school population nationally is designated having Fragile X Syndrome (FXS). The present study aims to analyze the pedigrees of children with FXS. ***Methods: In the present study 86 children having FXS from different parts of Kerala were selected based on their Intelligence Quotient. The investigator prepared questionnaire for collecting the details of their family and on the basis of the data obtained, pedigree charts were prepared**.** ***Results:*** Pedigree is acting as one of the important tool to assess patients with FXS, as it plays a significant role in assessing the modes of inheritance, analysis, treatment, intervention programmes and moreover in planning of future generation. In the present study, detailed pedigree was collected from all the children with FXS, and the study proved that parents of affected children were scared of conceiving another child with same abnormality. ***Conclusion:*** A three generation pedigree revealed the problems like foetal loss, miscarriage, different genetic diseases in and among family members and others with clues to the unknown etiology. The study proved that there is a positive correlation between FXS and pedigree analysis.

Key words: Dyscalculia, Dysgraphia, Dyslexia, Fragile X Syndrome, Learning Disability, Pedigree.

Introduction

Fragile X Syndrome (FXS) is a genetic disease, which is the most common cause of LD. In 1943, two British physicians, Martin and Bell, described several generations of boys with severe intellectual disabilities or learning disabilities who all belonged to the same extended English family[(1)]. FXS is the most common inherited form of LD, it is due to appearance of a characteristic fragile site in the X chromosome of the affected individuals while staining of metaphase chromosome. A **c**hromosomal fragile site is a non- staining gap or discontinuity in chromatids or chromosome due to the failure of chromatin condensation during mitosis. Lehrke in 1972 reported that the genes coding for intellectual function is located on X chromosome [(2)]. FXS is a distinct entity among X-linked mental disability conditions, estimated to account for the majority of the male predominance and they are the most severe, pervasive, and chronic form of LD [(3)].

The incidence of FXS has been estimated in different countries and its occurrence ranges from 1-75% of the school population[(4)]. The National Institute for Mentally Handicapped, Secunderabad, India conducted a study, which claimed the incidence to be 4%. The Neurological Institute in Kerala conducted a survey, which revealed that 10% of schools going children are learning disabled. Clinical studies and reports suggest that the nonautistic members of the families share various language and other cognitive problems with the autistic person, but have them in a less severe form[(5)].

Pedigree is a diagram which represents family relationships, uses symbols to represent people and lines to represent genetic relationships. These diagrams make it easier to visualize relationships within families, particularly in extended families. Pedigrees are often used to determine the mode of

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inheritance of genetic diseases. For identifying children with FXS, family history will be most beneficial by allowing enhanced patient care, including better identification of individuals at risk of disease and also helpful for earlier detection and management of diseases. Earlier testing and screening or foetal analysis in pregnancies at risk should be useful for taking precautions at proper time.

Materials and methods

For the present study 86 LD children from different areas of Kerala, in the age group of 7-15years , who were attending various therapies in Institute of Communicative and Cognitive Neurosciences (ICCONS) Trivandrum were selected, For the study Ethical Clearance was obtained from the Human Ethics Committee of the institution. The epidemiological and clinical data of the study subjects were collected by using questionnaires. Information pertaining to age, religion, health status, medical, educational and family history were recorded. Those with family history of FXS were subjected to detailed pedigree analysis. Three generation pedigrees of all children were constructed. Each generation is labeled at the left with a Roman numeral beginning with the first generation with their ages underneath.

Results

All the children selected for the study exhibited different types of learning disabilities, 53.5 per cent of the children exhibited Dyslexia was poor in academic performance, Dyscalculia was showed 40.7 per cent and the remaining 5.8 per cent children expressed Dysgraphia.

Health status assessment showed 73.2 per cent of the children with moderate health conditions, which altered from time to time in various physical and climatic conditions, 16.3 per cent children showed high health propaganda and were less affected by the common diseases. Food habits of these children did not show much variations and 89.5 per cent of the children were non-vegetarians and 10.5 per cent children were vegetarians. The duration of sleeping showed much variation in the present study and is recorded as 9-11 hours. In this investigation, consanguinity was also analysed, among the families selected, five consanguineous marriages were identified. Attention Deficit Hyperactive Disorder was observed in 26.7 per cent and 20.9 per cent of the study groups children were identified as having Autism like behaviour. Family history of the parents of the study subjects were also collected for preparing the pedigree. Their food habits revealed that 94.2 per cent were non-vegetarians. Health assessment conditions, 11.6 per cent with high health propaganda and the remaining 9.3 per cent always affected by common diseases.

Pedigree analysis in the first generation shows that most of the grand parents were phenotypically normal. In the second generation families such as 26, 45, 62, 68 and 70 showed consanguineous marriages with FXS children, a member of family 32 have Down's syndrome and in family 38 and 63 two members with congenital renal disease. It was also found out that in family numbers 8, 10, 14, 17, 32, 41, 51, 58 and 80 one of the parents was suffering from different types of LD and 69.7 percentage of their children were proved to be having FXS. In the third generation pedigree showed that 37 children from different families are affected with FXS and in family 12, 29, 40, 49, 55 and 72, the siblings were also affected by FXS. In family 19 is having a child with Prader- Willi Syndrome. Detailed three generation pedigrees of all children with FXS were prepared and some of them have remarkable features are shown in figure 1 - 4.

Fig :1

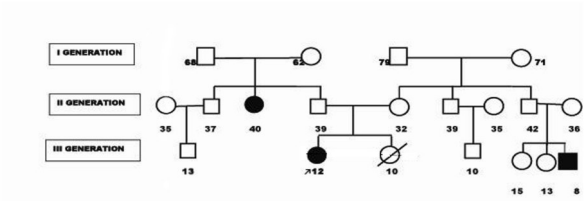


Fig: 2

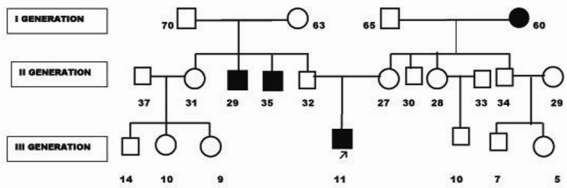


Fig:3

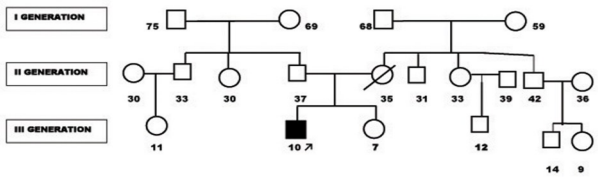
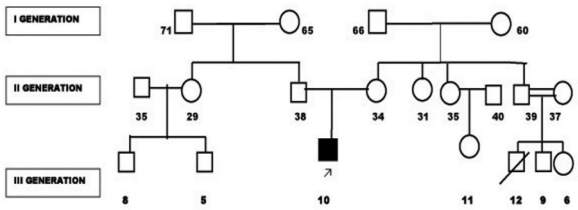
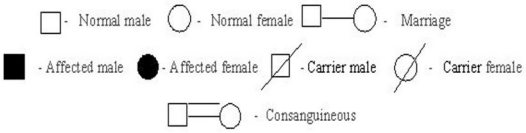


Fig:4



Figures:1to 4 – Represents the Pedigrees of children with FXS



Discussion

Pedigree analysis is an important criterion for any genetic study. The pedigree is critical in the diagnosis of FXS as it not only involves the affected children but also potentially has significant health consequences for multiple generations in each family. The health status of the children with FXS is concerned most of them had a moderate health and was less affected by the common diseases and food habits of these children did not show much variation[6], the present study is also agreement with this report. Multifactorial and single gene mutations are commonly associated with consanguinity, which has been shown to double the rate of risk of birth defects. Studies indicates that some Middle Eastern countries and parts of North Africa and South Asia, the rate of consanguinity was reported as high as 20 to 50 per cent[7]. Consanguinity not only increases the risk of multifactorial conditions, but also has the tendency to expose rare autosomal recessive conditions in offsprings through shared inheritance of gene mutations. So it was important to evaluate the possible role of consanguinity in the etio-pathogenesis of FXS. In the present study 5 families with consanguineous marriages were identified and their children are having FXS[8]. These children showed different types of learning difficulties and they were at greater risk of having genetic abnormalities in the next generation. Pedigree charting of FXS not only would enable at risk families to receive accurate reproductive counseling to the immediate and extended family but also could allow for appropriate intervention in infancy. LD often occurs in conjunction with other disorders or conditions, especially in FXS, in which a comprehensive and thorough assessment is critical for a differential diagnosis. It is estimated that between 30 to 50 per cent of undiagnosed LD may be genetic in origin. The present study made an effort to differentiate the LD children with and without FXS and pointed out the probable chance of occurrence of the disease in the successive generations. Pedigree analysis is very much useful for providing information regarding the inheritance pattern and variability of the clinical phenotype in people being affected. Pedigree reveals the options for reproductive planning for adults at risk of having affected children and provides information to assist families who need the support of organizations.

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