Chromosome features of children with fragile x syndrome

Manjula TS

ABSTRACT

Background: Fragile X syndrome is the most common genetic cause for mental retardation. Reports suggest a sizeable proportion of school children in Kerala are suffering and seeking treatment for this disorder.

Aim: To analyze the mitotic chromosome features of children with Fragile X syndrome and to compare with that of normal.

Method: Eighty six children with Fragile X syndrome from Kerala in the age group of 7-15 years were randomly selected. Peripheral blood samples (5 ml) were collected for mitotic analysis and to measure the arm of chromosomes.

Results: Autosomes and the Y chromosomes of all age group showed significant differences from the normal, but X chromosome showed least variability in their arm lengths.

Conclusion: Chromosome size has a great role in detecting the character of an individual. In this study, X chromosome showed least variation in measurements. For analyzing Fragile X syndrome, greater attention should be given to the sex chromosomes of an individual.

Keywords: fragile X syndrome, fragile site, mitosis, arm lengths

NTRODUCTION

Fragile X syndrome (FXS), Martin–Bell syndrome or Escalante's syndrome is a genetic syndrome, and is the commonest single-gene cause of autism and most common inherited cause of intellectual disability. In 1943, two British physicians, Martin and Bell described several generations of boys with severe intellectual disabilities who belongs to the same extended English family.[1] FXS is a distinct entity among X-linked mental retardation conditions, estimated to account for the male predominance.[2,3] There are genes coding for intellectual function located on X chromosome.[4] It is believed that mutations of genes on the X chromosome contribute significantly to this gender inequality.[5] FXS shows an X-linked inheritance pattern and is characterized by symptoms ranging from impaired learning abilities to severe retardation and autistic behaviors and a X linked loci that influence intelligence levels.[6]

A chromosomal fragile site is a non staining gap or discontinuity in chromatids or chromosome due to the failure of chromatin condensation during mitosis. These discontinuities usually have a strand of visible material across them under electron microscope or chromosome is broken at the fragile sites. The presence of a fragile site in long arm of X chromosome in children with learning disability is noted.[7] Cytogenetic methods for detecting this foliate-sensitive fragile site, FRAXA were developed during early 1980.[8]

Many studies in relation to human chromosomes have been conducted considering the length of the normal arm lengths and centromere indices of mitotic chromosomes; relative lengths of the short and long arms of each of the autosomes (in male and female samples) and association of variations in human karyotype and sexual and congenital anomalies.[9,10] The present study aims at to analyze various measurements of mitotic chromosomes in children with the FXS of different age groups and to identify whether any significant difference in measurements exists between autosomes and X chromosome.

MATERIALS AND METHODS

Children with FXS were selected from the Institute for Communicative and Cognitive Neurosciences (ICCONS) Trivandrum and Shornur. Ethical clearance was obtained from the Human Ethical Committee under Government of Kerala. Eighty six

children in the age group of 7-15 were randomly selected. Standard IQ test was conducted to screen the children. 5 ml of peripheral blood samples were collected to study the mitotic chromosome features. The chromosome preparations were made using the standard method modified by Manjunatha.[11] Chromosome size was estimated by ocular micrometry by placing it on the metal diaphragm in the eye piece of the microscope. Photomicrographs were taken by an oil-immersion lens with a magnification of 20 x and 50 x. Individual chromosomes were arranged as homologous chromosome pairs numbered and grouped according to the method recommended by Paris Conference (1971).[12] The chromosome number, length of short and long arm, total arm length and the centromere index were assessed and recorded. All measurement was taken from an average of twenty five readings. The arm ratios of each bivalent was determined by getting the ratio of the short over the long arms multiplied by 100, while the centromere index was obtained from the ratio of the length of the shorter arm to the length of the entire half bivalent multiplied by 100.

RESULTS

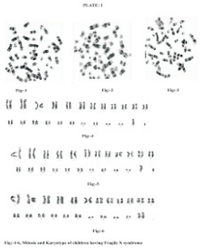
X chromosome showed the least variability in arm lengths. The short arm lengths ranges from 2.00 - 2.03 µm. The long arm length was in between 3.55 - 3.58 µm and S/L ratio was in between 0.55 - 0.57. Minimum and a maximum arm length recorded were 5.55 µm and 5.61 µm respectively. Majority of age groups showed the total arm length as 5.59 µm. The average short arm length of Y chromosome in all the age group ranged from 0.43 - 0.56 µm and long arm length ranges between 1.63 - 1.87 µm, S/L was between 0.23- 0.33. Total arm length measured at a minimum of 2.15 µm and a maximum of 2.32 µm accordingly. Mitotic chromosome analysis is another salient feature of the present study. The study highlighted the differences in short and long arm lengths of X chromosomes of different age groups. All these values showed marked differences from the normal.

Both sexes in each age group do not showed any obvious consistent pattern of differences to distinguish between the male and female chromosomes. While there were some definite indications of differences within the chromosomal groups, these were not as easily interpreted as the consistent differences in the size of the autosomes. The short arms of the female chromosomes were found to be significantly longer relative to their long arms than in the male cells.

Table -1: Mitotic chromosome measurements of participants

Chrosome number	Short arm length	Long arm length (Mean)	5/L ratio (Mean)	Total arm Length (Mean)
1	3.56	4.86	0,73	8.42
2	2.97	5.46	0.54	8.43
3	3.35	4.00	0.84	7.35
4	1.64	4.87	0.34	6.51
5	1.43	3.66	0.39	5.09
6	1.96	3.49	0.56	5.45
7	1.75	3.19	0.55	4.94
8	1.79	3.60	0.50	5.39
9	1.71	3.23	0.53	4.94
10	1.50	3.43	0.54	4.93
11	1.86	3.54	0.53	5.4
12	1.84	3.45	0.53	5.29
13	0.85	3.15	0.27	3.95
14	0.62	3.04	0.20	3.66
15	0.75	2.99	0.25	3.74
16	1.00	1.98	0.50	2.98
17	0.77	1.94	0.37	2.71
18	0.70	1.92	0.36	2.62
19	0.97	1.26	0.77	2.23
20	1.00	1.19	0.84	2.19
21	0.58	1.42	0.41	2
22	0.47	1.39	0.34	1.86
x	2.03	3.50	0.58	5.53
y	0.51	1.81	0.28	2.32

Figure-1-6. Mitosis and Karyotype of children having Fragile X syndrome



DISCUSSION

Our study reported that the short and long arm measurements of all the chromosomes including

the sex chromosome in females were consistently longer than the corresponding chromosomes in male similar to an earlier study.[3] This study highlights remarkable differences in short and long arm lengths of all the chromosomes from the normal which is similar to the findings by Bender and Kastenbaum.[10] The females have significantly higher arm ratios and the short arms of the female chromosomes are longer relative to their long arms than in the male cells. Chen and Falek found that variations in the human karyotype was associated with sexual abnormalities, congenital anomalies and mental retardation that have received much attention in the literature.

CONCLUSION

FXS children with learning disability were having short arm length in range of 2.01 - 2.03 µm; long arm length in between 3.55 - 3.58 µm and majority of the age groups showed long arm length as 3.57µm. Total arm length also showed least variation from the normal in most of the age groups. It is an important disorder in which proper and earlier genetic investigation is necessary to modify lifestyles of people who are affected.

ACKNOWLEDGEMENT

The author is deeply thankful to Dr. Raveendran Ankathil, Former Additional Professor, Department of Cytogenetics, R.C.C. Trivandrum, Dr. Suresh P.A, Director, Institute of Communicative and Cognitive Neurosciences, Trivandrum, Dr. Vijaya Lekshmi L., Professor of Biochemistry and H.O.D, Applied Nutrition, Government Medical College, Trivandrum, for their kind guidance and valuable support.

AUTHOR NOTE

Manjula Thulasi S, Assistant Professor**,** Contact no-09744798408,
Email: dharpraveent@gmail.com
(Corresponding Author)
Department of Anatomy, Dr.S.M.C.S.I. Medical College, Karakonam, Trivandrum, Kerala.

REFERENCES

1. Martin JP, Bell J. A pedigree of mental defect showing sex-linkage. *J Neurol Psychiatry.* 1943;6(3-4):154-7.
2. Opitz JM, Sutherland GR. Conference report: International Workshop on the fragile X and X-linked mental retardation. *Am J Med Genet*. 1984;17(1):5-94.
3. Neri G, Chiurazzi P, Arena F, Lubs HA, Glass IA. XLMR genes: update 1992. *Am J Med Genet.* 1992 ;43(1-2):373-82.
4. Lehrke RG. X-linked mental retardation and verbal disability. Birth Defects. *Orig Artic Ser.* 1974;10(1):1-100.
5. Opitz JM. On the gates of hell and a most unusual gene. *Am J Med Genet*. 1986;23(1-2):1-10.
6. Turner G, Webb T, Wake S,et al.Prevalence of fragile X syndrome . *Am J Med Genet.* 1996 12;64(1):196-7.
7. Lubs HA. A marker X chromosome. *Am J Hum Genet.* 1969 May;21(3):231-44.
8. Sutherland GR. The fragile X chromosome. *Int Rev Cytol,* 1983; 81:107-43.
9. Penrose LS. A note on the mean measurements of human chromosomes. *Ann Hum Genet.* 1964;28:195-6.
10. Bender MA, Kastenbaum MA. Statistical analysis of the normal human karyotype. *Am J Hum Genet*. 1969;21(4):322-51.
11. Manjunatha KR, Rao BSS, Narayanan HS, Girimaji SR,Shobha S, Gandhi DH, Sangvi R. Fragile X syndrome: The first case report from India. *Genome*. 1988;30(1): 205.
12. Paris Conference 1971 and 1975. Standardisation in Human Cytogenetics. Birth defects; orig artic Ser, XI: 9. New York: The National Foundation.
13. Chen AT, Falek A. Cytological evidence for the association of the short arms of the X and Y chromosomes in the human males. *Nature*. 1971 Aug 20; 232(5312):555-6.