

Cytogenetic Analysis of Mentally Retarded Patients in Srikakulam

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ABSTRACT The present study is undertaken to analyze the frequency of chromosomal abnormalities in mentally retarded patients (mild, moderate and severe), and to determine the types of chromosomal abnormalities that play a major role in causing mental retardation. Thirty subjects of both gender in the age group of 05-50 years were selected for study from "Behara Manovikas Kendram" of Srikakulam. Peripheral blood samples were collected from the patients with the help of technicians from TRIMS, Visakhapatnam and the samples were subjected to chromosomal analysis. Physical features like microcephaly, seizures, status of retardation etc., were also noted. The metaphase studies clearly revealed 5p deletions, Mosaic Down syndrome, 5q additions. One case revealed translocation in 9 and 17 chromosomes which also showed blast cells in Blood Smear. Chromosomal abnormalities play a vital role in causing mental retardation and its frequency increases with severity of mental retardation. We concluded that chromosomal studies in mentally retarded patients help in accurate diagnosis and proper prognosis followed by genetic counseling and management rehabilitations.

INTRODUCTION

The incomplete development of mental capacities and associated behavioural abnormalities are referred to as Mental Retardation. At least 7.6 million children are born globally every year with severe congenital malformations. 90 percent of mentally retarded people are born in countries with low incomes (Kaur and J R Singh 2010). In India, it is difficult to collect precise data on Mental Retardation (MR), causes for disorders, because of diversified social and cultural factors. Many reports are available on mentally retarded patients at global level, such as Speed et al. (1976) reports on Scotland, Jacobs et al. (1978) report on North America, Sutherland et al. (1976) reports on South Australia, Kondo et al. (1980) reports on Japan. The first report from India on cytogenetic abnormalities was published by Moghe et al. (1981). Subsequently Isaac et al. (1985) reported a survey on Down syndrome in Hyderabad, Verma et al. (1998) reported cases from Delhi region, Modi et al. (1998) reported cases in Baroda region. Jain et al. (1998) screened 1206 children with MR and found 6.38 percent positive for fragile-

X syndrome. Sex anomalies were also established by many scientists which include Turner syndrome, Klinefelter's syndrome. Micro deletion syndromes were detected in 73 cases among 374 by Madon prochi et al. (2010). First report from Jammu and Kashmir on chromosomal anomalies was reported by Parvinder Kumar et al. (2010) and they reported 11.2 percent Turner syndrome cases and 6.8 percent Klinefelter syndrome cases. Rajasekhar et al. (2010) analyzed 1400 referral cases for cytogenetic analysis and reported karyotype 45X in 36.17 percent cases. Reports on congenital anomalies are also available from different parts of India. Mishra and Baveja (1989), Aggarwal et al. (1991), Kumar et al. (1994), Patel and Adhia (2005) assess overall incidence of malformations which include Neural Tube Defects, Microcephaly, Cleft lip / palate, Hydrocephalus and Heart diseases.

With reference to Andhra Pradesh (AP), very little information is available on the data on prevalence of Mental Retardation, except work by Jyothy et al. (2000), who recorded cytogenetic data obtained from 1001 patients of Down syndrome and their parents over a period of 20 years (Jan 1979 – Jan 1999) in Hyderabad area of AP.

The present study has been undertaken with an intent to determine the frequency and types of chromosomal abnormalities in mentally retarded patients of Srikakulam district of AP, India. Furthermore, this type of study from Srikakulam has not been reported. However, the number of individuals investigated was not sufficient

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to permit statistical analysis and patients who are not institutionalized have not been included.

SUBJECTS AND METHODS

In the Behara Mano Vikasa Kendram of Srikakulam, Andhra Pradesh, India, we have physically examined 50 subjects. Based on deformities we have selected 30 subjects of both sexes in the age group of 05-50 years for Karyotypic study. Peripheral blood samples were collected from the patients, with the help of the technicians from TRIMS, Visakhapatnam and chromosomal analysis was conducted. Peripheral blood samples were collected in sodium heparin vacutainers. Cultures were initiated using rpm 1640 including 15 percent serum, Glutamine, antibiotics and phytohemagglutinin. The cultures were terminated on 3rd day by adding colchicine. Metaphase preparations were made and GTG banding was done. Well spread metaphases were scored for chromosomal analysis. 30 metaphases were scored to estimate numerical abnormalities and 3 metaphases were karyotyped to analyze structural abnormalities. Physical features were also noted like Microcephaly, seizures and magnitude of retardation etc.

RESULTS

All 30 subjects are known mentally retarded patients, among them 66.66 percent were under weight (Table 1), 13.33 percent were dumb, 10 percent were suffering from dermatological disorders like dry skin, 16.60 percent were with skeletal deformities, 10 percent were microcephalic, 6.66 percent were suffering from seizures and 6.66 percent were with long faces.

Fifty percent of the subjects are categorized as Mild MR (Table 2), 30 percent are Moderate MR and 20 percent are suffering from severe Mental Retardation.

Out of 30 subjects, 9 showed chromosomal aberrations (30.0%) included 7 (23.3%) structural variations, 2 (6.66%) numerical anomalies (Table 3). Structural variations include Deletions, Inversions, Translocations and Additions. Numerical variations included Down syndrome. Surprisingly no sex chromosomal abnormalities were noticed.

Sex-wise 36.36 percent males (Table 4) and 12.5 percent females were suffering from chromosomal anomalies. Age showed no impact on chromosomal aberrations.

Table 1: Physical findings of sample population

Finding	Sample size	Prevalence (N %)
	30	All are mentally retarded
<i>Weight</i>		
Under weight		20 (66.6%)
Over weight		2 (6.6%)
Normal		8 (26.6%)
Dumb	30	4 (13.33%)
Dermatological disorders	30	3 (10.0%)
Skeletal disorders	30	5 (16.66%)
Microcephaly	30	3 (10.0%)
Seizures	30	2 (6.66%)
Long face	30	2 (6.66%)

Table 2: Degree of MR among the patient groups (n=30)

Abnormality	Age group	Males	Females	Total	%
Mild MR	6-50 yrs	11	4	15	50
Moderate MR	6-50 yrs	7	2	9	30
Severe MR	6-50 yrs	4	2	6	20

Table 3: Different chromosomal anomalies found among the positive subjects in the present study (n=9) (Figs. 1 to 9)

Case No.	Chromosomal abnormality	Sex	Age in years	Clinical status
1	47 XY + 21	Male	8	MILD MR
2	46 XY Del 5(p)	Male	26	MILD MR
3	46 XX inv 9(p12-q13)	Female	30	MILD MR
4	46 XY t(9q; 17q)	Male	50	MILD MR
5	46XY t(15q; 17q)	Male	40	MILD MR
6	46 XY Del (5p)	Male	14	MODERATE MR
7	46 XY add(15q)	Male	12	MILD/SEVERE MR
8	46 XY add(4q)	Male	17	MILD MR
9	46 XY(10) / 47 XY +21(02)	Male	09	MILD MR

Table 4: Influence of age and sex

S. No.	Sex and age	Total cases	No. of abnormal cases	%
1	Female	8	1	12.5
2	Male	22	8	36.36
3	Below 15 years	15	4	26.66
4	Above 15 years	15	5	33.3

Chromosomal study in individuals suspected to be suffering from genetic disorders has been carried out by Kanata (1986 a), Kanata (1986b), Latha (1996), Anderlid et al. (2002), Chethan et

al. (2007), Jeong et al. (2010), Kumar Parvinder et al. (2010), Rajasekhar et al. (2010), Yeshwanth (2010). These workers reported wide variations in the frequencies of chromosomal aberrations in their study. In the present study (Table 5) chromosomal aberrations were detected in 30.3 percent and as such this figure is higher than most of the previous reports except, 56.32 percent as reported by Kumar Parvinder et al. (2010).

Table 5: The percentage of chromosomal abnormalities reported previously by various authors in subjects with MR

S. No.	Investigation	Year	Subjects studied (n)	Subjects with chromosomal anomalies (n)	%
1	Kanata S	1986	56	9	16.1
2	Latha P	1996	100	18	18.0
3	Anderlid et al.	2002	111	10	9.0
4	G K Chetan et al.	2007	100	12	12.0
5	Radhakrishnan Yeshwanth	2010	176	32	18.8
6	Parvinder kumar et al.	2010	161	91	56.32
7	M Rajasekar et al.	2010	1400	343	24.5
8	Seon-Yong Jeong et al.	2010	431	60	13.9
9	Present Study	2010	30	9	33.3

DISCUSSION

Abnormal Physical Features

The physical features of the subjects clearly showed symptoms of mild, moderate and severe Mental Retardation. 66.66 percent are under weight patients. This may be due to malnutrition and the inability of the subject to gulp food. This underweight condition coincides with their low red blood cell count and Hb levels (Oddbjorn Hove (2004).Jaya Kumari and Mythili (2010) worked on weight survey of MR patients and reported that patients with severe MR were more likely to be underweight and people with mild MR were more likely to be stout. Food refusal and self induced vomiting were present among persons who are underweight. Simila and Niskanen (2008) reported that 29.5 percent of the MR subjects of their study were underweight, an obvious consequence of the different feeding and dietary problems connected with their multiple disabilities. Al-Sharbaty Marwan (2003) reported 20 percent of the patients of their study were

underweight. The subjects of the present study are living in a home organized by a social worker. Due to paucity of funds, they are not providing balanced diet to the MR patients.

The incidence of microcephaly is not known in India. Present study reported 10 percent microcephalic cases, with 3.3 percent abnormal karyotypes. This figure is higher than the 9 percent microcephalic cases reported by Kaur et al. (2003). Microcephalic condition in some cases is due to monogenic abnormalities, the others might have been due to injuries during delivery or infections like Rubella during early stage of pregnancy. Cases with apparently normal chromosomal complement may have some monogenic abnormality or complex structural rearrangements that are beyond the detection of G-banded chromosome analysis. Kaur et al. (2008) also reported 3 microcephalic cases with chromosomal aberrations like 2p deletion, 18p deletion and ring chromosomes.

Many reports are available on physical deformities of MR with skeletal disorder, seizures, but dumb cases are not yet reported. The cytogenetic analysis of 3 dumb patients of the present study was also normal.

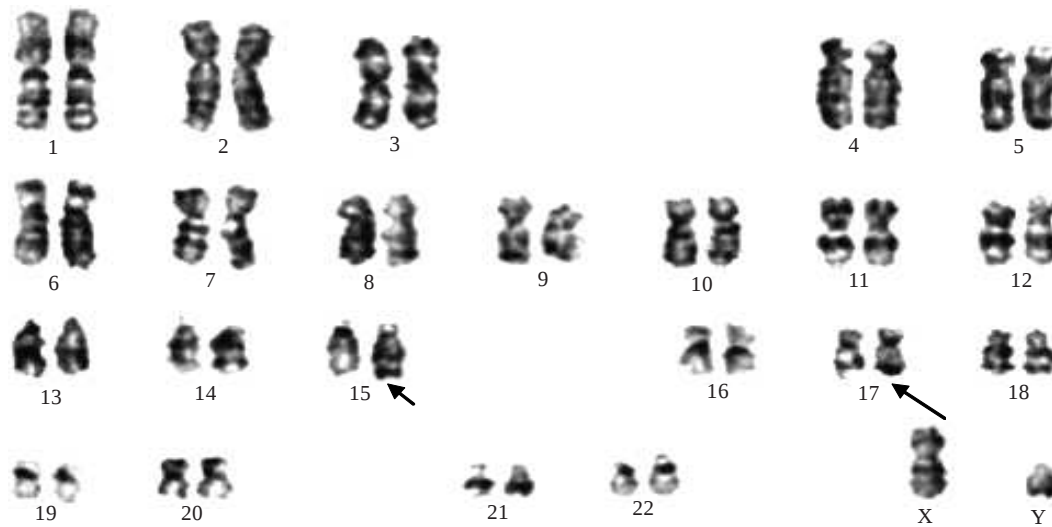
Five patients (16.66%) were suffering from different skeletal disorders like spinal cord deformation, limb deformation. Among this, 2 karyotypes (40%) showed abnormality, one with translocation 46 XY t (15q: 17q) (Fig. 1) and one with addition 46XY (15q) (Fig. 2). Ventroto et al. (2005) reported that balanced reciprocal translocation 2:8(q:32;p:13) leads to multiple skeletal abnormalities. Emanuel Beverly et al. (2010) reported that patients with t8: 22 have some deformation of the fingers. Jung (2007) reported that 46 XY t(3:17) is associated with multiple muscular and skeletal abnormalities.

According to Peng-Cheng-Fang et al. (2008), MR patients are suffering from seizures. Steffenburg Ulf et al. (1996) also reported that 50 percent of the MR children had seizures. But present study reports only 6.6 percent of seizures among MR patients. Among these patients 50 percent showed trisomy for 21 chromosomes (Fig. 3).

Abnormal Karyotypes

Among 30 subjects, 9 showed abnormal karyotypes (30%) among them 6.6% are numerical abnormalities and 23.3 percent are structural abnormalities.

Only 2.6 percent cases related to Down syn-

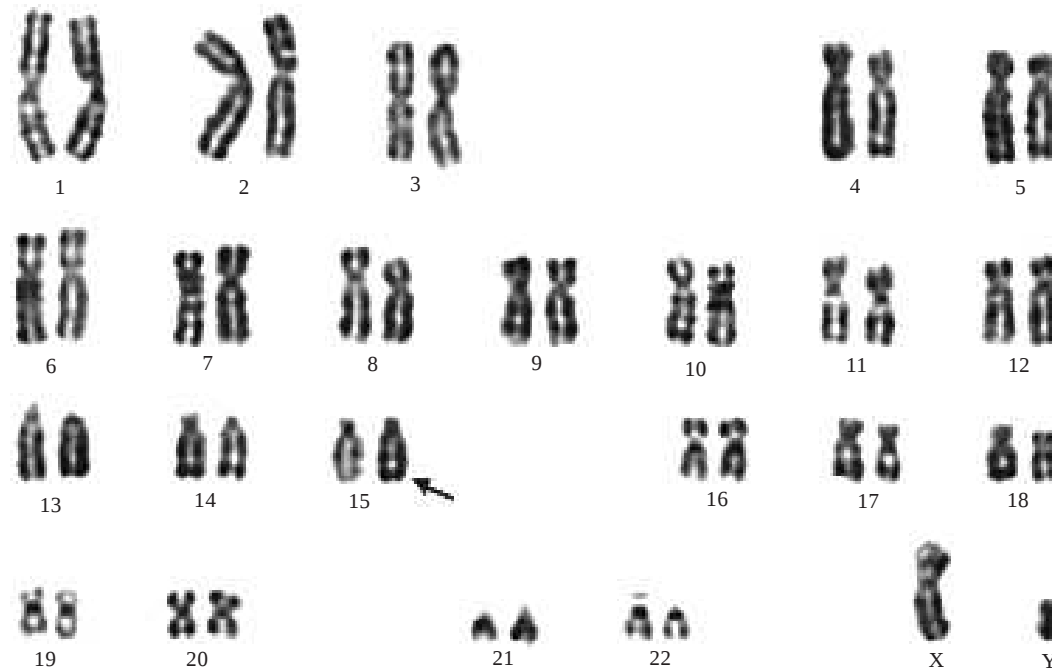
**Fig. 1.**

Karyotype: 46, XY, t(15q; 17q).

IMPRESSION: Presence of t(15q; 17q) in 100% of metaphases.

drome and Down syndrome with mosaicism reported among numerical abnormalities among which one free trisomy was reported (Fig. 3)

and one had a mosaic cell line (80 percent of his cells are normal, the other cells being trisomic for chromosome no.21.) In the cytogenetic analy-

**Fig. 2.**

Karyotype: 46, XY, add(15q).

IMPRESSION: Presence of add(15q).

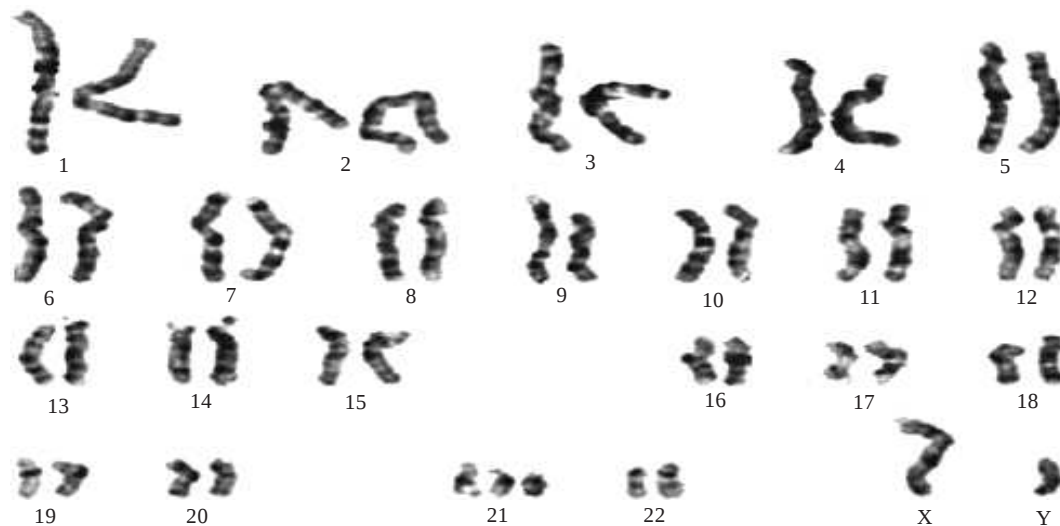


Fig. 3.
Karyotype: 46, XY, +21.
IMPRESSION: Down's syndrome.

sis, out of 40 metaphases counted, 8 metaphases revealed trisomy of chromosome no.21 (Fig. 4). This abnormality is less than 11.3 percent reported by Kaur and Singh (2010), 27 percent

reported by Thomas et al. (1992), 12.09 percent by M.Rajasekhar et al. (2010).

Prevalence of Down syndrome is more in India and many scientists worked on this elabo-



Fig. 4.
Karyotype: 46, XY, [10] / 47, XY, +21[02].
IMPRESSION: Presence of trisomy 21 in 20% of metaphases (Mosaic Down's syndrome).

rately. Hence more statistical data is available on Down syndrome with reference to India. Verma et al. (1998) reported a frequency of 0.81/1000 in Delhi region. Patel et al. (2005) reported incidence of trisomy 21 was 1 in 1200 in Mumbai region.

Rajgam et al. (1977) reported the associated malformation in cytogenetically confirmed Down syndrome patients and among them 5.52 percent are osteoarticular malformation. In the present study, the Down syndrome patients are not suffering from this malformation.

5p deletion is a rare abnormality and the estimated prevalence is about 1 in 50,000 live births. The prevalence among individuals with MR is about 1.5 in 1000. In the present study, among 9 positive subjects, 2 are (22.22%) with 5p deletions (Figs. 5 and 6) and they are males only. Dave Usha and Shetty Dhana lakshmi (2010) were reported 5.2 percent deletions of 7q, 18p, 16q and Xq. Rajasekher et al. (2010) were reported 18.75 percent of deletions in their study with two 5p deletions and one 18q deletions. Chetan et al. (2010) reported 33.33 percent deletions of three 15q and one Xq in their study on Idiopathic MR.

Translocation anomaly is the most common among structural deformities and vast literature

is available on it. The chromosomes involved in translocations reported were t(2;8) translocation by Ventruto et al. (2005), t(3;17) by Jung et al. (2007), t(8;22) by Emanuel Beverly et al. (2010), t(3;10) by Chetan et al. (2010), t(11q;16q), t(12p;17q), t(3q;14q), t(Xq;10q), t(14p;21p) by Dave and Shetty (2010), t(9;22), t(14;7), t(16;22) by Rajasekher et al. (2010). In the present study, translocations are reported at t(9q;17q) (Fig.7) and t(15q;17q) (Fig.7) which are rare translocations. Nampoothiri et al. (2008) claimed that for the first time they have reported a translocation between q arms of chromosome 9 and 17. Lowwage et al. (1987) have reported one case of Philadelphia positive chronic myeloid leukemia which showed a high promyelocytic component associated with a variant t(15q-17q). In our study also patient with 15q-17q is suffering from leukemia as the blood smear showed blast cells. The other case of translocation is with microcephaly.

One female karyotype showed inv 9(p12-q13) (Fig. 8) which is a structural variant that has been found in both normal populations and patients with various abnormal phenotypes and diseases. Babu V Rao et al. (2006) and Balkan et al. (2010) reported high frequency of inv 9(p12-q13) and 9(p13 q13). Rajasekher et al. (2010) reported

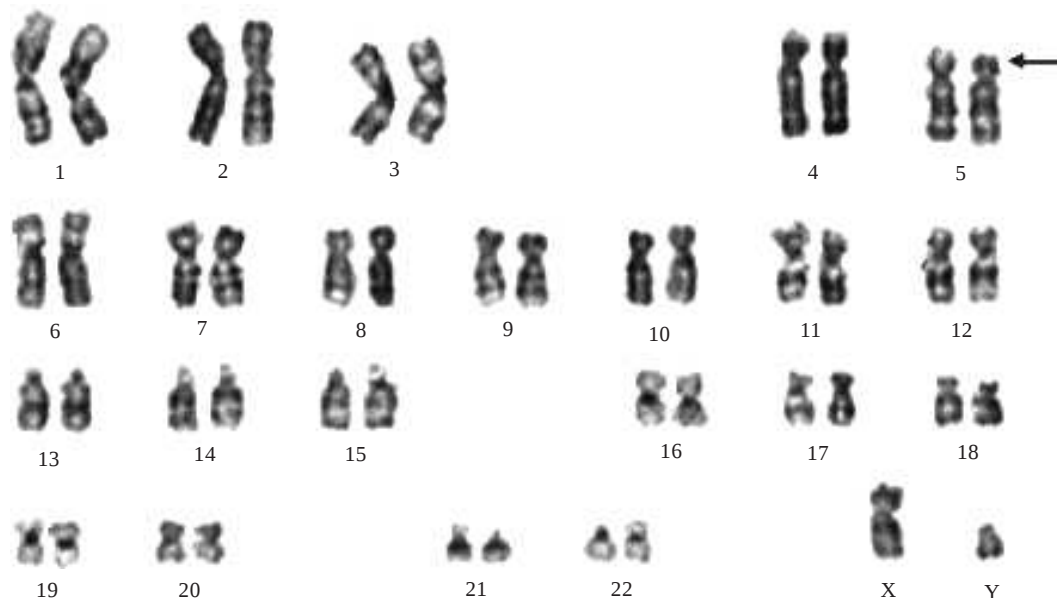
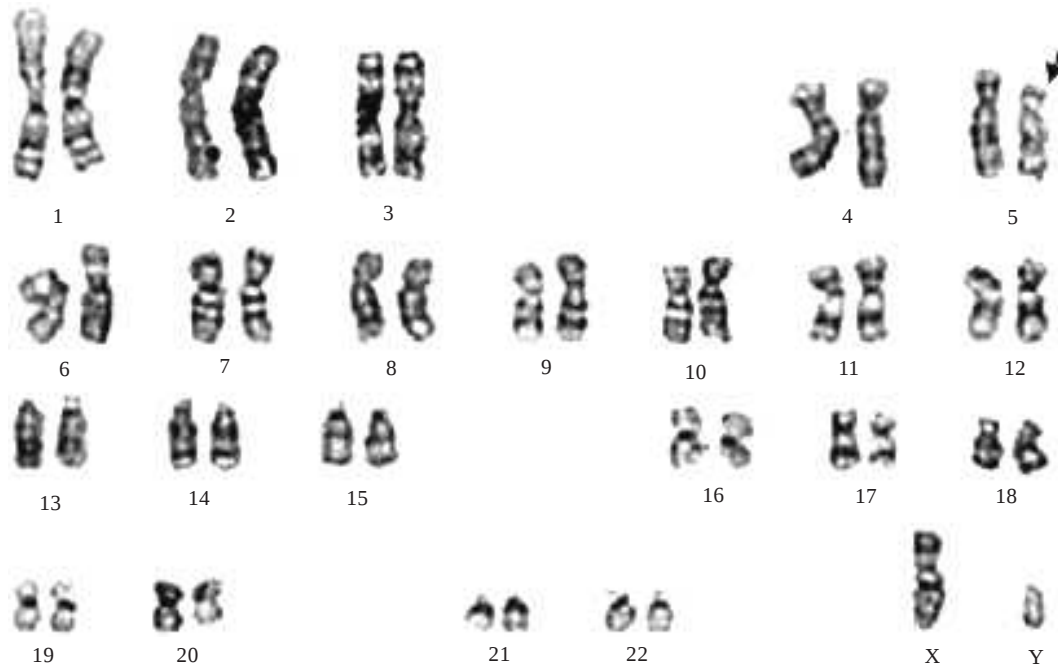


Fig. 5.

Karyotype: 46, XY, del(5p).

IMPRESSION: Presence of del(5p) in 100% metaphases.

**Fig. 6.**

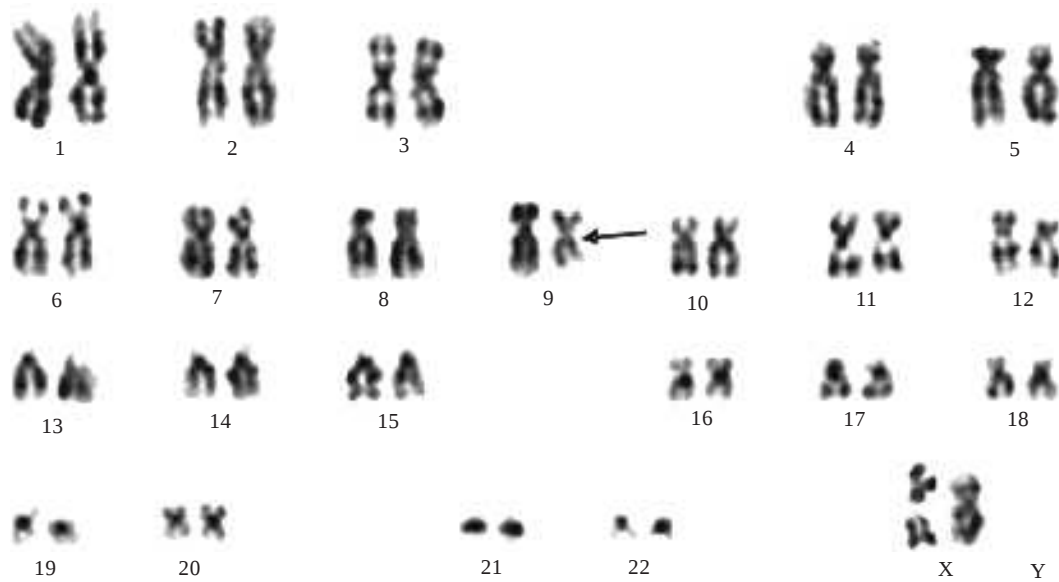
Karyotype: 46, XY, del(5p).

IMPRESSION: Presence of del(5p) in 100% metaphases.

**Fig. 7.**

Karyotype: 46, XY, t(9q; 17q).

IMPRESSION: Presence of t(9q; 17q) in 100% metaphases.

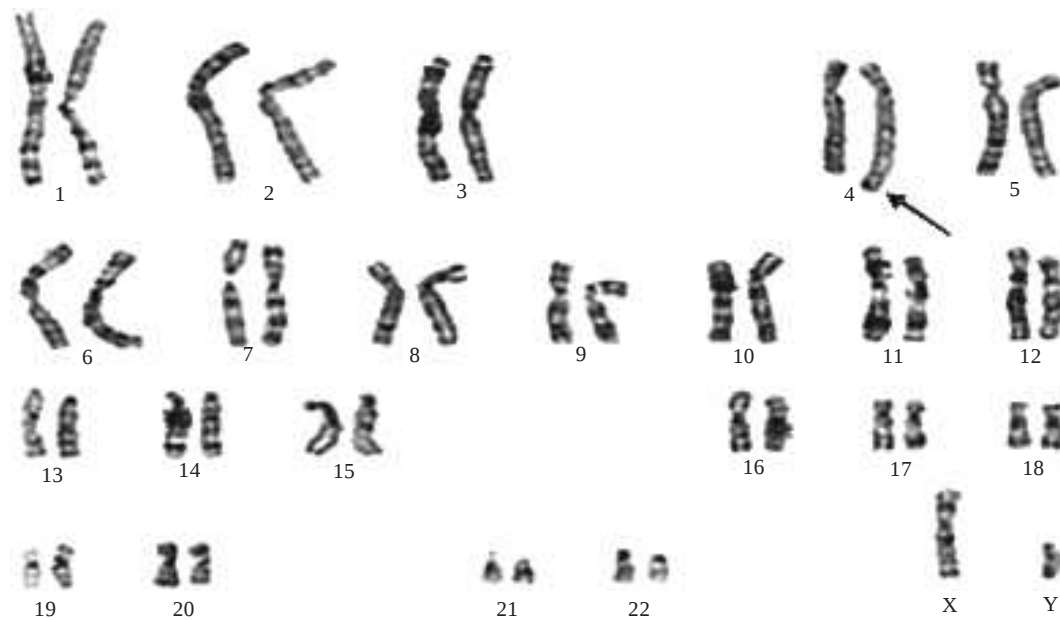
**Fig. 8.**

Karyotype: 46, XY, inv 9(p12-q13).

IMPRESSION: Pericentric inversion of chromosome No.9 is a structural variant that occurs frequently in normal population. It is considered as a normal variant.

inversion of 7 and 8 chromosomes. Dave Usha and Shetty Dhanalaxmi (2010) also reported 7.2

percent of inversions of which 8, 9, 11, 17 and X chromosomes are involved. Jeong (2010) re-

**Fig. 9.**

Karyotype: 46, XY, add(4q).

IMPRESSION: Presence of add(4q).

ported 13.3 percent inversion frequency of 9(p11-q13) with congenital anomalies. Gaber Khaled et al. (2010) for the first time reported phenotypically normal female carrying structural variant on both the chromosome 1 and 9 leading to recurrent miscarriages.

Two cases showed positive 4q and 15q additions (Figs. 9 and 2). Chromosome 4, partial trisomy of distal 4q is a rare disorder in which a portion of the 4th chromosome appears 3 times rather than twice in cells of the body. The common symptom of the disorder is MR, defects of the hand and feet. The patient of the present study had mild MR, long head and skeletal deformity. Patel et al. (2007) also reported clinical features including absence of right thumb and claw like fingers on both hands with duplication of majority of 4q. Rajasekher et al. (2010) reported duplication of 18, 14 chromosomes but Dave Usha and Shetty Dhanalaxmi (2010) reported 4q addition along with 5p,6q,9p,11p, and 16q.

15q addition is an extremely rare chromosomal disorder. A few reports are available on this as Ruggenbuck et al. (2004) reported this abnormality in 3 patients. The patient of the present study showed long upper lip and short neck.

CONCLUSION

1. 33.3 percent of the study population showed chromosomal abnormalities.
2. Males are suffering more in comparison with females.
3. Rare translocations are observed in the positive cases with Leukemic conditions t(9q 17q) and t(15q 17q).
4. Rare 4q, 15q Additions are reported in the positive subjects.

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REFERENCES

- Aggarwal SS, Singh U, Singh PS, Singh SS, Das V, Sharma A 1991. Prevalence and spectrum of congenital malformations in a prospective study at a teaching hospital. *Indian J Med Res*, 94: 413-419.
- Al-Sharbaty Marwan M, Al-Hussaini Ala'Aldin A, Sajjeev X Antony 2003. Profile of child and adolescent psychiatry in Oman. *Saudi Med J*, 24(4): 391-395.
- Anderlid BM, Schoumans J, Anneren G, Sahlen S, Kyllerman M, Vujic M, Hagberg B, Blennow E, Nordenskjold M 2002. Subtelomeric rearrangements detected in patients with idiopathic mental retardation. *Am J Med Genet*, 107(4): 275-284.
- Balkan M, Akbas H, Isi H, Oral D, Turkyılmaz A, Kalkanli S, Simsek S, Fidanboy M, Alp MN, Gedik A, Budak T 2010. Cytogenetic analysis of 4216 patients referred for suspected chromosomal abnormalities in Southeast Turkey. *Genetics and Molecular Research*, 9 (2): 1094-1103.
- Chetan GK, Manjunatha KR, Venkatesh HN, Balu S, Venkataswamy E, Roy S 2010. Cytogenetic studies of idiopathic mental retardation: A report. *Int J Hum Genet*, 10(1-3): 33-39.
- Dave Usha, Shetty Dhanalaxmi 2010. Chromosomal abnormalities in mental retardation: Indian experience. *Int J Hum Gen*, 10(1-3): 21-32.
- Emanuel Beverly S 2010. Researchers Find New Translocation; Weak Spots in DNA Cause Genetic Disease. *American Journal of Human Genetics*, published online July 29.
- Gaber Khaled R, El-Bassouy Hala T, El-Gerzawy Asaad 2010. Pericentric inversion of chromosome 1 and 9 in a case with recurrent miscarriage in Egypt. *Journal of American Science*, 6(8): 154-156.
- Isaac GS, Krishnamurthy PS, Reddy YR, Ahuja YR 1985. Down's syndrome in Hyderabad, India. *Acta Anthropogenet*, 9: 256-260.
- Jain U, Verma IC, Kapoor AK 1998. Prevalence of fragile X (A) syndrome in mentally retarded children at a genetics referral centre in Delhi. *Indian J Med Res*, 108: 12-16.
- Jayakumari V, Mythili K 2010. Haematological Abnormalities in Intellectually Disabled Persons. Paper presented in the International Conference on "Environmental Pollution, Water Conservation and Health" in University of Bangalore, Bangalore, July 29 to 31, 2010.
- Jeong Seon-Yong Kim, Bo-Young Yu, Jae Eun 2010. De novo pericentric inversion of chromosome 9 in congenital anomaly. *Yonsei Medical Journal*, 51(5): 775-780.
- Jacobs PA, Matsuura JS, Mayer M, Newlands IM 1978. A cytogenetic survey of an institution for the mentally retarded: 1. Chromosome abnormalities. *Clin Genet*, 13(1): 37-60.
- Jyothy A, Kumar KS, Rao GN, Rao VB, Swarna M, Devi BU, Sujatha M, Kumari CK 2000. Cytogenetic studies of 1001 Down syndrome cases from Andhra Pradesh, India. *Indian J Med Res*, 111: 133-137.
- Kanata S 1986a. A chromosomal study on 56 cases with heavy mental retardation and behavior disorders. *Proc Japan Acad*, 62B: 165-168.
- Kanata S 1986b. A chromosomal study on 121 cases with heavy mental retardation. *Proc Japan Acad*, 62B: 314-316.
- Kaur A, Mahajan S, Singh JR 2003. Cytogenetic investigations in mentally retarded individuals. *Int J Hum Genet*, 3: 13-16.
- Kaur A, Singh JR 2010. Chromosomal abnormalities: Genetic disease burden in India. *Int J Hum Genet*, 10(1-3): 1-14.
- Kaur A, Dhillon S, Garg PD, Singh JR 2008. Ring chromosome 7: In an Indian Woman. *J Intellect Dev Disabil*, 33(1): 87-94.
- Kondo, Hamaguchi H, Nakajima S, Haneda T 1980. A cytogenetic survey of 449 Patients in a Japanese Insti-

- tution for the mentally retarded. *Clin Genet*, 17: 177-182.
- Kumar Parvinder, Gupta Ashma, Fotra Roopali, Upma, Raina Sunil, Sethi Surbhi, Raina TR, Gupta Subash 2010. Chromosomal anomalies in referred cases with suspected genetic disorders: First Report from Jammu and Kashmir. *Int J Hum Genet*, 10(1-3): 41-47.
- Kumar V, Singh A J, Marwaha RK 1994. An epidemiological study of congenital malformations in rural children. *Indian Pediatr*, 31: 909-914.
- Latha P 1996. *Cytogenetics of Autosomal Fragile Sites: Association and Their Implications in Subjects with Mental Retardation*. Ph. D Thesis, Bangalore: NIM-HANS.
- Lowwaige AC, Mecucci C, Criel A, Vanhoof A, Van Den Berghe H 1987. Variant translocation t (15q:17q) accompanying a Premyelocytic accelerate phase of Rh-Positive Chronic myeloid Leukemia. *Cancer Genetics and Cytogenetics*, 28(2): 349-35.
- Madon Prochi F, Athalye Arundhati S, Sanghavi Kunal, PaInt Firuza R 2010. Microdeletion syndromes detected by FISH -73 Positive from 374 cases. *Int J Hum Genet*, 10(1-3): 15-20.
- Mishra PC, Baveja R 1989. Congenital malformations in the newborn: A prospective study. *Indian Pediatr*, 26: 32-35.
- Modi UJ, Nayak U, Aiyer S, Bharani S, Master DC, ShahT, Anerao M 1998. Study of malformations and Down syndrome in India (SOMDI): Baroda region. *Indian J Hum Genet*, 4: 93-98.
- Moghe M, Patel ZM, Peter JJ, Amfani LM 1981. Cytogenetic studies in a selected group of mentally retarded children. *Hum Genet*, 58: 184-7.
- Nampoorthiri S, Lakshman LR, Anilkumar A, Thampi M 2008. Partial trisomy 9q due to maternal 9q and 17q translocation. *Indian Pediatric*, 45(7): 595-8.
- Oddbjørn Hove 2004. Weight survey on adult persons with mental retardation living in the community *Research in Developmental Disabilities*, 25(1): 9-17.
- On Jung, Jung-Hyun Lee, Chung-Sik chun 2007. Sprengel's deformity associated with a de novo balanced translocation involving chromosome 3 and 17. *Korean Journal of Pediatrics*, 50(3): 311-314.
- Patel VM, Raghuveer TS, Persons DL, Myers SA 2007. Trisomy 4q Syndrome: A rare syndrome phenotypically similar to trisomy 18. *The Internet Journal of Pediatrics and Neonatology*, 7(2): 1-6.
- Patel ZM, Adhia RA 2005. Birth defects surveillance study. *Indian J Pediatric*, 72: 489-491.
- Peng-Cheng Fang, Yung-Jung Chen, Inn-Chi Lee 2008. Seizure precipitants in children with intractable epilepsy. *Brain and Development*, 30: 527-532.
- Radhakrishnan Yashwanth, Nallathambi Chandra, Gopinath PM 2010. Chromosomal abnormalities among children with congenital malformations. *Int J Hum Genet*, 10(1-3): 57-63.
- Rajasekhar M, Murugesan R, Rekharao, Shetty H, Jyothirao, Gopinath PM, Satyamoorthy K 2010. Cytogenetic analysis of 1400 referral cases: Manipal experience. *Int J Hum Genet*, 10(1-3): 49-55.
- Rajgam S, Hegde S, Thomas IM 1997. Down syndrome associated malformations. *Indian J Med Sci*, 51: 390-393.
- Rao Babu V, Kerketta Lily, Korgaonkar Seema, Ghosh Kanjaksha 2006. Pericentric inversion of chromosome 9[inv(9)(p12q13)]: Its association with genetic diseases. *Indian Journal of Human Genetics*, 12(3): 129-132.
- Simila S, Niskanen P 2008 Underweight and overweight cases among the mentally retarded. *Journal of Intellectual Disability Research*, Article first published online: 28 June.
- Speed RM, Johnson AW, Evans HS 1976. Chromosome survey of population of mentally subnormal in North-East of Scotland. *J Med Genet*, 13: 295-306.
- Steffenburg Ulf, Hagberg Gudrun, Kyllerman Marten 1996. Characteristics of seizures in a population-based series of mentally retarded children with active epilepsy. *Epilepsia*, 37(9): 850-856.
- Sutherland GR, Murch AR, Gardina AJ, Carter RF, Wiseman C 1976. Cytogenetic survey of a hospital for the mentally retarded. *Hum Genet*, 34(3): 231-245.
- Thomas IM, Rajangam S, Hegde S 1992. Cytogenetic investigations in Down syndrome patients and their parents. *Ind J Med Res*, 96: 366-371.
- Verma IC, Anand NK, Kabra M, Menon PSN, Sharma N1998. Study of malformations and Down syndrome in India (SOMDI): Delhi Region. *Indian J Hum Genet*, 4: 84-87.
- Ventruto V, Pisciotto R, Renda S, Festa B, Maria Michela Rinaldi, Stabil M, Maria Luigia Cavaliere, Esposito M, Opitz John M 2005. Multiple skeletal familial abnormalities associated with balanced reciprocal translocation 2;8(q32;p13) *Am J Med Genet*, 16(4): 589-594. Article first published online: 2 June.