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RESEARCH ARTICLE

INCIDENCE OF DOWN SYNDROME IN MENTALLY RETARDED PEOPLE OF NORTH COASTAL ANDHRA PRADESH

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ABSTRACT

Background: Mental Retardation (MR) (also called mental handicap) is a term for a pattern of persistently slow learning of basic motor and language skills ("milestones") during childhood, and a significantly below normal global intellectual capacity as an adult. Down syndrome is the most first and common genetic cause of mental retardation. The aim of the present study was to estimate the frequency of Down syndrome in mentally retarded people of North Coastal Andhra Pradesh.

Methods: This study was carried out an approximately on 100 mentally retarded children from North Coastal Andhra Pradesh and a control group consists of 100 normal individuals of same age group. The blood sample was collected from mentally retarded children and controls for the evaluation of the chromosomal abnormalities. The karyotype of all mentally retarded cases were assessed by conventional cytogenetic techniques (GTG –banding).

Results: Out of 100 mentally retarded people analyzed, 88 (88%) had normal karyotype and remaining 12 (12%) were Down syndrome. Among them regular free trisomy constituted 8 (8%) cases, Robertsonian translocations in 2(2%) cases and mosaicism was recorded in 2 (2%) cases.

Conclusions: The study confirmed the findings of earlier studies carried out in India and other countries. It emphasizes free trisomy 21 was found to be the most frequent autosomal aberration of Down syndrome when compared with Robertsonian translocations and mosaics.

INTRODUCTION

Mental retardation (MR) is the manifestation of brain dysfunction that originates during developmental period, resulting in the limitation of two or more adaptive skills, that is, communication, self care, home living, social skills, self direction, health, safety, leisure and work (Medicine net.com 2011). Mental retardation results as a defect in the structure and function of neuronal synapse (Chechlacz *et al.,* 2003). The incidence of mental retardation (IQ<70) is found to be 2-3% worldwide (Lewis, 2007). Its incidence in developing countries is about 2-3 times more as compared to developed countries. Males are found to be more affected than females. The risk of mental retardation is found to be higher in children with congenital structural defects (Decoufle *et al*., 2001). The cause of mental retardation may be genetic (30%) or environmental, congenital (for example, fetal exposure to teratogenic agents, chromosome disorders), or acquired (for example, central nervous system infection, head trauma). Chromosomal aberrations account for 15% of mentally retarded individuals (Mulley *et al.,* 1992). Monosomies and trisomies are reported to be more frequent than tetrasomies, pentasomies, double aneuploids, polyploidy, etc., whereas subtelomeric rearrangements account for 5% of mental retardation /malformation syndrome (Archer *et al.,* 2005). Several types of structural aberrations are also known to cause mental retardation, the common ones being deletion, duplication, inversion, translocation and isochromosome formation (Flint *et al.*, 1995; Walter *et al.,* 2004; Holinski-Feder *et al.,* 2007). Down syndrome (DS) or trisomy 21, with its characteristic clinical features is the most frequently observed autosomal aneuploidy with an incidence of about 1 in 700 live births. The prevalence of DS in India is 0.88 per 1000 (1 out of 1139) to 1.09 per 1000 (1 out of 916) and three DS children are reported to be born every hour (Rajangam and Thomas, 1992; Verma, 2000; Malini and Ramachandra, 2006). In general, over 95% of Down syndrome individuals possess free trisomy 21 resulting from non-disjunctional error of chromosome 21 during gametogenesis in one of the parents. While about 2-4% result from a translocation of chromosome 21 on to a D or G group chromosome, 1-2% are mosaics showing a normal cell line additionally, due to mosaicism (Nussbaum *et al.,* 2001).

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MATERIALS AND METHODS

This study was carried out an approximately on 100 mentally retarded children from North Coastal Andhra Pradesh and a

control group consists of 100 normal individuals of same age group. The blood sample was collected from mentally retarded children and controls for the evaluation of the chromosomal abnormalities. The cerotype of all mentally retarded cases were assessed by conventional cytogenetic analysis.

Culture technique: Obtain 5-7 ml of venous blood mix with heparin. Prepare a culture tube with 8 ml of Tc 199 medium, 2 ml of fetal calf serum, 0.2 ml of phytohemagglutinin, 0.5 ml of whole blood for micro culture. For macro culture centrifuges the blood and add buffy layer. Incubate for 72 hours at 37°c. Add few drops of colchicine 2 hours prior to harvesting the cells. Centrifuge for 10min at 800-1000 r.p.m. Remove the supernatant fluid. Resuspend cells in 5 ml hypotonic solution. Leave for 15-20 min at 37^{O}c. Centrifuge for 10min at 800-1000 r.p.m. Remove supernatant fluid. Resuspend cells in 0.5 ml of resting fluid. Add fixative carefully leave for 10-15 min. Centrifuge for 10 min at 800-1000 r.p.m. Remove supernatant fluid then add fresh fixative. Keep in refrigerator for 1-2 hours. Centrifuge for 10 min at 800-1000 r.p.m. Remove supernatant fluid then add enough fixative to obtain a cell suspension adequate for preparation of slides. Stain the slides with Giemsa, mount with DPX and screen for good metaphases.

GTG Banding: Prepare solutions A and B.

- A solution: 0.9078 gms of KH_2PO_4 (Potassium dihydrogen orthophosphate) for 100 ml of distilled water.
- B solution: 1.1876 gms of $Na_2H\ PO_4$ (Disodium hydrogen orthophosphate) for 100 ml of distilled water. Take 25 ml of solution A and 25 ml of solution B in a jar, add 0.01 gms of Trypsin to the solution and mix it thoroughly. Give 3 dips for the slide. Stain the slides with Giemsa, mount with DPX and then screen for good banded metaphases.

RESULTS

100 MR cases and 100 cases of age and sex matched healthy controls were included in the present study. Age and sex wise distribution of MR and controls were represented in Table 1.Highest number of MR males (45) females (25) and highest number of control males (53) females (21) were present in 11-20 years age group category. Lowest number of MR and control males and females were present in both 31-40 and 41-50 age groups respectively. The karyotype could be determined in 100 mentally retarded cases subjected to chromosomal analysis.

Table 1. Age and Sex wise distribution of MR and controls

S.No	Age group (yrs)	MR				Controls			
		M	F	T	%	M	F	T	%
1	0-10	4	12	16	16	5	13	18	18
2	11-20	44	25	69	69	53	21	74	74
3	21-30	5	5	10	10	4	2	6	6
4	31-40	2	-	2	2	1	-	1	1
5	41-50	-	3	3	3	-	1	1	1
Total number of samples		55	45	100		63	37	100	

Table 2. Chromosomal abnormalities of MR patients

Without chromosomal abnormalities	With chromosomal abnormalities		
	Trisomy	Robertsonian translocation	Mosaicism
88	8	2	2

Table 3. The percentage of chromosomal abnormalities reported previously by various authors in MR patients

S.No.	Investigation	Year	Subjects studied(n)	Subjects with chromosomal anomalies	%
1.	Steve *et al*.,	1976	2134	455	21.32
2.	Kanata	1986	56	9	16.1
3.	Latha	1996	100	18	18.0
4.	Anderlid *et al*.,	2002	111	10	9.0
5.	Anupam Kaur *et al*.,	2003	143	92	64.3
6.	Chetan *et al*.,	2007	100	12	12.0
7.	Frenny Sheth et al.,	2007	382	324	84.8
8.	Parvinder kumar	2010	161	91	56.32
9.	Rajasekar *et al*.,	2010	1400	343	24.5
10.	Seon-Yong Jeong *et al*.,	2010	431	60	13.9
11.	Mythili *et al*.,	2010	30	9	33.3
12.	Chandra *et al*.,	2010	1102	924	83.82
13.	Jayalakshamma	2010	874	759	86.84
14.	Joice Biselli *et al*.,	2010	387	357	92.2
15.	Jaouad *et al*.,	2010	852	820	96.24
16.	Usha Dave *et al*.,	2010	1760	555	31.53
17.	Surbhi Mahajan *et al*.,	2011	183	32	17.4
18.	Nasiri *et al*.,	2013	865	205	23.6
19.	Jami Sagar Prusti *et al*.,	2014	50	39	78
20.	Present study	2015	100	12	12

Fig.1 Normal Metaphase

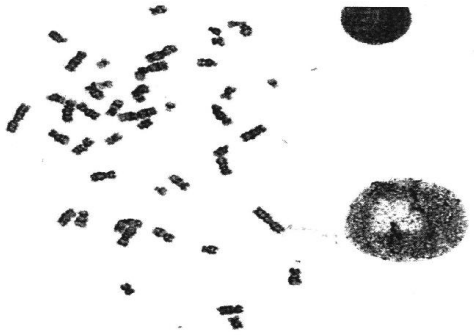


Fig.1 Normal Karytype

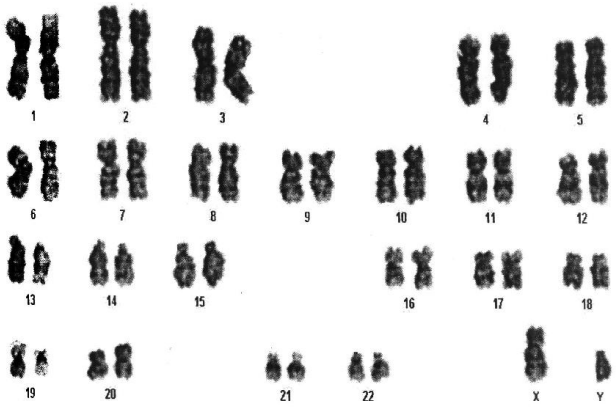


Fig.2 Trisomy 21 Metaphase

Fig.2 Trisomy 21 Karyotype

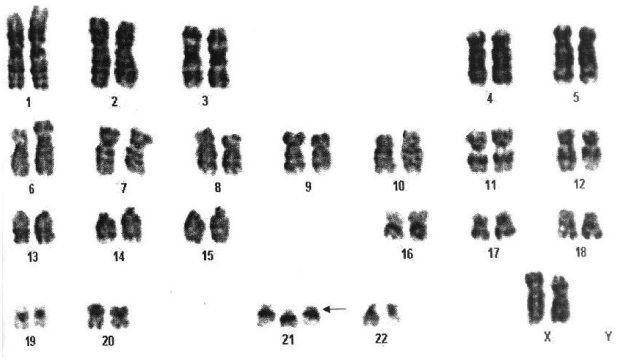


Table 2 represents the chromosomal abnormalities of the MR patients. According to the results of karyotype, out of 100 mentally retarded patients 88 patients presented normal karyotype (Fig. 1). The predominant chromosomal abnormality was trisomy 21in 8 cases (Fig. 2) followed by Robertsonian Translocation (Fig. 3) and Mosaicism in 2 cases each.

Fig.3 Robertsonian translocation Metaphase

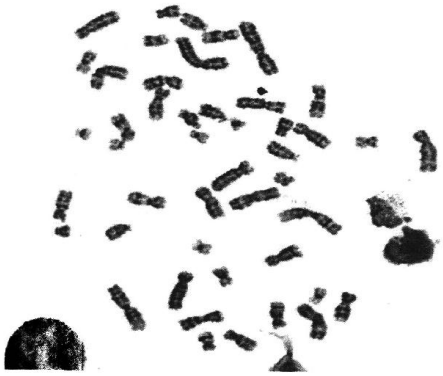
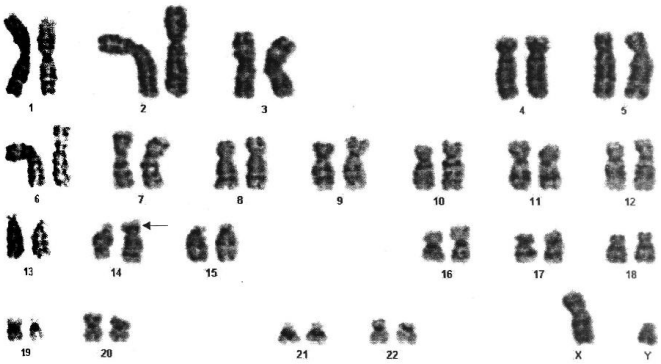


Fig.3 Robertsonian translocation Karyotype



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 were available on mentally retarded patients at global level. Table 3 represents chromosomal abnormalities reported by various authors in MR patients. Chromosomal abnormalities of individuals suffering from genetic disorders from mentally retarded patients has been carried out by Steve,1976; Kanata,1986; Latha, 1996; Anderlid *et al*., 2002; Anupam Kaur *et al*., 2003; Chetan *et al*., 2007; Frenny Sheth *et al.,* 2007; Parvinder kumar, 2010; Rajasekar *et al*., 2010; Seon-Yong Jeong *et al.,* 2010; Mythili *et al*., 2010; Chandra *et al*., 2010; Jayalakshamma, 2010; Joice Biselli *et al.,* 2010; Jaouad *et al*., 2010; Usha Dave *et al*., 2010; Surbhi Mahajan *et al.,* 2011; Nasiri *et al.,* 2013; Jami Sagar Prusti *et al*., 2014; Present study, 2015.

DISCUSSION

Since genetic causes attributes to about half of the known aetiologies, it is generally believed that about 50% of all mental retardation cases have a genetic origin (Curry *et al.,* 1997; Stevenson *et al*., 2003; Winnepenninckx *et al*., 2003). Trisomy 21 or Down syndrome is a common birth defect and is the most frequent and most recognizable form of mental retardation. A maternal meiotic nondisjunction occurs in approximately 90% cases of Down syndrome, which correlates with the most frequent cytogenetic variant being Trisomy 21.Another

mechanism for this aneuploidy is that one of the parents, especially the mother, exhibits mosaicism. The most common translocation in Down syndrome is rob (14; 21), followed by rob (21; 21) or I (21q) (Mutton *et al*., 1996; Sheth *et al*., 2007). With reference to Andhra Pradesh, very little information is available 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 Andhra Pradesh. Mythili and Jaya Kumari, 2011 conducted cytogenetic work on 100 MR patients in the Behara Mano Vikasa Kendram of Srikakulam, Andhra Pradesh.

The present study has been undertaken with an intent to determine the frequency and types of chromosomal abnormalities in mentally retarded patients of Visakhapatnam district of Andhra Pradesh. Furthermore, this type of study from Visakhapatnam has not been reported. However, the number of individuals investigated was not sufficient to permit statistical analysis. According to literature, Down syndrome is a consequence of free tisomy of chromosome 21 in about 95% of cases, translocation in 3-4% and mosaics in 1% (Newberger, 2000).In the present study 100 mentally retarded individuals were cytogenetically analysed. Chromosomal anomalies were seen in 12% cases. Out of 12% cases, 8% were pure 21 trisomies, robertsonian translocations and mosaics occurred in 2% each. Publications on cytogenetic studies of patients with Down syndrome have shown differences in the frequencies of the Chromosomal abnormalities. In the present study, Chromosomal aberrations were detected in 12% of MR patients. The frequency of Chromosomal anomalies were higher than that found by Dereymaeker *et al.,* 1988 (13.3%); Fryns *et al*., 1986 (15.03%); a Fryns *et al*., 1990 (17.6%), Gustavson *et al*., 1977(32%); Laxova *et al*., 1977 (32.2%). The differences in the frequencies of chromosomal abnormalities among these studies are probably due to variations in the criteria for inclusion of patients and the cytogenetic methodology applied.

In the present study, among the three cytogenetic types of Down syndrome the occurrence of trisomy 21 in 8% cases, Robertsonian translocations in 2% and mosaics in 2%.The frequencies of trisomy 21, Robertsonian translocations and mosaics of the present study were lower than the other studies of Astete *et al.,*1991;Thomas *et al.,* 1992; Jyothy *et al.,* 2000; Biselli *et al*., 2000; Kava *et al*., 2004; Sheth *et al*., 2007; Jayalakshamma *et al*., 2010; Chandra *et al*.,2010; Jami Sagar *et al.,* 2014. In the study of Anupam Kaur *et al.,* 2003 the trisomy 21 frequency is more but translocation frequency is similar with the present study. In Staples *et al.,* 1991 study, the frequency of mosaics is equal to the present study unlike the trisomy 21 and Robertsonian translocation. The studies of Delvin *et al.,* 2004 and Azman *et al.,* 2007 shows lower Robertsonian translocation frequencies and higher frequencies of trisomy 21 and mosaics when compared with the present study. Because the prevalence of mosaicism was higher than that reported in the literature, it should emphasize the importance of appropriate studies in individuals with few Down syndrome traits or with intellectual disabilities of unknown origin. The differences between various studies may be because of the sample and methodology.

The studies of Mutton *et al.,*1996; Mokhtar *et al*.,2003 ; Jaouad *et al.,* 2010 shows lower mosaic frequencies when compared with the present study where as the frequencies of trisomy 21 and Robertsonian translocations were more. In India, early marriage and early reproductive life are customary, because of which the occurrence of trisomy 21 associated to older maternal age may be decreased. In conclusion, the cytogenetic pattern of Down syndrome is variable among different studies. Free trisomy of chromosome 21, resulting from a chromosomal nondisjunction is the most frequent cause. All cases with a clinical diagnosis of Down syndrome should be referred to a genetic counseling service.

Conclusions

The present study suggests the importance of not only estimating the prevalence but also for evaluating the chromosomal abnormalities of MR patients of North Coastal Andhra Pradesh. The data indicates the 12% of the chromosomal abnormalities occurred in MR patients whereas controls were having normal karyotype. In conclusion, chromosomal abnormalities are an important cause of MR emphasizing the need for cytogenetic evaluation. However, few cases with a clinical suspicion of certain syndromes exhibiting normal karyotype. Molecular studies could have thrown light on the precise genetic constitution of those patients.

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REFERENCES

Anderlid, B.M, Schoumans, J, Anneren, G, Sahlen, S, Kyllerman, M, Vujic, M, Hagberg, B, Blennow, E, Anupam Kaur, Surbhi Mahajan, and Jai Rup Singh. 2003. Cytogenetic Profile of Individuals with Mental Retardation © Kamla-Raj *Int J Hum Genet*., 3(1): 13-16.

Anupam Kaur, Surbhi Mahajan and Jai Rup Singh. Cytogenetic Profile of Individuals with Mental Retardation © Kamla-Raj 2003 *Int J Hum Genet*, 3(1): 13-16.

Anupam Kaur, Surbhi Mahajan and Jai Rup Singh.2003. Cytogenetic Profile of Individuals with Mental Retardation © Kamla-Raj *Int J Hum Genet*, 3(1): 13-16.

Archer, HL, Gupta, S, Enoch, S, Thompson, P, Rowbottom, A, Chua, I. 2005. Distinct phenotype associated with a cryptic subtelomeric deletion of 19p13.3-pter. *Am J Med Genet.*, 136(1): 38-44.

Astete, C, Youlton, R, Castillo, S, Be, C, Daher, V.1997. Analisis clínicoy citogenético en 257 casos de syndrome de Down. *Rev Chil Pediatr.,*62: 99-102.

Azman, B,Z, Ankathil, R, Siti Mariam, I, Suhaida, M.A, Norhashimah, M. and Tarmizi, A.B, *et al*.2007. Cytogenetic and clinical profi le of Down syndrome in Northeast Malaysia. *Singapore Med J*;48:550-554.

Chandra, N, Cyril, C, Lakshminarayana, P, Nallasivam, P, Ramesh, A, Gopinath, P.M, *et al*. 2010. Cytogenetic

evaluation of Down syndrome: a review of 1020 referral cases. *Int J Hum Genet*, 10:87-93.

Chandra, N, Cyril, C, Lakshminarayana, P, Nallasivam, P, Ramesh, A, Gopinath, P. M, *et al*.,2010. Cytogenetic evaluation of Down syndrome: a review of 1020 referral cases. *Int J Hum Genet*.,10:87-93.

Chechlacz M, Gleeson JG 2003. Is mental retardation adefect of synapse of str Lewis RA. 2007.Columbia University Pediatric Faculty Practice. New York, Review provided by Vermid.From <http://www.nlm.nih.gov/medlineplus/ency/article/001523.htm> (Retrieved November 12, 2007).

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.

Curry CJ, Stevenson RE, Aughton D, Byrne J, Carey JC, Cassidy S, Cunniff C, Graham Jr JM, Jones MC,

Curry CJ, Stevenson RE, Aughton D, Byrne J, Carey JC, Cassidy S, Cunniff C, Graham Jr JM, Jones MC, Kaback MM, Moeschler J, Schaefer GB, Schwartz S, Tarleton J, Opitz J of the American College of Medical Genetics 1997. Evaluation of mental retardation: Recommendations of a consensus conference. *Am J Med Genet*., 72: 468-477.

Dave Usha, Shetty Dhanlaxmi. 2010. Chromosomal abnormalities in mental retardation: Indian experience. *Int J Hum Gen.*, 10(1-3): 21-32.

Decoufle P, Boyle CA, Paulozzi LJ, Lary JM. 2001. Increased risk for developmental disabilities in children who have major birth defects: A populationbased study. Pediatrics., 108(3): 728-734.

Dereymaeker, A.M., Fryns, J.P., Haegeman, J., Deroover, J. and Van Den Berghe, H. 1988. A genetic-diagnostic survey in an institutionalized population of 158 mentally retarded patients. The Viaene experience. *Clin. Genet*., 34: 126-134.

Devlin L, Morrison PJ.2004. Accuracy of the clinical diagnosis of the Down syndrome. *Ulster Med J* ;73:4-12.

Flint, J., Wilkie, A.O.M., Buckle, V.J., Winter, R.B., Holland, A.J., and McDermid, H.E.1995. The detection of subtelomeric chromosomal rearrangements in idiopathic mental retardation. *Nat Genet*., 9:132- 139.

Fryns, J.P., Kleczkowska, A., Dereymaker, A., Hoefnagels, M., Heremans, G., Marien, J. and Van Den Berghe, H. 1986. A genetic diagnostic survey in an institutionalized population of 173 severe mentally retarded patients. *Clin. Genet*., 30: 315-323.

Fryns, J.P., Volcke, P.H., Haspeslagh, M., Beusen, L. and Van Der Berghe, H. 1990. A genetic survey in an institutionalized population of 262 moderately mentally retarded patients: the Borgerstein experience. *J. Ment. Defic. Res.*,34: 29-40.

Gustavson, K.H., Hagberg, G. and Sars, K. 1977. Severe mental retardation in a Sweedish county. Epidemiology, gestational age, birth weight and associated CNS handicaps in children born 1959-70. *Acta Paediatr*. Scand.,66: 373-379.

Holinski-Feder E, Reyniers E, Uhrig S, Golla A, Wauters J, Kroisel P 2000. Familial mental retardation syndrome ATR-16 due to an inherited cryptic subtelomeric translocationt (3;16) (q29;p13.3). *Am J Hum Genet*, 66: 16-25.

Jami Sagar Prusti, Sitansu K. Panda, Santosh K. Sahu, Dharma N. Mishra, Geetanjali Arora, Mahesh C. Sahu. 2014. Incidence of Down s syndrome with Chromosomal pattern in the Eastern *India.Journal of Evolution of Medical and Dental Sciences.*,3;8185-8196.

Jaouad IC, Cherkaoui Deqaqi S, Snatiq A, Elkerch F, Sefiani A. 2010.Cytogenetic and epidemiological profiles of Down syndrome in a Moroccan population: a report of 852 cases. *Singapore Med J*., Feb; 51(2):133-6.

Jayalakshamma, Mary Margaret, S Amudha, Preetha Tilak, Rema Devi and Sayee.Rajangam.2010.Cytogenetic Analysis in Down syndrome. *Int J Hum Genet*, 10(1-3): 95-99.

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.

Joice Biselli, Eny Goloni-Bertollo, Mariângela Ruiz and Érika Pavarino-Bertelli.2010**.** Cytogenetic profile of Down syndrome cases seen by a general genetics outpatient service in Brazil, doi:10.3104**.**

Jyothy A, Kumar KS, Rao GN, Rao VB, Swarna M, Devi BU, 2000. Cytogenetic studies of 1001 Down syndrome cases from Andhra Pradesh, India. *Indian J Med Res*.,111:133-137.

Jyothy A, Kumar KS, Rao GN, Rao VB, Swarna M, Devi BU.2000. Cytogenetic studies of 1001 Down syndrome cases from Andhra Pradesh, India. *Indian J Med Res*., 111:133-137.

Kaback MM, Moeschler J, Schaefer GB, Schwartz S, Tarleton J, Opitz J of the American College of Medical Genetics 1997. Evaluation of mental retardation: Recommendations of a consensus conference. *Am J Med Genet*., 72:468-477.

Kanata S .1986b. A chromosomal study on 121 cases with heavy mental retardation. *Proc Japan Acad.,* 62B: 314-316.

Kava MP, Tullu MS, Muranjan MN and Girisha KM. 2004.Down syndrome: clinical profile from India. *Archives of Medical Research*. 35: 31-35.

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.

Latha P. 1996. *Cytogenetics of Autosomal Fragile Sites: Association and Their Implications in Subjects with Mental Retardation*. Ph. D Thesis, Bangalore: NIMHANS.

Laxova, R., Ridler, M.A.C. and Bower-Bravery, M. 1977. An etiological survey of the severely retarded Hertfordshire children who were born between January 1, 1965 and December 31, 1967. *Am. J. Med. Genet*., 1: 75-86.

Malini SS, Ramachandra NB. 2006. Influence of advanced age of maternal grandmothers on Down syndrome. *BMC Med Genet.*, 147: 4.

Mokhtar MM, Abd el-Aziz AM, Nazmy NA, Mahrous HS.2003. Cytogenetic profile of Down syndrome in Alexandria, Egypt. *East Mediterr Health J.,* 2;9:37-44.

Mulley JC, Kerr B, Stevenson R, Lubs H. 1992. Nomenclature guidelines for X-linked mental retardation. *Am J Med Genet*, 43: 83-89.

Mutton D, Alberman E, Hook EB. Cytogenetic and epidemiological findings in Down syndrome, England and Wales 1989 to 1993.1996. National Down Syndrome

Cytogenetic Register and the Association of Clinical Cytogeneticists. *J Med Genet* ;33:387-394

Mutton D, Alberman E, Hook EB. Cytogenetic and epidemiological findings in Down syndrome, England and Wales 1989 to 1993.1996. National Down Syndrome Cytogenetic Register and the Association of Clinical Cytogeneticists. *J Med Genet*., 33:387-394.

Mythili K. and V. Jaya Kumari.2011.Cytogenetic Analysis of Mentally Retarded Patients in Srikakulam, *Int J Hum Genet*., 11(3): 183-192.

Nasiri F., F Mahjoubi, F Manouchehry,F Razazian, F Mortezapour, and M Rahnama.2012. Cytogenetic Findings in Mentally Retarded Iranian Patients. *Balkan J Med Genet.*, 15(2): 29–34.

Newberger DS. 2000.Down Syndrome: Prenatal Risk Assessment and Diagnosis. American Family Physician., 62: 825-832, 837-838.

Nordenskjold M. 2002. Subtelomeric rearrangements detected in patientswith idiopathic mental retardation. *Am J Med Genet.*,107(4): 275-284

Nussbaum RL, McInnes RR, Willard HF .2001. *Thompson and Thompson Genetics in Medicine.* Philadelphia: WB Saunders Company

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.

Sheth F, Rao S, Desai M, Vin J, Sheth J. 2007.Cytogenetic analysis of Down syndrome in Gujarat. *Indian Pediatr*., 44: 774-777.

Sheth F, Rao S, Desai M, Vin J, Sheth J. Cytogenetic analysis of Down syndrome in Gujarat., *Indian Pediatr* 2007;44:774-777.

Sheth F, Rao S, Desai M, Vin J, Sheth J.2007. Cytogenetic analysis of Down syndrome in Gujarat. *Indian Pediatr*., 44:774-777.

Steve J, Funderburk, M. Anne Spence, and Robert S. Sparkes.1977. Mental Retardation Associated with "Balanced" Chromosome Rearrangements. *Am J Hum Genet,* 29:136-141.

Surbhi Mahajan, Anupam Kaur and Jai Rup Singh. 2011. Cytogenetic Investigations in Mentally Challenged Individuals. *Int J Hum Genet*., 11(2): 93-98.

Thomas IM, Rajangam S, Hegde S.1992. Cytogenetic investigations in Down syndrome patients and their parents. *Indian J Med Res* .,96:366-371.

Verma IC, Anand NK, Kabra M, Menon PSN, Sharma N.1998. Study of malformations and Down syndrome in India (SOMDI): Delhi Region. *Indian J Hum Genet*.,4: 84-87.

Walter S, Sandig K, Hinkel GK, Mitulla B, Ounap K, Sims G 2004. Subtelomere FISH in 50 children with mental retardation and minor anomalies, identified by a checklist, detects 10 rearrangements including a de novo balanced translocation of chromosomes 17p13.3 and 20q13.33. *Am J Med Genet*., 128(4): 364-373.

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