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Chromosomal Anomalies in Referred Cases with Suspected Genetic Disorders: First Report from Jammu and Kashmir

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ABSTRACT In a four year period (2005-2009), a total of 161 individuals of different age group presenting clinical profile like genetically uncertain syndrome, multiple congenital anomalies, short stature, facial dysmorphism, abnormal behaviour, unclassified mental retardation and Down syndrome were referred to the Human Genetic Research cum Counselling centre, Jammu.Chromosome study was carried out in all the referred cases, when the chromosomal abnormalities were detected in 91 (56.52%) individuals. Besides chromosome study, some non-cytogenetic factors like maternal age, male: female ratio, birth order and consanguinity have also been studied to find out the possible association of these factors with chromosomal aberrations in referred patients.

INTRODUCTION

Chromosomal abnormalities, the leading cause of human congenital anomalies make major contribution to human morbidity and mortality (Verma and Dosik 1980; Navsaria et al. 1993; Mohammad 1997 and Anupam et al. 2003).These abnormalities may be fatal when the developing fetus fail to reach full term and gets aborted or the fetus may be compatible with intra uterine life, but the child is born with gross phenotypic anomalies making the child distinct and help clinicians to suspect the condition (Berry 1991).Congenital anomalies having a chromosomal cause, besides causing gross phenotypic anomalies also remain the leading cause of mental retardation (Pashayan et al. 1973; Anupam et al. 2003). So far, more than 100 chromosomal disorders have been reported, however, Trisomy 21 remains the commonest with its incidence 1:650-1:1000 live births (Hassold and Sherman 2000; Sanjeev et al. 2002). Trisomy 21 causes Down syndrome, the human congenital anomaly of special interest. Besides being the leading cause of mental retardation, this syndrome survives for a longer period (Sanjeev et al. 2002). Non-disjunction of chromosome number 21 causes its aneuploidy (Wright 1990). The exact cause of non-disjunction remains unknown, although attempts have been made on the association of maternal age with the birth of Down syndrome. Birth order, socio-economic conditions, rural/urban background, consanguinity, sex of the affected child and parental age are some of the additional parameters that need to be worked out extensively.

Chromosome study carried out in 161 referred cases was aimed at finding out the incidence of chromosomal aberrations in the referred cases. Besides chromosome study, attempts have also been made to work out the possible associations of non-cytogenetic parameters like maternal age, birth order, socio-economic conditions, rural/urban background, and sex of the affected children with the birth of Down syndrome the common congenital anomaly.

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MATERIAL AND METHOD

Chromosome study in 161 referred cases was carried out from GTG banded metaphase plates following Seabright (1971).Well spread GTG banded complements were karyotyped. Table 1 shows clinical categorization of the referred cases.

RESULTS

Results observed from chromosome study

Table 1: Categorizing of clinically referred cases (161)

S. No.	*Clinical diagnosis*	*Number of patients*	*Percentage*
1.	Down syndrome	80	49.7
2.	Delayed milestones	50	31.1
3.	Turner syndrome	18	11.2
4.	Klinefelter syndrome	11	6.8
5.	Patau syndrome	02	1.2
	Total	161	100.0

and karyotypes prepared are given in table 2 Trisomy 21, XO, XXY and Trisomy 13 were the chromosomal abnormalities detected in 91 of the 161 referred cases. Trisomy 21 free as well as mosaic was the commonest chromosomal abnormality detected in 71 of the 91 cases. Amongst the 80 clinical Down syndromes, typical Trisomy 21 was detected in 59 cases while the remaining 21 cases had normal karyotype and amongst the 50 cases with delayed milestones, mosaicism of Trisomy 21 was detected in only 12 cases while the remaining 38 cases had normal karyotype. Thus making a total of 71 cases where Trisomy 21 was detected (see Fig. 1 and 2).

Of the 18 clinical Turner females, 11 were found to have XO sex chromosome constitution (see Fig. 3) and the remaining seven had normal karyotype where both the X-chromosomes were intact. 7 out of 11 clinical Klinefelter syndromes were found possessing 47, XXY sex chromosome constitution (see Fig. 4). Trisomy 13 could be detected only in 2 cases and both these cases were clinically diagnosed as Patau syndrome (Table 2).

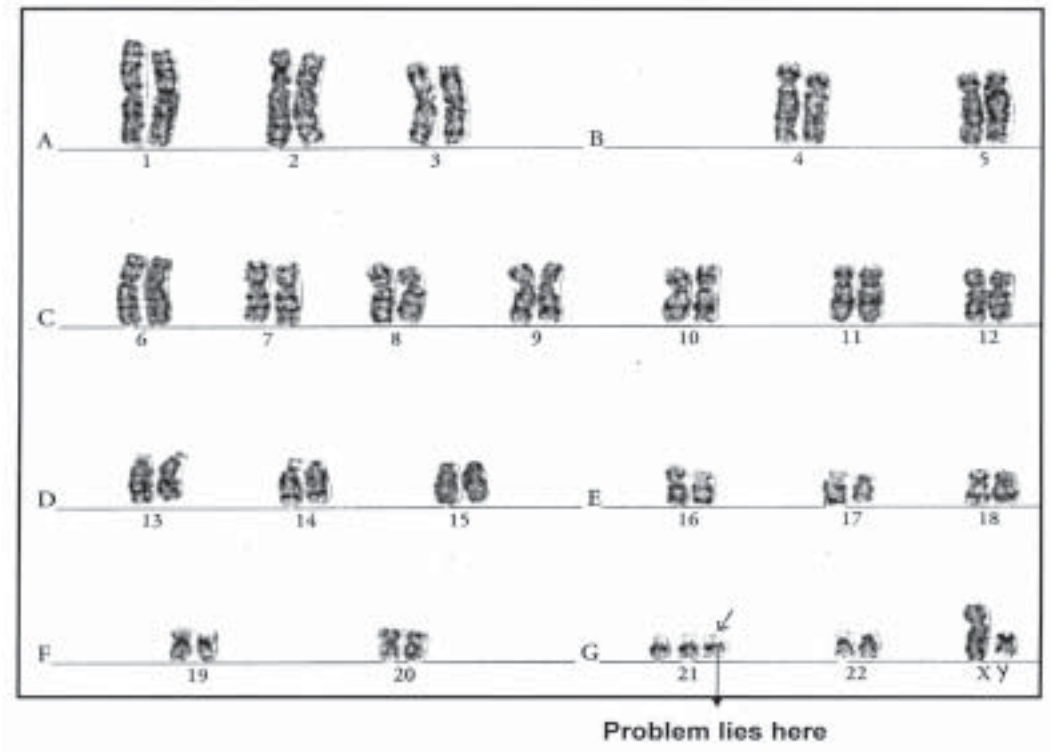


Fig. 1. Photokaryotype of a male Down syndrome

Maternal Age: Birth rate of 71 cases having Trisomy 21 (both free and mosaicism) was the highest amongst mothers between 26-30 years age (Table 3).

Sex of the Child: From the 71 genetically confirmed Down syndromes (Both with free Trisomy 21 and Mosaicism of 21), 45 (63.38%) were males and 26 (36.61%) were females with approximate 2:1 male to female ratio.

Birth Order: Majority (54.92%) of the Down syndrome children were born as 1st issue (Table 4).

Consanguinity: Majority of the couples were non-consanguineous.

Total Couples=71
Non Consanguineous Couple=58 (81.69%)
Consanguineous Couple=13 (18.30%)

DISCUSSION

Chromosome study carried out in 161 cases of congenital abnormalities showed chromosomal abnormalities in 91 cases (56.52%) with Trisomy 21 being the commonest (78%). Higher percentage of chromosomal abnormalities could be attributed to the fact that majority of the referred case had full blown features of different

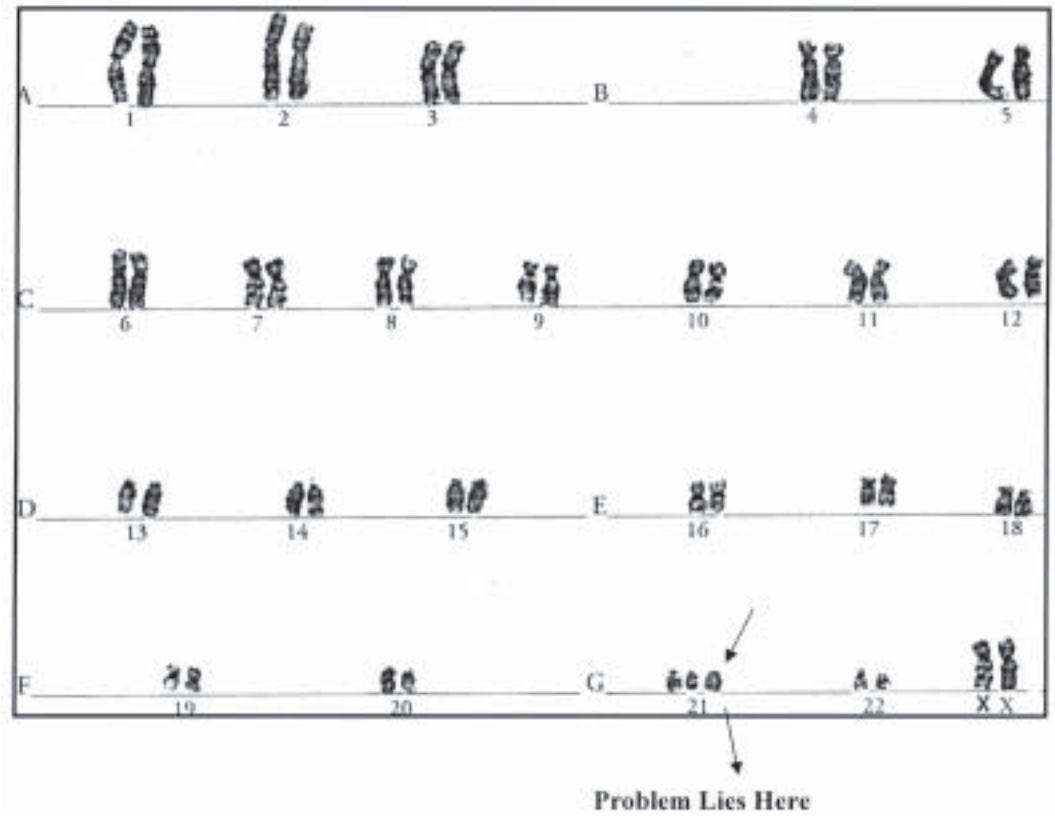
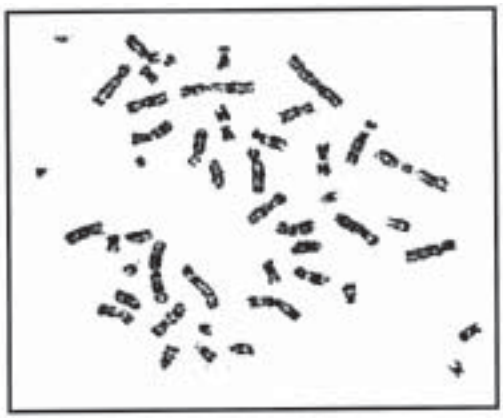


Fig. 2. Photokaryotype of a female Down syndrome

Table 2: Chromosomal abnormalities detected.

Total number	*Free trisomy 21*	*Mosaic trisomy 21*	*XO condition*	*XXY condition*	*+13*
91	59	12	11	07	02



syndromes. Trisomy 21 detected in 71 cases remained the commonest chromosomal abnormality in the present study. Following Trisomy 21, the next chromosomal abnormality was XO condition (12.08%).

Chromosome study in individuals suspected of having Genetic Disorders has been carried out by Verma and Dosik (1980), Shah et al. (1990), Nkanza and Tobani (1991), Mohammad (1997), Waheid et al. (2008b) and various other workers. These workers have reported wide variations in the frequency of chromosomal abnormalities in their study. In the present work, chromosomal aberrations were detected in 56.52% and as such this figure is higher than most of the previous reports.

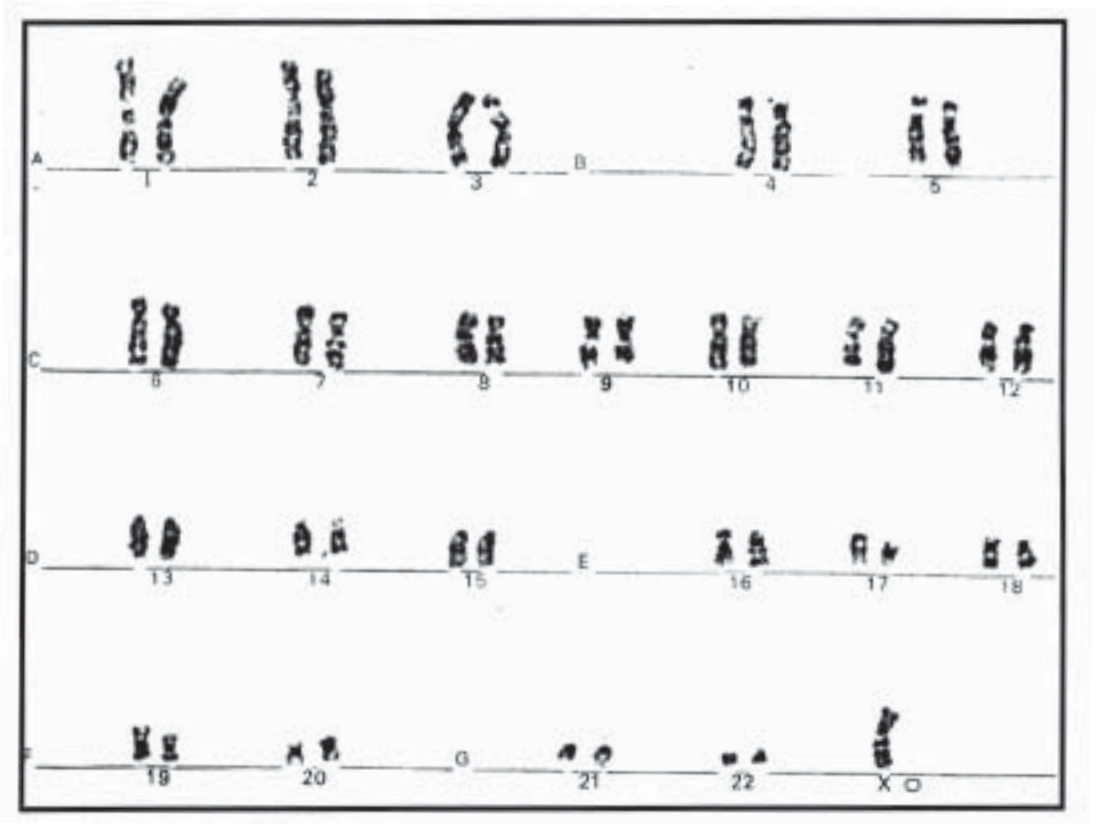


Fig. 3. Photokaryotype of a Turner syndrome

Table 3: Relation between maternal age and birth of Down syndrome.

S. No.	*Maternal age (in years)*	*Number of births*	*Percentage*
1.	20-25	20	28.2
2.	26-30	35	49.3
3.	31-35	10	14.1
4.	36-40	06	8.4
	Total	71	100.0

Table 4: Percentage frequency of birth order of Down syndrome patients.

S. No.	*Birth order*	*Number of patient*	*Percentage*
1.	1st Birth Order	39	54.9
2.	2nd Birth Order	19	26.8
3.	3rd Birth Order	08	11.3
4.	4th Birth Order	02	2.8
5.	5th Birth Order	03	4.2

Existing literature on chromosomal aberrations shows Trisomy 21 to be the commonest .Present findings are akin to the available reports. Trisomy 21 in the present study was 78%. This value is nearly similar to the earlier reports, wherein Trisomy 21 in congenital anomalies has been recorded to be 74.6% (Gardener and Sutherland 1996). However the frequency of mosaicism in Down syndrome vary between 0-4% (Wright 1990; Sanjeev et al. 2002). In the present study about 13.18% patient with Down syndrome had mosaicism. Majority of the mosaic Down syndrome were born to mothers below 30

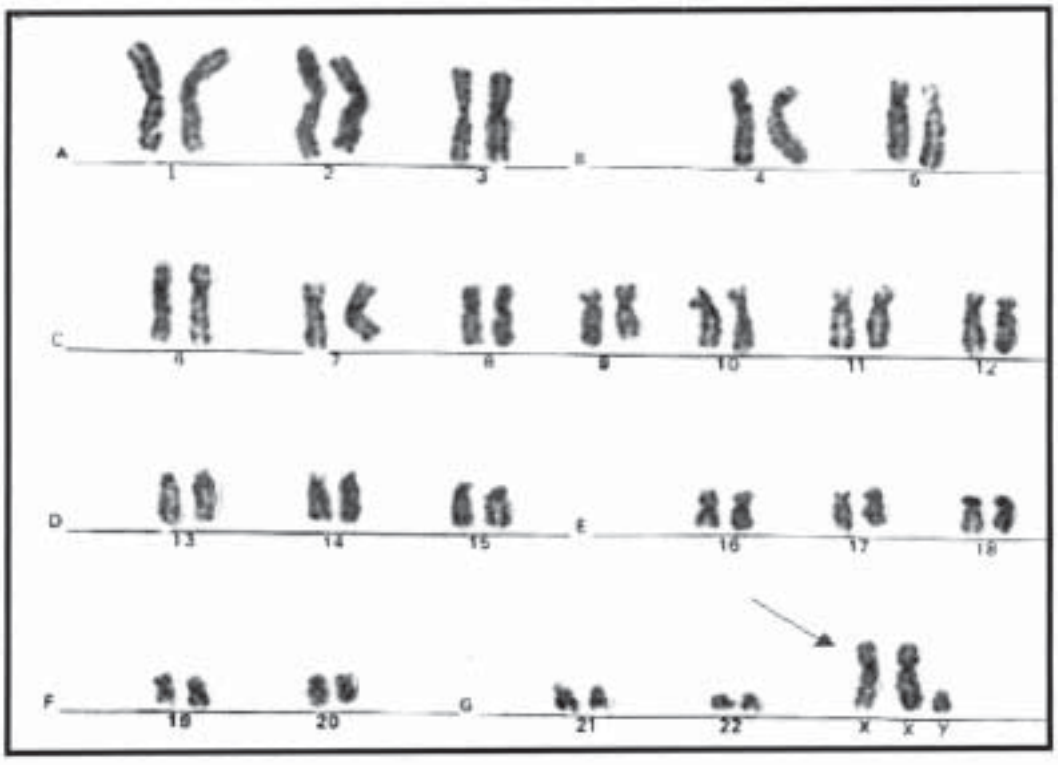


Fig. 4. Photokaryotype of a Klinefelter syndrome

years of age. Therefore in the present study the percentage frequency of mosaicism in Down syndrome is higher then the earlier reports.

The Down syndrome birth has often been associated with maternal age by various workers (Multon et al. 1996; Sanjeev et al. 2002; Anupam et al. 2003; Waheid et al. 2008a). As reported by the workers, increased maternal age has generally been associated relationship with non disjunction of chromosome number 21. This may be attributed to over ripening of the ovum. It is estimated that 80% of Down syndromes are born to woman <35 years, however, in the present study only 6 (8.4%) females were in the age group >35 years. Therefore, in the present study, majority of the mothers were <35 years. Trisomy 21 could be the consequence of non-disjunction that might occur during gametogenesis or in the 1st or 2nd cleavage (Pullian and Huether 1986; Wright 1990). Non-disjunction could occur at any time, therefore children with Trisomy 21 can be born to mothers of all age groups. Since in the present study majority of mothers are <35 years, it may therefore, be attributed to the fact that most pregnancies occur in younger woman. Hence, the present findings on the association of maternal age with the birth of Down syndrome are similar to the earlier reports.

Down syndrome is usually regarded as Exhaustion product (Berry 1991). In the present study, 39 (54.92%) Down syndrome were 1st in birth order and 19 (26.76%) in 2nd birth order. Following 2nd birth order the incidence was very low .Present findings are therefore contrary to the previous reports, reporting Down syndrome as the commonest congenital anomaly.

CONCLUSION

Among a group of individuals with phenotypic abnormalities where the karyotyping was done, the frequency of autosomal chromosomal aberrations was found to be much higher than sex chromosomal anomalies. Trisomy 21 was the most frequent. The precise delineation of a major autosomal Trisomy is only possible using clinical examination and cytogenetic tools. Recognition of parents with chromosomal abnormalities is important, as the risk of recurrence is high in some cases. This knowledge allows proper genetic counselling to be produced.

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