



## Karyotypic Detection of Chromosomal Abnormalities in Referred Cases with Suspected Genetic Disorders

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### ABSTRACT

*In the present study, a total of 150 individuals in 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 to rule out chromosomal abnormality. Chromosome study was carried out in all the referred cases, and the chromosomal abnormalities were detected in 77 (51.33%) 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.*

**KEY WORDS:** Down syndrome, Mental retardation, Multiple congenital anomalies, Facial dysmorphism.

### INTRODUCTION

Chromosomal abnormalities, the leading cause of human congenital anomalies make major contribution to human morbidity and mortality [1,5,7,14]. 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 [2]. Congenital anomalies having a chromosomal cause, besides causing gross phenotypic anomalies also remain the leading cause of mental retardation [1,9]. 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 [4,11]. 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 [11]. Non-disjunction of chromosome number 21 causes its aneuploidy [15]. 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 are being worked out extensively.

Chromosome study carried out in 150 referred cases was aimed at finding out the incidence of chromosomal aberrations in the referred cases. Besides chromosome study, some non-cytogenetic parameters like maternal age, birth order, socio-economic conditions, rural/ urban background, and sex of the affected child with the birth of Down syndrome have also been studied.

### MATERIAL AND METHOD

Chromosome study was carried out from GTG banded metaphase plates following Seabright [12]. Well spread GTG banded metaphase plates were karyotyped.

**Table1:** Showing clinical categorization of the referred cases.

S.No.	Clinical Diagnosis	Number of Patients	Percentage Frequency
1.	Down syndrome	70	46.66%
2.	Delayed milestones	49	32.66%
3.	Turner syndrome	16	10.66%
4.	Klinefelter syndrome	13	8.66%
5.	Patau syndrome	02	1.33%
	TOTAL	150	

**RESULTS**

Results obtained from chromosome study and karyotypes prepared are given in Table2.

Table2: Chromosomal abnormalities detected.

Total Number	Free Trisomy 21	Mosaic Trisomy 21	XO condition	XXY Condition	+13
77	47	12	09	07	02

Trisomy 21, XO, XXY and Trisomy 13 were the chromosomal abnormalities detected in 77 of the 150 referred cases.

Trisomy 21 free as well as mosaic was the commonest chromosomal abnormality detected in 59 of the 77 cases. Amongst the 70 clinical Down syndromes, typical Trisomy 21 was detected in 47 cases while the remaining 23 cases had normal karyotype and amongst the 49 cases with delayed milestones, mosaicism of Trisomy 21 was detected in only 12 cases while the remaining 31 cases had normal karyotype. Thus, making a total of 59 cases where Trisomy 21 was detected.

Of the 16 clinical Turner females, nine were found to have XO sex chromosome constitution and the remaining seven had normal karyotype where both the X-chromosomes were intact.

7 out of 13 clinical Klinefelter syndromes were found possessing 47, XXY sex chromosome constitution.

Trisomy 13 could be detected only in 2 cases and both these cases were clinically diagnosed as Patau syndrome.

As in the present study, the incidence of Down syndrome was the highest, therefore, some of the Non-Cytogenetic factors such as Maternal age, sex of the Proband and Birth order were also studied to find out any association of these factors with the birth of Down syndrome child.

**Maternal age**

Birth rate of 59 cases having Trisomy 21 (both free and mosaicism) was the highest amongst mothers between 26-30 years age (Table<sup>3</sup>).

Table3: Relation between Maternal age and birth of Down syndrome.

S.No.	Maternal Age (yrs.)	Number of births	Percentage of Frequency
1.	20-25	15	25.42%
2.	26-30	28	47.45%
3.	31-35	10	16.94%
4.	36-40	06	10.16%
	TOTAL	59	

**Sex of the Child**

From the 59 genetically confirmed Down syndromes (Both with free Trisomy 21 and Mosaicism of 21), 38 (64.4%) were males and 21 (35.6%) were females with approximate 2:1 male to female ratio.

**Birth order**

Majority of the Down syndrome children were born as 1<sup>st</sup> issue (55.93%)-Table 4.

Table 4: Percentage Frequency of Birth order of Down syndrome patients.

S.No.	Birth Order	Number of Patient	Percentage of Frequency
1.	1 <sup>st</sup> Birth Order	33	55.93%
2.	2 <sup>nd</sup> Birth Order	14	23.72%
3.	3 <sup>rd</sup> Birth Order	07	11.86%
4.	4 <sup>th</sup> Birth Order	02	3.38%
5.	5 <sup>th</sup> Birth Order	03	5.08%

**Consanguinity**

Majority of the couples were non-consanguineous.

Total Couples=59

Non Consanguineous Couple=48 (81.35%)

Consanguineous Couple=11 (18.65%)

## DISCUSSION

Chromosome study carried out in 150 cases of congenital abnormalities showed chromosomal abnormalities in 77 cases (51.33%) with Trisomy 21 being the commonest (76.62%). Higher percentage of chromosomal abnormalities could be attributed to the fact that majority of the referred case had full blown features of different syndromes. Trisomy 21 detected in 59 cases remained the commonest chromosomal abnormality in the present study. Following Trisomy 21, the next chromosomal abnormality was XO condition (11.68%).

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 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 51.33% and as such this figure is higher than most of the previous reports.

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 76.62%. This value is nearly similar to the earlier reports, wherein Trisomy 21 in congenital anomalies has been recorded to be 74.6% [3]. However the frequency of mosaicism in Down syndrome vary between 0-4% [11,15]. In the present study about 15.58% patient with Down syndrome had mosaicism. Majority of the mosaic Down syndrome were born to mothers below 30 years of age. Therefore in the present study the percentage frequency of mosaicism in Down syndrome is higher than the earlier reports.

The Down syndrome birth has often been associated with maternal age by various workers [1,11]. 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 1<sup>st</sup> or 2<sup>nd</sup> cleavage [6,10,15]. 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 [2]. In the present study, 33 (55.93%) Down syndrome were 1<sup>st</sup> in birth order and 14 (23.72%) in 2<sup>nd</sup> birth order. Following 2<sup>nd</sup> 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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