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Cytogenetic and Dermatoglyphic Patterns of Down's Syndrome Cases

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Abstract

Trisomy 21, is the most common autosomal anomaly among mental retardation . The frequency in general population is about 1 for every 660 live births. A correlation has been shown concerning the risk of a child being born with Trisomy 21 which increases exponentially with maternal age. In the present investigations, the results of cytogenetic and dermatoglyphic patterns confirm the clinical diagnosis and the etiology of the syndrome. Of the 20 cases studied, only one showed mosaic trisomy 21. Most of the trisomy 21 cases exhibited sterotyped dermatoglyphic features. These findings were useful in genetic counselling of the parents of the affected child.

Key words -

Down's syndrome,
Maternal age,
Dermatoglyphics,
Trisomy

Trisomy 21, the most common autosomal anomaly among mental retardation was first described by Lejeune et al. [1]. It was first described by Seguin [2], by the name 'Fur furaceous idiocy'. However, the first clinical account was given by Langdon Down [3] in 1866 who named it the 'Mongolian idiocy'. Later this name was changed to 'Down's syndrome'. Over the past two decades the terminology widely accepted is '21 trisomy'. Jacobs et al. [4], Ford et al. [5] and Book et al. [6], independently confirmed the findings of Lejeune et al. [1]. They reported that the extra chromosome probably represented a trisomic state. Since then, numerous reports have been accrued on the cytogenetics of 21 trisomy.

The frequency of this anomaly in general population appears to be 1.45 per 1000 on about 1 for 660 - 700 live births [7]. However, this incidence rate is not constant over all maternal ages and the risk of a child being born with 21 trisomy increases exponentially with increased maternal age [2], [3], [4], [5], [6], [7], [8], [9].

The association of maternal age with non-dysjunction is of utmost importance in understanding the aetiological

significance, in most of the autosomal trisomic conditions.

The first reports on the dermatoglyphic patterns of 21 trisomy was reported by Penrose [10], Holt [11], Priest [12] and Lafourcade and Rethore [13], in that all Down's possess stereotyped patterns which have significant diagnostic value.

Keeping in view the extensive researches conducted on Down's syndrome cases, the present study was undertaken to understand the cytogenetic and dermatoglyphic features from this part of the country.

In most of the clinically diagnosed cases the results of the cytogenetic investigations appeared to be of diagnostic value.

Material and Methods

Twenty patients, (Thirteen males and seven females) (Table-I) clinically diagnosed as Down's syndrome cases within the age group of 1 to 19 years formed the material for the study. These patients were referred from the Mental Retardation Clinic at NIMHANS from July 1984 to June 1985.

Table I - Age-sex distribution of cases

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Figures 1-4 show some of the important clinical features characteristic of the Down's syndrome.

- ***Clinical photo of a male patient aged 5 years***
- ***Clinical photo of a female patient aged 8 years***
- ***Enlarged photograph of the foot of the patient (figure 2) showing wide space between great and 2nd toe***
- ***Clinical photo of a male patient aged 18 years***

Details of the parental age, the detailed physical examination and other psychosocial aspects of these cases are presented in the results.

Cytogenetic Investigations

Chromosomal preparations were made with short culturing of leukocytes from whole blood according to the method of Arakaki and Sparkes [14]. Chromosome analyses were done using the GTG (Seabright) [15], CBG (Scheres) [16] and QFQ (Casperson et al) [17] chromosome banding techniques, which allows easier identification of the homologue chromosomes. Cytogenetic studies involved analysis of 25 random G-banded metaphase spreads. Structural assessment was done by detailed analysis of 5 metaphase spreads and one of them was karyotyped for presentation.

Dermatoglyphic studies include taking of impressions of the palm and the finger-tips for detailed assessment (Figs 5-7).

- ***Photograph showing simian crease (single -transverse palmar crease) and clinodactyly of the fifth finger in the palm (left)***
- ***Photograph showing simian crease in the palm (right) and the fifth finger showing single inter phalangealflexion crease and also clinodactyly***
- ***Photograph showing simian crease (partial) and sydney line (partial) on the left palm***

Results

Twenty cases, clinically diagnosed as Down's syndrome in the age range of 1-19 years and of both sexes were studied (Table I). It is observed that more number of cases (40%) were distributed in mothers within the age group of 20-24 years as compared to the rest and there is a uniform distribution of cases in the age groups 25-34, 35-39 and 40-44. No cases were seen in the 45 and above age groups (Table II). There were 55 % and 45 % of cases distributed in 20-39 and 40-50 age group (range) of father respectively (Table III). It has been observed that if the average sibship size is taken as 6 then 70 % of the cases are distributed in sibships below and 30 % in sibships above 6. From the details of the family and birth history of the cases (Table IV), 25 % of the cases showed parental consanguinity and 75 % had delayed milestones and in 30 % cases there was severe degree of mental retardation.

Table II - Distribution of cases (age-sex wise) in different groups of mothers

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Table III - Distribution of cases (age-sex wise) in different age groups of fathers

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Table IV - Family & birth history of Down's syndrome patients

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In majority of the cases there was speech problem. There was no persistence in the generalised behavioural and emotional manifestations in majority of the cases. Most of them exhibited friendliness and in a few cases aggressive behaviour and restlessness were noticed. Many of them have shown special liking for music.

Table V shows the detailed findings on physical examination, wherein majority of the cases showed uniform distribution of clinical features.

In addition to the common clinical features characteristic of Down's syndrome cases presented in Table V, there were some salient features occasionally seen in these patients which are presented in Table VI.

Table V - Finding on physical examination of Down's syndrome cases

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Table VI - Few important clinical features present in Down's syndrome cases

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The details of the dermatoglyphic patterns are presented in Table VII. In general, the dermatoglyphic studies revealed significantly elevated incidence of stigmata typical of Down's syndrome.

Table VIIa - Dermatoglyphic patterns in Down's syndrome patients .

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Abbreviations used : UL - Ulnar Loop, W - Whorl, RL - Radial Loop, TFRC - Total Finger Ridge Count, t" - Distal position of axial triradius, L - Loop without accessory triradius, O-Open field, v - Vestige without tendency towards loop, Lv - Vestige with tendency towards loop, Lt - Left, Rt - Right.

All 20 cases diagnosed clinically as Down's syndrome showed an extra chromosome 21 in their G-banded karyotypes. The details of the cytogenetic findings are presented in Table VIII. A female patient aged 13 years, showed mosaic 21 trisomy, in that 18 % of the cells had 46, XX and 82 % of the cell lines had 47, XX+21 chromosome constitution. She showed most of the clinical symptoms characteristic of Down's syndrome but her parents were not available for further investigations.

Table VIII - Cytogenetic findings in Down's syndrome's cases

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Figures 8-11 indicate that, in our series, trisomy 21 is seen in all the karyotypes. Besides trisomy 21, some of the cases showed chromosomal polymorphic variants, such as 9qh+, 15p+, 21s+ and 22s+ in their karyotypes. None of the cases showed any 21 translocation either with D group (13-14-15) or with G group (21-22).

Table IX - Maternal age & percentage of Down's syndrome cases in India

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.Karyotype of a trisomy 21 Down's syndrome male showing large satellite on one of the chromosome numbers 21 (21s+)

.Karyotype of a trisomy 21 Down's syndrome male showing large secondary constriction on one of the chromosomes 9(9qh+) and a large satellite on one of the chromosome 22(22s+)

.Karyotype of a trisomy 21 Down's syndrome male showing large secondary constriction on one of the chromosomes 9(9qh+) and a large satellite on one of the chromosomes 21(21s+)

.Karyotype of trisomy 21 Down's syndrome female showing enlarged short arm of the chromosome 15 (15p+)

Discussion

Between July 1984 and June 1985 out of 800 cases registered at the M. R. Clinic, 20 were clinically diagnosed as Down's syndrome. This gives an approximate incidence of 2.5 / 1000 and is in agreement with the 2.66 / 1000 as observed by Subbe Gowda [18].

Based on some of the reports available [19], the incidence of Down's syndrome in India appears to be 1-2/1000 births. However, it is very difficult to emphasize the general frequency since the surveys are conducted on a small size of population.

Cytogenetic studies revealed definite 21 trisomy in all these cases and no incidence of translocation

Down's were noticed. One female showed a mosaic cell line for 21 trisomy, wherein 18 % of the cell lines had 46, XX and 82 % showed 47, XX+21 chromosome constitution. Clinically the patient had all the features characteristic of Down's syndrome. It has been recently reported by many workers that the parental mosaicism is seen in 21 trisomy Down's syndrome patients which is important to some extent in establishing the etiological factor in Down's syndrome [20]. They also reported that, mosaicism was found more commonly in mothers than in fathers, however, more data are needed for confirmation of the phenomenon.

The presence of minor chromosomal variants, in a few cases, such as, large secondary construction on the long arm of chromosome 9 (9 qh+), the enlarged short arm on chromosomes 15 (15 p+), and the presence of large satellites on chromosomes 21 (21s+) and 22 (22s +), are associated with the 21 trisomy karyotypes.

However, the phenotype-karyotype correlation in the presence of the polymorphic chromosomal variants is not known in 21 trisomies, since such chromosomal polymorphic variants have been reported in patients with mental retardation and also exists in normal, healthy relatives of mentally retarded patients (Fryns et al. [21]). It is known that, such variants exist:

(a) in children with congenital malformations and chromosomal abnormalities,
(b) in children with congenital malformations and normal karyotypes and
(c) in phenotypically normal parents with an increased risk of reproductive failure [22].

From the present study, it is very clear that, dermatoglyphic pattern is very important in characterising the syndrome and is of great diagnostic value in clinical assessment [10], [11], [12], [13]. In this context, a comparative and comprehensive data on dermatoglyphic patterns of Down's syndrome cases from different parts of India as compared to the control population is worth studying.

In the present study, about 25 % of cases showed parental consanguinity. Recently Alfi et al. [23] showed a correlation regarding increased incidence of Down patients among offsprings of consanguineous parents. They also suggested the existence of a rare autosomal recessive gene which, in the homozygous state causes mitotic non-dysjunction in Down's zygote. However, these reports are contradicted by those of Devoto et al. [24] who studied 242 Down's children, in that they have not noticed any increase in the frequency of consangineous marriages among their parents with respect to the general population, as it has been reported in cases such as PKU, Friedreich ataxia, Cystic fibrosis and Werner syndrome [25], [26], [27], [28].

It is well known that the parental age and incidence of Down's syndrome depends significantly on the maternal age with a non linear increase after the age of 30-35 years [29]. On the contrary, the earlier reports of Jenkins [8] and Penrose [9] suggested that the risk of a child being born with 21 trisomy increases exponentially with an increased maternal age (Table X).

Table X - Occurence and risk figures for Trisomy 21 by maternal age .
From Miller & Dill, 1965, Birth Defects Reprints Series

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In more recent reports, there is a general decline in the average maternal age and a possible effect on the incidence of Down's syndrome. A concomitant decrease in the incidence, but also of an increase in some maternal age groups, specially in younger age groups has been reported by several workers [29],

[30], [31], [32], [33], [34], [35].

The mean maternal age noted in the present study was 28.9 years, unlike previous observations of 31 years from this centre [18] and of 28.2 years in the general population [7].

The mean paternal age of the children with Down's syndrome was 38 years.

The recent observations by Leisti et al. [29] recorded that a permanent reduction in the mean maternal age from 36.3 years to 31.7 years seems to have occurred over a period of 15 years. They have also observed that there is a decrease in the percentage of Down's syndrome children born to mothers aged 35 years or older. However, there is a proportional percentage of increase in younger mother age groups.

In the present study a similar observation was made and the comparative data is presented (Table IX) and in general there is a marked increase in the percentage of children with Down's syndrome born to mothers of 34 years and below, as compared to a proportional decrease in the mothers over 40 years of age.

Considering the influence of maternal age there is need to give a serious thought for establishing centres where facilities for amniocentesis and counselling are available.

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