STUDIES ON DOWN’S SYNDROME AND MATERNAL AGE

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SUMMARY
Details of clinical, genetic and karyotyping investigations carried out on thirty patients with Down’s syndrome are described. All the patients showed Trisomy-21. The information relating to the maternal age revealed that women in the age group of 15-35 also had cases of Down’s syndrome which is in contrast to the findings made in western countries.

Langdon Down, in 1866 was the first to single out ‘Mongols’ from a heterogenous collection of mentally retarded (MR) subjects and this enabled physicians to undertake a detailed study of their physical character (Down 1866). A number of workers reported on various physical features viz., head and face, jaws, eyes, heart, among others. The occurrence of ‘Mongolism’ was established to be independent of the father’s age (Kirmann 1975) and of birth order (Penrose 1951). Dermatoglyphic studies showed a tendency to transverse arrangement of dermal ridges, with a high axial tri-radius (Richards 1970). Biochemical studies carried out have revealed low blood calcium, reduced excretion of tryptophan, increased UDG galactose transferase and immunoglobulin A levels were found to be high in Mongols (Kirmann 1975, Mellan et al. 1964). After the introduction of karyotyping by Tjio and Levan the studies of Lejeune established the trisomy state in Down’s cases (Tjio & Levan 1956, Subbegowda 1984). Thus, if one summarises the salient observations made in cases of Down’s syndrome in the past one hundred years, three discoveries have been of outstanding importance; it is recognisable at sight, it is associated with late maternal age, and affected subjects have an extra chromosome.

There have been a number of reports from India and abroad indicating that maternal age has an influence on the occurrence of Down’s syndrome. This paper reports a study conducted at this centre to determine the influence of maternal age on the occurrence of Down’s syndrome.

Material and Methods
The clinical material was obtained from patients coming for consultation to the mental retardation clinic at the department of Psychiatry of National Institute of Mental Health and Neuro Sciences, Bangalore. In all these cases detailed clinical history was obtained which included the genetic history. This included collecting information relating to history of consanguinity among the parents and or similar or other psychiatric illness among relatives. Physical examination was carried out in all the cases. The body fluids were collected to screen for possible metabolic defects. Cytogenetic studies were also carried out. For comparison age-sex matched mentally retarded subjects who were not mongols were investigated besides healthy subjects.

Results
There were 18 male and 14 female patients of Down’s syndrome included in this study. In all these cases, trisomy-21 was present. The age-sex distribution of the
cases are indicated in Table 1.

| Age group (in year) | Male | Female | Total |
|---------------------|------|--------|-------|
| 2 - 4               | 5    | 3      | 8     |
| 5 - 7               | 1    | 4      | 5     |
| 8 - 10              | 0    | 0      | 0     |
| 11 - 13             | 4    | 4      | 8     |
| 14 - 16             | 4    | 2      | 6     |
| 17 - 19             | 0    | 0      | 0     |
| 20 +                | 4    | 1      | 5     |
| Total               | 18   | 14     | 32    |

In order to examine the influence of maternal age on the occurrence of Down's syndrome the cases noted in different age groups were classified under different age groups of the mother. This is indicated in Table 2.

| Age of Maternal age (in years) | Down's Syndrome | Controls |
|--------------------------------|-----------------|----------|
| 20-25                          | 4               | 3        |
| 26-30                          | 1               | 2        |
| 31-35                          | 1               | 2        |
| 36-40                          | 1               | 2        |
| 41-45                          | 3               | 2        |
| 46-50                          | 2               | 1        |
| <17                            | 1               | 1        |
| Total                          | 10              | 8        |

It was noted that the cases were distributed almost uniformly in all the age groups and not many were there in the age group above 45.

The data obtained in other centres in India and the present one indicates that majority of the children were born to mothers in the age group of 20 - 29 with lesser number in the other age groups. However, if the data is redistributed in the age group of 15 - 34 and 34 and above some interest-

ing observations are noted, as indicated in Table 3.

| Maternal Age (in years) | 15 - 34 | 34 & above |
|-------------------------|---------|------------|
| Down's syndrome in other parts of India | 67.0% | 33.0% |
| Down's syndrome in present study | 60.0% | 40.0% |
| Controls                | 92.6% | 7.4% |

From the above data it can be noted that the prevalence rate of Down's syndrome in India is higher in the age group below 34 years.

The data relating to mean maternal age in Down's syndrome cases and controls reported from different centres in the world are indicated in Table 4.

| Country | Down's Syndrome | Controls |
|---------|-----------------|----------|
| Australia | 33.7            | 28.0     |
| Canada  | 34.9            | 27.8     |
| Denmark | 34.6            | 28.3     |
| U. K.   | 35.1            | 28.4     |
| Finland | 34.9            | 28.2     |
| Formosa | 36.6            | 28.3     |
| Germany | 34.2            | 27.1     |
| Japan   | 33.2            | 28.2     |
| Sweden  | 35.4            | 28.7     |
| U. S. A | 33.3            | 27.7     |
| U. S. S. R. | 33.7     | 27.9     |
| All Countries | 34.43 | 28.9     |
| Present Study | 32.2      | 25.2     |

It can be observed that the mean maternal age is lower in the present series. One of the reasons could be that women get married at an earlier age and have children at a relatively earlier age than in the west.
The data of Collmann and Stoller quoted by Richards (1970) indicated that high maternal age was not always obligatory for the birth of a Down's case. Therefore, quite a sizeable proportion of mongols are born independent of maternal age. These are termed as class-A mongols by Penrose (1966) and maternal age dependent ones as class-B. Some suggestions are also there to indicate that maternal infective hepatitis, and parental radiation may lead to mongolism. Collman and Stoller (Richards 1970) noted that one out of every 2300 mothers below 30 years had a child who was a mongol while one out of 40 children born to mothers over 45 years was a mongol, that is a 50 fold increase was noted in late aged mothers. From the figures reported from West it looks as if that whenever there is a fall in maternal age there was lesser chances of mongols being born. It is interesting to note that while there is no definite association of late maternal age with the incidence of Down's syndrome in the present series, the clinical diagnosis was confirmed by cytogenetic investigations. It is likely that secular changes in maternal age at child birth are responsible for much of the variations in incidence in different geographical areas and in different years. Usually in India women marry and have children at a relatively earlier age. In this connection it is interesting to note that in Yugoslavia, a very low mean maternal age at child birth was noted (Richards 1970).

The association of maternal age with the incidence of Down's syndrome has been attributed to several factors. One of them being, non-dysjunction of the 21-chromosome. If there is no association, the proportion of mongols born to younger mothers could be due to causes independent of maternal age influence. Casual influences other than maternal age thus becomes increasingly important to the investigator.

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