

## A STUDY OF 361 CASES OF SEVERE UNCLASSIFIED MENTAL RETARDATION WITH RECURRENCE IN THE FAMILIES

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### SUMMARY

Detailed family history obtained from 361 cases of severe mental retardation revealed that more than one sib was affected in a majority of the cases where consanguinity was present in more than one generation. The need for studies in general population is indicated for purposes of evolving strategies for genetic counselling.

### Introduction

Severe mental retardation (IQ level below 50) is usually pathological. The known causes of severe M.R. are varied. Berg & Kirman, (1959) and Narayanan and Rao (1977) found that approximately 50-60% cases were clinically unrecognisable. In this group, genetic factors are important. Bunday and Carter (1974) found that in the undiagnosed group there are small but definite recurrence risks to the sib. Penrose (1938) studied 1280 cases of mental retardation without specific diagnosis and found the risk to be 3.4%. Hallgren and Sjogren (1959) found a recurrence risk of 8.4% in rural population of undifferentiated mental retardation. The following are the recurrence risk found by other workers viz., 5.6% (Akkesson 1961); 4.7% in hospital admitted case (Angeli & Kirman 1970) 2.7% in 179 families who had patients with nonspecific mental retardation (Bunday & Carter 1974), Narayanan et al (1973), Rao and Narayanan (1976) found relatively high prevalence of parental consanguinity in females where more than one sib was affected (including those with metabolic

defects). Somasundaram et al (1976) have reported that genetic factors are important in the etiology of mental retardation. One cause for mental retardation which is revealed only by cytogenetic investigations is the fragile x syndrome.

The present study was aimed to study the clinical and genetic aspects in families which had more than often one sib affected in an unclassified group of mental retardation.

### Material and Methods

The clinical material was obtained from cases, attending the M. R. Clinic of NIMHANS, Bangalore. The mental retardation cases belonged to both sexes and all ages. Their IQ was below 50. In all these cases, detailed family history was obtained and pedigree charts drawn. In all cases, clinical, genetic and biochemical investigations were done. Psychometry was also done in all the cases.

All M. R. cases of known aetiology and well known syndromes like Bardet Bidaal syndrome, Delange syndrome were excluded. The remaining unclassified group of

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severe M.R. (IQ below 50) were studied.

### Results and Discussion

The total number of severe mental retardation cases examined were 4950, out of which 2329 cases could be classified on the basis of known aetiology or syndrome. The remaining 2621 (53%) index cases were unclassifiable. In these 2621 unclassified group there were 361 (14%) cases with one or more sib affected with mental retardation.

The consanguinity rate in the unclassified group was studied. The unclassified group was divided into Group A, where one or more sib was affected and Group B, where the other sib was not affected.

The data in Table 1 clearly shows the increased rate of consanguinity in families where one or more sib is affected with mental retardation. The differences between the two groups was highly significant.

Table 1  
Rate of consanguinity among A & B groups

(a) Parents	Group A	Group B
Consanguinity present	751	251
Not present	1509	110
Total Index cases	2260	361
$\chi^2 = 173.68302, df = 1, p < 0.001$		
(b) Grand parents	Group A	Group B
Consanguinity present	82	155
Not present	2178	206
Total	2260	361
$\chi^2 = 5.847757, df = 1, p < 0.001$		

Bell (1940) estimated that the frequency of first cousin marriages in the parents of patients admitted to general hospital was 0.8%. Davison (1973) reported that the frequency of cousin marriages of parents of

people resident in the Oxford area was as high as 0.5%. Davison (1973) studied consanguinity in relation to mental retardation in 93 families where one or more other sib was affected with M.R. and found that in the families the rate was 8.6%. In the present study consanguinity among the unclassified group, it was noted that parental consanguinity among group A where one or more sib affected, the ratio is twice that in families of group B where other sib was not affected. Another interesting finding during the present study was that the consanguinity rate among grand parents in the group A was several times more than in group B.

In addition there were some rare types of congenital abnormalities. There were eight index patients having partial or complete deafness, two patients with albinism, five with cataract, eight with retinitis pigmentosa, two with microphthalmia, one with bifid tongue and four had congenital heart disease.

Table 2  
Age and sex distribution of 361 Index M.R. Patients

Age group	Male	Female	Total
0 - 4	73	44	117
5 - 9	67	36	103
10 - 14	48	28	76
15 - 19	36	5	41
20 +	14	10	24
Total	238	123	361

### Sibs of Index Patients:

There were 1471 live born sibs, 74 abortions and 10 still births. On detailed enquiry and examination there were 318 male and 222 female mentally retarded patients. The age distribution is given in Table 3.

Out of these 240 sibs, 66 male sibs and 43 female sibs died. Out of a total 109 men-

Table 3  
Age distribution of other sibs having  
mental retardation

Age	Number	Percentage
0 - 4	173	32.0
5 - 9	141	26.1
10 - 14	92	17.0
15 - 19	84	15.6
20 +	50	9.3

rally retarded, 36 were found to have died at the time of subsequent followup while 73 had died earlier and in these cases the parents were definite that these children had similar illness as noted in index patients and the parents wanted to know the future probability. Out of the remaining 931 sibs who were not mentally retarded 111 children had died in infancy. The parents reported that 30 of their children had epilepsy.

Most of the studies have shown that the male children tend to suffer more from M. R. than females. Lekhre (1972) postulated a specific x-linked gene for mental retardation and he stated that nearly 20% of male mental retardation is due to linkage. Davison (1973) studied 141 families where at least two numbers were severally retarded, and the cause of defect was not known, reached a similar conclusion. She found a remarkable excess of pedigrees which are compatible with x-linked inheritance.

In 79 out of 361 families almost all the sibs were mentally retarded as indicated below.

Sibship size	Total No. of M. R. Children
2	46
3	22
4	5
5	1
6	5
Total	79

The data reported clearly indicates the influence of genetic factors in the aetiology of severe M. R. For instance in families with parental consanguinity there was greater chance of having more than one sib affected. None of the cases included in the present study had microcephaly or fragile x-syndrome as evidenced by clinical and biological and cytogenetic investigations. Surprisingly greater number of males are affected. Considering that these studies are based on hospital data, there are strong indications that population surveys would be more useful. This would help in utilising the information for purposes of genetic counselling and minimize the chance of having severe M. R. in families. If the same trend is noted genetic counselling has to be directed to avoid future mis-haps of similar nature thus helping in reducing the morbidity of severe M. R.

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