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Consanguinity and familial mental retardation

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Summary. Studies made in a group of patients with mental retardation showed that there was a high degree of parental consanguinity of the order of 30.3%. Index cases with parental consanguinity showed a relatively higher prevalence where more than one sib was affected. Cases with metabolic defects were also more common among cases with parental consanguinity. There is a need for studies in the general population in order to understand the biological significance of consanguinity.

Among the psychiatric disorders, mental retardation occupies a unique position because in many cases a genetic aetiology has been established and some of them also have associated metabolic defects. For many varieties of mental retardation, a polygenic mode of transmission is currently thought to be the probable basis for the condition, resulting from unfavourable polygenic combinations (Sinclair, 1972). Consanguineous marriage would considerably increase the risk of such combinations occurring in the offspring and the risk increases with the closeness of the relationship of the parents (Centerwall and Centerwall, 1966). Since consanguinity is widely practised in this part of India, it was considered worth while to study this aspect at this centre.

Subjects and methods

The clinical material consisted of cases attending the mental retardation clinic, the mental hospital, and a general hospital. The mental retardation cases belonged to both sexes and were less than 15 years of age. To serve as controls, cases of schizophrenia attending the mental hospital and a group of women admitted for delivery in the maternity section of a general hospital were selected (in these controls the ages ranged from 20 to 40 years). In all the three groups, clinical, genetic, and biochemical investigations were conducted.

Observations

The material for this study was collected from 1034 cases with mental retardation, 2172 schizophrenics, and 470 mothers admitted in a maternity unit. The cases with mental retardation were distributed as follows: profound, 172; severe, 286; mild, 367; and borderline, 209. The 1034 cases with mental retardation do not include those with a recognizable pathology (such as Down's syndrome) or metabolic defects (such as phenylketonuria). The controls from the maternity clinic did not have any physical or mental disease.

The distribution of parental consanguinity noted in the three groups are indicated in Table I.

As can be seen from this table, the rate of parental consanguinity was found to be almost the same in cases with mental retardation and in controls.

TABLE I

	MR	Schizophrenics	Controls
Total number of cases	1034	2172	470
Number of cases with parental consanguinity	314	412	152
Percentage of parental consanguinity	30.3	19	32.3

TABLE II

Consanguinity	Mental Retardation		Schizophrenia		Controls	
	No.	%	No.	%	No.	%
In parents only	173	55.2	380	92.3	112	73.6
In parents and grandparents	73	23.3	22	5.4	38	25.0
In parents, grand- and great-grandparents	68	21.5	10	2.3	2	1.4
Total	314		412		152	

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TABLE III

Religion	Man Marrying His*	Mental Retardation No.	Mental Retardation %	Schizophrenia No.	Schizophrenia %	Controls No.	Controls %
Hindus	SD	139	52.7	177	50.0	63	47.2
	MBD	69	24.8	98	27.7	35	37.2
	FSD	66	22.5	79	22.3	29	15.6
Other religions	SD	3		5		1	
	MBD	1		2		–	
	FSD	–		–		–	
Muslims	FBD	39	66.5	28	77.5	16	66.7
	MSD	12	33.5	8	22.5	8	33.3

* SD—sister's daughter; MBD—mother's brother's daughter; FSD—father's sister's daughter; FBD—father's brother's daughter; MSD—mother's sister's daughter.

It is surprising that the rate of parental consanguinity is very low in the schizophrenic material. This definitely calls for a population survey with respect to the prevalence of parental consanguinity in the general population.

It was noted that in many cases with mental retardation, a history of consanguineous union was noted in parents as well as in grand- and great-grandparents and the figures are indicated in Table II.

Regarding the type of consanguinity, it was noted that there was a difference between Hindus and Muslims. Among the Hindus, marriage between a man and his sister's daughter was commonly noted and rather less often marriage with mother's brother's daughter and father's sister's daughter, whereas such unions were not seen among Muslims. Among Muslims, frequently a man married his father's brother's daughter and less often his mother's sister's daughter, and these types of unions were not seen among Hindus. Thus there was a wide difference in the consanguineous unions in the two religious groups. The distribution of data in the three groups relating to consanguinity among the various religions is indicated in Table III.

This difference in the type of consanguineous union noted among Hindus and Muslims is perhaps due to restrictions placed by the two religious groups relating to marriages among parallel and cross cousins. It is also interesting to note that in North India, even Hindus cannot marry anyone who is related to them within five or even seven generations and, therefore, one may assume that consanguinity is virtually absent among the northern Hindus (Centerwall, Savarinathan, and Mohan, 1969).

Another significant point noted was that in the group with mental retardation, a considerable number of the index cases showed more than one sib affected with mental retardation in the same sibship where there was parental consanguinity.

Apart from the cases with mental retardation included in this study, there was another group of 26 cases with some pathological or metabolic defect, and these also showed a relative increase in the sibships with more than one sib affected Table V.

There was parental consanguinity in all the index cases as indicated in Tables IV and V. Besides these cases, parental consanguinity was noted in other cases with metabolic defects, i.e. in 7 additional cases of phenylketonuria, 6 of Hurler's syndrome, and 2 of Hartnup's disease. The present series of cases with metabolic defects among those with mental retardation appear to be the largest of such cases to be detected from any one centre in India.

Discussion

In the inheritance of human diseases regulated by recessive genes, chances of like genes coming together are augmented by consanguineous union among parents, especially in susceptible families. Consanguinity is a custom still prevalent in many

TABLE IV

More Than One Sib Affected	Mental Retardation Parental Consanguinity Seen	Not Seen	Total	Schizophrenia Parental Consanguinity Seen	Not Seen	Total
Seen	92	36	128	138	21	159
Not Seen	222	684	906	274	1739	2013
Total	314	720	1034	412	1760	2172

TABLE V

Diagnosis	Index Cases	Other Affected Sibs	No. of Families
Phenylketonuria	5	5	5
Homocystinuria	1	2	1
Hurler's syndrome	3	5	3
Down's syndrome	4	6	4
Laurence–Moon–Biedl syndrome	5	6	5
Microcephaly	8	10	8

parts of south India (Dronamaraju and Khan, 1963; Sanghvi, 1966; Centerwall and Centerwall, 1966) and the significance of utilizing this opportunity for understanding certain human disease states has been emphasized by Centerwall (1965) who has done pioneering work in this field. Consanguinity in marriage is rare in North India (Centerwall *et al*, 1969) and so far only one report is available on this topic from the north (Sinclair, 1972).

During this study it was noted that the rate of parental consanguinity was the same in cases with mental retardation and among controls. In a preliminary study from this centre (Rao, Narayanan, and Reddy, 1971) it was noted that the rate of parental consanguinity was the same in the general population. The rate appears to vary among the different states of South India (Centerwall and Centerwall, 1966; Rao, Inbaraj, and Jesudian, 1972).

It was noted that in index cases with parental consanguinity, increase of sibships was present with more than one sib affected. A similar observation has been reported by Wortis, Jerdresek, and Wortis (1967) among mentally retarded cases. There appears to be a relation between metabolic defects and sibships, with more than one sib affected, since Priest, Thuline, and Jarvis (1961) noted that the chances of finding rare clinical or metabolic types associated with mental retardation was greater in these than in singly affected sibships. In the present study cases with metabolic defects showed the same trend.

An increased association of congenital anomalies with parental consanguinity was noted by Centerwall (1965) who concluded his report by stating that, 'In the absence of a specific disease on which to focus, knowledge of the empirical overall increased risk associated with consanguinity is not expected to have a measurable effect upon this ancient cultural custom of South India.' In this respect it would also be useful to recall the statement of Alstrom who has stated that, 'In certain social groups in India, reasonably high degrees of inbreeding have existed for centuries. Reliable data are lacking concerning the 'historical evidence' for the same conditions existing in South India 2000 years ago. Because of the uncertain hypothetical conditions, it is somewhat rash to conclude that the practice of consanguineous marriages in India should have resulted in an appreciable reduction in the incidence of hereditary recessive defects and diseases' (Alstrom, 1970).

In view of these interesting observations made in a hospital population it seems useful to extend these studies in the general population in order to understand the biological significance of consanguinity. Centerwall and Centerwall (1966) have stated that South India with its unusually high rate of consanguinity is a natural 'laboratory' for such work.

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