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The Genetic Effects of Consanguinity on Morbidity : A Population Study

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ABSTRACT The effect of inbreeding on morbidity is assessed through genetic load estimates in terms of detrimental equivalents among the Ezhavas of Alappuzha, by using a random sample of 1204 marriages. The genetic burden manifested in total morbidity was estimated between 1.0973 and 1.1136 detrimental equivalents per gamete. It suggests that an average person carries in heterozygous condition 2-3 abnormal equivalent genes that, if made homozygous, would produce recognizable defects and diseases. The high B/A ratio obtained (67.28) is suggestive that genetic load disclosed by inbreeding in the group is predominantly from mutational load. Compared with unrelated parents, offspring of consanguineous marriages have a higher risk of morbidity (Relative risk (RR) = 4.4 to 13.22). The attributable risk (AR) for the whole sample is about 50%. It shows that inbreeding has a major impact on morbidity.

INTRODUCTION

Inbreeding, as exemplified by consanguineous marriages in man, increases the frequency of homozygotes in the population and decreases the frequency of heterozygotes. Disadvantages effects of harmful recessives are sheltered by their normal counterparts and thus escape selection. These concealed genetic variants constitute the genetic load, which is considered to be the harmful burden borne by the population. With the work of Chetverikov (1926) many researchers attempted to document genetic load and study the forces which operate in maintaining genetic variability in natural populations. One of the most vexing problems associated with genetic load concept has been that of deciding how these variants are maintaining and affecting the fitness of their heterozygous carriers. As a mean of alleviating this dilemma Morton et al. (1956) in a pioneering paper gave a method for determining from inbred and outbred individuals, whether the genetic load in the population was mainly due to deleterious genes maintained by mutation pressure (Mutational load) or due to genes maintained because the heterozygote were superior to the homozygotes (Segregational load). Morton, Crow and Muller (1956) have applied their method to some human mortality data from France and the United States and suggested that an appreciable fraction of the genetic load is mutational and that the component of the genetic load tend to act nonsynergistically when brought to the manifestation in homozygotes. This has stimulated a great deal of research on the subject and generated considerable controversy. Both the validity of the approach as well as the interpretation of the results have been questioned on mathematical and theoretical grounds by (Li, 1963; Sanghvi, 1963; Schull and Neel, 1965) and defended by Crow (1963).

The MCM (Morton, Crow and Muller's) concept of genetic load originally devised for use with respect to mortality data in terms of lethal equivalents and later the concept of lethal equivalents has been extended to specific detrimental effects as detrimental equivalents (Morton, 1960). Since the publication of original theory many investigators have used the data on inbreeding and morbidity to estimate the genetic load in man (Morton, 1960; Neel and Schull, 1962; Cavalli-Sforza and Bodmer, 1971; Rao and Inbaraj, 1977; Kaku and Freire-Maia, 1992; Reddy, 1992; Sudhakaran, 1996).

Despite, India being a vast conglomerate of various endogamous castes, communities and tribes providing excellent material for consan-

guinity studies, reports on such investigation are fragmentary and only a few reports on genetic load are available (Kumar et al., 1967; Chakraborty and Chakravarty, 1977; Rao and Inbaraj, 1977; Rao and Murty, 1990; Devi et al., 1994: Sudhakaran and Vijayavalli, 1996a, b, 1997). The data on the effects of inbreeding on morbidity among the Ezhavas of Alappuzha district of Kerala is used here for estimating the detrimental load in the group. The magnitude of genetic load due to morbidity expressed by inbreeding has not been estimated previously in the population groups of Kerala.

MATERIALS AND METHODS

The Ezhavas are the major Hindu backward (socio-economically) community of Kerala. Numerically they are the single largest group among Hindus, constituting more than 21% of the total population of the state. They are almost evenly distributed, mostly in the central and southern districts of the state including Alappuzha, among whom the practice of related marriages has long been favoured and encouraged. Data were collected exclusively from door to door survey. The effects of inbreeding on morbidity was computed from the data on total number of surviving children/couple (during survey period 1993-1996), with a sample of 1204 marriages drawn randomly from the urban (265), sub-urban (330) and rural (609) regions of the district through intensive interviewing of the spouses by using an elaborate questionnaire. Non consanguineous families from the same socio-economic status of the community was taken as control. Morbidity data have been collected and analysed under four broad categories namely physical defects (Polydactyly, Syndactyly, Brachydactyly, Dwarfism, Club foot, Cleft lip ± Cleft palate) mental defects (Mental retardation) sensory defects (Blindness, Deafness, Sluttering/Stammering, Squient eyes) and a few systmic diseases (Asthma, Diabetics, Tuberculosis, Epilepsy, Heart, Kidney and Lung diseases). Estimation of genetic load was made through an analysis of regression of morbidity on the coefficient of inbreeding using the weighted regression equation :

$$L_D = -\log (1-P_D) = A+BF \text{ (Morton, 1960).}$$

Where, L_D is the detrimental load, and P_D is the frequency of affected individuals among the people whose inbreeding is measured by F.

Inbreeding was represented by only a few individuals in our sample. Hence it is likely that observed viability to be zero in certain inbreeding classes, which results in an undefined logarithm, and hence a small size correction was made before performing the regression. The appropriate correction used for a logrithm regression was :

$$\ln \left(\frac{x_i+1}{n_i+2}\right) = -A-BF \text{ (Templeton and Read, 1983).}$$

The relative risk (RR) and proportional attributable risk (AR) was calculated following Grant et al. (1994).

RESULTS

A sample of 1204 marriages was studied, out of which 13.62% were consanguineous with F=0.0087. The effects of consanguinity at various stages of morbidity are presented in table 1. The computed frequency distribution of physical (2.0%) mental (0.60%) and sensory defects (1.60%) and diseases (3.0%) among the offspring of consanguineous parents have been found higher than control (physical 0.46%, mental 0.33%, sensory 0.19% and diseases 0.58%). Estimate of detrimental load and equivalents by type of defect and their B/A ratios are also presented in table 1. A and B were computed separately for each type of defect and collectively for total morbidity. In all cases, B values were found higher than A values. Of these highest B value obtained for diseases and lowest for mental defects. Estimates of A and B obtained for the total morbidity was 0.016308 and 1.0973, respectively with a B/A ratio of 67.28.

The proportional attributable risk (AR) for

Table 1 : Estimate of detrimental load in terms of A and B statistics by type of defect among the Ezhavas

Consanguinity type	*Total no. surviving children*	*Frequency of abnormalities*									
		Physical		*Mental*		*Sensory*		*Diseases*		*Total*	
		n	%	*n*	%	*n*	%	*n*	%	*n*	%
IC	420	7	1.67	3	0.71	8	1.90	13	3.10	31	7.38
ICI	4	-		-		-		-		-	
2C	76	3	3.95	-		-		2	2.63	5	6.58
Total	500	10	2.00	3	0.60	8	1.60	15	3.00	36	7.20
NC	3070	14	0.46	10	0.33	6	0.19	18	0.58	48	1.56
A			0.00495		0.00361		0.00286		0.00625		0.01631
B			0.32538		0.11228		0.31958		0.49100		1.09726
B/A			65.78		31.11		111.73		78.59		67.28

Note : IC = First cousin, ICI = First cousin once removed, 2C = Second cousin, C = Consanguineous, NC = Nonconsanguineous

the effects of consanguineous marriages on morbidity for different levels of relative risks (RR) calculated are presented in table 2. A breakdown by type of defect showed that offspring of consanguineous marriages have a higher risk of morbidity than controls (RR = 4.4 to 13.2), corresponding differences were observed in their AR values also (AR = 77.27% to 92.44%). The AR value for total morbidity was estimated to be 88.04%

Table 2: Estimates of relative risk (RR) and proportional attributable risk (AR) by type of defect among the Ezhavas

Type of defect	*Relative Risk*	*Attributable Risk*
Physical	8.194	87.80
Mental	4.398	77.27
Sensory	13.219	92.44
Diseases	9.596	89.58
Total	8.358	88.04

DISCUSSION

The morbidity profile for a specific community or population within the context of their unique demographic and environmental circumstances can help in understanding the relative influence of various epidemiological, genetic and environmental factors on human health. The new born are subject to differential risks of congenital malformations and various diseases. Some may be severe enough to cause death at various stages. Many abnormalities do not substantially increase the death but can handicap the bearer in various ways. It is difficult to partition such defects and diseases which contribute to morbidity in man into genetic and nongenetic entities with certainty. However, a variety of Mendelian conditions are believed to have been related to many metabolic abnormalities, inborn errors of metabolism, physical, mental and sensory disorders and diseases (McKusick, 1987).

In estimating the genetic load of the sample, the concept of detrimental equivalents (in terms of A and B statistics) advanced by Morton (1960) was employed. His estimates of the number of detrimental equivalents are derived by assuming that the ratio of physical, mental and sensory defects and diseases between consanguineous and control populations are an expression of detrimental or abnormal genes of varying degress of penetrance. By performing linear regression of the log proportion of nondefective children onto the respective F values, A can be determined from the Y-intercept at zero inbreeding (F=0), and B is given by the slope of the regression.

Data on morbidity type and their respective detrimental equivalents are given in table 1. The results show that various types of defects measured by detrimental recessive genes have different probabilities of responding to inbreeding. The genetic burden manifested in total morbidity in the group is estimated between 1.0973 and 1.1136 detrimental equivalents per gemete. The result of inbreeding effects suggests that an average person carries in

heterozygous condition 2-3 detrimental equivalent genes that if made homozygous, would produce recognizable defects and diseases. The high B/A ration (67.28) suggests that the morbidity disclosed by inbreeding in the group is predominantly from mutational load.

To suppress the erratic nature of the data on the effect of consanguinity, caused by nongenetic variation in the background morbidity rates, A and B values calculated as above were incorporated into relative risk (RR) and proportional attributable risk (AR) estimates for total consanguinity by type of defect (Grant et al., 1994 *cf.* Bittles, 1994). The relative risk, defined as the ratio of morbidity in the consanguineous versus control group is calculated by using the formula:

$$RR = 1+BF/A$$

and proportional attributable risk, which measures the extent of excess risk within consanguineous group, is calculated by the formula :

$$AR = BF/A+BF$$

RR value calculated for type of defect (Table 2) shows that among the children of consanguineous marriages the frequency of abnormalities are 4.4 to 13.22 times higher than control. AR values calculated for total consanguinity by type of defect shows that 87.8% of Physical defect were associated with the expression of detrimental recessives genes, with equivalent values of 77.27%, 92.44% and 89.58% for Mental defect, Sensory defects and Diseases respectively. Calculation of the population proportional attributable risk (Khoury et al., 1987) which estimates the fraction of total morbidity associated with consanguinity in the study sample, indicate that 50% of the morbidity was associated with inbreeding. The last value shows the amount by which the frequencies of abnormalities and diseases would decrease in the population, if consanguineous marriages could be eliminated.

These findings suggest that among the population, with prolonged and medium levels of consanguinity (<15%) the effect of inbreeding on genetically determined defects and diseases are greater than among those with high levels of inbreeding, as had from the studies on other South Indian populations (Rao and Inbaraj, 1977; Babu et al., 1994). This is consistent with genetic theory, which predicts that under prolonged and high levels of inbreeding, there would have been a marked decline in the frequency of deleterious genes due to their elimination by segregation, thus lowering the equilibrium allele frequencies for detrimental genes. The reducing effect of such genes have their manifestation in the consanguinity-associated morbidity also.

REFERENCES

Babu, B.V., Kusuma, Y.S. and Naidu, J.M. : Genetic load among four Andhra caste populations. *Soc. Biol.*, **41**: 127-129 (1994).

Bittles, A.H. : Role and significance of consanguinity as a demographic variable. *Popu. Dev. Rev.*, **20**: 561-584 (1994).

Cavalli-Sforza, L.L. and Bodmer, W.F. : *The Genetics of Human Populations*. W.H. Freeman and Co., San Francisco (1971).

Chakraborty, R. and Chakravarty, A. : On consanguineous marriges and the genetic load. *Hum. Genet.*, **36**: 47-54 (1977).

Chetverikov, S.S. : On certain aspects of evolutionary process from the stand point of morden genetics. *Am. Phil. Soc.*, **105**: 167-195 (1926).

Crow, J.F. : The concept of genetic load : A reply. *Am. J. Hum. Genet.*, **15**: 310-315 (1963).

Devi, N., Dhathri, S., Vishnupriya, K., Ravikumar, R. and Padma, T. : Consanguinity and genetic load in the families affected by retinitis pigmentosa. *Med. Sci. Res.*, **22**: 355-356 (1994).

Kaku, M. and Freire-Maia, N. : Inbreeding effect on morbidity : IV Further data in Brazilian populations. *Am. J. Med. Genet.*, **42**:420-423 (1992).

Khoury, M.J., Cohen, B.H., Chase, G.A. and Diamond, E.: An epidemiological appraoch to the evaluation of the effect of inbreeding in prereproductive mortality. *Am. J. Epidemiol.*, **25** : 251-262 (1987).

Kumar, S.R, Pai, A and Swaminathan, M.S. : Consanguineous marriages and the genetic load due to lethal genes in Kerala. *Ann. Hum. Genet.*, **31**:141-147 (1967).

Li C.C. : The way of load works. *Am.J. Hum. Genet.*, **15**:316-321 (1963).

McKusick, V.A. : *Mendeliam Inheritance in Man*. John Hopkins University Press, Baltimore (1978).

Morton, N.E. : The mutational load due to detrimental genes in man. *Am. J. Hum Genet.*, **12**:348-364 (1960).

Neel, J.V. and Schull, W.J. : The effect of inbreeding on mortality and morbidity in two Japanese cities. *Proc. Natl. Acad. Sci.(USA)*, **48**:573-582 (1962).

Rao, P.S.S. and Inbaraj, S.G. : Inbreeding effects on human reproduction in Tamil Nadu of South India. *Ann.Hum.Genet.*, **41**:87-98 (1977).

Rao, V.V. and Murty, J.S. : Role of marital migration in the expression of inbreeding load in different castes of Andhra Pradesh. *J.Hum. Ecol.*,**1**:43-46 (1990).

Reddy, B.M. : Inbreeding effects on reproductive outcome : A Study based on a large sample from the endogamous Vadde of Kolleru Lake, Andhra Pradesh, India. *Hum.Biol.*, **64**:659-682 (1992).

Sanghvi, L.D. : The concept of genetic load : A critique. *Am. J. Hum. Genet.*, **15**: 298-309 (1963).

Schull, W.J. and Neel, J.V. : *The Effect of Inbreeding on Japanese Children*. Harper and Row, New York (1965).

Sudhakaran, M.V. : *Studies on Consanguinity and Its Effects in Certain Castes and Communities in Alappuzha (Kerala)*. Ph.D. Thesis, University of Kerala (1996).

Sudhakaran, M.V. and Vijayavalli, B. : Effects of inbreeding on mortality in Ezhavas of Alappuzha, South India. *J. Cytol. Genet.*, **31**: 179-183 (1996a).

Sudhakaran, M.V. and Vijayavalli, B. : The genetic effects of inbreeding on mortality among the Pulayas of Alappuzha. *Dmography India*, **25**: 199-204 (1996b).

Sudhakaran, M.V. and Vijayavalli, B. : An estimate of genetic load in the Nayars of Alappuzha, Kerala. *J. Hum. Ecol.*, (in press) (1997).

Templeton, A.R. and Read, B. : The elimination of inbreeding depression in a Capative Herd of Speke's Gazelle. In : *Genetics and Conservation : A Reference for Managing Wild Animal and Plant Populations*. C.M. Schonewald-Cox, S.M. Chambers, B. MacBryde, W.L. Thomas (Eds.). Benjamin/Cummings Publishing, Co., USA (1983).