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AN ESTIMATE OF GENETIC LOAD DISCLOSED BY INBREEDING AMONG THE MUSLIMS OF ALAPPUZHA, KERALA

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ABSTRACT

A cross sectional samples of 515 marriages of the Muslims of Alappuzha district of the state of Kerala were studied for estimating the component of genetic load operating in the prenatal and postnatal stages. Consanguinity-associated prenatal and postnatal mortality was found to be 4.84 to 5.07 times higher than control. The genetic burden manifested in total prereproductive mortality in the group was estimated between 3.1009 and 3.1379 lethal equivalents per gamete. It suggests that a normal 'healthy' human being carries in heterozygote condition 7 lethal equivalent genes, if made homozygyous, they would kill an individual between birth and maturity. The high B/A ratio (83.74) is suggestive that mortality disclosed by inbreeding in this group is predominantly from mutational load.

Key words: Muslim, consanguinity, mortality, genetic load.

Based on the pioneering work on Chetverikov[1], Haldane attempted to document the expression of deleterious recessive genes as detrimental to the fitness of population [2]. Muller [3] has developed this proportion as 'genetic load' to describe mortality and morbidity in human population. Morton *et al.* [4] have found it helpful to express the load in terms of lethal equivalent to study the influence of inbreeding on the viability or sterility of progeny. Many investigators have used the data on inbreeding on mortality to estimate the genetic load in man[5-9]. A precise estimation of such genetic damage in a population should weigh genes by their lethal effects.

Despite India being a vast conglomerate of various endogamous castes, communities, tribes and a variety of racial isolates, and great prevalence in the practice of inbreeding, only a few reports on genetic load are available in literature [10-14] and are almost lacking in Kerala[15-22].

The present study aims to assess the effect of inbreeding on prereproductive mortality and to estimate the genetic load among the Muslims of Alappuzha district of the state of Kerala (South India). The magnitude of genetic load due to mortality expressed by inbreeding has not been estimated previously in this population group of Kerala.

MATERIALS AND METHODS

The Muslims of Kerala forms the third largest population group, constituting more than 19.5% of the total population of the state. They are socio-economically backward community, among whom the practice of related marriages has long been favoured and encouraged. In the present study data were collected exclusively from door to door survey. The effects of inbreeding on prereproductive mortality was computed from the data on the reproductive histories of couples (during the survey period 1993- 1996) drawn randomly from the urban, sub-urban, and rural regions of the district through intensive interviewing of the spouses by using an elaborate questionnaire. Nonconsanguineous families from the same socio-economic status of the community was taken as control. Chi-square tests have been used to test the significance of the differences between the proportions. Estimation of genetic load was made through an analysis of regression of prereproductive mortality on the coefficient of inbreeding using the weighted regression equation:

$$S = e^{-(A+BF)} \qquad \ldots \quad [4]$$

Where,

S = the viability or probability of survivors
e = 2.7183
A = panmitic load (random load)
B = inbred load.
F = Coefficient of inbreeding

Incidence of inbreeding was represented by only a few individuals in our sample. Hence, it is likely that the observed viability being zero in certain inbreeding classes, which results in an undefined logarithm. Thus a small size correction was necessary before performing the regression. The appropriate correction used for this study, is the one that proposed by [23], for a logarithm regression:

$$\ln(x_i + 1/n_i + 2) = -A - BF$$

Where, x_i = number of individual surviving
n_i = total number of births

RESULTS AND DISCUSSION

A cross sectional sample of 515 marriages was studied, out of which 10.68% were consanguineous with F = 0.005959. The effects of consanguinity at various stages of preproductive mortality are presented in Table 1. The computed frequency distribution of prenatal (5.96%) postnatal (11.93%), and total prereproductive mortality (17.89%) among the offspring of consanguineous parents have been found higher than control (Prenatal 1.23%, postnatal 2.35%, total preproductive mortality 3.58%). Postnatal ($p < 0.01$), and total preproductive mortality ($p < 0.02$) was found to be positively associated with consanguinity. Estimate of genetic load in terms of A and B statistics (Table 2) were computed separately for prenatal and postnatal mortality and collectively for total prereproductive mortality. In all cases B values were found higher than A values. Estimates of A and B obtained for the total mortality was 0.03703 and 3.1009 respectively with a *B/A* ratio of 83.74.

Table 1. Effect of consanguinity on mortality among the muslims of Alappuzha

Parameter	No. of cases studied	Nonconsanguineous (F = 0)		Consanguineous (F = 0.09375)	
		n	%	n	%
Abortion	32	20	1.12	12	5.50
still birth	3	2	0.11	1	0.46
Prenatal	35	22	1.23	13	5.96^{*}
Infant	21	11	0.61	10	4.59
Neonatal	2	2	0.11	-	-
Postneonatal	10	9	0.50	10	4.59
Child	25	11	0.61	14	6.42
Juvenile	22	20	1.12	2	0.92
Postnatal	68	42	2.35	26	11.93^{**}
Total Mortality	103	64	3.58	39	17.89^{**}
Total Survived	1900	1721	96.42	179	82.11
Total Pregnancy	2003	1785	100.00	218	100.00

$^{*}0.90>p>0.80$ $^{**}p < 0.01$ $^{***}p < 0.02$

Table 2. Estimate of genetic load in terms of A and B statistics for prenatal, postnatal and total mortality among the muslims of Alappuzha

Mortality	A	B	A + B	B/A
Prenatal	0.01293 ± .003	1.0531 ± .34	1.06601	81.45
Postnatal	0.02448 ± .004	2.0053 ± .47	2.02978	81.91
Total	0.03703 ± .005	3.1009 ± .60	3.13793	83.74

Natural population of presumably all diploid and outbreeding organisms carry burden or load of genetic defects which may sometimes be expressed phenotypically or remain hidden in heterozygous conditions. These hidden recessive genetic variants are not ordinarily expressed, but may be revealed by inbreeding. Genotypes that confer a fitness distinctively below the mean of adaptive values may periodically be eliminated from the gene pool during prenatal and postnatal stages and the components of concealed genetic load become expressed more frequently in inbred progeny. Many inbreeding studied world over, have highlighted increased rates of prenatal and postnatal deaths in consanguineous progeny than control [5, 6, 15-20]. In the present study consanguinity-associated prenatal and postnatal mortality was found to be 4.84 to 5.07 times higher than control (Table 1). These findings are consistent with genetic mechanisms, since inbreeding increases the frequency of autosomal recessive genes in inbred offspring.

To analyse the inbreeding effects in the study sample, the concept of lethal equivalents [4] has been employed. The procedure adopted here was to fit a linear function to the natural logarithm of surviving children (of age 0 to 20 years) in each sibship as a function of kinship coefficient (F) of the parents, using weighted least square regression analysis. On this model, random load (A) can be determined from the Y- intercept at zero inbreeding (F=0) and inbred load (B) is given by the slope of the regression. According to the genetic load theory, A value measures the mortality of noninbred fraction (F=0), while B reflects the hidden or concealed genetic damage revealed by inbreeding, if random gametes were made homozygous (F =1). The total genetic damage per gamete is equal to the sum of B and the genetic component of A and hence lies between B and $B + A$. The consanguinity ratio (B/A) provides critical information on the relative importance of mutational and segregational loci in maintaining the genetic load [24].

In this present group of Muslim, A and B parameters, B/A ratios and their standard errors have been calculated from the data in Table 1. The genetic burden manifested in total prereproductive mortality in the group is estimated between 3.1009 to 3.1379 lethal equivalents per gamete (Table 2). The result of inbreeding effects suggest that an average person carries in heterozygous condition 7 lethal equivalent genes, that if made homozygous, they would kill an individual between birth and maturity. The estimate of mean number of lethal equivalents per gamete of 3.1009 obtained for Muslims, appear to be high in comparison with previously published data on Ezhavas [17] (A = 0.07847, B = 2.2877, B/A = 29.15), Nayars [19] (A = 0.05699, B = 2.3664, B/A = 41.53), and Viswakarmas [20] (A = 0.0428, B = 1.8365, B/A = 43.29). However, the estimated values of B for Muslims are found to be in good agreement with the values obtained for Pulayas of Kerala [18]. The consistently high B/A ratios obtained in all three parameters of mortality, suggest that mortality disclosed by inbreeding in this group is predominantly from mutational load.

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