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INBREEDING LOAD IN THE NEWBORN OF HYDERABAD

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SUMMARY

The population of Andhra Pradesh has been considered ideal for the study of inbreeding effects in view of its high incidence of consanguinity. Information for the present investigation was obtained from 1,091 consecutive hospital single births to study the genetic load in the newborn in terms of mortality and malformation as a consequence of inbreeding. The nature of consanguinity was examined and the frequency of uncle-niece marriages was found to be lower than in other parts of Andhra Pradesh. The mortality load in the newborn was found to be two lethal equivalents per individual, while the malformation load at birth was half the mortality load.

INTRODUCTION

Populations are continuously impaired by genetic loads which are the result of reduction in fitness due to deleterius genes. Genetic load has been defined as the proportion by which the fitness of an average genotype in the population is reduced in comparison with the optimum genotype.

The load, generally measured as mortality, sterility, or malformation, can be estimated from the effects of consanguinity by expressing the load L as a function of inbreeding F, (Morton et al. 1956). Thus $1 - L = \exp - (A + BF)$, which for low levels of inbreeding and low values of A may be approximated by $L = A + BF$. The statistic A is an estimate of the random-mating load, while B is an estimate of the inbred load; $A + B$ therefore represents the total load. The ratio B/A gives an estimate of the number of loci with heterotic alleles, a low value of which indicates that the load is segregational, i.e., due to the segregation of superior heterozygotes. A high value represents a mutational load which is due to deleterius mutations balancing selection. When the load is measured as mortality it is expressed in lethal equivalents, and when measured as malformation it is defined in terms of detrimental equivalents.

In view of the prevalence of a high degree of consanguinity, the population of Andhra Pradesh forms an ideal source for the measurement of genetic loads. Several studies (e.g. Dronamraju 1964, Sanghvi 1966) report the incidence of inbreeding in the state and the factors responsible for it, but studies on its effects remain largely empirical.

The present study is designed to estimate the genetic load in terms of mortality and malformation in the newborn. Estimates of the load in the newborn are

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useful as they are free from genetic and environmental causes that influence mortality or impairment after birth. The random mating component of this load involves the effects of in-utero environment alone.

Information was collected on 1,091 consecutive single births in a period of over three months from 1st April 1969 from the Maternity Unit of the Niloufer Hospital for Women and Children.

Each infant was examined for the presence of major visible congenital anomalies within 36 hours after birth. Infant mortality up to the third day was noted. Information on parental consanguinity was obtained directly from the mother and verified with an accompanying relative.

RESULTS

Consanguinity

The average inbreeding coefficient of the present series (0.0134 ± 0.0009: Table I) is less than the figures reported for Coastal Andhra (0.023: Dronamraju and Meera Khan 1963; and 0.015 – 0.048: Sanghvi 1966). This figure is also less than the average, 0.029, obtained in a study of 1,037 newborn in a Vellore hospital in Tamil Nadu (Centerwall and Centerwall 1966). However, this result is about the same as that obtained by Rajyalakshmi (1970) in a random sample of 100 families of Hyderabad. Sanghvi (1966) also reports a fairly low level in the Telangana region of Andhra Pradesh.

TABLE I

CONSANGUINITY, MORTALITY, AND MALFORMATIONS

Relationship	Present Series						Vellore Sample	
	F	N	% of total	Mortality (%)	Malformed (%)	% among malformed	N	% of total
Unrelated	0.0000	880	80.66	3.7	0.91	61.5	649	62.6
Second cousins once removed	0.0078	2	0.18	—	—	—	—	—
Second cousins	0.0156	8	0.73	12.5	—	—	—	—
First cousins once removed	0.0313	8	0.73	—	—	—	23	2.2
First cousins	0.0625	121	11.09	6.6	2.48	23.17	184	17.8
First and second cousins	0.0781	39	3.57	10.3	5.13	14.8	—	—
First and double second cousins	0.0937	16	1.46	12.5	—	—	—	—
Uncle-niece	0.1250	11	1.01	18.2	—	—	137	13.2
Second cousins once removed and uncle-niece	0.1258	4	0.37	—	—	—	—	—
Others	—	2	0.18	—	—	—	23	2.2

Malformation

Among the 1,091 newborn, a total of 13 malformed babies (1.18%) having 16 individual malformations (1.46%) was found. Three cases of multiple anomalies include (*a*) hydrocephalus with meningocoel, (*b*) hydrocephalus with cleft lip, and (*c*) cleft lip and palate with hypospadias. The cases with single malformations were: anencephaly 3, oesophageal atresia 1, exomphalus 1, polydactyly 2, deformed pinna 1, gross skeletal malformations 1, and hydrocephaly 1.

Genetic load

The estimates of A and B for the genetic loads obtained through weighted regression (Smith 1967) are given in Table II along with the χ^2 values for testing the adequacy of relationship between morbidity and inbreeding. The newborn of Hyderabad may be seen to carry a load of two lethal equivalents and one detrimental equivalent per individual. The load in both cases is mainly mutational as is evident from the high B/A ratios.

TABLE II

ESTIMATES OF A AND B

	A	B	B/A	χ^2
Malformation	0.0069 ± 0.006	0.4709 ± 0.271	69	0.545 with 1 *DF*
Mortality	0.0596 ± 0.008	0.8672 ± 0.381	14	9.002 with 4 *DF*

DISCUSSION

The present study confirms the generally lower incidence of inbreeding in Hyderabad and other areas of the Telangana region as compared to Coastal Andhra Pradesh or Vellore of Tamil Nadu. This difference in inbreeding could in part be attributed to the low frequency of uncle-niece marriages in Telengana region. The frequency of such marriages in the Telangana region are 1% (present study), 0.04% (Rajyalakshmi 1970), and 2-5% (Sanghvi 1966), as compared to 6-10% (Dronamraju and Meera Khan 1963) and 10-20% (Sanghvi 1966) in Coastal Andhra Pradesh, or to 13.2% (Centerwall and Centerwall 1966) and 11% (Jacob and Jaibal 1971) in Vellore of Tamil Nadu.

The incidence of congenital anomalies in different populations normally varies with the ethnic background and the estimates are complicated by diagnostic procedures and objective follow-up after birth. In view of the small sample size, the present investigation (and that of Centerwall and Centerwall 1966) is inadequate to give a reliable estimate of the incidence of congenital anomalies; in fact, it has pri-

marily been designed to study the effects of number and consanguinity. However, the number and spectrum of malformations found in this study is different from that obtained by Centerwall and Centerwall (1966) in Vellore in a study of similar sample size and with the objective of finding out the inbreeding effects. The reasons may be many, including ethnic differences and inbreeding levels.

Comparable estimates of genetic loads for perinatal mortality are not quite available excepting those by Sutter and Tabah (1952) who found in France a load similar to ours ($B = 1.124$, $B/A = 14.4$) and by Bigozzi et al. (1970) who found a load of about two lethal equivalents in Italy. Kumar et al. (1967) report a load of 3-4 lethal equivalents for stillbirths and neonatal deaths.

Considering all genetic deaths, i.e., mortality up to adult age, a load of 3-5 lethal equivalents was reported among Caucasians, (Morton et al. 1956) and 8-9 lethal equivalents among Keralites (Smith 1969), but this was an estimate from the families of hospital in-patients admitted for different sorts of diseases. Thus, about one third to one half of the genetic load in man seems to be expressed at birth.

We find the genetic load due to malformation to be one detrimental equivalent, i.e., half the mortality load in the newborn. Bigozzi et al. (1970) also found a load of 1.6 detrimental equivalents for congenital defects.

This investigation supports the conclusions of Morton et al. (1956) and Kumar et al. (1967) that the genetic load in man is more mutational than segregational. Further, the high frequency (64%) of unrelated matings among the parents of malformed children (Table I) points out to nongenetic and/or mutational components in the incidence of these malformations, and thus provides another evidence for the mutational component of the genetic load.

This result regarding the nature of the load and the incidence of malformation needs further consideration. The population of Coastal Andhra is highly inbred and Sanghvi (1966) makes an attempt, based on theoretical considerations, to show that the frequency of deleterious alleles would have declined considerably over a period of two thousand years in a population under such inbreeding. But as the level of inbreeding in Hyderabad and other Telengana areas of Andhra Pradesh is low, the efficiency of inbreeding in eliminating deleterious genes may not be as striking as envisaged by him. Nonetheless, the low incidence (1.18%) of congenital malformations and the fact that the load is nonsegregational point out to the role of inbreeding in this population.

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Riassunto

La popolazione dell'Andhra Pradesh è stata considerata ideale per lo studio degli effetti dell'endogamia, data la sua elevata incidenza di consanguineità. I dati per l'attuale ricerca sono stati ricavati dall'ospedale di Hyderabad, dove un campione di 1091 nascite semplici consecutive sono state rilevate in modo da studiare il carico genetico sui neonati in termini di mortalità e malformazioni come conseguenza dell'endogamia. La natura della consanguineità è stata esaminata e la frequenza di matrimoni zio-nipote è risultata inferiore che in altre parti dell'Andhra Pradesh. Il carico della mortalità nei neonati è risultato di due geni-equivalenti letali per individuo, mentre il carico delle malformazioni alla nascita è risultato della metà.

Résumé

La population de l'Andhra Pradesh a été considérée idéale pour l'étude des effets de l'endogamie, étant donnée sa fréquence élevée de consanguinité. Les données pour cette recherche ont été obtenues de l'hôpital d'Hyderabad, où un échantillon de 1091 naissances simples consécutives a été considéré afin d'y étudier le poids génétique en termes de mortalité et malformations en conséquence de l'endogamie. La nature de la consanguinité a été examinée et la fréquence de marriages oncle-nièce a été trouvée inférieure à celle d'autres régions de l'Andhra Pradesh. Le poids de la mortalité des nouveaux-nés est de deux gènes-équivalents léthaux pour individus, alors que celui des malformations est de la moitié.

Zusammenfassung

Ihrer hohen Blutsverwandtschaftsrate wegen eignet sich die Bevölkerung des Andhra Pradesh besonders zum Studium der Inzuchtswirkung. Um den Erbeinfluss der Inzucht auf die Sterblichkeit und die Missbildungen der Neugeborenen zu untersuchen, wurden im Hospital zu Hyderabad Erhebungen an einem Muster von 1091 hintereinander erfolgten Einzelgeburten vorgenommen. Es wurde dabei der Grad der Blutsverwandtschaft untersucht, u. es zeigte sich, dass Onkel-Nichten-Ehen weniger zahlreich waren als in anderen Gegenden des Andhra Pradesh. Der Einfluss der Neugeborenensterblichkeit entspricht zwei letalen-äquivalent-Genen pro Person; die Missbildungen bei Geburt hingegen betragen die Hälfte.

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