

Inbreeding and post-natal mortality in South India: effects on the gene pool

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Abstract. Consanguineous marriages have been favoured throughout South India for many generations. On theoretical grounds it was proposed that long-term inbreeding would have resulted in the elimination of deleterious, recessive lethal and sub-lethal genes. As part of a newborn screening programme for amino acidopathies, data were collected on the level of inbreeding in the current populations of the cities of Bangalore and Mysore, and on the relationship between consanguinity and mean numbers of liveborn and living children. Mean consanguinity was 32.24%, equivalent to a coefficient of inbreeding in the newborns, $F = 0.0271$. There were no significant differences between the various inbreeding classes in the number of liveborn or living children, nor was a significant consanguinity-related effect on the proportion of survivors detectable. In the light of these findings, the effects on the gene pool of multiple generations of inbreeding are discussed.

Keywords. South India; inbreeding; liveborns; living children.

1. Introduction

The four southern states of India - Andhra Pradesh, Karnataka, Kerala and Tamil Nadu (figure 1) - are of considerable interest to geneticists as their inhabitants, who totalled more than 164 millions in the 1981 Census of India, strongly favour consanguineous marriages. In general, inbreeding in South India is negatively correlated with socio-economic status (Dronamraju and Meera Khan 1963a; Centerwall *et al* 1969; Rao and Inbaraj 1977a; Venugopal Rao and Murty 1984), but the actual rates and types of consanguineous unions vary between and within each state (Sanghvi 1966a; Kumar *et al* 1967; Rao *et al* 1971; Hann 1985), between the major religious groups (Asha Bai *et al* 1981; Radha Rama Devi *et al* 1982; Rao 1983) and, in the majority Hindu population, by caste (Rao *et al* 1971; Ray 1979; Papa Rao and Rami Reddy 1983). Since it is believed that high levels of inbreeding have been practised by the Dravidian peoples for some 2,000 years, it was proposed that the overall, long-term effect on the gene pool would be a significant reduction in the number of lethals and sub-lethals (Sanghvi 1966b). Although this hypothesis was contradicted by analysis of a survey on perinatal mortality and congenital malformations (Chakraborty and Chakravarti 1977) conducted in Maharashtra, the southern part of which follows the Dravidian inbreeding tradition (Sanghvi 1966a; Malhotra 1979), supporting evidence was claimed in large-scale prospective and retrospective surveys on fetal and infant deaths in Tamil Nadu (Rao and Inbaraj 1977b, 1979a). The aim of the present study was to further investigate

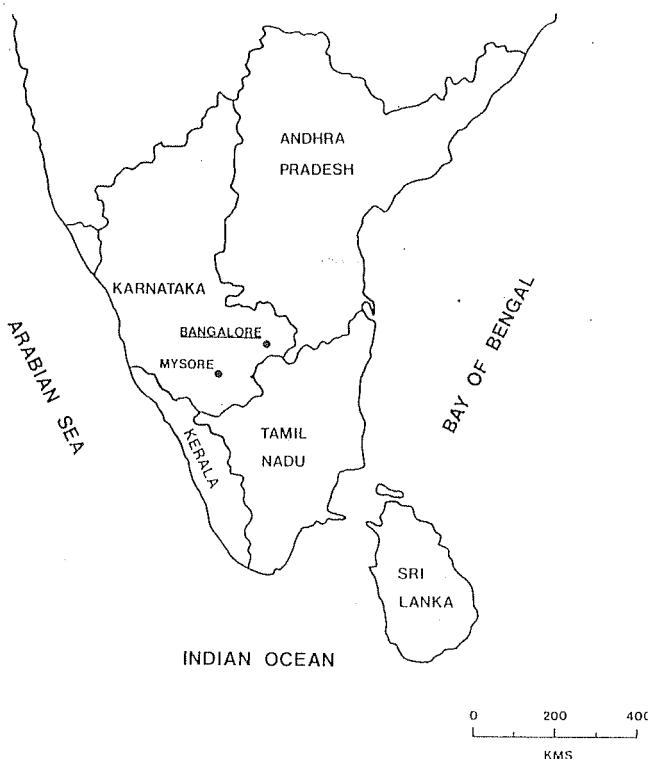


Figure 1. Location of the survey.

the effect(s) of inbreeding on the levels of post-natal mortality in Karnataka as earlier, preliminary findings had indicated no significant consanguinity-related increase in this parameter (Radha Rama Devi *et al* 1981).

2. Materials and methods

The data on post-natal mortality were collected as an integral part of a project designed to estimate the incidence of disorders of amino acid metabolism in newborn infants (Bittles *et al* 1982). The programme, which was established in 1980, is based in the Indian Institute of Science (IISc) and operates in fifty hospitals and maternity homes located throughout the cities of Bangalore and Mysore. There is no pre-selection of subjects and the programme operates without charge to those tested. As a result, the families sampled are reasonably representative of all sections of the populations of both cities, although there may be some under-sampling of the poorest stratum of society, that is, those without fixed abode.

In Bangalore, sample collection from the newborns was carried out by trained, female, paramedical staff from the Department of Biochemistry, IISc, who also interviewed each mother and recorded family details on maternal age, the degree of genetic relatedness of the husband and wife, the religion(s) of both partners, and the number of liveborn and living children, including the recently delivered infant(s).

Table 1. Religious profile of the total population

Religion	Total number	Percentage
Hindu	34,660	78.83
Muslim	7,426	16.89
Christian	1,744	3.97
Others	6	0.01
Unspecified	132	0.30

Random cross-checks on the collected data failed to detect any evidence of systematic bias in the mothers' answers. In Mysore, sampling was similarly conducted by paramedical and nursing staff and all interview data were transmitted to Bangalore by post along with the blood specimens. The inbreeding classes recorded were, uncle-niece (in the offspring, $F = 0.125$), first cousin ($F = 0.0625$), second cousin ($F = 0.0156$), beyond second cousin ($F < 0.0156$) and non-consanguineous ($F = 0$). Only data on inbreeding in the current generation was considered. All interviews were conducted in the mother's own language, predominantly Kannada. As a result of the rapid expansion of Bangalore during the last thirty years, in a small percentage of cases translation was required from the languages of the three neighbouring states, Andhra Pradesh (Telugu), Kerala (Malayalam), and Tamil Nadu (Tamil).

The families on which the current study is based were sampled between 1980 and 1984. Following collection, all family details were punched on to cards, verified, and stored prior to analysis using a DEC 10 main-frame computer. In order to make the variance between each consanguinity class homogeneous, arcsin transformations of the data were made. Multiple analyses of variance were then run to determine whether statistically significant differences could be detected with inbreeding in the total population and between each major religious group.

3. Results

Data on a total of 43,968 newborns were analyzed; these comprised 43,334 single births, 311 pairs of twins and 4 sets of triplets. The religious profile of the population is presented in table 1 and the frequencies of the main consanguinity classes are shown in table 2. The results, which are in close agreement with those calculated on this

Table 2. Consanguinity classes in the total population

Marital type	Coefficient of inbreeding (F)	Total number	Percentage
Non-consanguineous	0	27,891	63.43
Beyond second cousin	< 0.0156	1,099	2.50
Second cousin	0.0156	956	2.17
First cousin	0.0625	4,826	10.98
Uncle-niece	0.125	6,389	14.53
Unspecified	—	2,807	6.38

Table 3. Percentage of each stated consanguinity class by religion

Marital type	Hindu	Muslim	Christian
Non-consanguineous	65.64	74.46	80.69
Beyond second cousin	2.81	2.06	2.32
Second cousin	2.20	2.86	2.50
First cousin	11.00	16.33	6.62
Uncle-niece	18.34	4.28	7.87

population for the year 1980 only (Radha Rama Devi *et al* 1982), indicate that of the pregnancies in which consanguinity data were available 32.24% were inbred. This figure is comparable with the overall levels reported for previous generations in South India (Dronamraju and Meera Khan 1963b; Rao *et al* 1971), and so it would appear that an earlier prediction of a rapid reduction in consanguineous marriages in the region (Dronamraju 1964) was premature. In table 3 it can be seen that the total, percentage, stated inbreeding was greatest in the Hindu community (34.36%), intermediate in Muslims (25.54%) and least among Christians (19.31%). However, as shown in table 4, the coefficient of inbreeding for Hindus ($F = 0.0301$) was virtually double that of Muslims ($F = 0.0159$) because of the preference for uncle-niece marriages among Hindus, as opposed to the first cousin unions favoured by Muslims. The rate of uncle-niece marriages in the Hindu community (18.34%) was the highest yet recorded for a major, South Indian urban population. Among the Christian group, which included Roman Catholics, the coefficient of inbreeding ($F = 0.0143$) was comparable to that of the Muslim population, due to the relatively high rate of Christian uncle-niece marriages (7.87%).

In table 5, the maximum, minimum and mean numbers of liveborn and living children, and standard errors of the means, are shown for each consanguinity class in the total population. To put the figures for liveborn and living children into perspective, the mean total marital fertility for Karnataka in 1978 had declined to 3.7 in rural areas and 3.0 for urban groups (Vital Statistics Division, 1982). The mean numbers of liveborn and living children were smallest in the nonconsanguineous group but no statistically significant trends in either parameter could be correlated with increasing levels of inbreeding. The proportions of survivors observed in the total population and in each of the major religious groups are reproduced in table 6, sub-divided into consanguinity classes. Again, no significant consanguinity-related trends were detected by analyses of variance in the total population or separately in any of the three major

Table 4. Coefficient of inbreeding by religion

Religion	Coefficient of inbreeding (F)
Hindu	0.0301
Muslim	0.0159
Christian	0.0143
Total population	0.0271

Table 5. Consanguinity class, number of liveborns and number of living children

Marital type	Number of liveborns				Number of living children			
	Maximum	Minimum	Mean	SEM	Maximum	Minimum	Mean	SEM
Non-consanguineous	20	1	2.32	0.0084	20	1	2.21	0.0079
Beyond second cousin	10	1	2.49	0.0435	10	1	2.38	0.0414
Second cousin	10	1	2.39	0.0472	10	1	2.24	0.0423
First cousin	14	1	2.43	0.0209	9	1	2.30	0.0195
Uncle-niece	10	1	2.38	0.0173	10	1	2.25	0.0163

religious groups. There was the possibility of some disadvantageous inbreeding effect in the majority Hindu population, $p = 0.0789$, while the small Christian group tended to indicate a slight advantage with respect to consanguinity, $p = 0.0762$.

4. Discussion

The results of the present study amply confirm the abiding popularity of consanguineous marriages among the populations of South India. It has been suggested that the main reason for this popularity is the perceived degree of social stability offered by marriage to a close relative, allied to the maintenance of property within the family (Dronamraju and Meera Khan 1963b; Reid 1973). Therefore a rapid shift to non-consanguineous unions appears unlikely, although, given the marked decline in average family size and the increased overall mobility of the population, it seems equally improbable that uncle-niece marriages will remain at their present high level (Radha Rama Devi *et al* 1982).

As noted by Haldane (1963), the major question to be answered in any South Indian population study must be, what effect(s) have been exerted on the gene pools of the Dravidian peoples as a result of their preference for consanguinity? The findings presented here initially appear to concur with the hypothesis advanced by Sanghvi (1966b), that the long-term practice of inbreeding would have led to a marked elimination of deleterious genes. However, before acceptance of this postulate a number of factors require consideration:

Table 6. Mean proportion of survivors by consanguinity class: total population and by religion

Marital type	Coefficient of inbreeding (F)	Proportion of survivors		
		Total population	Hindu	Muslim
Non-consanguineous	0	0.9528	0.9520	0.9571
Beyond second cousin	< 0.0156	0.9563	0.9576	0.9533
Second cousin	0.0156	0.9336	0.9433	0.9134
First cousin	0.0625	0.9469	0.9462	0.9530
Uncle-niece	0.125	0.9458	0.9450	0.9610
				0.9450

(i) Given the probable effects of recurrent wars, droughts, famines and epidemic diseases, on population numbers and structure during the time-span envisaged by Sanghvi, that is, the last 2000 years, the assumption of an uninterrupted supply of close relatives, with the sexes in more or less equal numbers, thus ensuring the possibility of consanguinity in each and every generation, seems unwarranted. Nevertheless, in the Hindu community the effect of occasional non-consanguineous marriages on the cumulative coefficient of inbreeding may have been minimized by the probability that marriage partners, almost certainly would have been of the same endogamous caste. Thus, although not directly related genetically, they would have been subject to substantial positive assortative mating.

(ii) The assumption that in every marriage the husband necessarily was the biological father of all offspring is also potentially erroneous. Among recent generations in developed countries this has been shown not to be the case, to a significant extent. Non-recalled adoptions would have similar consequences, that is, the maintenance of genetic heterogeneity.

(iii) The hypothesis also fails to allow for reproductive compensation, a phenomenon identified in Japan both in a small-scale inbreeding study on the island of Kuroshima (Schull *et al* 1962) and later in an extended survey on Hirado (Schull *et al* 1970; Schull and Neel 1972). Confirmation subsequently has been provided that stillbirths and the early deaths of malformed infants are associated with the initiation of replacement pregnancies at reduced birth intervals (Record and Armstrong 1975; Erickson *et al* 1979). Although not statistically significant, the higher mean levels of live-born and living children observed in all consanguinity classes in the present study are strongly suggestive of reproductive compensation. As excess deaths due to inbreeding must be presumed to result from the expression of rare, single recessive genes or polygenic combinations of rare recessives, in two-thirds of cases the net effect of reproductive compensation would be replacement of the expired homozygote by an obligate heterozygote for the disorder. Contrary to the supposition of Rao and Inbaraj (1979b), this would significantly prevent elimination of the deleterious gene(s) from the gene pool. Since the majority of pre-reproductive mortality is, and has been, in the first year of life both in developing and developed countries (Schull and Neel 1972), the opportunities for reproductive compensation would be concomitantly optimized.

Thus, potent reasons exist to suspect the validity of Sanghvi's hypothesis and, in fact, complementary investigations in Karnataka on amino acid disorders in newborns (Bittles *et al* 1982) and on sick children referred with a wide variety of symptoms (Radha Rama Devi *et al*, in preparation), suggest that the levels of many deleterious, recessive genes remain at high frequency in the total gene pool.

If indeed there has been no marked diminution in the numbers of lethals and sub-lethals in the gene pool, what explanation(s) can be advanced for the failure to observe the generally expected consanguinity-related increase in childhood mortality? In addition to the points discussed above, a number of factors can be identified which not only interfere with interpretation of the present data but are common to all inbreeding studies conducted in developing countries:

- (i) There is an absence of written records relating to the marital patterns of previous generations, associated with the general low level of literacy in the population. As a result, it is not possible to assess the cumulative coefficient of inbreeding values and, hence, the total influence that consanguinity has exerted on the current gene pool.
- (ii) There may be failure to control adequately for socio-economic differentials

between the various consanguinity classes. The distortional effects of such differentials were clearly evident in studies on Hiroshima and Nagasaki (Schull and Neel 1965). In Bangalore and other urban growth centres, the population is largely composed of migrants who have made their homes in the cities during the last 20 years but whose marriages predominantly were contracted in their native towns and villages scattered throughout South India. Under these circumstances, the exact nature of the relationship(s) between socio-economic status and consanguinity is almost impossible to define.

(iii) There are high, residual levels of childhood mortality in sections of the population, caused by environmental agents. For example, among non-consanguineous offspring in Tamil Nadu first year mortality rates of between 9.3% and 13.2% were reported (Rao and Inbaraj 1977b, 1979a), while pre-reproductive mortality in Andhra Pradesh ranged from 29.3% to 53.6% according to socio-economic status (Venugopal Rao and Murty 1984). While these levels of mortality are significantly greater than in the current combined Bangalore and Mysore populations (tables 5 and 6), substantial numbers of severe infectious and nutritional disorders are still observed in Karnataka. Against such a background, estimation of the genetically-determined component of mortality becomes extremely difficult.

Obviously the identification of multiple, potential data base and interpretational problems means that any conclusions relating to the effect(s) of long-term inbreeding on the gene pool must be made with considerable caution. Nevertheless, this is a fundamental area of human biology which directly affects the lives of many millions of individuals living both within and far beyond the boundaries of South India, for example, in Muslim communities throughout the world. As such it requires a definitive answer. With our continually expanding data base and a gradual decline in pre-reproductive mortality due to environmental causes, the conditions necessary for such a positive response will soon be met.

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