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REVIEW PAPER

Consanguinity in Kerala: Patterns, Prevalence and Effects

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Abstract

Highlight of major findings of consanguinity study in 51 communities of the Kerala region is provided, considered in relation to the patterns, frequency and effects of the phenomenon. The patterns in the order of incidence are First cousin (1C), Second cousin (2C), First cousin once removed (1.5C), Uncle-Niece (UN) and Double First Cousin (DFC). Consanguinity was quantified chiefly by two measures (a) frequency and (b) coefficient of consanguinity (F), which is the probability that a consanguineous offspring is an identical homozygote; such as 1/8, 1/16 and 1/64 for UN, 1C and 2C respectively. A wide range of frequencies occurs in the Kerala communities ranging from 1.5% (Christian Malai Arayas, Kottayam) to 97% (Kurumbapulaya tribe, Idukki), the highest ever known. Fairly high rates occur in most tribals (>70%) and medium (20-40%) in the others. A variety of socio-economic factors influence the incidence of consanguinity in the state, of which literacy the foremost, negatively co-related. A declining trend was evident from the older generations to the younger. Consanguinity effects include social, reproductive/fertility and genetic. Notable social effect is the security/ freedom of young brides in consanguineous households. There was consistent hike in fertility profile, considered primarily due to reproductive compensation, especially evident in the tribals owing to low age at marriage. The genetic effects are dependent on the degree of spousal relationship, the nature, number and frequency of lethal recessive genes. The risk effects would be high in consanguineous families with rare hereditary diseases/defects. The harmful effects evaluated in terms of consanguinity-related mortality, found to range from 3-39%, the highest in certain tribals of Palakad Dt. The differentials of mortality/morbidity were significant, and positively correlated with the rate of consanguinity, which in turn negatively with literacy level. Effective genetic counselling and adequate literacy promotion are required among the tribals.

Keywords: Consanguinity, Kerala, patterns, frequency, effects.

INTRODUCTION

Consanguinity or human inbreeding is referred to as the phenomenon of marital union between spouses who are related to each other by common ancestry. Since all humans, in broad sense, are descendants of some common ancestors in the distant ancient past, all people, especially those in geographically isolated regions and islands could be all related to each other in appreciable degree, and sharing common genes at various loci. The probability of two related spouses to possess the same genes inherited from the common ancestors would be pretty high, and inbreeding would bring them together resulting in higher frequencies of homozygous offspring in consanguineous families. Detrimental effects of inbreeding arise as a result of genetic homozygosis of lethal/sublethal recessive genes, and the homozygous children are likely to meet with developmental abnormalities *in utero* or after birth, and become nonviable leading to mortality at various pre-reproductive stages and of morbid conditions of genetic predisposition, and succumb to various genetic diseases and congenital defective conditions (Mathew and Jyothilekshmi, 2017). It is from this expectation that the effects of consanguinity are interpreted and evaluated. The major risk of

blood-related alliances is the expression in the consanguineous offspring of various autosomal recessive detrimental conditions on account of both the parents being carriers of the same deleterious alleles.

The earliest consanguinity study in India is that of Dronamraju and Meerakhan (1963), and those in Kerala are of Kumar *et al.* (1967) and Abraham and Mathew (1969). This was followed by a more meaningful and systematic study initiated by the author in the 1980's in the Kerala University Botany Department; and during the past few decades an extensive consanguinity study was accomplished in over 70 inbreeding communities of Kerala and of the Kanyakumari district of Tamil Nadu; and the results were published in a series of papers and one book, the relevant major ones of which are: Pillai and Mathew 1995, 1996, 1997; Joseph and Mathew (2002, 2003, 2005); Balachandran *et al.* (2005); Begum *et al.* (2008); Sindu and Mathew (2010, 2012, 2013); Sindu *et al.* (2001); Jyothilekshmi and Mathew (2016, 2017); Mathew (2005, 2017, 2018); Mathew & Devipriya (2010); Mathew and Jyothilekshmi (2016, 2017) and Mathew *et al.* (2006, 2007). This paper highlights the major findings emerged from the consanguinity studies in 51 communities of the Kerala region belonging to diverse social classes hailing from mostly the districts of southern and central Kerala and a few from the north in respect of the patterns, prevalence and effects of the phenomenon of consanguinity in them.

Influencing Factors

The factors which influence the consanguineous unions in general include parental inbreeding, size of the mating unit, marital distance and traditional systems based on social, cultural, economic, linguistic, religious and geographic variables. Economic reasons like conservation of family property, bridal payment etc have been foremost motivating factors in most Kerala communities. In Kerala, great many Hindu castes and communities, particularly the tribals have been practising closely related marriage alliances for centuries as part of their social custom and tradition. Certain social customs operate in many communities, particularly aimed at avoiding conflicts in the interpersonal relationships between a new wife and her in-laws. The relationship is believed to be more congenial if the mother in-law is the girls' father's/mother's sister. The joint family system and the custom of arranged marriages still vogue in the region are also striking influencing factors. The linguistic preference is a strong factor among most tribal groups.

Patterns and Measures

Very close degrees of human matings like parent-offspring, brother-sister are incestuous and taboo in almost all communities. The consanguinity patterns commonly practised in the Kerala communities, in the order of preference and prevalence are First cousin (1C), Second cousin (2C), First cousin once removed (1.5C), Uncle-Niece (UN) and Double First Cousin (DFC). The first cousin pattern is further subdivided based on the position occupied by the male spouse, by a second level such as (a) patrilateral parallel cousin (PPC) which is the union between a man and his father's brother's daughter, (b) matrilateral parallel cousin (MPC) the relation between a man and his mother's sister's daughter, (c) patrilateral cross cousin (PCC) the relation with his father's sister's daughter, and (d) matrilateral cross cousin (MCC), the relation with his mother's brother's daughter. Although the four subtypes are genetically similar, there is discrimination based on social customs and traditions held as sacred regarding choice of the specific subtype. Of the four subtypes, the cross cousin subtype is the most favoured first cousin pattern, with the MCC having a clear edge.

The basic measures of consanguinity applied for describing and quantifying genetic relatedness are (1) the frequency of consanguinity, (2) the coefficients, considered and computed at three levels such as (a) the Coefficient of consanguinity (F), (b) Coefficient of relationship (r) and (c) the Mean Coefficient of the population F (Wright, 1922). The frequency of consanguinity is the rate at which all the different patterns together occur, calculated as the percentage of the total sample. The 'r' is a probability that both the related spouses share a gene identical by descent (inherited from the common ancestor), while F is the probability that a consanguineous offspring is an identical homozygote. Among the allelic genes, there are two sorts (1) genes with the same phenotypic effect irrespective of their origin, referred to as genes 'alike in state'. But, when the spouses are related to each other by common ancestry, each of them is at heterozygous state for an allele which is replica of one and the same gene possessed by the common ancestor (eg. A_1). Such alleles are referred to as genes identical by descent. When the related spouses mate, they would each pass on to the offspring a gene identical by descent such that the offspring becomes an identical homozygote (A_1 A_1) and thus the coefficient of consanguinity (F) is the probability that the consanguineous offspring is an identical homozygote for any of the four alleles identical by descent, ie A_1 A_1, A_2A_2, A_3A_3 or A_4A_4 at a given locus.

The 'r' and 'F 'values are computed by two methods (1) the path coefficient method (Wright 1933) and (2) the probability method (Malecot, 1945). The 'r' and 'F' values for the different degrees of spousal relationships are as in Table 1.

Table 1
Coefficients 'r' and 'F' of different patterns of consanguinity

Pattern	r	F
Uncle-Niece/Aunt Nephew	¼	1/8 (0.125)
Double First cousin	¼	1/8 (0.125)
First cousin	1/8	1/16 (0.0625)
First cousin once removed	1/16	1/32 (0.0313)
Second cousin	1/32	1/64 (0.0156)
Third cousin	1/128	1/256 (0.0039)

Table 2
Recessive gene frequency and harmful effect of consanguinity

q_0	R_0	Fpq	R_1	R_1/ R_0
0.4	0.16	0.015	0.175	1.09
0.2	0.04	0.010	0.050	1.25
0.1	0.01	0.0056	0.156	1.56
0.01	0.0001	0.00062	0.00072	7.19
0.001	0.000001	0.0000624	0.0000634	63.4

q_0 = Initial gene frequencies; R_0, R_1 : Recessive genotype frequency without inbreeding and with inbreeding; F = Coefficient of Consanguinity

Table 3
Frequency and genetic effects (mortality/morbidity)of consanguinity in Kerala communities.

Social class	Frequency Consanguinity %		Mortality %			Morbidity %
			Prenatal	Postnatal	Total	
Forward Class (4)	1.2 – 1.8	NC	2 – 11	0.6 – 6.3	4 – 16.7	1.8 – 6.5
		C	4 – 16	4.9 – 8.5	9 – 24.2	5.7 – 28.3
Backward Class (19)	10 – 54	NC	2 – 5.3	0.5 – 5.8	4 – 7.9	1.2 – 8.6
		C	4.9 – 16.90	2.8 – 11.9	10.7 – 23.5	3.5 – 19.9
Scheduled Class (13)	5 – 81	NC	0.6 – 5.2	0.5 – 4.9	1.3 – 10.2	1.2 – 8.3
		C	1.5 – 14.1	3.9 – 20.3	5.2 – 24.5	2.4 – 22.2
Scheduled Tribe (15)	1.5 – 97	NC	1.1 – 7.2	0.9 – 13.1	3.1 – 15.0	0.6 – 3.4
		C	2.1 – 10.2	4.1 – 23.3	8.3 – 39.9	2.3 – 11.5

Frequencies (Prevalence) of Consanguinity

A wide spectrum of frequency levels of consanguinity is known in diverse world population groups, ranging from less than 0.5% to as high as over 97%, with corresponding levels of mean Fs which range from 0.0009 to 0.0620. The lowest known rates occur in USA and many European countries and Australia. The notable low levels in these Christian countries are due to the impact of Church ban coupled with increased morbidity, industrialization, urbanization and education, and the consequent socio-economic advancement. The rates observed in the 51 inbreeding communities of the Kerala region also show wide variation (1.5-97%), which can be grouped under 5 rate classes such as <10%, 10-30%, 30-50%, 50-70% and >70% (Mathew and Jyothilekshmi, 2017). A social class-wise distribution of the rates is furnished in Table 3. The lowest rates occur in the Christian Malai Arayas of Kottayam District (1.5%) followed by 4.84% in the Latin Catholics. The very low rates in the Christian communities are due to strong church ban prohibiting marriages upto the second cousin degree together with higher literacy in them. However, another Christian denomination, the 'Knanayas', which practise tight endogamy, shows fairly high (33%) rate. They are of two denominational groups in the state: (1) Catholic Knanayas of the Vijayapuram Diocese, Kottayam and (2) the Jacobite Knanayas with concentration in Ranni and Chingvanam. By custom and tradition the Knanayas take mates only from within their closed group which inevitably leads to higher consanguinity rates. The pooled inbreeding frequencies among the different social classes of the state are 12-18% (forward class), 10-15% (backward class), and 5-81 % (scheduled caste and 1.5-97% (scheduled tribes) The rates of blood-related marriage alliances in the state are found to be dependent on a variety of socio-economic covariables, customs and tradition and also on certain demographic determinants. The major socio economic factors are education, occupation and family income, and demographic factors include year of marriage and spousal age at marriage. In almost all communities studied, the literacy factor was negatively correlated with the related alliance. Increased educational and financial status played prominent role in younger generations inhibiting the propensity and prevalence of related marriages. In most communal groups a descending trend of consanguinity was evident from the older to the younger generation, very much associated with increased educational and economic levels. The study by period of marriage in the communities, surpassing social class difference, showed higher consanguinity rates in marriages contracted in the earlier periods (1960's), and the declining trend in the rates was highly significant in many of them. The study also showed higher rates of related alliances associated with low age at marriage of spouses, especially women.This was more evident among the tribal groups in which the mean age at marriage of women was below 17.

Effects

The practice of blood related alliances have implications on various realms of human life which include social effects, reproductive effects in terms of fertility/fecundity, and genetic effects in terms of prereproductive mortality and morbidity, of which the latter two directly concern human survival and public health.

Social Effects

Consanguinity can be beneficial to man's social life in many ways. It can strengthen the family relationship. The system of dowry payment and bridal wealth are less frequent in families involved in consanguineous alliance. The women, their husbands and children of consanguineous families benefit from the premarital transfer of wealth and gifts. Very often, related marriages represent an attractive strategy in Kerala, especially among the poor families. Prenuptial arrangements are greatly simplified. In cases of blood-related marriages, the bride who moves to her in-law's household, has a feeling of being at home, and she has no concern nor any anxiety of insecurity, because her mother-in-law is her own aunt. There is also greater marriage stability, which has favourable impact on the health and well-being of the children of such families. Domestic abuses and estrangements and associated conflicts and problems are minimum in consanguineous family set ups. There are also other welcome social effects like gender equality, female autonomy etc.

Fertility Effect

Human fertility is conventionally measured in terms of three reproductive parameters such as conception, live birth and child survival. Available information has projected three trends of association between consanguinity and human fertility such as (a) lower fertility differentials among the inbreds (Lazo *et al.*, 1996) (b) significant higher association (Bener and Ali, 2006), and (c) no clear association (Rao and Imbaraj, 1977). Many reasons are known explaining the increased fertility rates in consanguineous families, which include operation of genetic, immunological,

social and psychological factors. Sharing of common Histo-Compatibility Antigen (HLA) by related spouses is suggested to have a selective advantage during pregnancy owing to greater immunological compatibility of the mother and the foetus. There are reports of reduced levels of primary and/or secondary sterility in consanguineous couples suggesting intrauterine lower mortality profile (Philippe, 1974). A range of proximate determinants exert direct influence on fertility which include age at menarche, and menopause, sterility/fecundity, lactational amenorrhoea etc. (Wood, 1989). Reproductive compensation through replacement of infants dying at an early age provides another convincing explanation for the positive association between consanguinity and fertility. This appears to have happened in several Kerala communities, especially the tribals (Joseph and Mathew, 2005; Mathew *et al.*, 2006). Initiation of a further pregnancy closely following the death of a breast-fed infant is mainly a biological phenomenon on account of cessation of lactational amenorrhoea. The Kerala communities belonging to different social classes, including the tribals, displayed some sort of differing trends of association between couple fertility and consanguinity. A few of the socio-economically developed communities (Nair, Brahmin, Ezhava) have relatively low fertility means, and only marginal differentials, while most of the backward class communities and socio-economically under-developed and illiterate scheduled caste and tribal groups showed fairly significant fertility differentials associated with consanguinity. A number of social and demographic factors may be implicated for the greater fertility profile in such communities which include younger maternal age at marriage as in the tribals who have registered increased fertility rates on account of longer cohabitation period and consequent extended reproductive span. The overall picture emerged from the analysis of fertility data of Kerala group of communities appears to be suggestive that the higher fertility differentials in them could be more a reflection of reproductive compensation and greater reproductive span, rather than representing any underlying biological difference in fecundity ascribable to consanguinity.

Genetic effects

The magnitude of harmful effects of consanguinity depends on a variety of genetic and nongenetic parameters such as the degree of spousal relationship, the nature, number and frequency of the deleterious recessive genes and also the prevalence and duration of inbreeding.

Spousal Relationship

The probability of the offspring of consanguineous unions to be homozygous dominant/recessive would be greater than p^2 and q^2 respectively by an amount each by 'e', and to be heterozygous correspondingly less than 2pq − 2e (Mathew and Jyothilekshmi, 2017). The increase factor 'e' by inbreeding is a function of the inbreeding coefficient 'F' and of the two gene frequencies p and q such that e = Fpq. Assuming a hypothetical panmictic population with frequencies of the dominant (A) and recessive (a) genes at a given locus to be p = 0.4 and q = 0.6 such that its genotypic constituition as per Hardy Weinberg expectation to be AA = p^2 = 0.16; Aa = 2pq = 0.48 and aa = q^2 = 0.36. Consider the population as resorting to matings of different spousal relationships in the order of the degrees such as Uncle-Niece (UN), First cousin (1C), Second cousin (2C) and Panmixis(RM). The F values of the different degrees are 1/8 for UN, 1/16 for 1C, 1/64 for 2C and F = 0 for RM. The respective numerical equivalents of the corresponding 'e' values (Fpq) are 0.03 = e_1, for UN; 0.15 = e_2 for 1C; 0.007 = e_3 for 2C and 0.0 = e_0 for RM. The resulting genotype frequencies in respect of the different degrees of spousal relationships are 0.390 for UN, 0.375 for 1C, 0.365 for 2C and 0.360 for RM. It can be seen that the recessive genotype frequencies are positively associated with the degree of spousal relationships. The increase of recessive homozygosity is maximum for the highest degree (UN) and minimum for the least (2C) and nil for RM, implying that the magnitude of the effect of inbreeding on homozygosity is dependent on the degree of spousal relationship.

Nature of gene

The harmful effect of consanguinity depends very much on the degree of lethality of the recessive gene. If the gene is fully lethal and severely detrimental, serious effect may be expected; and conversely if the gene is less lethal or not lethal, there is little or no risk effect. In communities with highly defective genetic conditions, the recessive genotypes would be completely eliminated every generation, resulting in a steep decline of the recessive gene frequency in successive generations. The frequency of such recessive genes after 'n' generations of complete selection against the recessive genotypes is denoted by the expression.

where q_0 is the initial recessive gene frequency, 'n' the number of generations, and q_n the frequency of the recessive gene after n generations (Mathew and Jyothilekshmi, 2017). After several

generations, the deleterious recessive gene may be completely dispensed with, and from that point on, consanguinity has little or no harmful effect.

Number of genes

The harmful effect of consanguinity also depends on the number of deleterious recessive genes in a population. Since the coefficient of consanguinity (F) for first cousins is 1/8, the probability of any one of the children of a first cousin family being affected is ¼ x 1/8 = 1/32 = 3.1 %, and being unaffected is 100 − 3.1 = 96.9 %. The probabilities of being affected with different numbers of such genes are:

with 1 gene= 1-0.969=3.1%

2 genes= $1\text{-}0.969^2$=6%

3 genes= $1\text{-}0.969^3$=9%

8genes= $1\text{-}0.969^8$=22.4 %

n genes = $1\text{-}0.969^n$

This would imply that the harmful effects of consanguinity increase exponentially with increasing number of lethal recessive genes.

Frequency of recessive gene

The expected harmful effect (R_1/Ro) of consanguinity: eg. First cousin in terms of the deleterious recessive gene frequency (q) is determined by the expression (Mathew and Jyothilekshmi, 2017) as:

$$\frac{R_1}{R_0} = \frac{q+\frac{1}{16}pq}{q^2} = \frac{q\,(1+15q)}{16+\,a^2}$$

where p and q are the dominant and recessive gene frequencies; 1/16 the F for first cousin pattern; R_1 the recessive genotype frequency with inbreeding and R_0 without inbreeding. The values of different 'q', Fpq and $\frac{R_1}{R_0}$ are furnished in Table 2. It can be seen that the values of harmful effect ($\frac{R_1}{R_0}$) are very low for higher qs (0.4, 0.2, 0.1), and for lower qs (0,001), the harmful effect is exceptionally high, in which the Fpq factor (the effect exclusively by inbreeding) is the major component of the harmful effect. This would imply that the frequency of lethal recessive genes in the consanguineous families matters very much, indicating that the harmful effect of consanguinity is very much high in communities with very rare hereditary diseases and defects.

Mortality effect

Mortality in humans is the loss of progeny from early stage to the pre-reproductive juvenile stage. Various genetic and nongenetic reasons have been implicated for consanguinity-related moratlity/morbidity. The detrimental effects associated with consanguinity are caused by the expression of lethal/sublethal recessive genes inherited from the common ancestor, and such unions are expected to elevate the frequency of affected recessive homozygotes, the effect being more conspicuous when the genes are rare. Most studies have suggested significant levels of adverse effects, others marginal and still others no effect. There is, however, a strong view that homozygosity for deleterious recessive genes, does result in offspring which become nonviable leading to loss by mortality at both prenatal and postnatal stages, and also by morbid conditions (Bittles 2008, 2012).

Prenatal mortality refers to pregnancy wastage by foetal loss at various stages before birth such as early (abortion), intermediate (miscarriage) and late (still birth). It has been estimated that 15−20% of all implanted pregnancies are lost by spontaneous abortions during the early months of gestation due to various reasons. The effect of consanguinity in prenatal mortality includes failure of conception and deleterious effect on embryonic development. In consanguineous unions, the foetuses produced are at an increased risk of getting aborted due to high heterozygosity of alleles, and there are also higher risk of preterm birth, and the child being under-weight. The deleterious genes exposed by inbreeding may be causative for many miscarriages and still births. Several factors are known to contribute to increased prenatal loss in consanguineous families which include (a) increase of homozygosity of lethal genes which affect growth and development of embryo leading to intrauterine growth retardation and consequent abortions and still births, (b) effect of additively active polygenes which elevate foetal loss linearly with degree of inbreeding, (c) increased antigenic difference between the mother and the foetus under inbreeding. The consanguinity study in the Kerala group of communities has displayed significant differentials in most communities (Table 3). The rates of prenatal loss ranged from 4 – 16% in the Forward classes; 4.8-16 % in Backward classes; 1.5-14.1% in Scheduled castes, and 2.1 – 10.2 % in the Tribals, the differentials being significant in all.

Postnatal mortality refers to loss of offspring after live birth upto the age of reproduction (neonatal, postneonatal, infant, child, juvenile). In most cases the bulk of postnatal deaths occur in infant stages. It has been estimated that aggregation

of homozygosity for lethal recessive genes by related matings can adversely affect the survival of the offspring between birth and juvenile stage, and it implies that consanguinity carries a risk of death mostly in the early span of human life. The postnatal mortality profile in the Kerala group of communities showed 4.9 – 8.5% in the Forward classes; 2.8 – 1.9 % in Backward classes; 3.9 – 20.3% in Scheduled castes, and 4.1 – 23.3 % in the Tribals, the differentials being highly significant in most of them. The severity of postnatal loss was much graver in the Tribals.

The significant levels of pre and postnatal mortality were duly reflected in the total mortality profiles of the communities as well, and this ranged from 9 – 24.2% in the Forward classes; 10.7 – 23.5 % in Backward classes; 5.2 – 24.5 % in Scheduled castes, and 8.3 – 39.1 % in the Tribals. Total mortality was the highest in the tribe Paniyani of Palakkad dt (39.04%), followed by 37% in the 'Mudugars' (Table 3).

Morbidity refers to various kinds of diseases and congenital abnormalities/defects involving a variety of defective conditions commonly classified as sensory, physical, psychiatric and systemic. Severe morbidity causes death during the postnatal and thereafter, while many others handicap the bearer impairing functions of various organs. The practice of consanguineous unions has been attributed to susceptibility to a host of human diseases and defects. The morbid conditions examined in the Kerala communities constituted a variety of infirmities and congenital defects broadly classified as physical (polydactyly, syndactyly, ectrodactly, dwarfism, microcephaly, hydrocephaly and cleft foot, cleft lip/palate), sensory (deaf, dumb, squint eye, blindness) and mental (epilepsy, schizophrenia, alzhimer) defects and systemic diseases (tuberculosis, leprosy, bronchitis, whooping cough, diabetes, cordiac problems, cancer, etc). As the number of different individual morbid conditions was not large enough, only the pooled data comprising all the morbid elements together considered for analyses. The incidence of this ranged from 5.7 – 28.3% in the Forward classes, 3.5 – 19.9 % in Backward classes, 2.4 – 22.2% in Scheduled castes, and 2.3 – 11.5 % in the Tribals, the differentials being fairly significant in all (Table 3).

In almost all the communities studied, the magnitude of harmful effects in terms of consanguinity related mortality/morbidity was significant and positively correlated with the rate of consanguinity, which in turn negatively with socio-economic covariables, especially the literacy factor. Blood-related marriages with significant implications on recessive diseases and defects have remarkable social relevance and also public health impact. The higher degree of harmful outcome of consanguinity among the socio-economically weaker sections of the society including the illiterate tribals is an intricate and alarming social problem. This calls for urgent remedial measures to be taken by the state and also the social organization and the NGOs, aimed at minimizing the degree and extent of the risk effects of the phenomenon of consanguinity, which may be termed an 'avoidable social evil', still in vogue conspicuously in many of the tribals. The plausible major means for minimising the consanguinity-associated harmful effects proposed are two-fold (Mathew and Jyothilekshmi, 2017): (1) effective genetic counselling and (2) adequate literacy promotion, particularly among the poor, ignorant and marginalised tribals.

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