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Impact of Kinship on the Chosen Autosomal Anomalies in Sivagangai, Tamil Nadu, India

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Abstract

Significance of study: Prevalence of consanguinity and their impact on the autosomal recessive anomalies such as diabetes mellitus, hearing impairments, epilepsy, limb defect and eye defect among Sivagangai population was studied. The present investigation provides a new plat form for pinpointing out the genetic causes leading to congenital autosomal recessive disorder, so that in future newer gene therapy approaches can be developed to treat such anomalies. In our study, an attempt has been made to evaluate the association of the most common causes of autosomal recessive impairment among heterogeneous Sivagangai population.

Objective: To determine the effect of endogamy on the hereditary anomalies of Sivagangai population.

Study design: Human health survey.

Method: The impacts of kinship against autosomal recessive disorder among the selected population of Sivagangai were studied. In this study, 2376 families were taken for assessment by face-to-face interviewed in the local language according to the standard procedures.

Result: Consanguineous marriage was significantly higher in current generations (29.62%) than the previous generations (37.94%). The occurrences of abnormality were higher among inter breeding populations (67.34%) than non consanguineous population (32.65%). The highest Odd ratio was recorded in epilepsy, followed by hearing impairment, limb defect and eye defects, while, the lowest value was observed in diabetic population. The highest P value, odd ratio and 95% Class Interval recorded were 0.001, 26.48 and 18.63-37.63 respectively. The highest degree of consanguinity reported in the study was 2nd degree in epilepsy.

Conclusion: The present study showed that the hereditary anomalies were higher among cognate population than out breeding population. The children of such con sanguineous couples have higher risk of expressing recessive gene disorders.

Keyword*: Endogamy, Lethality, **e**pilepsy, hearing impairment, limb defect, diabetics and eye defect.*

Introduction

Kinship refers to the culturally defined relationships between two people who share a common ancestor or blood. Consanguineous marriages have been practiced for hundreds of years in many communities throughout the world[1]. Historically, the prevalence of consanguineous marriages is very high in south India. However, marriages between biological relatives are quiet common not only in developed countries but also in developing countries. More than one billion peoples around world are consanguineous [2 and 3]. In India, cognate marriage is a customary practice in some communities. They won't prefer non-consanguineous marriage because of their cultural differences between families. This is based on either matrilineal or patrilineal. The

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endogamous population increases the level of autosomal recessive homozygosity, which leads to biological unfitness of population. This phenomenon is known as inbreeding depression[4]. The children of consanguineous unions have the highest chance for expression of single-gene disorders inherited from their recessive parents. The risk of autosonal anomalies increases with degree of genetic relationship between the parents. In the present study, an attempt has been made to assess the prevalence of consanguinity and their impact on the autosomal recessive anomalies such as diabetes mellitus, hearing impairments, epilepsy, limb defect and eye defect among Sivagangai population. The present investigation provides a new plat form for pinpointing out the genetic causes leading to congenital autosomal recessive disorder, so that in future newer gene therapy approaches can be developed to treat such anomalies.

Autosomal recessive defect selected for the present study

Diabetes mellitus

It is a type of heterogenous metabolic disorder causes high blood sugar level for a prolong period of life. Hence it is called as hyperglycemia. It is due to either the disinfection of beta cells of pancreases to secrete insulin or irresponsiveness of body cells to insulin hormone. Based on this, diabetes can be classified into Type 1 and Type 2 diabetes.Type1 diabets is caused by insufficient production of insulin by pancreas and also called as Insulin dependent diabetes mellitus (IDDM) or juvenile diabetes. Type 2 is caused by insulin resistance power of the cells in our body and also known as non-insulin dependent diabetes mellitus (NIDDM) or adult onset diabetes. Any defective 3 genes for type I and 20 genes for II diabetes are responsible for these anomalies. These genes are localized in 2,3,4,5,6,7,8,10,11,12,13,15,17,19, and 20th chromosomes[5].

Epilepsy

It is a clinically heterogeneous neurological disorder, commonly called as seizures. Seizures are caused by a disturbance in the electrical activity of the brain. Thus the nerve cell produce excessive and abnormal activity at the cortex region of the brain. Epilepsy may occur as a result of genetic disorder and acquired brain injury such as a trauma or stroke. During a seizure, a person experiences abnormal behaviour, symptoms and sensations leads to the loss of consciousness. There are various types of seizures, but all are not involve in convulsion, unconsciousness and shaking. Some of them are caused by single gene defect and many of them were caused by multiple gene defect. Epilepsy is usually treated by medication and in some cases by surgery, devices or dietary changes.

Limb Defect

Congenital Limb defect is the most common complex disorders among human population. This disorder occurs during the specification of upper or lower limb development. This defect is a common congenital disorder next to cardiac anomalies. The impact of congenital limb malformations are reduction of limb size, direction of bone angle, polydactyly and syndactyly. These are genetic syndromes produced by number of point mutations during cell fate determination and regulation during embryogenesis.

Eye Defect

The development of eye is specified through a complex program during the embryonic development. Any anomalies in this specification of eye cause profound defects in the eye. The most common congenital inborn errors in eyes are **anophthalmia, microphthalmia, coloboma, aniridia** and **optic nerve hypoplasia.** The other minor defects are myopia, hypermetropia, presbyopia, astigmatism and cataract.

Ear defect

The ear defect is a problem in recognizing different types of sound from the birth. It is a hereditary disorder due to the loss of certain factors in the uterus during development. More than 50% of the ear defect is caused by genetic factors. The hearing loss is an autosomal dominant or autosomal recessive or X-linked pattern of inheritance. Approximately, about 5% of the population has some sort of such ear malformation. The frequently encountered congenital ear problems are protruding ear and external ear microtia.

The characteristics of nonsyndromic hearing loss vary among the different types.Hearing loss can affect one ear (unilateral) or both ears (bilateral). Degrees of hearing loss range from mild (difficulty understanding soft speech) to profound (inability to hear even very loud noises). The term “deafness” is often used to describe severeto-profound hearing loss. Hearing loss can be stable, or it may be progressive, becoming more severe as a person gets older. Particular types of nonsyndromic

hearing loss show distinctive patterns of hearing loss. For example, the loss may be more pronounced at high, middle, or low tones. Most forms of nonsyndromic hearing loss are described as sensorineural, which means they are associated with a permanent loss of hearing caused by damage to structures in the inner ear. The inner ear processes sound and sends the information to the brain in the form of electrical nerve impulses. Less commonly, nonsyndromic hearing loss is described as conductive, meaning it results from changes in the middle ear. The middle ear contains three tiny bones that help transfer sound from the eardrum to the inner ear. Some forms of nonsyndromic hearing loss, particularly a type called DFNX2, involve changes in both the inner ear and the middle ear. This combination is called mixed hearing loss. Depending on the type, nonsyndromic hearing loss can become apparent at any time from infancy to old age. Hearing loss that is present before a child learns to speak is classified as prelingual or congenital. Hearing loss that occurs after the development of speech is classified as postlingual.[5]

Methodology

The present study was a cross sectional based population investigation, carried out in Sivagangai thaluk, which have many native populations. A total number of 2376 families were investigated. These families were selected by simple random sampling. The details about their subjects in terms of history, clinical features, consanguinity, disorder and pregnancy outcomes in the present generation as well as the previous generation by face-to-face interview in the local language according to the standard procedure[6 and 7]. The maximum care was taken to avoid any wrong interpretation by the respondents. Information was collected through personal visit to the selected families. The collected data were then processed to get the prevalence of consanguinity and defects. The types of disorder were then classified.

Odds ratios were calculated based on the influence of endogamy on autosomal recessive anomalies status in the current generation as well as the respondent's children. For the current generation, cases of respondent's offspring of consanguineous union and non-consanguineous union were experimental and control respectively. Chi-square test was used to ascertain the associated between two or more categorical variables. Since the sample size was small (2x2 tables), the Fisher exact test (two-tailed) was applied. Mantel-Haenszel method was used to calculate Relative risk and confidence level at 95% interval. All statistics test were two-sided and $p<0.05$ was considered statistically significant.

Result

The 2376 families were selected for the cross sectional studied. A total of 704 consanguineous (29.62%) and 1672 non consanguineous (70.38%) union in parental generation were observed. The maternal grand parents of 916 were consanguineous and 1460 non - consanguineous and the paternal grand parents were 887 consanguineous and 1489 non-consanguineous (Figure 1). The overall prevalence of consanguinity among parents was 29.62% and grandparental generation was 37.94%. This showed that th econsanguinity was higher among the grandparent generation than the current generation.

Figure 2 depicts various types of abnormalities among the consanguineous and non consanguineous population. The highest number of anomalies were recorded among consanguineous population. The total number of abnormalities among consanguineous population was 67.34%. The maximum number of degree of consanguinity recorded in 2nd degree.

The P value, odd ratio and 95% CI for diabetes mellitus were 0.02, 8.75 and 6.34-12.09 respectively, for hearing impairment were 0.0006, 22.53 and 15.17-33.47, epilepsy were 0.001, 26.48 and 18.63-37.63 respectively. In the case of Limb defects and eye defects, the P value, odd ratio and 95% CI were 0.0108, 18.24 and 10.99-30.26, and 0.319, 14.44 and 9.53-21.87 respectively (Table 1).

Table1: Odd ratio and P value of consanguineous and non-consanguineous population.

	Consanguineous		Non consanguineous		Odd Ratio	95% Confidence Interval	P value
	Affected individuals	%	Affected individuals	%			
Diabetes	96	60	64	40	8.75	6.34-12.09	0.02
Hearing impairment	120	78.94	32	21.06	22.53	15.17-33.47	0.0006
Epilepsy	168	60	112	40	26.48	18.63-37.63	0.001
Limb	64	80	16	20	18.24	10.99-30.26	0.010
Eye	80	71.42	32	28.58	14.44	9.53-21.87	0.319

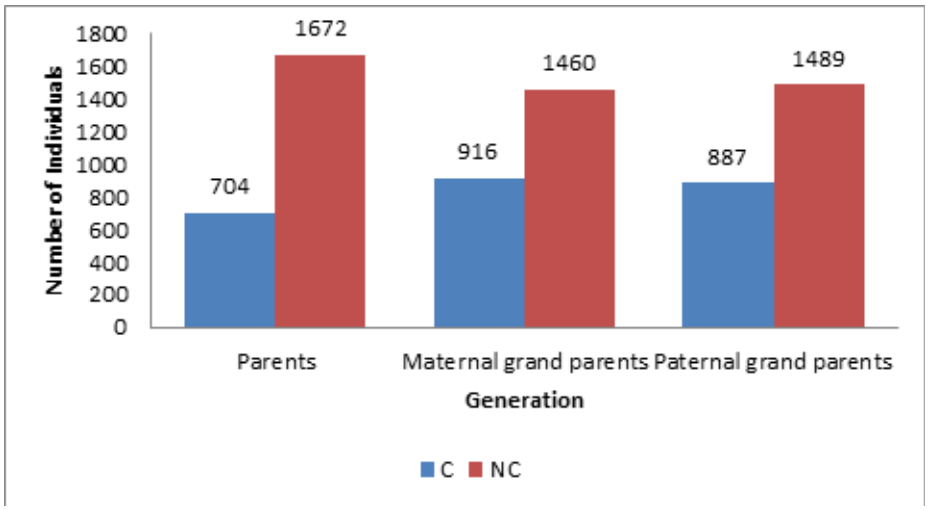

Figure 1: Prevalance of consanguineous and non consanguineous marriages

C: Consanguineous NC: Non Consanguineous

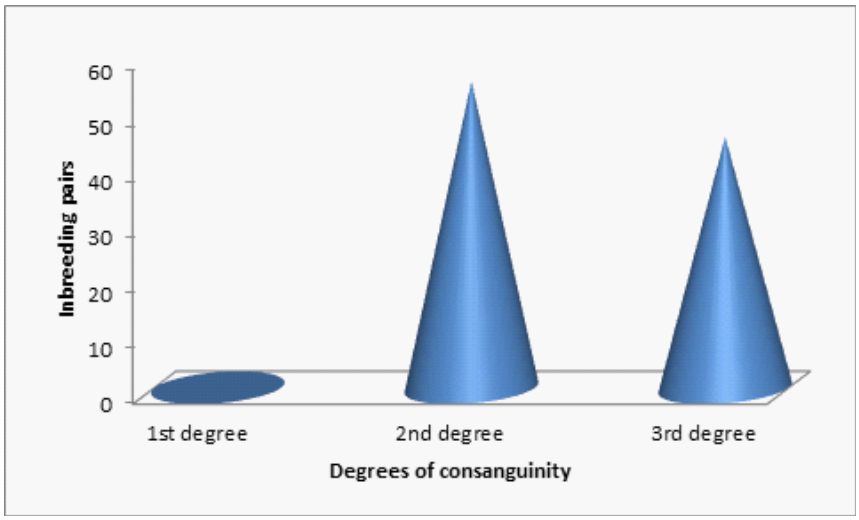

Figure 2: Degrees of endogamy in current generation and parental generation

Discussion

Consanguinity is a couple of biologically blood related individuals of second cousins or more closer to one another[8]. It promotes family stability with significant social and economic advantages[9 and 10]. Kuntla *et al.,* (2013)[11] estimated that the prevalence of consanguineous marriage among Indian population was 38.2%. In this study, consanguineous marriage was higher among grand parents generation (37.94%) than the current generation (29.62%). Among the selected population, 704 couples were consanguineous and 1672 were non-consanguineous of current generation, where as 916 and 1460 of maternal grandparents and 887 and 1489 of paternal grand parents were consanguineous non-consanguineous respectively. The calculated P value was statistically significant. The highest Odd ratio was recorded in epilepsy, followed by hearing impairment, limb defect and eye defects, while, the lowest value was observe eye defectd in diabetic population. The highest degree of consanguinity reported in the study was 2nd degree. The reported marriages were first cousin type. According to the study of Roychoudhury (1976)[12] and Badaruddoza (1998)[13] that the frequency of first cousin marriages in different parts of South India varied from 5 to 57 %. The intra familial marriages have the possibilities of transmitting recessive identical lethal genes from parents to offspring. Such lethal genes cause number of anomalies in children. Congenital malformations are the major reasons for prenatal mortality during gestation in developing countries like India [14 and 15]. In the present study, the prevalence of abnormalities were higher in consanguineous population (64.5%) than the non consanguineous population (34.5%). The studies of Verma *et al.* (1992)[16] and Becker *et al* (2015)[17] had recorded the significant number of congenital malformations among the children of consanguineous couples than the non-consanguineous one. The babies born with congenital anomalies were found to be 3.4 times more from consanguineous parents than non-consanguineous. In the present investigation, the risk of deleterious anomalies was found to be statistically significant.

Diabetics are a most common defect in India. It may be heritable. It may be due to insufficient secretion of insulin by pancreas. Epilepsy is also called as seizure. It is due to any disturbance in the electrical activity of brain. The limb defect is a type of autosomal dominant or autosomal recessive or x-linked anomalies. These genetic defects are caused by primary intrauterine inhibition or intrauterine destruction of normal embryonic tissues. It can also occur with various syndromes in offspring. Teratogenic agents (eg, thalidomide, vitamin A) are known causes of hypoplastic or absent limbs. The other congenital limb anomaly is amniotic band-related limb deficiency, which loose strands of amnion entangle or fuse with fetal tissue. Hereditary hearing loss is an autosomal recessive or X-linked recessive as well as by mitochondrial inheritance. The defective genes cause syndromic or non-syndromic with dominant or recessive genes hereditary hearing loss. The syndromic hearing loss is a hearing impairment associated with specific traits. The dominant deafness is caused by only one faulty gene from the mother or father with hearing impairment. The recessive deafness is because of faulty gene from both the mother and father. There are more than 200 forms of such syndromic hereditary hearing impairment. The human eye is programmed by a complex system of specification during embryonic development. The common congenital eye malformations are anophthalmia, microphthalmia, coloboma, aniridia, and optic nerve hypoplasia. The eye is completely developed in the first trimester of pregnancy. Many genes have been found to have a role in this complicated process. Any alternation in these genes due to point mutations can cause abnormal development in eyes.

Considering the above, the practice of consanguinity should be avoided by educating the public about the adverse effect of blood related marriages. The present investigation provides a new plat form for providing proper health care to public regarding the transmission of lethal endogamic disorders.

Author statement section

Ethical approval – Ethical approval is not required for this study, because we had not used any experimental samples (Blood/ saliva) from the individuals. Before sampling, consent certificate had been received from each individual. We collected data by individual face to face interview.

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Competing Interest- None declared

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