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Influence of Intra Familial Relationship on Hypertension among the Population of Sivgangai, Tamil Nadu

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Abstract: ***Consanguineous marriage is one of the customary practices in South India. It is a type of inbreeding among the populations who share a common ancestor. First cousin marriages were the most common practice among South Indian population. Genetically, it was proven that consanguinity increases the chance of transmitting identical recessive gene, which leads to the possibility of incurable hereditary diseases. The present study was undertaken to determine the rate of consanguinity and its effect on high blood pressure among the selected Sivagangai population. High blood pressure is a common hereditary disorder in South India. It increases the chance of various cardiovascular impairments. In the current study, a total of 1062 families were selected and interviewed about their consanguinity and their prevalence of high blood pressure. Among the total population, 34.18% were consanguineous and 65.81% were non-consanguineous marriages in the parent generation, and 8.47% were consanguineous and 91.52% were non-consanguineous in the grandparent generation. The incidence of high blood pressure is higher in consanguineous populations (60%) than non-consanguineous populations (40%). This showed that congenital abnormalities were double-fold higher among inbreeding populations than out breeding populations. The genes associated with high blood pressure are CYP11B (11-beta hydroxylase gene) on chromosome 8q CYP11B2 (aldosterone synthase gene) on 8p, WNK1, WNK4 (lysine-deficient protein kinase 1 and 4 genes) on 12p, KLHL3 on 5q, CUL3 (cullin 3 gene) on 2q, SCNN1B, SCNN1G (Amilorid-sensitive sodium channel, beta and gamma subunit gene encoding two subunits of the ENaC sodium channel) on 16p, CYP17A1 (steroid 17-hydroxylase/17, 20 lyase gene) on 10q, HSD11B2 (11-beta-hydroxy steroid dehydrogenase 2 gene) on 16q, NR3C2 (mineralocorticoid receptor gene)on 4q and KCNJ5 (potassium inwardly rectifying channel gene, subfamily J, member 5)on 11q. Genetic factors associated with this disease were due to the occurrence and transmission of lethal identical recessive genes. The preference for out breeding is the only way to remove the lethal genes from the gene pool of human population.***

Keywords: Inbreeding, homo-zygosity, Mineralocorticoids, Endogamy

1. Introduction

Hypertension is a current major health problem in both children and adults around the world. It results from various complex genetic aspects, epigenetic, and environmental interplay. Due to these multifactorial influences, altering single and specific genetic influences lead to the development of hypertension. Nevertheless, various gene mutation and epigenetic studies have enhanced our understanding of hypertension modulation and its genetic programming of blood pressure. Consanguinity is the practice of marrying within close relative families, which causes enormous influences on the risk of genetic diseases. When closely interrelated people have progenies together, there is an increased possibility that any heritable mutations or disease-producing genes that they carry will be passed on to their descendants. Intra-familial marriage relationships (consanguinity) enhance the occurrence of identical recessive genes and the transmission of such anomalies from parents to offspring (Subalakshmi and Jepa, 2018). Consanguineous marriage is the marriage between two people who are blood relatives who share a common ancestor. At present, about 20% of the world's population lives in communities with a preference for consanguineous marriage (Modell and Darr 2002). Consanguineous marriages are common in the South Indian population. Various studies on consanguinity also showed that different kinds of consanguineous unions are preferred by different sub-populations; for example, Hindu women in South India typically marry their maternal uncles, while Muslim populations favour first-cousin marriages (Iyer 2002). The prevalence of consanguinity and rates of first cousin marriage vary widely within and between communities, depending on ethnicity, religion, culture, and geography. Numerous reports on the effect of inbreeding on health have focused mainly on its impact on reproduction, childhood mortality, and rare Mendelian disorders (Bittles et al., 2002; Charlesworth, Charlesworth 1999; Ben Arab et al., 2004; Bittles, Bittles 2003; and Wright, 2001). Nevertheless, very limited information is available on the possible role of consanguinity and recessive genes in multi-factorial or polygenic common adult diseases (Jaber *et al.*, 1997; Bener and Hussain, 2006; and Bener *et al.*, 2001). High blood pressure is common in the South Indian population. Hypertension (BP) is a complex trait regulated by an intricate network of physiological pathways involving extracellular fluid volume homeostasis, cardiac contractility, and vascular tone through the renal, neural, or endocrine systems. Untreated high hypertension (HTN) is associated with increased mortality, and thus a better understanding of the pathophysiological and genetic underpinnings of blood pressure regulation to prevent the major impact on public health. However, identifying genes that contribute to hypertension has proved challenging. In this review, our current understanding of the genetic architecture of BP, which has accelerated over the past five years primarily

owing to genome-wide association studies and the continuing progress in uncovering rare gene mutations, epigenetic markers, and regulatory pathways involved in the physiology of hypertension. Blood pressure levels are affected by modifiable factors such as salt, alcohol consumption, obesity, physical activity, and chronic stress. However, twin and family studies have demonstrated that 30-50% of the individual risk comes from genetic factors. Over the last few decades, number of studies has been designed to understand the genetic basis of BP and the associated molecular alterations. This current study estimated the impacts of cognition on high blood pressure among the population of Sivagangai, South India.

2. Methodology

A cross-sectional study was conducted in the selected Sivagangai population to determine the impact of consanguineous marriages on common blood pressure diseases. The total samples of 1062 families were approached for this study during 2022. All information was gathered based on structured face-to-face interviews. This database was used for reviewing the prevalence of consanguineous marriages in Sivagangai population and for making an initial assessment of the association between consanguinity and high blood pressure.

3. Result

This study was carried out to determine the percentage of consanguineous marriage among the Sivagangai population and also to determine the effect of consanguineous marriage on high blood pressure. The prevalence of consanguineous and non-consanguineous marriages between the selected populations is depicted in Figure 1

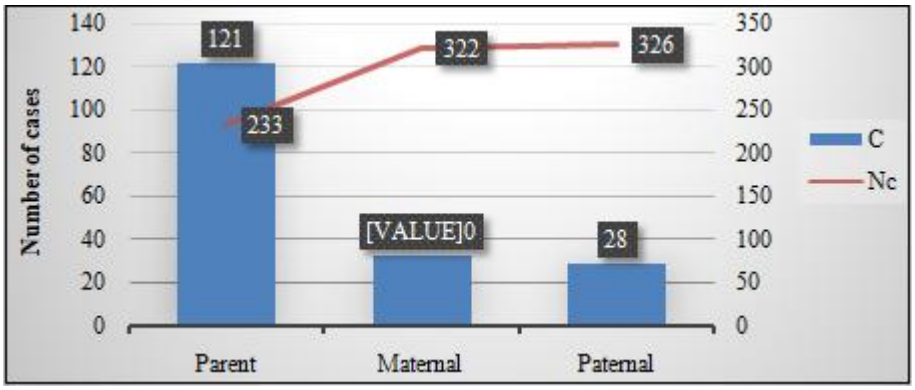

Figure 1: Prevalence of consanguinity

Among the total number of parents in the current generation, 121 were consanguineous, and 233 were non-consanguineous. The maternal parents of the couple were 32 consanguineous and 322 non-consanguineous marriages, and the paternal parents were 28 consanguineous and 326 non-consanguineous marriages. The percentage of consanguineous marriages was higher in the current generation (34.18%) when compared with the previous generation (8.47%). The prevalence of blood pressure among the consanguineous population is depicted in Figure 2. A total of 65 individuals had high blood pressure, of which 39 were consanguine and 26 were out breeding individuals. Figure3 shows the major genes and their location in the chromosome responsible for blood pressure. Most of the genes (CYP11B, CYP11B2 WNK1, WNK4, KLHL3, CUL3, SCNN1B, SCNN1G, CYP17A1, HSD11B2, NR3C2, and KCNJ5) were located in different chromosomes of various locus. They decode the formation of different proteins associated with multiple physiological functions.

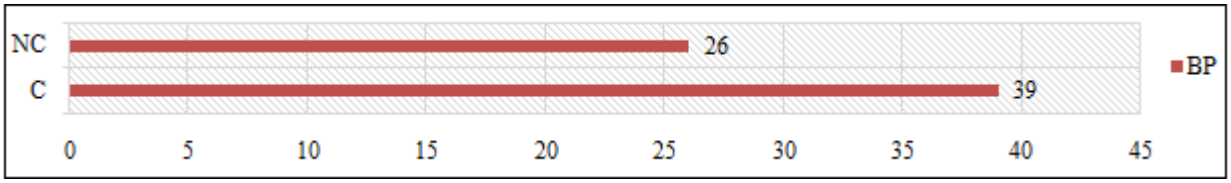

Figure 2: Percentage of High blood pressure associated with consanguinity.
NC-out breeding C-consanguineous

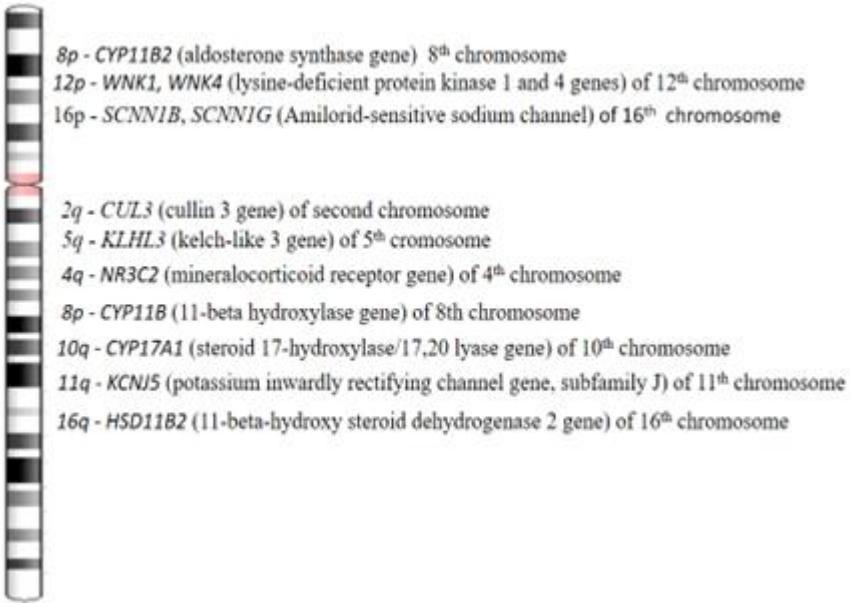

Figure 3: Major genes and their location in chromosome responsible for blood pressure

4. Discussion

High blood pressure is the most frequent classic cardiovascular risk factor for causing a number of cardiovascular mortality. Genetics and genomics provide a major opportunity to investigate the remaining variability of BP. There are a number of genes that are responsible for the physiology of maintaining blood pressure. Any mutation in the nitrogenous base pairs of these genes can alter their functions. Such anomalies can directly or indirectly lead to blood pressure anomalies and other associated physiological diseases. Data from family and twin studies suggest that 30 to 50% of BP is moderately heritable (Mial and Oldham 1963). The genes associated with high blood pressure are CYP11B (11-beta hydroxylase gene) on chromosome 8q (White et al 1991), CYP11B2 (aldosterone synthase gene) on 8p (Lifton et al 1992), WNK1, WNK4 (lysine-deficient protein kinase 1 and 4 genes) on 12p (Wilson et al 2001), KLHL3 (Kelch-like 3 gene) on 5q (Boyden et al 2012 and Louis et al 2012), CUL3 (cullin 3 gene) on 2q (Boyden et al 2012), SCNN1B, SCNN1G (Amilorid-sensitive sodium channel, beta and gamma subunit gene encoding two subunits of the ENaC sodium channel) on 16p (Shimket et al 1994 and Hansson et al 1995), CYP17A1 (steroid 17-hydroxylase/17, 20 lyase gene) on 10q (Goldsmith et al 1967), HSD11B2 (11-beta-hydroxy steroid dehydrogenase 2 gene) on 16q (Mune et al 1995), NR3C2 (mineralocorticoid receptor gene)on 4q (Geller et al 2000) and KCNJ5 (potassium inwardly rectifying channel gene, subfamily J, member 5)on 11q (Choli et al 2011). The present study highlights the role of consanguinity as a risk factor for the occurrence of high blood pressure. The trends in consanguineous marriages were higher in the current generation than in the previous generation, with percentages of 34.18% and 8.47%, respectively. Among the blood pressure population, 60% were consanguineous and 40% were non-consanguineous. This finding is in accordance with the earlier studies of consanguinity among the populations of South India, which ranged from 20% to 60%. The practice of consanguineous marriages has a relatively higher risk of producing the genetic disease associate with identical recessive genes. Subalakshmi and Jepa (2019 & 2021) pointed out the high risk of intra familial relationships on pregnancy outcome and other autosomal anomalies in Sivagangai. This amplified risk is dueto the fact that closely associated individual's are more probable to share genetic material, including risky mutations. As a result, the chances of recessive heritable disorders occurring in offspring of intra-familial unions are significantly higher. In some populations, consanguinity has been practiced for generations, which means that certaingenetic impairments can be more predominant in these populations. The communities of Middle Eastern and South Asian communities have high rates of recessive hereditary disorders such as, diabetics, thalassemia, epilepsy and sickle cell anemia, which are caused by point mutation (Subalakshmi and Japa, 2020). To mitigate the threat of hereditary impairments in kinship marriages, genetic screening and psychotherapy are recommended. These measures can support the couples to understand the probability of passing on hereditary disorders and support them make well-versed decisions about having kids. In some cases, pre-implantation inherited diagnosis or donor gametes may also be considered. Sivagangai district is considered as the hot spot of consanguinity for number of century. This customary practice of inbreeding leads to the chance of homozygosis associated with the expression of some lethal recessive genes. Thus, the present study reveals the impact of consanguinity on blood pressure and provided a preliminary platform for further studies.

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