Short Article

Consanguinity and chromosomal abnormality

S. Amudha, N. Aruna, S. Rajangam
Division of Human Genetics, St. John's Medical College, Bangalore, India

BACKGROUND: Consanguinity is defined as the marriage between close relatives. The deleterious effects associated with consanguinity may be caused by the expression of rare recessive genes inherited from common ancestors.
AIMS AND OBJECTIVES: The present study was undertaken to analyze the effect of consanguinity on chromosomal abnormality (CA).
METHODS AND MATERIALS: During last 6 years period, a total of 1465 cases with suspected genetic etiology like bad obstetric history, mental retardation, multiple congenital anomalies, Down syndrome, primary amenorrhea and primary infertility was referred to Division of Human Genetics for karyotyping and genetic counseling. The information regarding consanguinity was obtained through pedigree analyzes up to three generations from all the patients. Chi-square test was applied to test the significance.
RESULTS: Consanguinity was seen in 427 cases (29.14%), 305 cases were confirmed to have CA, among them 240 (78.7%) had numerical abnormality and 65 (21.3%) had structural abnormality. The presence of consanguinity in CA was seen in 53 cases (17%), including 43 (81.1%) with numerical and 10 (18.9%) with structural abnormality.
CONCLUSION: The effect of consanguinity on CA was almost significant ($P < 0.001$), whereas the effect was not significant for the type of CA. It may be because of the pooled types of consanguinity as well as the CA. Further information is needed to state categorically that there could be the effect of consanguinity on CA.

Key words: Chi-square test; chromosomal abnormality; consanguinity; genetic counseling.

Consanguinity may result in the homozygous condition for recessive autosomal/deleterious genes. The incidence of consanguinity reported in India is 5–60% and uncle-niece and first cousin are the more commonly occurring relationships in Indian population.[1] Chromosomal abnormality (CA) is defined as the genetic defects large enough to be seen under the light microscope. The CA is categorized as numerical and structural abnormality. Etiology for CA may arise in meiosis or mitosis because of advanced maternal age and any other risk factors. Nondisjunction and anaphase lag mechanism may produce numerical CA, whereas break and join phenomenon may result in structural CA such as translocation. And asymmetric segregation of structural rearrangements may produce an incorrect amount of part of the chromosome.

In spite of the available literature on consanguinity, there seemed to be limited information in India, associating consanguinity and CA. Hence, in the present study, it has been aimed to determine the effect of consanguinity on CA in the consecutively referred patients to Division of Human Genetics.

Methods and materials

Division of Human Genetics, since 1976, is a referral center for karyotyping and genetic counseling. A total of 1465 cases with suspected genetic etiology like bad obstetric history (BOH), mental retardation (MR), multiple congenital anomalies (MCA), Down syndrome (DS), primary amenorrhea and primary infertility was referred to Division of Human Genetics for karyotyping and genetic counseling. Data on consanguinity was traced from family pedigree lasting a minimum of three

Address for Correspondence : N Aruna, Division of Human Genetics, Department of Anatomy, St. John's Medical College, Bangalore – 34, India E-mail: sjmcdhg@yahoo.co.in

generations. Karyotyping was done from peripheral blood lymphocyte culture and Giemsa–Trypsin–Giemsa banding[2] findings were statistically analyzed with the application of chi square test of significance.

Results

Consanguinity was observed in 427 cases (29.14%) [Table 1]. The occurrence of consanguinity in relation to the chief complaints in the patients was found to be high in couples with BOH (42.38%). [Table 2] shows the consanguinity in relation to chromosomal abnormalities. A significant effect of consanguinity was observed among the patients with chromosomal abnormalities ($P < 0.001$). Among CA, numerical CA seemed to be prevalent in 78.6% of the cases [Table 3]. Even though numerical CA and consanguinity seemed to be associated, however, no significant difference was observed between consanguinity and nonconsanguinity ($P > 0.50$).

Discussion

It is a well-known fact that consanguinity may increase the chances of individuals having identical genes. The homozygosity may have effect on the clinical conditions such as BOH, MR, MCA, DS, primary amenorrhea and primary infertility with suspected genetic etiology.

The classified genetic etiologies are the single gene disorders, CA and multifactorial inheritance. The CA, numerical and structural, may occur as de-novo at post zygotic mitosis or transmitted because of the errors at meiosis in the parental gametogenesis. Consanguinity has been suspected to have its influence in the formation of CA.

Table 1: Consanguinity in relation to chief complaints at the time of referral

Chief complaint	Consanguinity	%	Nonconsanguinity	%	Total
BOH	181	42.38	454	44	635
MR/MCA	101	23.65	149	14.35	250
DS	40	19.13	169	16.28	209
Male factor	20	25.64	58	06	78
Female factor	85	29.82	200	19.26	285
Others	–	–	8	01	8
Total	427	29.14	1038	70.86	1465

Note: Female factors: amenorrhea; Male factors: hypogonadism/male infertility; Others: premarital counseling, immigration certificate, primary infertility, and adoptions.

BOH, bad obstetric history; MR, Mental retardation; MCA, multiple congenital anomalies; DS, down syndrome.

Table 2: Consanguinity in relation to chromosomal abnormalities

	Normal karyotype	Abnormal karyotype	Total
Consanguinity	374 (87.6%)	53 (12.4%)	427
Nonconsanguinity	786 (75.7%)	252 (24.3%)	1038
Total	**1160 (79.2%)**	**305 (20.8%)**	**1465**

Table 3: Consanguinity and types of chromosomal abnormalities

	Numerical abnormality	Structural abnormality	Total
Consanguinity	43 (81.1%)	10 (18.9%)	53
Nonconsanguinity	197 (78.1%)	55 (21.9%)	252
Total	**240 (78.6%)**	**65 (21.4%)**	**305**

In 1961 itself, it has been postulated that the high frequency of trisomic syndromes in children, born of young mothers, may be because of nondisjunction of chromosomes, in females married to their maternal uncles.[3] In India, in a hospital-based study, among consanguineous marriages, a higher frequency of DS has been noticed.[4] Another study has also observed an increased frequency of parental consanguinity, among the parents of the patients with DS.[5] Subsequently, one of the studies has failed to confirm a higher incidence of close consanguinity among parents of individuals with DS.[6]

The effect of consanguinity on MR and or multiple congenital malformations has been widely reported.[7] Consanguinity has not influenced the fertility or the prevalence of MCA, CA and genetic disorders, has also been found. However, the Verma et al.[8] have noticed a significantly higher rate of stillbirths and infant mortality, in consanguinity. A significant frequency has been reported between consanguinity and genetic disorders, congenital heart disease, MCA, neurological malformations, chromosomal disorders and MR.[9] It has been stated that the association of recessive genetic disorders to consanguinity may be negated by urbanization and the decreased family sizes, which predictably will lead to a decline in the consanguinity associated genetic disorders.[10]

In this study, a sample size of 305 cases with confirmed CA has been studied. Even though, the influence of consanguinity on CA has been observed, it has not been reflected on the types of CA, neither on

the numerical nor on the structural CA. The differences may be because of the sample size, the mode of selection and the pooling of the CA as well as the types of consanguinity.

The interpretations from the observations of the present study are:

1. Consanguinity may have its influence on MCA.
2. One of the genetic etiology for multiple congenital anomaly is CA.
3. The effect of consanguinity on CA, but not on the types of CA, may be because of its association to MCA rather than to CA. The role of consanguinity is always under speculation. The findings of the present study may be interpreted that until and unless definite clinical conditions with CA as the etiology have been known to be associated to the consanguinity; the socioeconomic advantages definitely may outweigh the advocacy against consanguinity especially in India.

Hence, it is apparent that at the time of counseling, it may be kept in mind, that consanguinity may have a higher risk than the general population risk on CA. The present study has provided information on the suggestive role of consanguinity on CA.

References

1. Mueller RF, Young ID. Elements of Medical Genetics. 11th Edn. Edinburgh: Churchill Livingstone; 2001. p. 100/245.
2. Seabright M. A rapid banding technique for human chromosomes. Lancet 1971;2:971–2.
3. Penrose LS. Mongolism. Br Med Bull 1961;17:184.
4. Puri RK, Khanna KK, Bhargava I, Balakrishnan S. Role of Consanguinity in Chromosomal syndromes. Indian J Med Res 1977;65:859–64.
5. Alfi OS, Chang R, Azen SP. Evidence for genetic control of nondisjunction in man. Am J Hum Gent 1980;32:477-83.
6. Sayee R, Thomas IM. Consanguinity, nondisjunction, parental age and Down syndrome. J Indian Med Assoc 1998;96:335-7.
7. Kulkarni ML, Kurian M. Consanguinity and its effect on fetal growth and development: a south Indian Study: J Med Genet 1990;27:348-52.
8. Verma IC, Prema A, Puri RK. Health Effects of Consanguinity in Pondicherry. Indian J Ped 1992;29:685-92.
9. Jain VK, Nalini P, Chandra R, Srinivasan S. Congenital malformations, reproductive wastage and consanguineous mating. Aust NZ J Obstet Gynaecol 1993;33:33-6.
10. Bittles AH. Endogamy, consanguinity and community genetics. J Genet 2002;81:91-8.