ACROCENTRIC ASSOCIATIONS IN COUPLES WITH REPRODUCTIVE DISORDERS

By

T. LALITHA GOVERDHAN, A. JYOTHY AND G. S. ISAAC

SUMMARY

The frequency and pattern of acrocentric associations were studied in 50 couples with a history of spontaneous abortions, still births, neonatal deaths and children with congenital abnormalities and compared with 20 couples with normal children. A high frequency of D/G association was observed in all the cases with a history of repeated abortions. The observed value was higher than the expected ratio in parents with history of repeated abortions and history of still births and neonatal deaths. The acrocentric chromosome association index was observed to be high in parents with history of repeated abortions and history of congenitally malformed children.

Introduction

The primary cause of aneuploidy, resulting in chromosomal abnormalities such as trisomy, monosomy and mosaicism is due to chromosomal non-disjunction during cell division. An increased frequency of associations among acrocentric chromosomes might predispose to non-disjunction during cell division (Ohno *et al* 1961). However their predisposition to non-disjunction is not well understood. The acrocentric chromosome association has been of special interest in couples with reproductive disorders to understand the predisposition to non-disjunction of satellated chromosomes. Therefore an attempt has been made in this to measure the frequency and pattern of associations of acrocentric chromosomes in couples with reproductive disorders.

From: *Institute of Genetics Hospital for Genetic Diseases, Osmania University, Begumpet, Hyderabad*-500 016.

Accepted for publication on 22-9-87.

Material and Methods

Fifty couples with reproductive disorders referred for cytogenetic investigations have formed the material for the study. These couples were divided into three sub-groups:

(1) 20 couples (20 males in the age range of 26-45 years and 20 females in the age rnage of 20-38 years) with a history of repeated abortions.

(2) 18 couples (18 males in the age range of 25-35 years and 18 females in the age range of 20-38 years) with a history of still births and neonatal deaths and

(3) 12 couples (12 males in the age range of 26-35 years and 12 females in the age range of 20-32 years with a his-

tory of congenitally malformed children.

20 normal couples (20 males and 20 females in the age range of 25-45 years and 20-35 years respectively) without such complications as indicated earlier, but had normal children were taken as indicated earlier, but had normal children were taken as controls.

The chromosomal preparations obtained from lymphocyte cultures were stained according to Seabright (1971) and Scheres (1974). The associations of satellated chromosomes were secored according to the standard procedure of Zang and Back (1967). In each metaphase spread, the following parameters were analysed:

(a) All types of associations.
(b) The number of each type of association.
(c) The number of D and G group chromosomes associated.
(d) The total number of acrocentric chromosomes associated and
(e) The total number of associations.

Results and Discussion

The assessment of satellite association frequency and pattern was performed in 50 couples of reproductive disorders and 20 cases with history of normal children as control group The association frequency results in each group are given in Table I. A slightly increased number of associations were observed in females in all the three groups. There was no significant difference in the number of associations per metaphase in the study groups and controls but the mean number of chromosomes associated per metaphase showed higher values in study groups.

The distribution of different types of associations in the study groups and controls is presented in the Table II. The association of two acrocentric chromo-

TABLE I

Frequency of Acrocentric Chromosome Associations in Study Groups and Control Group

Study groups	No. of cases observed	No. of Metaphases screened	No. of Metaphases with Association (%)	Mean Number of Associations/ Metaphase	Mean Number of Chromosomes Associated/ Metaphase	Mean Number of Chromosomes Associated/ Association
1. History of repeated abortions	F 20	400	48.5	0.48 ± 0.14	1.86 ± 0.66	3.65 ± 1.0
	M 20	400	43.0	0.40 ± 0.11	1.82 ± 0.38	4.39 ± 1.2
2. History of still births and neonatal deaths	F 18	360	42.5	0.43 ± 0.14	1.51 ± 0.58	3.69 ± 0.96
	M 18	360	43.3	0.43 ± 0.13	1.69 ± 0.42	3.98 ± 0.66
3. History of congenitally abnormal children	F 12	240	46.4	0.48 ± 0.16	1.91 ± 0.74	3.98 ± 0.38
	M 12	240	43.3	0.44 ± 0.14	1.96 ± 0.59	4.4 ± 0.65
4. Parents with Normal children	F 20	400	45.8	0.46 ± 0.12	1.74 ± 0.47	3.8 ± 0.58
	M 20	400	41.3	0.41 ± 0.11	1.39 ± 0.62	3.43 ± 0.72

F = Female. M = Male.

TABLE II

Distribution of Different Types of Associations of Acrocentric Chromosomes

Study Groups	Number of Metaphases screened	Types of Associations			Multiple				Total
		DG	DD	GG	III	IV	V	VI	
1. History of repeated abortions	F 400	154	62	44	46	17	1	1	325
	M 400	148	58	32	46	19	3	1	307
2. History of still births and neonatal deaths	F 400	92	58	30	34	22	1	1	238
	M 400	112	45	42	46	12	2	1	260
3. History of congenitally abnormal children	F 240	100	38	29	25	14	1	—	207
	M 240	86	40	28	37	10	3	—	204
4. Parents with normal children	F 400	106	64	46	45	27	—	—	288
	M 400	120	52	32	31	13	—	—	248

F = Female; M = Male.

somes, such as DG, DD, GG were most frequent in all the study groups. The DG type of association was high in the cases with history of repeated abortions.

The distribution of D and G group chromosomes in association is summarised in Table III. The number of D and G chromosomes participated in the association was high in 1 and 2 study groups (Table III) as compared with controls.

TABLE III

Distribution of D and G Group Chromosomes and D/G Ratio

Study groups	No. of Metaphases screened	Per cent Association		AI	D/G ratio	
		D	G		Observed	expected
1. History of repeated abortions	F 400	19.0	17.5	18.4	1.62	1.5
	M 400	17.9	17.6	17.8	1.52	1.5
2. History of still births and neonatal deaths	F 360	15.7	15.3	15.5	1.51	1.5
	M 360	16.3	16.8	16.7	1.54	1.5
3. History of congenitally abnormal children	F 240	19.8	20.8	19.5	1.47	1.5
	M 240	19.4	20.0	19.7	1.46	1.5
4. Parents with Normal children	F 400	16.8	17.1	16.9	1.47	1.5
	M 400	13.4	17.1	15.3	1.40	1.5

F = Female; M = Female; AI = Acrocentric Chromosome Association Index.

The observed value was higher than expected D/G ratio in 1 and 2 study groups. The acrocentric chromosome association index (AI) of associations was calculated by taking the total number of D and G group chromosomes available per association in each group. AI was observed to be high in 1 and 3 study groups than the controls.

The physical basis of satellite association is not clearly understood. However it is evident that the satellites present on the human acrocentric chromosomes would participate in the nucleolus organization. It is also evident that there exists an extensive polymorphism for the nucleolus organizers. The size of the satellites or the number of the copies of the major RNA genes located on the satellites are variable. Zankl and Zang (1974) and Schmid *et al* (1976) have shown that longer satellites produce higher association frequencies.

In the normal course of cell division, the nucleolus appears in the cell during the interphase and after its function is over, the nucleolus distintegrates and the nucleolar material will organize into satellites and by the time the cell division reaches metaphase and then anaphase, the chromosomes should be ready to move towards the respective poles. But due to satellite associations, some times they may fail to disjoin and therefore non-disjunction may takes place as a result of which aneuploidy may occur. Most autosomal aneuploids end in abortion thus leading to reproductive failure. However further studies are necessary to understand the role, the satellite associations have in predisposing to non-disjunction.

Acknowledgements

Authors are grateful to Prof. O. S. Reddi, Director, Institute of Genetics for extending facilities.

One of the authors (TLG) is thankful to Council of Scientific and Industrial Research, New Delhi for financial support.

References

1. Hayata, I., Oshimura, M. and Sandberg, A. A.: N-band polymorphism of human acrocentric chromosomes and its relevance to Satellite Association. Hum. Genet. **36**: 55-61, 1977.
2. Miller, D. A., Tantravahi, R., Dev, V. G. and Miller, O. J.: Frequency of Satellite Association of human chromosomes is correlated with amount of Ag—staining of the nucleolus organizer region. Am. J. Hum. Genet. **29**: 490-502, 1977.
3. Ohno, S., Trujillo, J. M., Kaplan, W. D. and Kinosita, R.: Nucleolus—Organizers in the causation of chromosomal anomalies in man. Lancet, **11**: 123, 1961.
4. Scheres, J. M. J. C.: A modified method of Scheres. Hum. Genet. **23**: 4, 1974.
5. Schmid, M., Krone, W. and Vogel, W.: On the relationship between the frequency of association and nucleolar constriction of individual acrocentric chromosomes. Human genetik, **23**: 267-277, 1976.
6. Seabright, M.: A rapid banding technique for human chromosomes. Lancet, **1**: 971-972, 1971.
7. Zang, K. D. and Back, E.: Individual Satellite Association patterns. Lancet, **11**: 1423, 1967.
8. Zankl, H. and Zang, K. D.: The Association frequency of human acrocentric marker chromosomes. Human genetik, **23**: 259-265, 1974.