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Chromosome Abnormalities in a Referred Population for Suspected Chromosomal Aberrations
: A Report of 4117 Cases

A cytogenetic study was performed on 4,117 Korean patients referred for suspected chromosomal abnormalities. Chromosome aberrations were identified in 17.5% of the referred cases. The most common autosomal abnormality was Down syndrome and Turner syndrome in abnormalities of sex chromosome. The proportions of different karyotypes in Down syndrome (trisomy 21 92.5%, translocation 5.1%, mosaic 2.4%) were similar to those reported in other countries. However, it was different in Turner syndrome (45, X 28.1%, mosaic 50.8%, 46, X, del (Xq) 4.4%, 46, X, i (Xq) 16.7%), in which proportions of mosaics and isochromosome, 46, X, i (Xq), were higher than those reported in other countries. In structural chromosome aberrations of autosome, translocation was the most common (43.6%), and duplication (21.3%), deletion (14.4%), marker chromosome (7.9%) and ring chromosome (4.0%) followed in order of frequency. Rates of several normal variant karyotypes were also described. Inversion of chromosome 9 was observed in 1.7% of total referred cases.

Key Words: *Chromosomal abnormalities; Cytogenetics; Down syndrome; Turner's syndrome; Inversion (genetics)*

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INTRODUCTION

Chromosome abnormalities cause diverse functional problems in various organs and are frequently accompanied with mental retardation, therefore the patients need continuing familial and social support. Even though economic status and strategies for prenatal diagnosis have progressed recently, patients with chromosome abnormalities still remain an important medical problem. This study was performed to evaluate the most recent frequencies of different chromosome abnormalities compared with those of decades ago when the number of siblings was higher and prenatal diagnosis was not common in Korea. We also analyzed data to evaluate ethnic differences in frequencies of major and variant chromosome abnormalities.

MATERIALS AND METHODS

Peripheral blood leukocytes were obtained from study subjects who were clinically suspected having chromosomal abnormalities and referred to cytogenetics laboratories of two university hospitals (Yonsei Medical Center, Seoul, Korea and Ajou University Hospital, Suwon, Korea) and a clinical laboratory (Green Cross Reference Laboratory, Seoul, Korea) from 1994 to 1997. Collected blood samples were prepared for conventional GTG (G bands by trypsin using Giemsa) banding technique. A specialized cytogeneticist in each laboratory analyzed karyotypes. The karyotypes, and other informations on sex, age and clinical features of the subjects were obtained. Patients with malignant tumors or anemias were excluded from the study and the karyotypes from a total of 4,117 cases (male 2,172, female 1,945) were analyzed.

RESULTS AND DISCUSSION

Of the 4,117 cases evaluated, 721 cases (17.5%) showed chromosome abnormalities (Table 1, 2). Among them, autosome abnormalities were found in 527 cases (73.0%)

Table 1. Autosomal chromosome abnormalities by karyotype among 4,117 referred cases in Korea and in other studies of different countries

Karyotype	Present study		Relative frequency(%)		
	No.	R. F (%)	Choi et al. (1) & Lee et al. (9)*	Nielsen et al. (10)†	Hook EB et al. (11)†
Numerical aberrations					
Down syndrome	295	56.0	75.2	27.6	31.6
47, XX(Y), +21	273				
46, XX(Y)/47, XX(Y), +21	7				
Translocation	15				
Edward syndrome	23	4.4	0.7	3.8	3.1
47, XX(Y), +18	19				
46, XX(Y)/47, XX(Y), +18	3				
Translocation	1				
Patau syndrome	5	0.9	-	1.1	1.3
8 Trisomy (46, XX/47, XX, +8)	1	0.2	-	0.5	-
9 Trisomy (47, XY, +9)	1	0.2	0.7	-	-
Structural aberrations					64.0§
Cri du chat syndrome	8	1.5	-	-	-
Translocation	88	16.7	7.1	50.3	
Duplication	43	8.2	5.7	1.6	-
Deletion	29	5.5	3.5	1.6	
Marker chromosome	16	3.0	2.1	13.0	
Ring chromosome	8	1.5	-	0.5	
Miscellaneous	10	1.9	5.0	-	
Total	527	100.0	141 (100.0)	185 (100.0)	225 (100.0)

* among 644 referred cases for suspected chromosome aberrations in Korea
† among 34,910 newborn children in Denmark
† among 56,952 newborn children
§ including structural abnormalities of sex chromosome

Table 2. Sex chromosome abnormalities by karyotype among 4,117 referred cases in Korea and in other studies of different countries

Karyotype	Present study		Relative frequency(%)		
	No.	R. F (%)	Choi et al. (1) & Lee et al. (9)*	Nielsen et al. (10)†	Hook EB et al. (11)†
Turner syndrome	114	58.8	37.8	13.0	1.6
45, X	32				
Mosaic	58				
46, X, del (Xq)	5				
46, X, i (Xq)	19				
Klinefelter syndrome	59	30.4	42.2	36.3	27.6
47, XXY	51				
46, XY/47, XXY	4				
48, XXXY	3				
48, XXYY	1				
47, XXX	3	1.5	2.2	22.1	15.6
47, XYY	5	2.6	2.2	26.0	27.6
Other sex chromosome abnormalities	13	6.7	15.6	2.6	27.6
Total	194	100.0	45 (100.0)	77 (100.0)	127 (100.0)

* among 644 referred cases for suspected chromosome aberrations in Korea
† among 34,910 newborn children in Denmark
† among 56,952 newborn children

and sex chromosome abnormalities were in 194 cases (26.9%). There was also a neonate with triploidy accompanied with clinical features of hydrocephalus, syndactyly and low birth weight. The rate of total chromosome abnormalities was lower than previously reported in Korea (29.3%) (1) and other country (27.2%) (2). Discordance of classification criteria and increased interest in genetic diseases by physicians could explain this difference. We classified inversion and heterochromatin as normal variants and referred patients with minor abnormalities, and normal karyotypes might decrease the overall frequency of chromosomal abnormalities.

The most common chromosome abnormality was Down syndrome of 295 cases (40.9%). And 273 cases (92.5%) was with trisomy 21, seven cases were with mosaics (2.4%) and 15 cases (5.1%) were with translocation of chromosome 21. Among the translocations, there were seven cases of t(21:21), four cases of t(14:21), two cases of t(13:21), and a case of t(6:21), t(21:22) apiece. The proportion of each karyotypes in Down syndrome was similar to those reported in a previous study on 877 cases in Korea (47, XX(Y), +21 88.4%, translocation 6.5%, mosaic 3.9%) (3) and on 1,672 cases in Sweden (47, XX(Y), +21 92.3 %, translocation 5.7%, mosaic 2.0%) (4).

There were a 14-year-old female with 8 trisomy mosaicism, and a neonate with 9 trisomy.

In structural chromosome aberrations, translocation was found most common (43.6%). Duplication (21.3%), deletion (14.4%), marker chromosome (7.9%) and ring chromosome (4.0%) followed in order of frequency. Cri du chat syndrome was found in eight cases. The rest consisted of insertion and other complex aberrations.

Translocation between chromosome 13 and 14 were found in 13 cases. Other types of translocation were observed less frequent than two cases apiece except t(15:22) (five cases). Six cases had duplication of 8p. And duplications of 14p (four cases), 15p (four cases), and 16p (three cases) were also found. Among ring chromosome abnormalities, there were four cases of r(18), three cases of r(13) and a case of r(14).

Turner syndrome was the most common sex chromosome abnormality (114 cases). Mosaicism was more common than monosomy 45, X. Of the 58 mosaics, nine cases had Y chromosome component (45, X/46, XY etc.). Isochromosome with karyotype 46, X, i(Xq) was also found in 19 cases. The relative frequencies of different karyotypes of Turner syndrome (45, X 28.1%, mosaic 50.8%, 46, X, del(Xq) 4.4%, 46, X, i(Xq) 16.7%) identified in this study were different from other western countries (45, X 50.2%, mosaic 37.2%, 46, X, del (Xq) 3.9%, 46, X, i(Xq) 8.7%) (5) (45, X 50.6%, mosaic 28.4%, 46, X, del(Xq) 8.4%, 46, X, i(Xq) 12.6%) (6). We classfied mosaics of normal karyotype with deletion or isochromosome of Xq as mosaicism. But, even after we adjusted the criteria to be consistent with other studies, the proportion of mosaics was higher than Hook et al. (5) (p=0.003) and the proportion of 46, X, i(Xq) was higher than Gravholt et al. (6) (p=0.001). The proportion of monosomy 45, X was similar to the result of other study reported in Korea (30.3%) (7) but lower than those in other countries. Though it is hard to explain the reason for these differences, there is yet no clue showing that particular types of chromosomal abnormalities have racial preferences. Therefore, a nationwide survey is needed in the future.

The most frequent sex chromosome abnormality in male was Klinefelter syndrome (59 cases) and 86.4% of them were 47, XXY. Other sex chromosome abnormalities were also observed including partial deletion.

Some variant karyotypes including inversion, heterochromatin and large Y chromosome were identified in 3.7% (152 cases) of tested individuals (Table 3). These karyotypes were generally considered as normal variants without phenotypic effects on the individuals carrying these aberrations. Nevertheless, there have been also debates on the association between these karyotypes and various clinical problems. The prevalence of inversion chromosome 9 in a normal population were reported as 1.65%, and higher incidence in aborted fetuses with normal karyotype (3.31%) and couples with a history of more than two spontaneous first trimester abortions (3.19%) (8). In the present study, inversion of chromosome 9 was observed in 1.7% of total referred cases. Among them, 45 cases (65.2%) were pericentric inversion and for the rest breaking point did not specifically mentioned. There were patients having inv(9) accompanied with delayed development or mental retardation (25.0%), congenital anomaly (23.1%), giving birth to babies with an inv(9) (15.4%) and habitual abortion (7.7%). However it was not possible to confirm whether inv(9) was responsible for these clinical features.

Other normal variant karyotypes included inversion of chromosome 6 (seven cases), large Y chromosome (five cases), and inversions or heterochromatin of different

Table 3. Relative frequency of normal variant karyotype among 4,117 referred cases in Korea

Karyotype	No.	Relative frequency (%)
46, XX(Y), inv (9)	69	45.4
46, XX(Y), 1h+	20	13.2
46, XX(Y), 16h+	18	11.8
46, XX(Y), 9h+	11	7.2
Others	34	22.4
Total	152	100.0

chromosomes.

When compared with other studies reported in the early 1980s in Korea, the rank of relative frequencies of different chromosome aberrations in this study showed similar results.

The proportion of Down syndrome among autosomal abnormalities was lower by about 20% than those Choi et al. (1) and Lee et al. (9) reported. It was assumed that this was partly due to wide application of prenatal diagnosis in the last ten years. The proportion of structural abnormalities was higher in the present study and it could be due to development of chromosome banding technique and improvement of karyotyping skills. However, major clinical features of referred subjects could be different among clinics or medical specialists. So the differences of relative frequency of each karyotype could not simply be explained by the results per se.

The relative frequencies of 47, XXX and 47, XYY in referred subjects were much lower than those reported in newborn children. Since these chromosomal aberrations usually do not manifest severe phenotypic abnormalities, many of those patients must not have been included in this study.

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