ORIGINAL ARTICLE

KARYOTYPE STUDY IN PATIENTS WITH HEARING DISABILITY

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ABSTRACT

Background: Hearing disability is the most common sensory disorder in humans. About 50% cases of congenital hearing loss are due to genetic causes. About 70% of genetic hearing loss is nonsyndromic and 30% is syndromic. Syndromic hearing loss is found as about 500 syndromes associated with chromosomal abnormalities. Genetic study of hearing loss include numerical chromosomal aberrations like trisomy 13, 18, 21 and structural chromosomal aberrations like deletion, translocation or invertion involving chromosome numbers 1, 2, 3, 5, 6, 7, 8,10,11, 12, 13, 15, 18, 21 and many more .
Materials & Method: The aim of this study was to carry out a cytogenetic profile of 25 clinically diagnosed patients of hearing loss from school of deaf & dumb and from ENT clinics, Ahmedabad to find out the chromosomal abnormalities in these patients. Karyotypes of all the patients were prepared from peripheral venous blood & photographed at genetic laboratory at B.J.Medical College, Ahmedabad.
Observations: Clinical & karyotype analysis revealed that out of 25 patients, 8 cases had positive family history of hearing loss. Positive history of consanguineous marriage was found in 6 patients. It was observed that 17(68%) cases had isolated(non-syndromic) hearing loss and 8(32%) cases had syndromic deafness. Among 17(68%) non-syndromic patients 13(52%) cases showed normal chromosomal constitution and in 4(16%) cases metaphase was not found and out of 8(32%) patients with syndromic deafness, one female (4%) & two males (8%) had trisomy 21, one female (4%) had monosomy of X chromosome and 4(16%) cases showed normal chromosomal constitution.
Conclusion: Cytogenetic pattern of hearing loss is variable among different studies.So, cytogenetic analysis of suspected hearing loss is of value to objectively confirm the diagnosis and to provide a basis for genetic counselling.

Keywords: Nonsyndromic hearing loss, syndromic hearing loss, karyotype

INTRODUCTION

Hearing is a prerequisite for the development of normal speech & language. The period from birth to 5 years of life is critical for development of speech and language; therefore, there is need for early identification and assessment of hearing loss and early rehabilitation in infants and children.

The incidence of pre-lingual (before acquisition of speech) deafness is 1 in 1000 new born. About 50% cases of congenital hearing loss are due to genetic causes. About 70% of genetic hearing loss is nonsyndromic and 30% is syndromic.

Around 80 chromosomal locations harbour genes which are involved in non-syndromic hearing loss. Connexin 26, DFNB1 locus is the most common cause of autosomal recessive, nonsyndromic, congenital hereditary hearing loss.

Syndromic deafness is found in about 500 syndromes associated with chromosomal abnormalities; e.g. Down's syndrome, Turner's syndrome, Usher syndrome, Pendred syndrome, Waardenburg syndrome, Branchio-Oto-Renal syndrome, Treacher Collins syndrome etc.

In genetic study of deafness numerical chromosomal aberrations like trisomy 13, 18, 21 and structural chromosomal aberrations like deletion, translocation or invertion involving chromosome numbers 1, 2, 3, 5, 6, 7, 8, 10, 11, 12, 13, 15, 18, 21 and many more were found.

The object of this work was to study the clinical and karyotypic profile of patients with hearing loss from

the school of deaf and dumb and from ENT clinics, Ahmedabad to detect chromosomal abnormalities and genetic causes of deafness so that proper management and genetic counselling can be done.

MATERIALS AND METHOD

Being a retrospective study, data has been gathered from the available information on 25 deafs, who have been karyotyped. For each individual, a detailed personal & family history has been complied. Blood samples of the patients were obtained in a heparinized container. Cultivation was done on the same day of the aspiration. After an incubation period of 69 hours at 37^0 C, the harvesting was done and finally the metaphases on the slides were obtained. Thereafter, those slides showing metaphase with good morphology were selected and kept under non-humid dry wooden boxes for aging process.

Approximately after 7 days of harvesting, banding procedure was done using freshly prepared EDTA-Trypsin solution and giemsa stain.

About 25 metaphase plates were observed in each case and a photograph was obtained from a good quality metaphase slide with the help of a black & white film loaded camera attached with a photomicroscope with an exposure time of 8-15 seconds.The chromosomal findings were described according to the International system of Human Cytogenetic Nomenclatures & finally, karyotype was prepared using conventional cut & paste technique. Ethical committee permission was taken.

RESULTS

In the present study out of 25 patients, 14 males & 11 females were studied for cytogenetic assessment. Out of them 8 cases had positive family history of hearing loss & positive history of consanguineous marriages were found in 6 patients. It was observed that 17(68%) cases had isolated (non-syndromic) hearing loss and 8(32%) cases with syndromic deafness.

Table 1: Clinical Features of Hearing Loss

Deafness	Non-syndromic	Syndromic
No. of Cases	17	8
Male:Female	8:9	6:2
Type of Deafness	Sensoryneural	Sensoryneural or mixed
Positive Family History	8	
Consanguinity	6 cases	

The cytogenetic evaluation was done by karyotyping & was as follows.

Table 2: Cytogenetic Observation in Non-syndromic Hearing Loss

No. of cases	17
Normal	13
Abnormal	-
Metaphase not found	4

Table 3: Cytogenetic Observation in Syndromic Hearing Loss

Cytogenetic Observation in Syndromic Hearing Loss		
Syndrome	**Cases**	**Chromosomal findings**
Down's syndrome	3	Trisomy 21
Turner's syndrome	1	Monosomy X
Cleftlip cleft palate	1	Normal
Congenital heart disease	1	Normal
Branchio- oto-renal syndrome	1	Normal

Table 4: Cytogenetic Findings in Non-syndromic hearing loss in Different Studies

Worker	Karyotype	FISH/CGH array/others
Dar H (1969)	Chromatid aberrations, Elongated secondary constriction of chromosome 9 Heterozygosity of chromosome16, Long Y chromosome	
Kabarity A. et al (1979)	No numerical or structural chromosomal aberration.	
León PE et al (1981)	No chromosome abnormalities	
A Veske et al, (1996)	No numerical or structural chromosomal aberration	(DFNB8) on the distal long arm of chromosome 21
Zhuang J et al (2000)	Chromosomal 15 satellite enlargement, karyotype 46, XY(X), PS++(15)	
Ramchander P. V et al (2004)	No numerical or structural chromosomal aberration	DFNB1 locus (connexin26 gene) at 13q12.(31)
G.Padma et al (2010)	Disomy of a part of chromosome 13q	
Present study	No numerical or structural chromosomal aberration	

Table 5: Cytogenetic Findings in Syndromic hearing loss in Different Studies

Worker	Deafness:Isolated/ associated disorders	Karyotype
Katano t et al (1978)	Trisomy 22	Trisomy 22
V.P.Prasher (1995)	Down's syndrome	Trisomy 21
Hultcrantz M et al (1997)	Turner's syndrome	Monosomy X
Present study	Down's syndrome	Trisomy 21
	Turner's syndrome	Monosomy X

Cytogenetic investigation of the 25 deafs gave the following observations.. Out of them 1 deaf female & 2 deaf males with Down's syndrome had trisomy 21, 1 deaf female with turner's syndrome had monosomy X & 17 patients showed normal chromosomal constitution. In remaining 4 deafs metaphase was not found.

DISCUSSION

Consanguinity & Positive family history is the most important factor in the genetically determined deafness. Consanguinity could be an aetiological factor in deaf mutism (Rajendra kumar P.V). A large family with childhood deafness, contained several consanguineous marriages (A Veske et al)**.**70% of the deaf children were from parents of consanguineous marriages (Mazin Al Khabori and Michael A. Patton). Out of 356 patients with hearing defect, consanguinity among the parents was found in 199(59%) patients (Ramchander P. V et al). Out of 140 deaf school pupils, Parental consanguinity was established for 121(86.4%) of deaf school pupils. (Sajjad M et al) Out of 535 children with hearing loss, 73 (13.7%) children had positive family history (Ishisawa H)Out of 45 children, 33(73%) had positive family history. (Fishman J.E.et al).Out of 356 patients with hearing defect, 129(36.2%) cases had positive family history (Ramchander P. V et al)

In the present study 25 patients (M: F::14:11) of hearing loss were studied. Out of them 8 cases have positive family history of deafness & positive history of consanguineous marriage found in 6 patients.

Chromosomal analysis in 129 children with congenital familial deafness, 4 children showed a high incidence of chromatid aberrations, 5 members of one family showed a conspicuously elongated secondary constriction of chromosome 9, one deaf child showed heterozygosity of chromosome 16 and another deaf child showed an unusually long Y chromosome (Dar H and Winter S T).Karyotype analysis of the family included 13 cases of heritable childhood deafness showed an apparently normal male chromosomal constitution of 46, XY in all cells examined with no numerical or structural chromosomal aberration. (Kabarity A. et al). A large family from Pakistan, Linkage analysis mapped the disease locus (DFNB8) on the distal long arm of chromosome **21** (A Veske et al)**.**

In the study of clinical and cytologic examinations in 6 deaf patients, the karyotype showed chromosomal 15 satellite enlargement, 46, XY(X), PS++ (15). A proband as well as his brother and sister suffered from gradual hearing loss at the age of 12 to 13 and big satellite 15 existed in chromatinic karyotype. Based on the fact that they had similar clinical phenotype and karyotype, their delayed deaf-mutism may be related to the structural abnormality of chromosome 15(Zhuang J et al).In a large kindred of hereditary deaf affected with a progressive sensorineural loss, no associated abnormalities have been detected in karyotypes. (Leon PE et al).Autosomal recessive nonsyndromic hearing impairment (ARNSHI) is the most common form with profound hereditary hearing impairment linked to DFNB1 locus (connexin26 gene) at 13q12. (Ramchander P. V et al).In a family of a male proband with prelingual, profound non-syndromic hearing impairment was arising as a result of maternal uniparental disomy of a part of chromosome 13q. (G.Padma et al)

In the present study out of 17 patients of nonsyndromic deafness 13(52%) cases showed normal chromosomal constitution and in 4(16%) cases metaphase was not found.

The disturbance of the auditory function is more severe in the complete trisomy 22 than in the partial trisomy(Katano t et al). Out of 201 adults with Down syndrome(trisomy 21), 23(11.9%) had moderate or severe impairment(V.P.Prasher).24 individuals with turner syndrome had presence of unpaired genes on the X chromosome may account for hearing loss (Sculerati N.et al).40 women with Turner's syndrome, mid frequency SNHL was frequently diagnosed and could be correlated to the karyotype (Hultcrantz M et al). Two chromosomal anomalies: a der(9)t(9;13) derived from a paternal translocation and a der(6)t(4;6) of unknown origin was found in the study of 27 deaf patients of CHARGE syndrome.(Sanlaville D).In the study of an eleven year old boy with unilateral high-graded and contralateral middle-graded hearing loss in addition to the known skeletal, orofacial disorders, hypothrophia and retardation & found that there is interstitial deletion of chromosome 1(q23-q31).(Schwemmle C et al)

In the present study 8 patients had syndromic deafness, out of them 3(12%) had deafness with Down's syndrome, 1(4%) had deafness with turner's syndrome, 1(4%) patient had deafness with congenital heart disease, 2(8%) had deafness with cleft lip & palate & 1(4%) had deafness with branchio-oto-renal syndrome.

CONCLUSION

For the present study 25 clinically diagnosed patients with hearing disability were selected from school of deaf & dumb & from ENT clinics, Ahmedabad. In all

cases, relevant history clinical findings & necessary investigations were noted. Blood samples were collected & cytogenetic/ karyotypic study was performed at genetic laboratory, B.J. Medical College, Ahmedabad.

Samples were cultured, harvested & finally slides were prepared. There after photographs were obtained from the slides showing good quality metaphase using photomicroscope & karyotypes were prepared using conventional cut & paste technique.

Cytogenetic evaluation was done. Out of 25 cases of hearing loss, chromosomal abnormaltities was found in 4 cases, 17 cases showed normal chromosomal constitution and in 4 cases metaphase was not found. The chromosomal abnormality was trisomy 21 in 3 cases & monosomy of X chromosome in 1 case. In the present study nonsyndromic deafness was observed in 68% cases and syndromic deafness was in 32% cases. Positive family history was found in 32% cases & consanguineous marriages were found in 24% cases.

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