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Analysis of the Chromosomal Deletions

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ABSTRACT Deletion involves loss of part of a chromosome resulting in monosomy for that segment of chromosome. In this paper, a data profile on the detected chromosomal deletions and its association to the phenotype is reported. Data was obtained from 55 probands referred to Division of Human Genetics, from 1974 to 2007. Chromosomal preparations included modified leucocyte microculture method. Deletions were observed in 14 autosomes (2,3,4,5,6,8,9,11,13,15,16,17,18,22) and in X and Y. Deletion in the autosomes was seen in 37 and in X in 13. Deletion, as single cell line was identified in 32 and in mosaic status in 23. Deletion in the long arm of chromosomes was seen in 40 (72.7%) and in short arm in 15 (27.3%) and the break points could be pinpointed in 36. Male to female sex ratio was 1.1:1 (29:26). In 29 males deletion in the autosomes was observed in 24 and in 26 females deletion in autosomes & in X was of equal occurrence (13/26). Chromosomes with deletion seen in both sexes were 3,5,8,9,11,15,18. Deletions were found to be 'de novo' in 9. Deletion was associated to multiple congenital abnormality and or mental retardation (26), amenorrhea (12), bad obstetric history (13) and abnormality in the skeletal (15) and genital systems (15). The analyzed chromosomal deletions and the loss of the chromosomal segments seemed to be associated to a range of clinical conditions and birth defects. The present study, may be for the first time reporting the data on deletion from India.

INTRODUCTION

Chromosomal abnormalities are classified as numerical or structural abnormalities. The numerical chromosomal abnormality includes loss or gain of one or more chromosomes in 'single or mosaic status'. The structural chromosomal abnormality occurs because of the breakage in the chromosomes and subsequent reunion in different configurations which result in balanced or unbalanced rearrangements. In general, the balanced structural rearrangements are considered to be 'normal', whereas the unbalanced chromosomal rearrangements give rise to severe clinical effects.

The reported incidence of chromosomal abnormalities at birth is 0.5 to 5% and for the unbalanced chromosomal rearrangements, it is around 10 in 10,000 births (Turnpenny and Ellard 2005) and deletion is included in the category of the unbalanced chromosomal rearrangements.

Deletion involves loss of part of a chromosome resulting in monosomy (only one copy) for that segment of chromosome. A very large deletion will be incompatible with survival to term and as a general rule, any deletion resulting in loss of more than 2% of the total haploid genome will have a lethal outcome, leading to hemizygosity or haploinsufficiency for several or many genetic loci (Young 2005).

In deletion, the single break results in shorter chromosome and acentric fragment, which being unstable is lost through the subsequent cell divisions. A deletion may be terminal (at the end of chromosome) or interstitial (within the chromosome). The clinical consequences depend on the size of the deleted segment and the number and function of the genes that it contained. At 550-band stage metaphase, the average chromosomal band contains approximately $5x10^6$ DNA base pairs coding for as many as 100 to 200 genes (Spinner et al. 2007). Hence, patients with cytogenetically detectable chromosomal imbalance involving gain or loss definitely demonstrate abnormality in phenotype. Deletions occur either as 'de novo' or inherited from parents as a result of malsegregation of parental balanced translocation. Microdeletions are not detectable with the regular microscopy preparations of the chromosomes and are less than 3 to 4 Mb and are also associated to a number of clinical syndromes and with sibling recurrence (Gardner and Sutherland 2006).

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The present study reports the data on the cytogenetically determined deletions and its association to a range of clinical conditions and birth defects. It is aimed to present the data on the following aspects in deletion, such as the chromosomes involved, deletions in single cell line and in mosaic status, breakpoints as per the arms of the chromosomes, sex ratio, 'de novo' or the inherited status of the deletion and the effect of deletion on the phenotype.

MATERIAL AND METHOD

-Data was obtained from 55 probands confirmed to have chromosomal deletions. Clinical profile was gathered retrospectively from the duly filled proforma. Chromosomal preparations include modified leucocyte microculture method of peripheral lymphocyte culture, Giemsa- Trypsin banding technique, photography and karyotyping (Mitelman 2005). There were 29 male and 26 female probands and their age ranged from neonates to 40 years. In case of deletion, cultures were repeated not only for further confirmation, but also, to assess the percentage of the anomaly.

Leucocyte Microculture Method for Cytogenetic Analysis (Arakaki And Sparkes 1963) Culture Setting: 5 ml of the culture medium (RPMI 1640 with antibiotics, 86 ml; Serum (FBS), 14 ml; PHA, 6 ml) are placed in 15 ml vials. 2 vials are set up for each sample / patient. 0.5 ml [6-8 drops without needle] of heparinised whole blood is added to each vial. Vials are accurately labeled. The vial is gently shaken and incubated at 37 °c for 72hrs.

Harvesting of Cultures: At 66th to 69th hour of incubation, 50 microlitres of colchicine and 100 microlitres of Ethidium Bromide are added to each vial. The vials are gently shaken and further incubated for an hour. At the end of the incubation period, the culture vials are gently shaken and the contents are transferred to 15 ml centrifuge tubes and centrifuged at 1000 rpm for 8 minutes. The supernatant is discarded and the cells mixed well using a cyclomixer. 5ml of Ohnuki solution (hypotonic solution) is added and mixed well and left in the dark for 1hr in room temperature. Ohnuki solution should be prepared one hour in advance and kept it in the incubator at 37°C. After one hour at room temperature, centrifuge the suspension for 8 minutes. Discard the supernatant, mix the pellet, and add freshly prepared chilled fixative drop by drop keeping the centrifuge tube on the cyclomixer. The total volume is made up to 5ml with fixative (methanol and glacial acetic acid, 3:1 ratio). The suspension is left at room temperature for at least 15 minutes to allow the cells to fix. After 15 minutes, centrifuge suspension for 8 minutes discard the supernatant, mix the pellet, and add 5ml more of fixative. This procedure is repeated once more. After three changes in fixative, the slides are prepared.

Preparation of Slides: After the last change in fixative about 0.3-0.5 ml of fresh fixative is added to the pellet and mixed well. Precleaned slides are refrigerated (4° C) in triple distilled water for 2-3 hours prior to harvesting. With a Pasteur pipette 1-4 drops of the cell suspension are dropped onto the slide surface starting from a distance of ¼" from the slide edge. Start dropping the cell suspension at the end away from the label and work toward the label. The slide is held at an angle while dropping is done and then heat dried on a slide warmer at 45-60° C for 1-2 minutes. Four to six slides are prepared for each case. The test slide is checked under the microscope for the concentration of cell suspension, spreading of chromosomes and mitotic index. Slides are aged for 2 to 3 days at room temperature or at 90°C to 95° C for 15 minutes before banding.

RESULTS

Among the 55 with deletion, in 37 cases autosomes were involved followed by X (13) and Y (5). The involved autosomes were 2, 3, 4, 5, 6, 8, 9, 11, 13, 15, 16, 17, 18 and 22 (Table 1).

Deletion as single cell line was identified in 32 (32/55, 58.2%) and as mosaicism in 23 (23/55, 41.8%) cases. Chromosomes with deletion, that were common both in single line and mosaicism were 3,5,9,18,X,Y. Chromosomes seen in a single cell line were 11,13,15,16,17,22 and in mosaicism, 2,4,6,8. Mosaicism involving one or two spreads with deletion was seen in 16, out of which deletion in the autosomes was of higher percentage (13/16, 81.3%). In these 16 probands (males 10; females 6), it was the normal chromosomal complement either 46,XY (9/10) or 46,XX (4/6), which had occurred to a higher percentage (Table 1, Fig. 1).

The chromosomes involved in deletion with the breakpoints both in the short (14) and long arm (25) were 3p[3], 3q, 4p, 4q[2], 5p, 5q, 9p[3],

Table 1: Chromosomes involved in deletion

S. No.	*Phenotype*	*Chromosome*	*Break points*
1	MR	2	46,XY[93.3%]/46,XY,del(2)(p)[6.7%]
2	DS	3	46,XY,del(3)(p22p24)
3	Delayed milestones		46,XY/46,XY,del(3)(p)
4	MCA		46,XX,del(3)(q22q24)
5	BOH		46,XY[95.8%]/46,XY,del(3)(p14)[4.2%]
6	MR	4	46,XY[93.3%]/46,XY,del(4)(p13-15)[6.7%]
7	Reproductive failure		46,XY[96%]/46,XY,del(4)(q21)[4%]
8	Primary sterility		46,XY[93.3%]/46,XY,del(4)(q)[6.7%]
9	MCA	5	46,XX,del(5)(p)
10	Delayed milestones, marquis syndrome		46,XY[44%]/46,XY,del(5)(q32q34)[56%]
11	Delayed milestones, MR	6	46,XX[78.4%]/46,XX,del(6)(q22)[21.6%]
12	BOH	8	46,XX(13h+)[93.3%]/46,XX,del(8)(q21)[6.7%]
13	PA		46,XX[93.3%]/46,XX,del(8)(q24)[6.7%]
14	Primary infertility		46,XY/46,XY,del(8)(q)
15	DS	9	46,XX,del(9)(p21)
16	Delayed milestones, MCA		46,XY,del(9)(p21)
17	SA		46,XX,del(9)(q)
18	BOH		46,XY[92.9%]/46,XY,del(9)(p21)[7.1%]
19	SA		46,XX[93.7%]/46,XX,del(9)(q11)[6.3%]
20	BOH		46,XX[96%]/46,XX,del(9)(q12)[4%]
21	BOH		46,XY/46,XY,del(9)(q12)
22	MR	11	46,XX,del(11)(q23)
23	Delayed milestones		46,XY,del(11)(q23)
24	MR with MCA, Jacobsen syndrome		46,XY,del(11)(q23.1)
25	Delayed milestones	13	46,XY,del(13)(q)
26	?Prader-Willi Syndrome	15	46,XX,del(15)(q11-13)
27	Obesity		46,XY,del(15)(q)
28	Difficulty in breathing	16	46,XY,del(16)(q22)
29	MR with epilepsy, ?Miller Dieker syndrome	17	46,XY,del(17)(p13)
30	MR		46,XY,del(17)(q)
31	MR	18	46,XY,del(18)(p)
32	MR		46,XY,del(18)(p)
33	MR		46,XX,del(18)(q)
34	MR, growth retardation cataract		46,XY,del(18)(q21)
35	Delayed milestones		46,XX[63.2%]/46,del(18)(q21)[36.8%]
36	MCA	22	47,XY+del(22)(q12)
37	CHD, tetralogy of Fallot, dysmorphic features		46,XY,del(22)(q13)
38	POF	X	46,X,del(X)(p)
39	PA		46,X,del(X)(q13)
40	PA		46,X,del(X)(q21)
41	PA		46,X,del(X)(q21)
42	MR		46,X,del(X)(q25)
43	PA		46,X,del(X)(q25)
44	PA		46,X,del(X)(q)
45	SA		46,X,del(X)(q)
46	PA		45,X/46,X,del(X)(p)
47	PA		45,X/46,X,del(X)(q)
48	SA		45,X/46,X,del(X)(q24)
49	PA		45,X[88%]/46,X,del(X)(q24)[12%]
50	BOH		46,XX[77.8%]/46,X,del(X)(p22)[22.2%]
51	Primary sterility	Y	46,X,del(Y)(q)
52	Delayed milestones		46,X,del(Y)(q12)
53	DS		46,X,del(Y)(q12)
54	Sterility		45,X/46,X,del(Y)(q11)
55	BOH		46,XY/46,X,del(Y)(q)

MR- Mental Retardation, DS- Down Syndrome, MCA- Multiple Congenital Anomaly, BOH- Bad Obstetric History, PA- Primary Amenorrhea, SA- Secondary Amenorrhea, CHD- Congenital Heart Defect, POF- Primary Ovarian Failure

9q[4], 17p, 17q, 18p[2], 18q[3], Xp[3], Xq[10]; only in short arm 2p; and in long arm 6q, 8q[3], 11q[3], 13q, 15q[2], 16q, 22q[2], Yq[5]. The break points in the deletion seemed to be more frequent in the long arm of the chromosomes (40/55) (Tables 1, 2).

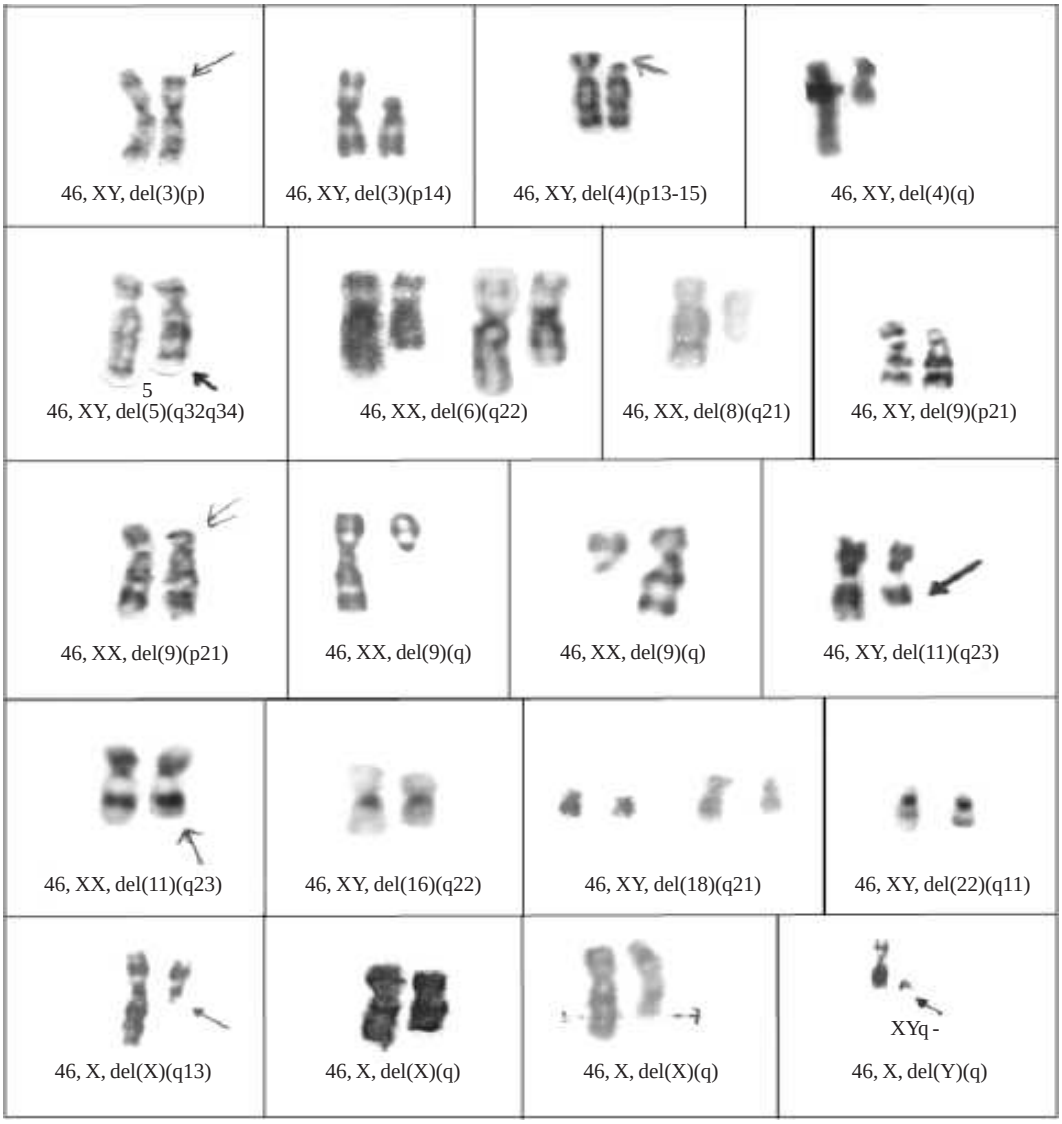

Fig. 1. Partial karyotypes of the deletions

The male to female sex ratio was 1.1:1 (29:26). Chromosomes with deletion seen in both sexes were 3,5,8,9,11,15,18; in male 2,4,13,16,17,22, Y and in female 6 and X. In male, the frequency of the chromosomes with deletion were Y (5), 9 (3) and 18 (3) and in female X (13) and 9 (4). Deletion in the autosomes was found in 24 male probands (24/29, 82.8%) and the remaining 5 had deletion in Y. In female, the autosomal (13/26, 50%) and the X chromosomal deletion (13/26, 50%) were of equal occurrence. Deletion in the long arm was seen in 19 males (19/29, 65.5%) and in 21 females (21/26, 80.8%). Deletion in the short arm of the chromosomes was preponderant in males (10/29, 34.5%) (Table 2).

In table 3 is shown the association of the deletion to the clinical conditions (mental retardation and or multiple congenital abnormalities, amenorrhea, bad obstetric history, difficulty in breathing, obesity, and the birth defects in obesity) and various systems of the body (respiratory, circulatory, skeletal, digestive, reproduc-

Table 2: Chromosomes and the arms involved in different groups

	Type of cell line	*Chromosomes involved*	*Chromosomal arms involved in the breakpoints*
General [55]	Total [55]	2, 3[4], 4[3], 5[2], 6, 8[3], 9[7], 11[3], 13, 15[2], 16, 17[2], 18[5], 22[2], X[13], Y[5].	2p, 3p[3], 3q, 4p, 4q[2], 5p, 5q, 6q, 8q[3], 9p[3], 9q[4], 11q[3], 13q, 15q[2], 16q, 17p, 17q, 18p[2], 18q[3], 22q[2], Xp[3], Xq[10], Yq[5].
	Single cell line [32]	3 [2], 5, 9 [3], 11 [3], 13, 15 [2], 16, 17 [2], 18 [4], 22 [2], X [8], Y [3].	3p, 3q, 5p, 9p [2], 9q, 11q [3], 13q, 15q [2], 16q, 17p, 17q, 18p [2], 18q [2], 22q [2], Xp, Xq [7], Yq [3].
	Mosaicism [23]	2, 3 [2], 4 [3], 5, 6, 8 [3], 9 [4], 18, X [5], Y [2].	2p, 3p [2], 4p, 4q [2], 5q, 6q, 8q[3], 9p, 9q[3], 18q, Xp [2], Xq [3] Yq [2].
Males [29]	Total [29]	2, 3 [3], 4 [3], 5, 8, 9 [3], 11 [2], 13, 15, 16, 17 [2], 18 [3], 22 [2], Y[5].	2p, 3p [3], 4p, 4q [2], 5q, 8q, 9p [2], 9q, 11q [2], 13q, 15q, 16q, 17p, 17q, 18p [2], 18q, 22q [2], Yq [5].
	Single cell line [17]	3, 9, 11 [2], 13, 15, 16, 17 [2], 18 [3], 22 [2], Y [3].	3p, 9p, 11q [2], 13q, 15q, 16q, 17p, 17q, 18p [2], 18q, 22q [2], Yq [3].
	Mosaicism [12]	2, 3 [2], 4 [3], 5, 8, 9 [2], Y [2].	2p, 3p [2], 4p, 4q [2], 5q, 8q, 9p, 9q, Yq [2].
Females [26]	Total [26]	3, 5, 6, 8 [2], 9 [4], 11, 15, 18 [2], X [13].	3q, 5p, 6q, 8q [2], 9p, 9q [3], 11q, 15q, 18q [2], Xp [3], Xq [10].
	Single cell line [15]	3, 5, 9 [2], 11, 15, 18, X [8].	3q, 5p, 9p, 9q, 11q, 15q, 18q, Xp, Xq [7].
	Mosaicism [11]	6, 8 [2], 9 [2], 18, X [5].	6q, 8q [2], 9q [2], 18q, Xp [2], Xq [3].

tive, central nervous system, endocrine). Deletions were associated to multiple congenital abnormality and or mental retardation in 26 (26/55, 47.8%) and in 23 cases the autosomes (23/26, 88.5%) were involved. Deletion was also associated to the referred couple with bad obstetric history (13) (3p, 4q[2], 8q, 9p, 9q, Yq[4] 8q, 9q, Xp] and amenorrhea (12) (8q, 9q[2], Xp[2], Xq[7]). Deletion was related to the abnormalities in the skeletal and reproductive systems in 15 cases respectively. Deletion in single cell line status was associated to the severity in the clinical conditions in 33 and to the system wise abnormality in 24.

It is the deletion in chromosome 11, which seemed to be involved to multiple congenital abnormality and or mental retardation (3) and to the abnormality in respiratory/ circulatory/ skeletal/ genital/ central nervous systems (6). X was associated to multiple congenital abnormality and or mental retardation (2) and to the defective functioning of the reproductive system (14) (Table 3).

The notable feature was the presence of the same breakpoints in 9 (9p21) and Y (Yq12), but with different manifestations. Deletion from 9p21 to pter manifested multiple congenital abnormality and or mental retardation in one of

Table 3: Deletion V/S Phenotype

Clinical conditions	*Chromosomal arms*	
	Male (n 29)	*Female (n 26)*
Mental retardation (MR)/Multiple congenital anomalies (MCA)	2p, 3p[2], 4p, 5q, 9p, 11q [2], 13q,17p, 17q, 18p[2], 18q, 22q, Yq	3q, 5p, 6q, 9p, 11q, 15q, 18q[2], Xq[2]
Amenorrhea	-	8q, 9q[2], Xp[2], Xq[7]
Bad obstetric history	3p, 4q[2], 8q, 9p, 9q, Yq[4]	8q, 9q, Xp
Others (difficulty in breathing, obesity)	15q, 16q, 22q	Xq
Systems	*Chromosomal arms Male (n 29)*	*Female (n 26)*
Respiratory system	5q, 11q, 16q, 18q	3q
Circulatory system	11q, 22q	-
Skeletal system	3p, 4p, 5q, 9p, 11q[2], 16q, 17p, 22q[2], Yq	3q, 6q, 15q, Xq
Gastrointestinal tract	5q	-
Genital system	4p, 11q, 16q, 22q, Yq[2]	8q, 9q[2], Xq[6]
Central nervous system	17p	11q
Endocrine system	-	18q
Incomplete data	(4)	(11)

the probands, but, in the other proband, the same segment expressed infertility. Proband with Yq12 to qter deletion manifested multiple congenital abnormalities and or mental retardation and another proband manifested infertility. (Table 3). Parental karyotyping was attempted only in 9 and the deletions in the chromosomes (4, 9, 11, 16, 18, Y) were found to be 'de novo'.

DISCUSSION

Deletions exist at two levels. A large chromosomal deletion can be visualized under the microscope such as the deletion in 4p to Wolf-Hirschorn syndrome and 5p to Cri-du-chat. Submicroscopic microdeletions also are identified with the help of high-resolution prometaphase and flurescent-in-situ- hybridization (FISH) studies, as in Prader- Willi and Angelman syndrome to 15q deletion. Microdeletions may involve only loss of a few genes at closely adjacent loci, resulting in 'contiguous gene syndrome (loci for X-linked disorder, retinitis pigmentosa and glycerol kinase deficiency very close to Duchenne- Muscular Dystrophy on Xp21). Recent studies on microarray comparative genomic hybridization (CGH) suggested that the submicroscopic chromosomal abnormality may be the cause in 10% of cases with ideopathic mental retardation. A number of malformations and syndromes, without any recognised cause, may be due to microdeletion or microduplication syndromes (Shapiro 1983; Reddy et al. 1984; Khalifa et al. 1993; Korenberg et al. 1994; Olson et al. 2004; FitzPatrick 2005).

In literature, it is opined, that almost the 23 chromosomes seemed to be involved in deletion. (de Grouchy and Turleau 1984; Jones 2006) In the present study, the chromosomes involved were 2, 3, 4, 5, 6, 8, 9, 11, 13, 15, 16, 17, 18, 22, X and Y. Deletion in the chromosomes 1, 7, 10, 12, 14 and 19 to 21 were not detected.

In literature, it is reported that deletion occurred both in the long and short arms for the chromosomes 1 to 12 and 16 to 20. On the other hand, for the chromosomes, 13, 14, 15, 21 and 22 deletion is observed only in their long arm; because, the short arms contain ribosomal RNA genes for the organization of nucleoli. In the case of X and Y, the tips of their short and long arms as pseudoautosomal regions are involved in recombination and exchange, during gametogenesis; hence the deletion is more frequent in their long arms rather than in the short arm. In the present study, the chromosomes involved in deletion with the breakpoints both in the short and long arm were 3p[3], 3q, 4p, 4q[2], 5p, 5q, 9p[3], 9q[4], 17p, 17q, 18p[2], 18q[3], Xp[3], Xq[10]; only in short arm 2p; and in long arm 6q, 8q[3], 11q[3], 13q, 15q[2], 16q, 22q[2], Yq[5].

The previous studies (Garcia-Minaur et al. 2005) have showed that the chromosomes with deletions associated to multiple congenital abnormality and or mental retardation are 3p, 3q, 4p, 4q, 5q, 6p, 9p, 9q, 11q, 17p, 17q, 18q, 22q. In the present study, the chromosomes found to be involved for the above mentioned conditions were 2p, 3p, 3q, 4p, 5q, 6q, 9p, 11q, 13q, 15q, 17p, 17q, 18p, 18q, 22q, Xq and Yq; 4q, 6p and 9q were not observed.

It is known, that deletions in X and Y may affect the normal reproductive function and stature (Gardner and Sutherland 1996). In the present study, X and Y chromosome showed the deletion in relation to the defective functioning of the reproductive system, such as bad obstetric history, amenorrhea and infertility. It is also known that X has influence on mental retardation and in the present study deletion in X was associated to mental retardation.

The notable feature was the presence of the same breakpoints in 9 (9p21) and Y (Yq12), but with different manifestations. Deletion from 9p21 to pter manifested multiple congenital abnormality and or mental retardation in one of the probands, but, in the other proband, the same segment expressed infertility. Proband with Yq12 to qter deletion manifested multiple congenital abnormalities and or mental retardation and another proband manifested infertility. The association could be co-incidental finding.

Deletions could occur de- novo or be inherited from the carrier parent as a result of malsegregation of the balanced translocation (de Grouchy and Turleau 1984; Gardner and Sutherland 1996; Jones 2006; Spinner et al. 2007). In the present study, in 9 cases, the deletion was found to be de-novo.

From literature, it is apparent, that for particular chromosomes and their break points, deletion whether macro or micro, is associated to the diagnosis of the syndromes (de Grouchy and Turleau 1984; Jones 2006), such as 4p in Wolf-Hirschorn syndrome; 8q24.11-q24.13 in Langer-Giedon Syndrome; 11q23 in Jacobsen

Syndrome; 15q11-13 in Prader-Willi and Angelman Syndromes; 17p13.3 Miller – Dieker Syndrome (M-DS); 18q- Syndrome and 22q11.21-q11.23 in DiGeorge/Shprintzen Velo-cardio-facial Syndrome. Even though, in the present study, for the above-mentioned specific chromosomes and the breakpoints, the deletions were seen; the assigned syndromes could not be confirmed, except for the Jacobson syndrome; which has been published (Reddy et al. 1984). Probands with Prader Willi and Miller Dieker syndromes had the phenotype, but the attempted, molecular cytogenetics could not confirm the deletion.

The findings from the present study either for the sex ratio or the phenotype could not be discussed further, since most of the reports in literature are as single case reports rather than a collective data profile. Moreover, it is also opined that in spite of the presence of the deletion, the effects on the phenotype may be non-significant (Mitelman 2005). For example, proband with 13q21 deletion in the present study showed mental retardation; but in literature it is stated that it may not lead to any effect.

Studies have shown that deletions may be associated to cancers. For example, monosomy 16q seemed to be involved in malignancies (Callen et al. 1993). In the present study, at the time of examination or follow up as part of genetic counseling, the probands have not shown any sign and symptoms towards any type of neoplasia.

The various hypotheses may be considered for the findings in the present study. The deleted segments from the determined chromosomes may have the direct and or indirect influence on the other active genes, spread in the 46 chromosomes (Shapiro 1983; Reddy et al. 1984; Khalifa et al. 1993; Korenberg et al. 1994; Olson et al. 2004; FitzPatrick 2005). Moreover, the parental origin also could not be attempted for all 55 cases, to give an idea about the parent of origin effect of the lost genes, in the deleted segments of the chromosomes.

The observed differences in the phenotype may be because of the ascertainment criteria, sample size, incomplete data, over lapping of the chromosomes involved, the single cell line and the mosaicism status, the preferential arms, the break points and the lost segments, the preponderance in the particular sex and the influence on the multisystem anomaly.

CONCLUSION

The present study has reported the data profile on the observed chromosomal deletions in the 55 individuals and its association to a range of clinical conditions and birth defects. Parents and the probands were counseled about the diagnosis, prognosis and management. The information conveyed were that due to the deletion, there is definitely the partial monosomy for the genes in the lost segments of the chromosomes and its influence on the various tissues and systems, in the body. The recurrence risk may be minimal and the prenatal diagnostic options for the subsequent pregnancy were also emphasized.

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