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Association of the Chromosomal Breakpoints in Reciprocal Translocation

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KEYWORDS Reciprocal Translocation. Chromosomes. Matrix of the Chromosomes. Breakpoints in the Arms. Sex of the Carrier.

ABSTRACT Reciprocal translocation involves break and exchange of the chromosomal segments between two non-homologous chromosomes. It is aimed to report the association between the breakpoints in the chromosomes and the clinical conditions and the sex of the carrier. The present study has analyzed the data from 42 carriers and there were 17 male and 25 female carriers. For the total sample, it was observed that 25 were in bad obstetric history; 25 chromosomes belonged to C group; chromosome 1 was involved 6 times with 2,3,9,14,15; the formation of the translocation between the long arms (q;q) was in 21 and the breakpoints in the long arm were 59. Bad obstetric history was associated to C group chromosomes in 15 and the long arm combinations were seen in 12 and the breakpoints in it were 29. In the female, 15 with bad obstetric history were carriers; C group was seen in 18 and in 11 it showed the association to bad obstetric history; the long arm combination was noted in 13 and in 8 it was in bad obstetric history; breakpoints in the long arm were 37 and 22 times it was in bad obstetric history and the translocation between 15q and 22q were associated to bad obstetric history. In the present study, the chromosomes and its arms and breakpoints and the clinical conditions were associated to female and bad obstetric history.

INTRODUCTION

Reciprocal translocation (rcpt) is defined as the structural rearrangement of the chromosomes with break and exchange between two chromosomes resulting in two new derivative chromosomes. The reported incidence of rcpt in the general population is around one in 500. Rcpt is one of the examples for the balanced structural chromosomal rearrangements; hence, the individuals with rcpt known as the carriers usually have 46 chromosomes and normal phenotype until and unless the break has damaged any functional gene. The association of the rcpt to the clinical conditions is reported (Gardner and Sutherland 1996; Tilak 2010). The carriers may manifest clinical conditions such as bad obstetric history (BOH), fertility failure (FF), amenorrhea (Ame), hypogonadism (HG), mental retardation (MR) and multiple congenital anomalies (MCA). The point to be noted is the existence of the risk to the carries to get offsprings with unbalanced chromosomal rearrangements and severely affected phenotype (Turnpenny and Ellard 2012).

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Objectives of the Study

From the available cytogenetically confirmed cases with rcpt, the aims and objectives of the study are to report the association between the chromosomes and the clinical conditions and the sex of the carrier. The step wise analysis includes: i) the observed rcpts ii) chromosomes involved in rcpt as per their grouping of A to G iii) the matrix of the chromosomes in rcpt iv) the formation of the rcpt between the long and or the short arms of the chromosomes v) the distribution of the breakpoints in relation to the arms and regions of the chromosomes.

MATERIAL AND METHODS

At Division of Human Genetics, St John's Medical College, Bangalore, from 1976 to 2007, in 42 individuals the breakpoints in rcpt could be pinpointed and reconfirmed. There were 17 male and 25 female carriers and their age ranged from newborn to 41 years.

RESULTS

It is observed from Table 1 that rcpt was observed in 25 cases with BOH (59.5%). Among

the 25 female carriers (59.5%) rcpt was associated in 15 to BOH. In 7 cases, the parental origin of the rcpt was determined and in 6 it was found to be maternal; out of which 4 were in female carriers with BOH.

Table 1: List of the rcpts (n42)

BOH-Male- rcpt (n10)	*BOH- Female- rcpt (n15)*
46,XY,t(1;14)(p36;q31)	46,XXt(1;15)(p35;q24) mat;pat
46,XY,t(2;4)(q13;q35)	46,XX,t(2;11)(q24;q13)
46,XY,t(2;13)(q32;q26)	46,XX.t(3;5)(p24;p15)
46,XY,t(3;11)(p21;q25)	46,XX,t(4;12)(q31;q24)mat
46,XY,t(4;21)(q34;q22)	46,XX,t(5;13)(p11;q33)
46,XY,t(5;6)(p15;p11)	46,XX,t(6;8)(q23;q24)
46,XY,t(7;13)(q31;q32)	46,XX,t(7;11)(q11;p15)mat
46,XY,t(8;14)(p23;q32)l	46,XX,t(7;18)(q34;p23)
46,XY,t(13;17)(q33;p11)mat	46,XX,t(10;14)(q11;p11)
46,XY,t(19;20)(p13;p11)	46,XX,t(11;16)(p11;q23)mat
	46,XX,t(15;20)(q13;q12)
	46,XX,t(15;22)(q22;q13)
	46,XX,t(15;22)(q22;q13)
	46,XX,t(20;22)(q11;q13)
	46,XX,t(X;12)(q23;q24)
FF- Male- rcpt (n2)	*FF- Female- rcpt (n1)*
46,XY,t(1;7)(q25;q11) mat	46,XX,t(X;22)(q22;p11)
46,XY,t(Y;Y)(q11;p11)	
HG- Male-rcpt (n3)	*Ame- Female- rcpt (n3)*
46,XY,t(3;12)(q11;p11)	46,XX,t(1;9)(q32;p24)
46,XY,t(8;11)(q11;q24)	46,XX,t(9;14)(q22;q32)
46,XY,t(10;11)(p24;p15)	46,XX,t(X;14)(q27;q24)
MR/ MCA- rcpt (n2)	*MR/ MCA- Female- rcpt (n6)*
46,XY,t(3;7)(q26;q36)	46,XX,t(1;2)(q32;q11)
46,XY,t(7;13)(q22;q22)	46,XX,t(1;3)(q42;p13)
	46,XX,t(2;9)(q32;q32)
	46,XX,t(2;18)(q21;p11)
	46,XX,t(15;17)(q26;q22)
	46,XX,t(15;18)(q24,p12)

In BOH, the chromosomes involved in rcpt that were common to both sex were 1 to 8,11,13,14, 20; chromosomes seen only in male 17,19,21 and in female 10,12,15,16,18,22,X. In BOH, chromosome 9 was not observed in rcpt status in both the sex and Y in male. In HG chromosome 11 was observed 2 times in male. In Ame, chromosomes 9 and 14 were observed 2 times in female. In MR/MCA chromosome 3 was seen in rcpt in both the sex; only in male 7,13 and in female 1,2,9,15,17,18.

Table 2 shows that 84 chromosomes were involved in the 42 rcpt. Chromosomes assigned to group C were found in 25 (29.7%) and A group in 17 (20.2%) instances. Grouping as per the clinical conditions showed C group in BOH in 15 (17.8%) and A group in MR/MCA in 7 (8.3%). Female carriers were found to have C group chromosomes in 18 (21.4%) and male in B group in 8 (9.5%). The association of the grouping to the clinical condition and the sex of the carrier revealed in female C group and BOH in 11 (13%) and in male in BOH and in HG in 5 (6%) each respectively.

Table 3 shows that chromosome 1 was involved 6 times in rcpt matrix and was associated to BOH,FF, Ame, MR/MCA. rcpt matrix only in BOH for the female carriers were between 4;12,5;13,6;8, 11;16,20;22 and for the male carriers 4;21,5;6,13;17,19;20. The association of the clinical condition and the sex of the carrier showed chromosome 15 in 4 female carriers with BOH. In both sex, rcpt starting with chromosomes 12,16 to 18, 21,22 were not observed; in female it was 8 and in the male it was 6,9,11,15,20,X.

Table 4 shows the formation of the 42 rcpt, the recombination between the short arms (p;p)

Table 2: rcpt: Chromosomal grouping of A to G; Clinical conditions and male and female carriers

Clinical conditions	*Sex*	*A*	*B*	*C*	*D*	*E*	*F*	*G*	*Total*
BOH	Female	03	03	11	06	02	02	03	30
-	Male	04	03	04	05	01	02	01	20
FF	Female	-	-	01	-	-	-	01	02
-	Male	01	-	01	-	-	-	02	04
HG	Male	01	05	-	-	-	-	-	06
Ame	Female	01	-	05	-	-	-	-	06
MR/ MCA	Female	06	-	01	02	03	-	-	12
-	Male	01	-	02	01	-	-	-	04
Total	Female	10	03	18	08	05	02	04	50
-	Male	07	08	07	06	01	02	03	34
Grand total	-	17	11	25	14	06	04	07	84
BOH	-	07	06	15	11	03	04	04	50
FF	-	01	-	02	-	-	-	03	06
HG	-	01	05	-	-	-	-	-	06
Ame	-	01	-	05	-	-	-	-	06
MR/MCA	-	07	-	03	03	03	-	-	16

Table 3: rcpt: Matrix of the chromosomes; Clinical conditions and male and female carriers

Chromosomes x Male/ Female; Male+ Female=Total; Clinical conditions=Male// Female

1 x 7,14/ 2,3,9,15; 2+4=6; FF,BOH// MR/MCA,MR/MCA,Ame,BOH
2 x 4,13/ 9,11,18; 2+3=5; BOH,BOH// MR/MCA,BOH,MR/MCA
3 x 7,11,12/ 3; 3+1=4; MR/ MCA,BOH,HG// BOH
4 x 21/ 12; 1+1=2; BOH// BOH
5 x 6/ 13; 1+1=2; BOH// BOH
6 x -/ 8; -+1=1; -// BOH
7 x 13,13/ 11,18; 2+2=4; BOH,MR/MCA// BOH,BOH
8 x 11,1 4/ - ; 2+-=2; HG,BOH// -
9 x -/ 14; -+1=1; -// Ame
10 x 11/ 14; 1+1=2; HG// BOH
11 x -/ 16; -+1=1; -// BOH
12 -
13 x 17/ -; 1+- =1; BOH// -
14 -
15 x -/ 17,18,20,22,22; -+5=5; -// MR/MCA,MR/MCA,BOH,BOH,BOH
16 -
17 -
18 -
19 x 20/ -; 1+- =1; BOH// -
20 x -/ 22; -+1=1 ; -// BOH
21 -
22 -
X x -/ 12,14,22; -+3 =3 ; -// FF,Ame,BOH
Y x Y/ -; 1+- =1 ; FF// -

was in 5 (12%); long arms (q;q) in 21 (50%) and short and long arms (p;q) in 16 (38%). The breakdown for the rcpt recombination for both the male (p;p 3, q;q 8, p;q 6) and female carriers (p;p 2, q;q 13, p;q 10) showed the preference between the long arms. The recombination between the long arms of the chromosomes was detected in BOH for 12 times. The association between the combination of the arms to the clinical conditions and the sex of the carrier showed in BOH for the female 8 times the long arm combinations.

Among the observed 50 breakpoints in BOH, in the short arm it was 16 and long arm 34. In chromosomes 11 (3 female,1 male), 13 (3male,1 female), 15 (4 female) the breakpoints were seen 4 times. Chromosomes 1,3,5, 17,18,19 showed breakpoints in the short arm; 2,4,7,10,1,13,15, 16,22,X in the long arm and 6,8,11, 14,20 short and long arm. Chromosomes 9 and Y were not involved in rcpt in BOH. The break in the short arm has occurred one time for the chromosomes involved in rcpt in male; whereas for female for 5 and 11, it was 2 times. In the male, the breakpoints in the long arm were either one or two times, except for 13 where it has occurred 3 times at q26,32,33 and in the female only in 15 it has occurred 4 times. The same breakpoints were seen at 5p11 and 13q33 for 2 male and 2 female carriers; at 12q24 and 15q22 each in 2 female and at 22q13 in 3 female. 6 breakpoints in FF were seen in 3 male and 3 female and 2 were in the short arms of 22(p11) and Y (p11)and 4 in the long arms of 1(25),7(11), X(22),Y (q11). In HG, in the 6 male for the 6 breakpoints, 3 were in the short (10p24, 11p15,12p11) and long arms (3q11,8q11, 11q24) respectively. Chromosome 11 was seen 2 times. Ame in 3 female showed breakpoints in one short arm (9p24) and in 5 (1q32,9q22, 14q24,q32,Xq27) long arms. Chromosomes 9 and 14 were seen 2 times. In MR/MCA the

Table 4: rcpt: Formation between the long and or short arms; Clinical conditions and male and female carriers

Arms	*BOH*	-	*FF*	-	*HG*	*Ame*	*MR/MCA*	-	*Total*
	Male	*Female*	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*	-
p;p	02	02	-	-	01	-	-	-	05
q;q	04	08	01	-	01	02	02	03	21
p;q	04	05	01	01	01	01	-	03	16
Total	10	15	02	01	03	03	02	06	42

breakpoints were 16 for the 2 male and 6 female carriers; out of which in the short arm it was 3 in female (3p13, 8p11,p12) and in the long arm it was 4 (3q26,7q22,q36,13q22) in the male and 9 (1q32,42,2q11,q21,q32,9q32, 15q24,q26,17q22)in the female. The breakpoints in the short or in the long arms were detected at region 11 in 19 instances: 10 in BOH, 4 in FF, 3 in HG and 2 in MR/MCA. It was associated to short arm 11 times and long arm 8 times and to 9 male and 9 female carriers. In BOH in 4 male and 3 female at p11 and in 3 female at q11; in FF at p11 in a male and female and at q11 in 2 male; in HG at p11 in a male and at q11 in 2 male; in MR/MCA at p11 and q11 in 2 female. (BOH: p11: 4 male: chromosomes 5,6,17,20 and 3 female: 5,11,14; q11: 3 female: 7,10,20. FF: male: Yp11,q11; 2 female: 22p11, 7q11. HG: 3 male: 3q11,8q11, 12p11. MR/MCA: male: 2q11; female: 8p11) It is noted that the same breakpoints in the same chromosomes such as 5p15 and 13q33 were seen in a male and female; 12q24 in 2 female; 15q22 in 2 female and 22q13 in 3 female in BOH. On the other hand, same breakpoints but 2 different conditions were observed; such as 1q32 in 2 female for Ame and MR/MCA; 2q32 to BOH in a male and to MR/MCA in a female; 11p15 in a male in HG and in a female in BOH; 14q32 and 15q24 in 2 female each to BOH and MR/MCA. The association of the chromosomes to the clinical condition and the sex of the carrier showed female carriers to BOH for 15 and 22; especially at 15q22 and 22q13; FF to Yp, Yq in male and to Xq in female; HG in male to 11p,11q; Ame in female to 9p,9q,14q and MR/MCA to 7q in male and to 2q in female.

The observed total number of breakpoints for the formation of the 42 rcpt were 84; 59 (70%) were noted in the 'q' arm and 25 in the 'p' arm (Table 5). The 'q' arm was seen in BOH 34 times (40%). In female, the 'q' arm was found to be 37 times (44%) and was associated to 22 female carriers with BOH (26%). Chromosomes 2,7 and 15 have shown 6 times each the breakpoints in the 'q' arm. The long arms of the chromosomes not involved in rcpt, in both the sex were 5,18,19; in male 6,9,10,12, 15,16,17,20,22,X and in female only 3. The breakpoints in 'p' arm were seen 11 times in male and 14 times in female. The short arms of 2,4,7,13,15,16,21,X were not involved in rcpt in both the sex; 9,14,18,22 in male and 6,8,10,12,17,19,20 in female.

Table 5: rcpt: Breakpoints in the long and short arms; Clinical conditions and male and female carriers

BOH	*Male*		*Female*		-
-	*p*	*q*	*P*	*q*	*Total*
1p35,p36	36	-	35	-	2
2q13,q24,q32	-	13,32	-	24	3
3p21,p24	21	-	24	-	2
4q31,q34,q35	-	34,35	-	31	3
5p11,p11,p15	11	-	11,15	-	3
6p11,6q23	11	-	-	23	2
7q11,q31,q34	-	31	-	11,34	3
8p23,8q24	23	-	-	24	2
9	-	-	-	-	-
10q11	-	-	-	11	1
11p11,p15,11q13,q25	-	25	11,15	13	4
12q24,q24	-	-	-	24,24	2
13q26,q32,q33,q33	-	26,32,33	-	33	4
14p11,14q31,q32	-	31,32	11	-	3
15q13,q22,q22,q24	-	-	-	13,22,22,24	5
16q23	-	-	-	23	1
17p11	11	-	-	-	1
18p23	-	-	23	-	1
19p13	13	-	-	-	1
20p11,20q11,q12	11	-	-	11,12	3
21q22	-	22	-	-	1
22q13,q13,q13	-	-	-	13,13,13	3
Xq23	-	-	-	23	1
Y	-	-	-	-	-
Total	8	12	8	22	50

It is seen from Table 6, that breakpoints were not observed in male for any of the clinical conditions for chromosomes 9,15,16,18,22,X and in female for 21. It is seen, that same breakpoints were observed at 5p15 and 13q33 in a male and female and 12q24 in two female in BOH. Same breakpoints in the same chromosomes but with different clinical conditions were observed at 1q32 to Ame and MR/MCA in 2 female; 2q32 to BOH in male and to MR/MCA in female; 11p15 to HG in a male and BOH in a female; 14q32 to BOH in a female and to Ame in another female; 15q24 to BOH and MR/MCA in 2 female and Xq22 to BOH and FF in 2 female.

The distribution of the 6 times breakpoints in chromosomes 1,2,7,11,15 were:

1: BOH:p35 female/p36 male; FF:q25 male; Ame:q26 female; MR/MCA:q32,q42 female, 2: BOH:q13,q32 male/q24 female; MR/MCA:q11,q21,q32 female, 7: BOH:q31 male/q11,q31 female; FF:q11 male; MR/MCA: q22,q36 male

11: BOH:q25 male/p11,p13,q13 female; HG:p15,q24 male

15: BOH:q13,q22,q22,q24 female; MR/MCA:q24,q26 female. In 3 female, association was found at 22q13 to BOH. X chromosome also showed in female adjacent breakpoints at q22 to FF, q23 to BOH and q27 to Ame. Moreover, the autosomes that were observed 2 times in HG in male was 11 and in Ame in female were 9 and14.

DISCUSSION

The literature survey for rcpt is quite vast; the published articles are either as case reports and or reviews and have reported the association of rcpt in pregnancy loss, infertility, hypogonadism, Mendelian conditions, cancer and in parents who have had offsprings with unbalanced chromosomal abnormality in the karyotype and severity in the phenotype. The findings of the present study are discussed with the relevant publications in literature. The reported incidence of chromosomal abnormality in literature is 90/ 1000 newborns; out of which the balanced structural rearrangements constitute 40 and that of rcpt is 1 in 500 individuals (Turnpenny and Ellard 2012). In 1978, the reported occurrence of 95 cases of rcpt involving the autosomes among the 10,000 patients is 0.95% (Aurias et al. 1978). At DHG, from 1976,

Table 6: rcpt: Chromosomes, arms, breakpoints, clinical conditions and male and female carriers

Chromosomes	*Breakpoints and clinical conditions*		*Total*	*Chromosomes*	*Breakpoints and clinical conditions*		*Total*
	Male	*Female*			*Male*	*Female*	
1	BOH:p36FF:q25	BOH:p35Ame:q32MR/MCA:q32,q42	6	13	MR/MCA:q22BOH:q26,q32,q33	BOH:q33	5
2	BOH:q13,q32	MR/MCA:q11,q21,q32BOH:q24	6	14	BOH:q31,q32	BOH:p11Ame:q24,q32	5
3	BOH:p21HG:q11MR/MCA:q26	BOH:p24MR/MCA:p13	5	15	-	BOH:q13,q22,q22,q24MR/MCA:q24,q26	6
4	BOH:q34,q35	BOH:q31	3	16	-	BOH:q23	1
5	BOH:p15	BOH:p11,p15	3	17	BOH:p11	MR/MCA:q22	2
6	BOH:p11	BOH:q23	2	18	-	MR/MCA:p11,p12BOH:p23	3
7	FF:q11BOH:q31MR/MCA:q22,q36	BOH:q11,q34	6	19	BOH:p13	-	1
8	BOH:p23HG:q11	BOH:q24	2	20	BOH:p11	BOH:q11,q12	3
9	-	Ame:p24,q22MR/MCA:q32	3	21	BOH:q22	-	1
10	HG:p24	BOH:q11	2	22	-	FF:p12BOH:q13,q13,q13	4
11	HG:p15,q24BOH:q25	BOH:p11,p15,q13	6	X	-	FF:q22BOH:q23Ame:q27	3
12	HG:p11	BOH:q24,q24	4	Y	FF:p11,q11	-	2
Total	-	-	48	-	-	-	36

on an average with the referral of 400 to 500 cases per year, it becomes 12,000 to 15,000 for the duration of the 30 years. Among them, the detected chromosomal abnormality of 1350 cases becomes 9 to 11.25%. Hence, the occurrence of 42 rcpt cases out of the total referral is 0.28% to 0.35% or 3% among the chromosomal abnormality. It is opined that the carriers with rcpt seemed to have a high probability in the formation of the chromosomally unbalanced gametes depending on the disjunction and segregation mechanisms during meiosis, hence, the expected and the observed effects may be the sterility, recurrent spontaneous abortions and birth of malformed children with unbalanced karyotype (Diedrich et al. 1983; Neri et al. 1983).

In male, the effect of the rcpt seen in infertility is because of the 'consequence of failure of pairing of homologous elements in the translocation chromosomes during meiosis, which promotes association of the quadrivalent with the sex chromosome vesicle leading to complete spermatogenic arrest' (Bourrouillou et al. 1985). The effect of rcpt in HG, may be because of the disturbances in the expression of the genes that may be involved in the cascade of events leading to the normal processes of sex differentiation, in male. In amenorrhea, whether primary or secondary, balanced rcpt has been reported (Tupler et al. 1994). In view of the frequency of the rcpt in population, the link between amenorrhea and rcpt is considered to be coincidental rather than causal (Gardner and Sutherland 1996).

In MR/MCA, there exists the likelihood, that the break and reunion in rcpt may have disrupted any functional gene (Brueton and Winter 1993) or shown the position effect (gene when put into a new environment may not permit the normal expression (Fantes et al. 1995). In the present study, (Table 1) among the total of 42 rcpts, 25 were associated to BOH and to 25 female carriers (59.5%). BOH includes couples who have had more than 2 recurrent abortions and or stillborn, neonatal deaths and normal live births. The referrals for BOH may be due to more number of referrals in the couples at the reproductive age with BOH for the detection of any genetic (chromosomal) abnormality, after the exclusion of other etiology such as anatomical, hormonal and environmental causes. The increase in the number of the female carriers is the reflection on the number of referrals with BOH. In the present study, the observed high percentage of the maternal origin of the rcpt (6/7, 85.7%) is in accordance with the reported observations in literature (Aurias et al. 1978). Even though, in literature, specifically, the association of rcpt as per the grouping of the chromosomes is not reported, the findings have indicated the frequent involvement of the C group chromosomes (Aurias et al. 1978; Neri et al. 1983). In the present study, (Table 2) C group chromosomes 6 to 12 and X were found to be frequent (n25,29,7%) for the total sample and in BOH (n15,17.8%) and female carrier (n18,21.4%) and the association was with female carriers with BOH (n11,13%).

From literature, it was noted, that rcpt X;14 and Y;Y were reported as case reports; but, the rcpt matrix between the autosomes of the chromosomes were different and were reported for recurrent abortions, hypogonadism, malformed children and infertility (Neri et al. 1983). In the present study, (Table 3) the rcpt matrix has shown the chromosomes involved exclusively for BOH, Ame, FF or a combination of the clinical conditions. It could be said that whether BOH or FF or HG or Ame, the chromosomes involved have affected the normal reproductive function in the carriers with rcpt. The rcpt matrix for chromosome 1 with 14 and 15 has shown its association to BOH, with 7 to FF, with 9 to Ame and with 2 and 3 to MR/MCA. The matrix of the rcpt in the X chromosome with the autosomes 12,14,22 were associated to BOH, Ame, FF in 3 female. In the male with FF, the rcpt matrix was between the homologous Y chromosomes. It is opined, that in X;autosome rcpt, the normal X is usually inactivated, so that the genes expressed from the autosomes are transcribed without much effect on the somatic systems in the carrier. The reported critical regions in X are the Xq13-q22 and Xq22-q27 for the normal gonadal function (Therman et al. 1990). The breakpoints within the region are associated to increased risk for the primary or secondary ovarian failure. The premature ovarian failure, defined as the secondary amenorrhea before the age of 40 is known to be associated with breaks in Xq26.1-q27 and Xq13.3-q21.1 regions and the gene clusters in these regions may be determining the ovarian activity (Powell et al. 1994). Pregnancy achieved with the help of oestrogen-progestin replacement therapy in

a female with premature ovarian failure and rcpt X;14(q21.2;q32.3) was reported and the breakpoint was at Xq21 (Katayama et al. 1991). Y;Y rcpt was reported in a male with small stature, skeletal deformity and neurological defects. The explanations for the formation of Y;Y translocation may be by centric fusion between two Ys in the male conceptus with 47,XYY status or isochromosome of Y. The genes in Yp are stated to have the effect on testis determination and Yq for azoospermia and the normal process of the spermatogenesis (Wahlstrom et al. 1976). In the present study, (Tables 5 and 6) in the 3 females with X;autosome rcpt, the breakpoints in X were within the reported critical region; hence, the carriers have manifested BOH with X;12 (q22;q13); FF with X;22 (Xq22;p11) and Ame with X;14(q27;q24) rcpts. The breakpoint in the long arm of Y may have disrupted the genes located in Yq for the normal process of spermatogenesis resulting in FF (Table 5). In the present study, (Table 4) the rcpt has occurred between the long arms in 21 cases (50%). Similar to the particular aspect, reports were not available in literature; but, the combination between the long arms in the formation of rcpt could be observed.

In the present study (Table 5), the predominance was seen for the long arm involvement in rcpt (n59,70%); in BOH (n34,40%); in female carriers (n37,44%) and the association was found for the female carriers with BOH (n22,26.2%). An excess of breakpoints was seen for the long arms of the chromosomes 2q,7q,15q (6 times each) and short arms of the chromosomes 3p,5p,6p,18p (3 times each). The observed deficiency of the breakpoints were for the short arms of 8 chromosomes (2,4,7, 13,15,16,21,X) and for the long arms of 3 chromosomes (5,18,19) for both the sex. The absence of the breakpoints in the short arms was seen in male for 4 chromosomes (9,14,18,22) and in female for 7 (6,8,10,12,17,19,20); likewise for the long arm in male for 10 (6,9,10,12, 15,16,17,20,22,X) and in female for only one chromosome (3) These findings differed from the studies on the systematic analysis of 95 rcpt involving autosomes (Aurias et al. 1978). The authors reported an excess of break points for the chromosome arms 4p,9p,10q, 21q,22q and deficiency for 1p,2p. The break-points were based on R banding and also mostly on their location to the terminal segments of the chromosomes. The criteria of ascertainment of the sample included the rcpts between the autosomes in parents who have had children with unbalanced chromosomal abnormality and in couples with spontaneous abortions, children with malformation/mental retardation, parents with trisomy 21 children, sterility and miscellaneous.

In Tables 7 and 8 are given as examples the review on the observed chromosomes involved in the rcpt matrix and the breakpoints in the short and long arms of the chromosomes in rcpt.

The chromosomes involved either for recurrent or spontaneous abortions or BOH were different. Deficiency was noted for the breakpoints in the chromosomes 2p,15p,17q,20p,21p, 22p,Xp, Yp,Yq. On the other hand some of the breakpoints were at the same location: in the present study, in BOH in a female and male at the breakpoints seen at 4q31 and 4q35 were also observed in recurrent abortion at 4q31 in a female (Diedrich et al. 1983) and in spontaneous abortions at 4q35 in a male (Neri et al. 1983).

Neri et al. (1983), stated that the total number of rcpt in their study and in literature series was 46, of which 33 ascertained through a malformed child, 11 for recurrent abortion and 2 for hypogonadism. The authors studied the number of times in which each chromosome was involved in translocation and the distribution of the breakpoints either in the short or long arms. The authors opined that in their material, no clear difference could be shown between the 3 groups of the ascertainment with respect to the regional position of the breakpoints, hence, the data were combined. The observed total number of breakpoints was 93, because of a double break in one chromosome in a case with rcpt (9;17), of which breakpoints in the short arm were 40 and long arm 53. It was concluded, that the distribution of the breakpoints appeared to be nonrandom both with respect to the individual chromosomes and to their arms. The breakpoints seemed to be in excess on chromosomes 5,9,13 and 15 and they have occurred in R-positive bands (68.8%) than in G bands (22.8%). Each chromosome arm were subdivided into 3 portions as terminal, centromeric and median; accordingly the breakpoints were classified and more than half of the translocations were of the Terminal/Median type (56.5%).

In the present study**,** the sample consisted of 25 with BOH, 3 with FF, HG and Ame respectively and 8 with MR/MCA. From the combined

Table 7: Review: Breakpoints in rcpt

Aurias et al. 1978 (n12) Spontaneous abortions		*Neri et al. 1983 (n11) Recurrent abortions*	
Male (n5)	*Female (n7)*	*Male (n3)*	*Female (n8)*
1;10(p32;) 2;5(q33;) 3;7(p25;q31) 7;11(p15;p15) 10;18(q26;q21)	1;4(p22;p14) 3;14(q21;) 4;15(q26;q23) 5;15(q35;) 6;7(q11;p22) 9;12(q22;q24) 9;17(q34;p11)	1;6(q32;q26) 2;8(q37;q22) 9;13(p22 or 23; q14 or 21)	3;8(p14;q24) 3;21(p22;qter) 4;9(q35;q12) 4;14(q32;qter) 5;15(p13;qter) 7;13(p15;qter) 9;17 10;15(q26;q21)

Diedrich et al. 1983 (n9) Spontaneous abortions		*Present study 2012 (n25) BOH*	
Male (n2)	*Female (n7)*	*Male (n10)*	*Female (n15)*
2;3(q1;p2) 10;18(q11;q11)	1;8(p22;q22) 1;16(p3;p1) 4q;15q 4;10(q31;q22) 4;X(p16;q13) 7;22(q11;q13) 11;22(q23;q11)	46,XY,t(1;14)(p36;q31) 46,XY,t(2;4)(q13;q35) 46,XY,t(2;13)(q32;q26) 46,XY,t(3;11)(p21;q25) 46,XY,t(4;21)(q34;q22) 46,XY,t(5;6)(p15;p11) 46,XY,t(7;13)(q31;q32) 46,XY,t(8;14)(p23;q32)l 46,XY,t(13;17)(q33;p11) 46,XY,t(19;20)(p13;p11)	46,XXt(1;15)(p35;q24) 46,XX,t(2;11)(q24;q13) 46,XX.t(3;5)(p24;p15) 46,XX,t(4;12)(q31;q24) 46,XX,t(5;13)(p11;q33) 46,XX,t(6;8)(q23;q24) 46,XX,t(7;11)(q11;p15) 46,XX,t(7;18)(q34;p23) 46,XX,t(10;14)(q11;p11) 46,XX,t(11;16)(p11;q23) 46,XX,t(15;20)(q13;q12) 46,XX,t(15;22)(q22;q13) 46,XX,t(15;22)(q22;q13) 46,XX,t(20;22)(q11;q13) 46,XX,t(X;12)(q23;q24)

Aurias et al. 1978 (n3) Ambiguous genitalia, hypospadias, clitoris enlarged		*Neri et al. 1983 (n2) Hypogonadism*	
Male (n2)	*Female*	*Male (n1)*	*Female (n1)*
2;6(q14;p12) 4;8(p16;q22)	11;17(q14,p13)	3;15(q24;q26)	3;12(q12;p13)

Present study 2012 (n3) Hypogonadism
Male (n3)
3;12(q11;q24) 8;11(q11;q24) 10;11(p24;p15)

-

Aurias et al. 1978 (n7) Affected spermatogenesis and sterility		*Present study 2012 (n3) FF*	
Male (n6)	*Female (n1)*	*Male (n2)*	*Female (n1)*
5;8(p14;q11) 6;13(q15;q13) 8;9(q23;pter) 10;13(q26;q11) 11;22(q23;q11) 11;22(q23;q11)	6;14(p12;q12)	46,XY,t(1;7)(q25;q11) 46,XY,t(Y;Y)(q11;p11)	46,XX,t(X;22)(q22;p11)

Aurias et al. 1978 (n14) Malformations and or mental retardation		*Neri et al. 1983 (n6) Malformed child*	
Male (n8)	*Female (n6)*	*Male (n2)*	*Female (n4)*
1;13(q21;q31) 1;16(q12;q12) 2;5(q35;q23) 3;15(q29;q11)	2;3(p12;p26) 2;6(p13;p25) 3;15(p25;q22) 5;7(p15;p11)	4;12(p15;p13) 5;21 (p14;qter)	2;13(q37;q14 or 21); 4;20(p16;q13) 5;10(p14;pter) 5;18 (p15;q21)

Table 7: Contd.....

Male (n8)	*Female (n6)*	*Male (n2)*	*Female (n4)*
4;10(p15;q11) 4;14(p15;q11) 5;15(q14;qter) 7;10(q35;q22)	10;12(q24;q13) 14;17(q32;q11)		
Present study 2012 (n8) MR/MCA			
Male (n2)		*Female (n6)*	
3;7(q26;q36) 7;13(q22;q22)		1;2(q32;q11) 1;3(q42;p13) 2;9(q32;q32) 2;18(q21;p11) 15;17(q26;q22) 15;18(q24;p12)	

Table 8: Review: Breakpoints: Abortions and BOH

-	*Spontaneous abortions*		*Recurrent abortions*		*Spontaneous abortions*		*BOH*	
Chromo-somes	*Aurias et al. 1978*		*Diedrich et al. 1983*		*Neri et al. 1983*		*Present study 2012*	
-	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*
1p	-	22	-	3,22	32	-	36	35
1q	32	-	-	-	-	-	-	-
2p	-	-	-	-	-	-	-	-
2q	33	-	1	-	37	-	13,32	24
3p	25	-	2	-	-	14,33	21	24
3q	-	21	-	-	-	-	-	-
4p	-	14	-	16	-	-	-	-
4q	-	26	-	q, **31**	-	32,**35**	34,**35**	**31**
5p	?	-	-	-	-	13	15	11,15
5q	-	35	-	-	-	-	-	-
6p	-	-	-	-	-	-	11	-
6q	-	11	-	-	36	-	-	23
7p	15	22	-	-	-	15	-	-
7q	31	-	-	**11**	-	-	31	**11,**34
8p	-	-	-	-	-	-	23	-
8q	-	-	-	22	22	**24**	-	**24**
9p	-	-	-	-	-	22 or 23	-	-
9q	-	22,34	-	-	-	12	-	-
10p	?	-	-	-	-	-	-	-
10q	-	26	**11**	22	-	-	-	**11**
11p	**15**	-	-	-	-	-	-	11,**15**
11q	-	-	23	-	-	-	25	13
12p	-	-	-	-	-	-	-	-
12q	-	**24**	-	-	-	-	-	**24,24**
13p	-	-	-	-	-	-	-	-
13q	-	-	-	-	-	ter, 14 or 21	26,32,33	33
14p	-	?	-	-	-	-	-	11
14q	-	-	-	-	-	ter	31,32	-
15p	-	?	-	-	-	-	-	-
15q	-	23	-	Q	-	ter	-	13,22, 22,24
16p	-	-	-	1	-	-	-	-
16q	-	-	-	-	-	-	-	23
17p	-	**11**	-	-	-	-	**11**	-
17q	-	-	-	-	-	-	-	-
18p	-	-	-	-	-	-	-	23
18q	-	21	11	-	-	-	-	-
19p	-	-	-	-	-	-	13	-

Table 8: Contd.....

-	*Spontaneous abortions*		*Recurrent abortions*		*Spontaneous abortions*		*BOH*	
Chromo-somes	*Aurias et al. 1978*		*Diedrich et al. 1983*		*Neri et al. 1983*		*Present study 2012*	
-	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*
19q	-	-	-	-	-	-	11	-
20p	-	-	-	-	-	-	-	-
20q	-	-	-	-	-	-	-	11,12
21p	-	-	-	-	-	-	-	-
21q	-	-	-	-	-	ter	22	-
22p	-	-	-	-	-	-	-	
22q	-	-	11	**13**	-	-	-	**13,13, 13**
Xp	-	-	-	-	-	-	-	-
Xq	-	-	-	13	-	-	-	23
Yp	-	-	-	-	-	-	-	-
Yq	-	-	-	-	-	-	-	-

Total

-	*Malformations and or MR*		*Malformed child*		*MR/MCA*	
Chromosomes	*Aurias et al. 1978*		*Neri et al. 1983*		*Present study 2012*	
-	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*
1p	-	-	-	-	-	-
1q	12,21	-	-	-		32,42
2p	-	12,13	-	-	-	-
2q	35	-	-	37		11,21, 32
3p	-	25,26	-	-	-	13
3q	28-	-	-	-	26	-
4p	15,15	-	15	16	-	-
4q	-	-	-	-		
5p	Ter	15,ter	14	15	-	-
5q	23	-	-	-		
6p	-	25	-	-	-	-
6q	-	-	-	-		-
7p	-	11	-	-	-	-
7q	35	-	-	-	22,36	-
8p	-	-	-	-	-	-
8q	-	-	-	-	-	-
9p	-	-	-	-	-	-
9q	-	-	-	-	-	32
10p	-	-	-	ter	-	-
10q	11,22	24	-	-	-	-
11p	-	-	-	-	-	-
11q	-	-	-	-	-	-
12p	-	-	13	-	-	-
12q	-	13	-	-	-	-
13p	-	-	-	-	-	-
13q	31	-	-	14 or 21	22	-
14p	-	-	-	-	-	-
14q	11	32	-	-	-	-
15p	-	-	-	-	-	-
15q	11,14	14,22	-	-	-	24,26
16p	-	-	-	-	-	-
16q	12	-	-	-	-	-
17p	-	-	-	-	-	-
17q	-	11	-	-	-	22
18p	-	-	-	-	-	11,12
18q	-	-	-	21	-	-
19p	-	-	-	-	-	-
19q	-	-	-	-	-	-

Table 8: Contd.....

-	*Malformations and or MR*		*Malformed child*		*MR/MCA*	
Chromosomes	*Aurias et al. 1978*		*Neri et al. 1983*		*Present study 2012*	
-	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*
20p	-	-	-	-	-	-
20q	-	-	-	13	-	-
21p	-	-	-	-	-	-
21q	-	-	ter	-	-	-
22p	-	-	-	-	-	-
22q	-	-	-	-	-	-
Xp	-	-	-	-	-	-
Xq	-	-	-	-	-	-
Yp	-	-	-	-	-	-
Yq	-	-	-	-	-	-
Total						

data a total of 84 breakpoints was obtained for the 42 rcpts and the breakpoints in the short arm were 25 and long arm 59. In the present study too, it may be opined that because of the pooled data, the distribution appeared to be non-random, since all the chromosomes were involved. The analysed breakpoints based on their location were from G bands and seemed to be in excess for chromosomes 1,2,7,11 and 15 From the table 7, it is seen that i) for some chromosomes some of the breakpoints were common (chromosome 1 at 1q32,4q31/34/35,5p11/15,8p23,8q24,9q22,12q24,15q22,21q22); ii) some were different (2q,5p,5q,6p,6q,10q,13q,14q,17q iii) breakpoints not observed in Neri et al. for 11,16,19,X, Y and 1p,7q,11p,14p,17q; in the present study 4p,7p,9p,10p,12p,15p,16p,18q, 19q, Xp; in both studies 2p,5q,13p,19q,21p,22p iv) between the 2 studies even though the breakpoints appeared to be common or different; the rcpt combination between the chromosomes were different.

Rare complexities associated to the breakpoints known as the vital points in the chromosomes in rcpt have been reported (Fantes et al. 1995; Gardner and Sutherland 1996). Among them, i) rcpt 1;11(q42.1;14.3) segregating with schizophrenia in a large kindred was hoped to enable the discovery of the causative gene. In the present study, in chromosome 1 the breakpoint at q42 was associated to MR/MCA ii) rcpt 6;7(p21.1;q11.23) to elastin gene when disrupted may cause supravalvular aortic stenosis. In the present study, 7q11 was seen in BOH. iii) 11p13 was associated to Aniridia.

In 1990, the cytogenetic studies in couples with repeated pregnancy losses has showed that the structural chromosomal abnormality such as translocations both reciprocal and Robertsonian and inversions were associated with a higher risk of pregnancy wastage (De Braekeleer and Dao 1990). In the present study, rcpt was associated to BOH.

The observed differences may be because of the differences in the ascertainment in the sample and the methodology. Moreover, it is stated that except for chromosome 22, an ascertainment bias may explain the nonrandom distribution of the breakpoints and chromosomal imbalance may vary as per the ascertainment (Aurias et al. 1978). It may be concluded, that the rcpt was associated to BOH and to female carriers. The affected individuals and their family are counseled about the prognosis, risk of recurrence, prenatal options and the medical management.

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