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Derivatives and Its Formation from the Meiotic Segregation in the Carrier Parents with Reciprocal Translocation

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ABSTRACT Chromosome derivatives are one of the outcomes in gametes, from the parents with reciprocal translocation. Individuals with derivatives have chromosomal imbalance, resulting in multiple congenital abnormalities and high mortality. The present investigation reports the observed derivatives in 19 probands; the sex ratio, parental origin and its association with meiotic segregation and the gain or loss in the chromosomes. From 1977 to 2007, 19 probands, who were referred for karyotyping and counseling to the Division of Human Genetics, St John's Medical College, Bengaluru, had cytogenetically confirmed derivatives. Their ages ranged from neonates to 14 years. 20 derivatives were observed in 13 males and 7 females; since one male showed 2 derivatives. The sex ratio was 1.7:1. 11 males and 7 females had 46 chromosomes and 1 male and 2 females had 47 chromosomes. 7 males and 2 females had derivatives of paternal origin and 5 males and 5 females had derivatives of maternal origin. 2:2 adjacent type 1 meiotic segregation was paternal in 9 and maternal in 7 probands. The subtype AB CB was paternal in 6 and maternal in 4; AD CD paternal in 4 and maternal in 2. The 3: 1 mode of maternal meiotic segregation in 3 showed AB CD CB or AD CD CB or AB AD CD sub types. The gain in partial trisomy was paternal in 9 and maternal in 15 and the loss in partial monosomy was paternal in 9 and maternal in 7. The article on the derivatives and its various aspects is reported for the first time in India.

INTRODUCTION

A derivative is defined as an 'unbalanced chromosome rearrangement; the chromosomal complement contains an incorrect amount of chromosome material which may lead to very serious clinical effects'. A derivative chromosome is a structurally rearranged chromosome generated by rearrangements involving 2 or more chromosomes e.g. the unbalanced products of translocation and derivative chromosomes are designated as 'der' (ISCN 2005; Schaffer and Tommerup 2005).

A few translocations are associated with a high risk, (as much as 20% or rarely higher), to produce a child with malformations and mental retardation, due to the parent transmitting an unbalanced chromosomal complement. At meiosis I, the 4 chromosomes (2 normal and 2 translocated) come together as a quadrivalent with segments in common lying side by side. At pachytene, in order to match the homologous segments, the 4 chromosomes enter into a cross shaped configuration. As the gametocyte enters metaphase, the 4 chromosomes release their points of attachment, except at the tips of the arms of the chromosomes resulting in the formation of the ring. In case of failure of attachment at one of the terminal pairings, a chain is formed, instead of a ring. Then, the 4 chromosomes separate from each other and are distributed to the 2 daughter cells i.e., they segregate in a number of ways. A 2:2 segregation, whether alternate or adjacent, refers to the two chromosomes going to one cell and two to the other; in 3:1 segregation, three go to one cell and one to the other. The propensity for a particular segregation outcome reflects the geometry of the quadrivalent; whether it forms a ring or chain **(**Gardner and Sutherland 1996).

In view of the lack of any published matter on derivatives from India, the present study was undertaken to report the various aspects of the derivatives in children with multiple congenital anomalies and mental retardation.

Aims

It is aimed to report the following findings:
- the observed derivatives and the chromosomes involved in the formation of the derivatives, from the karyotypes of the probands and the sex ratio, mortality in the probands,

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frequency of the derivatives and the familial status of the derivatives
- the parental origin of the derivatives from the parents with reciprocal translocation carrier status; the familial status of the reciprocal translocation
- the association of the sex of the probands with that of the parental origin for the types and the subtypes of the meiotic segregation of the chromosomes involved in the reciprocal translocation, the short and long arm combination of the chromosomes in the translocation status in the parents and the parental loss and gain in the segments of the derivative chromosomes.

MATERIAL AND METHODS

The Division of Human Genetics is a known referral center for karyotyping and counseling to individuals with multiple congenital anomalies and mental retardation. From 1977 to 2007, chromosome derivatives were observed in 19 probands. There were 12 male and 7 female probands and their age ranged from neonates to 14 years.The presence of the derivatives was confirmed with GTG banded peripheral leucocyte microculture. For confirmation, the cultures were repeated. Parental karyotyping and wherever required, karyotyping of the other members of the family were also done. At the outset, consent was duly obtained from the parents.

RESULTS

In Tables 1 and 2 are given the determined karyotypes in the probands with derivative chromosomes and the sex ratio, frequency of the derivatives, mortality in the probands and the familial status of the derivatives. Also given are the karyotypes of the parents with reciprocal translocation, the familial status of the reciprocal translocation, the parental origin of the derivatives and the frequency of the breakpoints in the chromosomes.

Derivatives were observed in 19 probands, out of which 12 were males (63.16%) and 7 females (36.84%) and the sex ratio was 1.7:1. One

Table 1: Karyotype in the probands with derivatives and in the parents with reciprocal translocation and the parental origin of the derivatives

S. No.	*Paternal origin*	*S. No*	*Maternal origin*
-	*Male Probands*	-	*Male Probands*
1	46,XY,der(21)pat 46,XY, t(2;21)(p22;q22)pat	10	47,XY,+der(21)mat 47,XYt(1;21)(q32;q11)mat Proband diseased
2	46,XY,der(3)pat 46,XY,t(3;15)(p25;q22)pat	11	46,XY,der(8)mat 46,XY,t(3;8)(p22; p21)mat
3	46,XY,der(5)pat, der(22)mat 46,XY,t(5;8)(p15;q22)pat 46,XX,t(11;22)(q23;q11.2)mat Proband diseased	12	46,XY,der(5)fam 46,XY, t(5;7)(p15;q33)mat aunt
4	46,XY,der(5)pat, familial 46,XY,t(5;8)(p15;q22)pat	13	46,XY,der(20)mat 46,XY,t(6;20)(p21;q13)mat
5	46,XY,der(18)pat 46,XY,t(7;18)(p21;q22)pat	14	46,XY,der(12)mat 46,XY,t(9;12)(p11;q24)mat
6	46,XY,der(9)pat, familial 46,XY,t(9;10)(p13;q24)pat Proband diseased	-	-
7	46,XY,der(18)pat 46,XY,t(13;18)(q14;q21)pat	-	-
-	*Female Probands*	-	*Female Probands*
8	46,XX,der(9)pat 46,XX,t(2;9)(p22;p21)pat	15	47,XX,+der(21)mat 47,XX,t(1;21)(p11;p11)mat
9	46,XX,der(14)pat, familial 46,XX,t(3;14)(q25;p10)pat	16	46,XX,der(8)mat 46,XX,t(3;8)(p22;p21)mat
-	-	17	46,XX,der(5)mat 46,XX,t(5;8)(p15;q22)mat
-	-	18	47,XX,+der(9)mat 47,XX,t(9;15)(q22;p12)mat
-	-	19	46,XX,der(9)mat 46,XX,t(9;21)(q22;q22) mat

Table 2: The breakdown of the derivatives in view of the parental origin is listed

Male probands with paternal derivatives in chromosomes 3,5(2),9,18(2),21
Female with paternal derivatives in 9,14
Male with maternal derivatives in 5,8,12,20,21,22
Female with maternal derivatives in 5,8,9(2),21
Male with only paternal derivative 3,5(2),18(2), 21
Female with only paternal derivative in 14
Male and female with paternal derivative in 9
Male with only maternal derivatives in 12,20,22
Female with only maternal in derivative 9(2)
Male and female with maternal derivatives in 5,8,21

male proband had 2 derivatives; hence, the total number becomes 20 derivatives in 19 probands i.e. 13 in males (65%) and 7 in females (35%). 16 probands (11 males, 7 females) (84.2%) had 46 chromosomes and 3 (1 male, 2 females) (15.8%) had 47 chromosomes. 3 male probands (case nos. 3, 6, 10) with der 5 (paternal origin) as well as der 22 (maternal origin), der 9 (paternal origin) and der 21 (maternal origin) were deceased within 2 years.

Derivatives 5 and 9 were observed 4 times each followed by derivative 21 in 3 times. Derivative 5 was noticed 3 times in male and one time in female probands; whereas derivative 9 was seen one time in male and 3 times in female probands.

Derivatives in the chromosomes 5,8,9 and 21 were found to be common in both the male and female probands; derivative 3,12,18,20 and 22 were seen only in male probands and derivative 14 only in female. In 2 probands, the derivatives were familial: case no 4 → male, derivative 5 was also confirmed in father's brother's son; case no 15 → female proband with derivative 21 was a case of translocation Down syndrome [47,XX,t(1;21),+21] mat; her parents' next conception also was derivative 21 (translocation Down syndrome [47,XY,t(1;21),+21] confirmed with amniocentesis and the parents medically terminated the conception.

The karyotype of 10 fathers (46,XY) and 8 mothers were normal (46,XX). One of the male proband's mother was deceased; hence the karyotype could not be ascertained. Nine fathers and 10 mothers had reciprocal translocation (rcpt). In 2 cases the reciprocal translocation status in the parents was found to be familial: case no 6 → father had translocation between 9 and 10 and the family study showed that his paternal grandmother, 3 paternal aunts and male paternal cousin also had the reciprocal translocation between 9 and 10; case no 9 → the reciprocal translocation seen in the female proband's father was also seen in the proband's sister.

The parental origin of the 20 derivatives was seen in 19 (95%)(11 males, 7 females) and one male had the maternal line origin (5%). For the case number 13, mother was deceased; the reciprocal translocation seen in the maternal aunt was between the chromosomes 5 and 7; hence, the origin of the derivative was stated to be from the maternal line. Among the 19, the paternal origin was determined in 9 (47.37%) and maternal in 10 (52.63%). The 9 derivatives of paternal origin was associated with 7 male (77.78%) and 2 female (22.22%) probands and the 10 derivatives of maternal with 5 male and 5 female probands, respectively (50% each).

Derivative 5 in 3 probands (2 males, 1 female) is because of the translocation in the parents between 5 and 8 (2 paternal, 1 maternal) and that too at the same breakpoints in the short and the long arms of the chromosomes 5 (5p15) and 8 (8q22). In one male proband, the derivative between 5 and 7 was seen in the maternal side (maternal aunt) and once again the breakpoint in 5 is at 5p15.

Derivative 9 was seen 4 times: in one male proband the translocation in the parent (paternal) is between 9 and 10 and in the 3 females, it is between 2 and 9 (paternal) or 9 and 15 (maternal) or 9 and 21 (mother). 2 mothers of 2 female probands, the same breakpoint in chromosome 9 in the long arm (9q22); the outcome is a derivative 9 with 46 chromosomes in one female proband but 47 in another female.

In Tables 3 and 4 are given the types and the sub types in the mode of the meiotic segregations, that which could have occurred during the parental gametogenesis resulting in the particular types of derivatives in the probands and their association to the sex of the probands.

2:2 adjacent type 1 meiotic segregation of the chromosomes involved in the reciprocal translocation carrier parents had occurred in 16 parents and it was paternal in 9 (56.25%) and maternal in 7 (43.75%). The 9 derivatives of paternal origin was associated with 7 male (77.78%) and 2 female (22.22%) and the 7 derivatives of maternal was seen in 4 male (57.14%) and 3 female (42.86%) probands.

In the adjacent 1 type segregation in 16, as per the quadrivalent pairing, the subtype AB CB

Table 3: Meiotic segregation, its types and sub-types and the outcome in the parents with reciprocal translocation

S. No.	*Schematic segregants*	*Chromosomal complement gametes*	*Origin*
	Adjacent I		*Male Probands*
1	AB CB	2, der(21)	46,XY,der(21)t(2;21)(p22;q22)pat 46,XY,der(21)(21pter→21q22::2p22→2pter) Loss of 21q22-21qter; Gain of 2p22-2pter Mother – 46,XX
2	AD CD	der(3), 15	46,XY,der(3)t(3;15)(p25;q22)pat 46,XY,der(3)(3qter→3p25::15q22→15qter) Loss of 3p25-3pter; Gain of 15q22-15qter Mother – 46,XX
3	AD CDAB CB	der(5), 8 der (22),11	46,XY,der(5)t(5;8)(p15;q22)pat 46,XY,der(5)(5qter→5p15::8q22→8qter) Loss of 5p15-5pter;Gain of 8q22-8qter Mother- 46,XX,der(22)t(11;22)(q23;q11.2)mat 46,XX,der(22)(22pter→22q11.2::11q23→11qter) Loss of 22q11-22qter;Gain of 11q23-qter
4	AD CD	der(5), 8	46,XY,der(5)t(5;8)(p15;q22)pat, familial 46,XY,der(5)(5qter→5p15::8q22→8qter) Loss of 5p15-5pter;Gain of 8q22-8qter Proband's fathers brother's son with der(5) Mother – 46,XX
5	AB CB	7, der(18)	46,XY,der(18)t(7;18)(p21;q22)pat 46,XY,der(18)(18pter→18q22::7p21→7pter) Loss of 18q22-18qter;Gain of 7p21-7pter Mother – 46,XX
6	AD CD	der(9), 10	46,XY,der(9)t(9;10)(p13;q24)pat, familial 46,XY,der(9)(9qter→9p13::10q24→10qter) Loss of 9p13-9pter;Gain of 10q24-10qter Paternal grandmother, three paternal aunts, male paternal cousin with der(9) Mother – 46,XX
7	AB CB	13, der(18)	46,XY,der(18)t(13;18)(q14;q21)pat 46,XY,der(18)(18pter→18q21::13q14→13qter) Loss of 18q21-18qter;Gain of 13q14-13qter Mother – 46,XX
8	AB CB	3, der(8)	46,XY,der(8)t(3;8)(p22;p21)mat 46,XY,der(8)(8qter→8p21::3p22→3pter) Loss of 8p21-8pter;Gain of 3p22-3pter Father – 46,XY
9	AB CB	6, der(20)	46,XY,der(20)t(6;20)(p21;q13)mat 46,XY,der(20)(20pter→20q13::6p21→6pter) Loss of 20q13-20qter;Gain of 6p21-6pter Father – 46,XY
10	AB CB	9, der(12)	46,XY,der(12)t(9;12)(p11;q24)mat 46,XY,der(12)(12pter→12q24::9p11→9pter) Loss of 12q24-12qter;Gain of 9p11-9pter Father – 46,XY
-	-	-	*Female Probands*
11	AB CB	2, der(9)	46,XX,der(9)t(2;9)(p22;p21)pat 46,XX,der(9)(9qter→9p21::2p22→2pter) Loss of 9p21-9pter;Gain of 2p22-2pter Mother – 46,XX
12	AB CB	3, der(14)	46,XX,der(14)t(3;14)(q25;p10)pat 46,XX,der(14)(14qter→14p10::3q25→3qter) Loss of 14p10-14pter;Gain of 3q25-3qter Sister- 46,XX,t(3;14)(q25;p10) Mother – 46,XX
13	AB CB	3, der(8)	46,XX,der(8)t(3;8)(p22;p21)mat 46,XX,der(8)(8qter→8p21::3p22→3pter) Loss of 8p21-8pter;Gain of 3p22-3pter Father – 46,XY
14	AD CD	der(5), 8	46,XX,der(5)t(5;8)(p15;q22)mat 46,XX,der(5)(5qter→5p15::8q22→8qter)

Table 3: Contd.....

S. No.	*Schematic segregants*	*Chromosomal complement gametes*	*Origin*
	Adjacent I		*Male Probands*
			Loss of 5p15-5pter;Gain of 8q22-8qter
			Father – 46,XY
15	AD CD	der(9), 21	46,XX,der(9)t(9;21)(q22;q22)mat
			46,XX,der(9)(9pter→9q22::21q22→21qter)
			Loss of 9q22-9qter;Gain of 21q22-21qter
			Father – 46,XY
-	*Adjacent II*	-	Male Proband
16	AB AD	5, der(5)	46,XY,der(5)t(5;7)(p15;q33)fam
			46,XY,der(5)(5qter→5p15::7q33→7qter)
			Loss of 5p15-5pter; Gain of 7q33-7qter
			Mother deceased. Father – 46,XY
			Maternal aunt had der(5)
-	3:!	-	*Male and Female Probands*
17	AB CD CB	1, 21, der(21)	47,XY,+der(21)t(1;21)(q32;q11)mat
			47,XY,+der(21)(21q11→21q32::1q11→1qter)
			Gain of 1q11-1qter; Gain of 21pter-21q11
			Father – 46,XY
18	AD CD CB	der(1), 21, der(21)	47,XX,+der(21)t(1;21)(p11;p11)mat
			47,XX,+der(21)(21qter→21p11::1p11→1pter)
			Gain of 1p11-1pter; Gain of 21p11-21pter
			Father – 46,XY
19	AB AD CD	9, der(9), 15	47,XX,+der(9)t(9;15)(q22;p12)mat
			47,XX,+der(9)(9pter→9q22::15p12→15pter)
			Gain of 9q22-9qter; Gain of 15p12-15pter
			Father – 46,XY

Table 4: Parental origin of the meiotic segregation as per the subtypes and their association to the short (p) and long (q) arms of the chromosomes involved in the reciprocal translocation

Segregation	*Arms*	*Male*		*Female*	
	-	*Paternal*	*Maternal*	*Paternal*	*Maternal*
Adjacent I					
AB CB (10)	p;q (05)	02	02	01	-
-	p;p (03)	01	-	01	01
-	q;q (02)	01	01	-	-
ADCD (6)	p;q (05)	04	-	-	01
-	q;q (01)	-	-	-	01
Adjacent II					
AB AD (1) 3:1 (3)	p;q (01)	-	01	-	-
AB CD CB	q;q (01)	-	01	-	-
AD CD CB	p;p (01)	-	-	-	01
AB AD CD	p;q (01)	-	-	-	01

was found in 10 parents (58.82%)(6 paternal → 60% and 4 maternal → 40%) and AD CD in 6 (41.18%)(4 paternal → 66.67% and 2 maternal → 33.33%).

The 6 with paternal origin for the subtype AB CB was associated with 4 male and 2 female probands and the 4 with maternal origin was associated with 3 male and 1 female probands. The 4 with a paternal origin of the AD CD was associated with 4 male probands and the 2 with a maternal origin was associated with 2 female probands.

Based on the karyotype of the maternal aunt, it was presumed that adjacent I subtype AB AD may have occurred in the deceased mother of the male proband. The 3: 1 mode of meiotic segregation was found to have 3 subtypes either AB CD CB (maternal in 1 male) or AD CD CB (maternal in I female) or AB AD CD (maternal in 1 male). (Figs. 1,2,3)

In Table 5 is given the combined observations for tracing the association between the chromosomal arms involved in the reciprocal translocation in the carrier parents with that of the parental origin of the derivatives, the sex of the probands and the types of the meiotic segregation in the parents.

The arrangement between the chromosomal arms in the parents with the reciprocal translocation, resulting in the 20 derivatives were p;p in 4 (21.05%) (2 paternal, 2 maternal); q;q in 4 (21.05%)(1 paternal, 3 maternal) and p;q in 12 (57.9%)(8 paternal, 4 maternal). The 2 cases with paternal origin of the p;p was associated to one male and one female proband and the 2 cases of maternal origin to 2 females; the one case of paternal origin of the q;q was associated to one male and the 3 cases of maternal origin

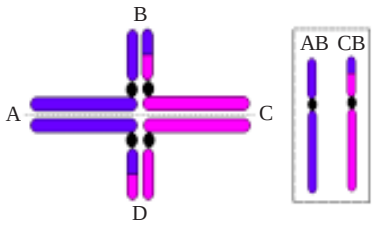

Fig. 1a. 2:2 Adjacent 1 meiotic segregation subtype AB,CB; arms involved p;p

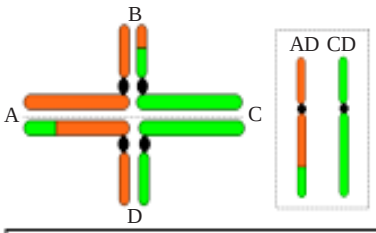

Fig. 1b. 2:2 Adjacent 1 meiotic segregation subtype AD,CD; arms involved p;q

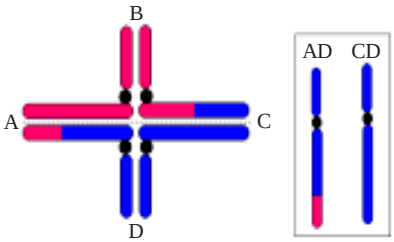

Fig. 1c. 2:2 Adjacent 1 meiotic segregation subtype AD,CD; arms involved q;q

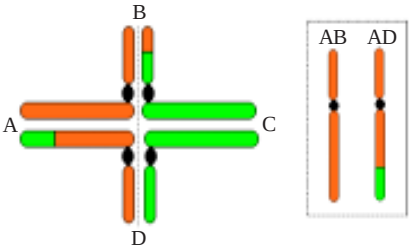

Fig. 2. 2:2 Adjacent II meiotic segregation subtype AB,AD; arms involved p;q

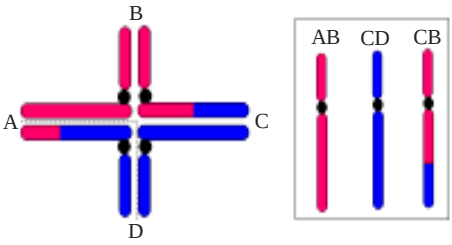

Fig. 3a. 3:1meiotic segregation subtype AB,CD,CB; arms involved q;q

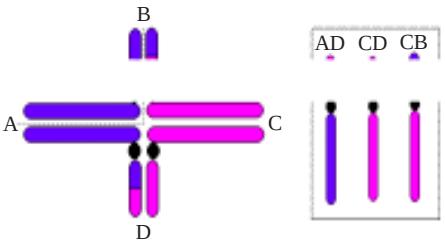

Fig. 3b. 3:1meiotic segregation subtype AD,CD,CB; arms involved p;p

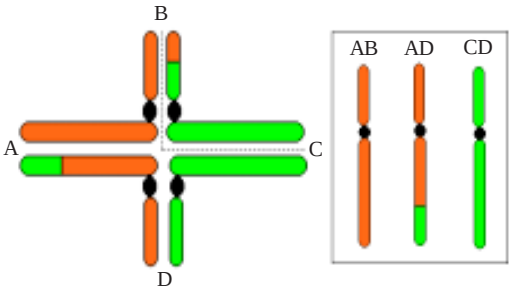

Fig. 3c. 3:1meiotic segregation subtype AB,AD,CD; arms involved p;q

Table 5: The association of the arms of the chromosomes and the sex of the probands to that of the parental origin is listed

Adjacent 1:p;q→ AB CB(5) →3 paternal →2 male and 1 female; 2 maternal → males
Adjacent 1:p;q → AD CD(5) →4 paternal→4 male; 1 maternal →female
Adjacent 2:p;q → AB AD(1) →1 maternal →male
3:1: p;q →AB AD CD(1) paternal → male
Adjacent 1:p;p→AB CB(3)→2 paternal→1 male and 1 female;1 maternal→female
3:1:p;p->AD CD CB(1)→1 maternal→female
Adjacent 1:q;q→ AB CB(2)→1 paternal→male; 1 maternal →male
Adjacent 1:q;q→AD CD→ 1 maternal→female or
3:1:q;q→ AB CD CB→1 maternal→male

to 2 males and one female and the 8 cases of paternal origin of the p;q were associated to 7 males and one female and the 4 cases of maternal origin to 2 male and 2 female probands.

In Tables 6 and 7 are given the partial trisomy and monosomy i.e., gain or loss of genetic material in the chromosomal segments and its association to the parental origin and the sex of the probands. The probands with 46 showed both gain as well as loss for the segments of the chromosomes involved in the derivatives; whereas the probands with 47 showed only gain in the chromosomes.

0In the total sample of 20 derivatives, partial trisomy was seen in 24 (60%) (14 males,10 females) and monosomy in 16 (40%) probands (12 males, 4 females). The number of chromosomes that showed gain in the q arm was 14 (9 males, 5 females) and in the p arm 10 (5 of each

Table 6: Derivatives: Correlation of trisomy or monosomy to the parental origin and the sex of the probands

Partial trisomy chromosomes	*Male*		*Female*	
	Paternal origin	*Maternal origin*	*Paternal origin*	*Maternal origin*
1	-	1q11→qter	-	1p11→pter
2	2p22→pter	-	2p22→pter	-
3	-	3p22→pter	3q25→qter	3p22→pter
6	-	6p21→pter	-	-
7	7p21→pter	7q33→qter	-	-
8	8q22→qter (2)	-	-	8q22→qter
9	-	9p11→pter	-	9q22→qter9q22→qter
10	10q24→qter	-	-	-
11	-	11q23→qter	-	-
13	13q14→qter	-	-	-
15	15q22→qter	-	-	15p12→pter
21	-	21q11→qter	-	21p11→pter21q22→qter
Partial monosomy chromosomes	*Male*		*Female*	
	Paternal origin	*Maternal origin*	*Paternal origin*	*Maternal origin*
3	3p25→pter	-	-	-
5	5p15→pter (2)	5p15→pter	-	5p15→pter
8	-	8p21→pter	-	8p21→pter
9	9p13→pter	-	9p21→pter	-
12	-	12q24→qter	-	-
14	-	-	14p10→pter	-
18	18q21→qter18q22→qter	-	-	-
20	-	20q13→qter	-	-
21	21q22→qter	-	-	-
22	-	22q11→qter	-	-

Table 7: The list of the gain and loss in the derivatives

Gain paternal p arm→ male: 2p,7p	Loss paternal p arm→ male: 3p,5p,9p
Gain paternal p arm→ female: 2p	Loss paternal p arm→ female: 9p,14p
Gain maternal p arm→ male: 3p.6p.9p	Loss maternal p arm→ male: 5p,5p,8p
Gain maternal p arm→ female: 1p,3p,15p,21p	Loss maternal p arm→ female: 5p,8p
Gain paternal q arm→ male: 8q,8q,10q,13q,15q	Loss paternal q arm→ male: 18q,18q,21q
Gain paternal q arm→ female: 3q	Loss paternal q arm→ female: NIL
Gain maternal q arm→ male: 1q,7q,11q,21q	Loss maternal q arm→ male: 12q,20q,22q
Gain maternal q arm→ female: 8q,9q,9q,21q	Loss maternal q arm→ female: NIL

sex) and the loss in the p arm 10 (6 males, 4 females) and q arm 6 (6males). The trisomy versus monosomy in the derivatives in the male probands was 14 versus 12 and the breakdown as per the paternal and maternal origin of the trisomy was 7 in each and the monosomy was 7 and 5. The trisomy versus monosomy in the derivatives in the female probands was 10 versus 4 and the breakdown as per the paternal and maternal origin of the trisomy was 2 and 8 and the monosomy was 2 and 2. Paternal gain for the total sample has occurred in 9 (7 males, 2 females) and maternal in 15 (7 males, 8 female); the paternal loss was 9 (7 males, 2 females) and maternal loss 7 (5 males, 2 females). The maternal gain was of higher percentage (68.2%) when compared to the loss (31.8%).

The gain in the q arm was paternal in 6 (5 males, 1 female) and maternal in 8 (4 males, 4 females) and the gain in the p arm was paternal in 3 (2 males, one female) and maternal in 7 (3 males, 4 females). The loss in the paternal and maternal q arm were seen in 3 male probands respectively and the loss in the p arm was paternal in 6 (4 males, 3 females) and maternal in 4 (2 males, 2 females).

DISCUSSION

The reported incidence of chromosomal abnormality is 90 per 10,000 live births (0.001%), out of which unbalanced structural rearrangements are 10 per 10,000 live births, which also include derivatives. The incidence of the reciprocal translocation is around 1 in 500 individuals (Connor et al. 2007).

At the Division of Human Genetics, an average of 500 patients per year, are referred for karyotyping and counseling. For the period of 30 years (1977-2007), 19 derivatives were identified.

In literature, it is seen that, the articles pertaining to the derivatives are found as case reports or are included in the review articles on genetic counseling for parents with Reciprocal and Robertsonian translocation and include estimated outcomes from the meiotic segregation of the translocation chromosomes resulting in offspring with derivatives and multiple congenital abnormalities. In the present study, only the discussion on meiotic segregation is done.

During gametogenesis (meiosis 1 and 2) carriers with reciprocal translocation, theoretically, could give rise to 16 types of chromosomal constitutions. But, the viability of the zygotes depends on normal chromosomal complement or the translocation status. The zygotes with partial trisomy or monosomy are also viable, depending on the severity of the phenotype, the size of the gain or loss in the segments of the chromosomes including the gene contents, the sex of the probands and the parental origin status.

In translocation carriers, in the 1st meiosis, the possible pairing is between quadrivalents, either as 2:2 or 3:1 segregation of the chromosomes. The 2:2 segregation is of alternate or adjacent types and in the adjacent type there are 2 subtypes, adjacent I and adjacent II.

The zygotes with normal or translocation status as in the parents may be produced due to the alternate mode of segregation of the chromosomes in meiosis (AB CD or AD CB).

The unbalanced chromosomal status in the zygotes with partial monosomy and partial trisomy of the chromosomes due to reciprocal translocation are because of adjacent I (non-homologous centromeres segregate together) (AB CB or AD CD) or adjacent II segregation (AB AD or CB CD). A 3:1 segregation invariably results in trisomy (AB AD CD or AB CB CD or AB AD CB or AD CB CD) or monosomy (AB or AD or CB or CD) in the zygotes (Turnpenny and Ellard 2007).Cohen et al. (1994) in a review of 1159 families, found the proportions of chromosomally unbalanced offspring as 71% adjacent -1; 4% adjacent-2; 22% tertiary trisomy/monosomy and 2.5% interchange trisomy.

Sperm karyotyping results from 27 men carriers for translocation showed that on an average, alternate (47%) and adjacent 1 (37%) segregants are the predominant types and adjacent -2 (12%) and 3: 1 (5%) are less frequently seen. It is opined, that a similar distribution or range of germ cell abnormalities may also be produced by their translocation heterozygous sisters. It is the conceptuses with less genetic imbalance, that result in the birth of an abnormal child (Gardner and Sutherland 1996).

In the present study, the unbalanced chromosomal status was ascertained in 19 probands with multiple congenital anomaly or mental retardation. Partial monosomy and trisomy was determined in 16 (84.2%) and trisomy on 3 (15.8%). In 17, it was due to adjacent I (78.9%) (AB CB- 10, AD CD- 6) and adjacent II (AB

AD- 1) mode of segregations in the parents with the reciprocal translocation, resulting in partial monosomy and trisomy for the segments of the chromosomes involved in the derivatives, in the probands. The observations of the present study, indicated the preponderance towards adjacent I segregation as reported in the literature.

Recently, Thomas et al. (2010) have reported the predominance in human of the paternal origin of the 'de novo' balanced translocation and its association with a significant increase in the paternal age. In the present study, the parental origin of the derivatives showed a high occurrence in male probands for adjacent I segregation with paternal origin. Moreover, in the present study, in 2 families the derivatives 5 and 9 were traced in the paternal cousins and the reciprocal translocation in the proband's sister also was paternal in origin.

The differences may reflect the bias in the sample its size and the criteria.

Inferences from the Present Study

1. Derivatives were preponderant in the male probands (13). The chromosomes involved in the formation of the derivatives (3,5,8,9,12,14, 18,20,21,22) and the preference as per the sex of the probands (male with derivatives in chromosomes 3,5,8,9,12,18,20,21 and 22; female with derivatives in 5,8,9,14 and 21) (only in males chromosomes 3,12,18,20 and 22 and in female 14), indicated that the zygotes with those chromosomes may survive as live births and there also could be preference as per the sex of the proband.

2. Maternal origin of the derivatives was of higher value (11/20); still the paternal origin of the derivatives was associated to the male probands (7/12) and the maternal origin to the female probands (5 out of 7).

3. Derivatives from 5 and 21 when paternal were seen in male proband; but the maternal derivatives were seen in both male and female. Derivative 9 of paternal originwas observed both in male and female; but of maternal origin only in the female. Derivatives 3 and 18 of paternal origin were noticed in male and derivative 14 of paternal origin in the female. Derivatives 12, 20 & 22 of maternal origin were seen in male; whereas derivative 8 of maternal origin was observed in both male and female. A maternal origin of derivatives that was transmitted only to the female was not observed.

4. 2:2 adjacent I segregation that was paternal in origin (8) was prevalent in male probands. The sub types AB CB and AD CD (paternal) showed a higher value in the male (4 each) and when maternal was equal in both sexes (2 in each). AD CD maternal segregation was not observed either in the male or the female probands.

5. The paternal origin of the derivatives as per the combinations of the short;long (p;q) arms of the chromosomes and AB CB as well as AD CD subtypes was associated with male probands. The maternal origin of the derivatives to the male probands from the p;p combination in AD CD was not detected. In female the parental origin of the derivatives whether maternal or paternal from the p;p combination in the ADCD subtype was not detected.

6. The gain in q arm is more in male (9) and also the maternal origin (8). The loss in paternal p arm or maternal p arm in the male is more (11). The loss in the paternal or maternal q arm is not observed in the female.

7. The maternal origin of the trisomy status seemed to be predominant (15). Paternal trisomy was associated to the male (7) and the maternal to the female (8) probands.

8. The gain in the paternal p arm common for both the sexes is 2p and for the maternal p arm 3p; whereas the loss for p arm paternal in origin common for both the male and female is 9p and maternal p arm is 5p,8p. The gain for the maternal q arm common in both the sexes is for 21q. The rest may be considered to occur exclusively as per the the parental origin and the sex of the probands..

9. The chromosomes not observed in the loss or gain in derivatives are 4,16,17,19,X and Y. Conceptions with derivatives for the chromosomes 4,16,17 and 19 may be lethal and derivatives for X and Y usually are associated with problems in the reproductive system than to multiple congenital anomaly and mental retardation.

10. Irrespective of the sample size, the findings may be reflecting the association between the parental origin of the derivatives and the types of the meiotic segregation to the sex of the probands:

(a) male conceptions with derivatives may be carried to term; (b) survival status to the zygotes with trisomy in the derivatives from maternal origin may be better than monosomy; (c) survival may not be better for the female zy-

gotes with monosomy; (d) the proposed spermatogenetic arrest especially in the X bearing sperms may lead to the decrease in the paternal origin of the derivatives in female live births.

Follow-up

In the present study, on follow up it was gathered that 3 male probands were deceased.

At the time of genetic counseling, it is important to examine the particular rearrangement (chromosomes, breakpoints, size of segments) and the sex of the carriers. The risk also depends on the mode of ascertainment of the reciprocal translocation, whether from the couples with infertility or bad obstetric history (abortions/ normal and abnormal live births) or recurrent abortions or individuals with amenorrhea or mental retardation and or multiple congenital anomaly. During genetic counseling, information is provided on the risk of recurrence and then the parents are recommended for prenatal diagnosis for the subsequent pregnancy.

CONCLUSION

The article on the derivatives and its various aspects is reported may be for the first time in India.

REFERENCES

Cohen O, Cans C, Mermet MA, Demongeot J, Jalbert P 1994. Viability thresholds for partial trisomies and monosomies.A study of 1,159 viable unbalanced reciprocal translocations. *Human Geneics*, 93: 188-194.

Connor JM, Pyeritz RE, Korf BR 2007. *Emery and Rimoin's Principles and Practice of Medical Genetics.* 5th Edition. Philadelphia, USA: Churchill Livingstone, Elsevier.

Gardner A, Howell RT, Davies T 2008. *Human Genetics.* New Delhi, India: Viva Books Private Limited.

Schaffer LG, Tommerup N 2005. *International System for Human Cytogenetic Nomenclature Cytogenetic and Genomic Research*, Basel: S Karger.

Thomas NS, Morris KJ, Baptista J, Ng LB, Crolla A, Jacobs PA 2010. de novo apparently balanced translocation in man are predominantly paternal in origin and associated with a significant increase in paternal age. *Journal of Medical Genetics*, 47: 112- 115.

Turnpenny PD, Ellard S 2007. *Emery's Elements of Medical Genetics.* 13th Edition. Philadelphia, USA: Churchill Livingstone, Elsevier.