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CASE REPORT

Dermatoglyphics and Reproductive Risk in a Family with Robertsonian Translocation 14q;21q

Selim Kolgeci[1], Jehona Kolgeci[3], Mehmedali Azemi[3], Aferdita Daka[4], Ruke Shala-Beqiraj[5], Ilir Kurtishi[2], Mentor Sopjani[2]

[1]Obstetrics and Gynecology Clinic, University Clinical Centre of Kosova, Prishtina, Kosova
[2]Faculty of Medicine, University of Prishtina, Prishtina, Kosova
[3]Pediatric Clinic, University Clinical Centre of Kosova, Prishtina, Kosova
[4]Dermatovenerology Clinic, University Clinical Centre of Kosova, Prishtina, Kosova
[5]Department of Histology and Embryology, University Clinical Centre of Kosova, Prishtina, Kosova

Corresponding author: Dr. Jehona Kolgeci, Pediatric Clinic, University Clinical Center of Kosova, Muharrem Fejza street nn, Prishtina, phone: +377(0) 44 469-475; E-mail: Jehonakolgeci@hotmail.com

ABSTRACT

Aim: The present study is carried out to evaluate the risk of giving birth to children with Down syndrome in a family with Robertsonian translocation 14q;21q, and to find the dermatoglyphic changes present in carriers of this translocation. **Methods:** Cytogenetics diagnosis has been made according to Moorhead and Seabright method, while the analysis of prints (dermatoglyphics analysis) was made with the Cummins and Midlo method. **Results:** Cytogenetic diagnosis has been made in a couple who suffered the spontaneous miscarriages and children with Down syndrome. Robertsonian translocation between chromosomes 14 and 21 (45, XX, der (14; 21) (q10; q10)) was found in a female partner who had four pregnancies, in two of which was found fetus karyotype with trisomy in chromosome 21 and pregnancies were terminated. The outcome of fourth pregnancy was twin birth, one of them with normal karyotype and another with Down syndrome due to Robertsonian translocation inherited by mother side. Specific dermatoglyphics traits are found in the child carrying Down syndrome, whereas several traits of dermatoglyphics characteristic of Down syndrome have been displayed among the silent carriers of Robertsonian translocation 14q;21q. **Conclusion:** Robertsonian translocation found in female partner was the cause of spontaneous miscarriages, of giving birth to a child with Down syndrome, and of trisomy of chromosome 21 due to translocation in two pregnancies.

Key words: Down Syndrome, Robertsonian Translocation, Spontaneous Miscarriages, Dermatoglyphics.

1. INTRODUCTION

Among the couples experiencing large number of spontaneous miscarriages, one of partners can be a Robertsonian translocation (RT) silent carrier (1, 2). These translocations represent the largest number of chromosomal aberrations in human population with an incidence of 1.23/1000 live births (3). RTs involve end-to-end fusion of two acrocentric chromosomes at or near the centromeres region. RTs silent carriers face high risk for spontaneous miscarriages and births of children with several anomalies. The risk level depends on the type of RTs (4, 5).

The carriers of RT between chromosome 21 and any other acrocentric chromosome (13q, 14q, 15q and 22q) face risk to give birth to children either with Down syndrome or to give birth to RT silent carrier inherited by their parent (6).

Changes in genotype can be manifested through changes in lines that form patterns on the skin (dermatoglyphics), especially on the fingerprints, palms of the hands and the soles of the feet.

It has been reported that dermatoglyphics patterns of people with Down syndrome due to RTs 13q;21q, 14q;21q and 15q;21q are approximately similar to those with Down syndrome caused by an extra chromosome 21 (7). However, the data of dermatoglyphics in silent carriers of RTs 13q;21q, 14q;21q and 15q;21q are contradictory. Some authors have found in RTs silent carriers 13q;21q, 14q;21q and 15q;21q combination of dermatoglyphic traits quite similar to those found among Down syndrome patients(8), whereas other authors have not found similarity between them, which is probably due to smaller number of analysis of the dermatoglyphics variables (9).

Results obtained by other authors showed intermediate dermatoglyphics patterns between RTs silent carriers and Down syndrome regarding the main lines and dermatoglyphics patterns on the fingertips, palms and the soles (10).

Authors involved in this field of study suggest that further research needed on dermatoglyphics of RTs silent carriers 13q;21q, 14q;21q and 15q;21q be done in order to gain better understanding and clarify the etiology of atypical forms of dermatoglyphics in genetic terms (8.10).

2. AIM

The aim of this study was that through analysis chromosomes and dermatoglyphics of a family affected by RT 14q;21q:

- Evaluate risk of giving birth to children with Down syndrome;
- Clarify genetic mechanism of formation of the embryos with trisomy 21 and the birth to children with balanced RT in this family;
- Establish dermatoglyphics characteristic of Down's syndrome also present in RT 14q;21q silent carrier.

3. METHODS

Cytogenetic diagnosis has been made in chromosome preparations of lymphocytes cultured from peripheral blood according to the Moorhead method (11). Standard method for G-banding by Seabright was used for precise identification of chromosomes (12). The digito-palmar dermatoglyphics were taken and analyzed according to the Cummins and Midlo methods (13). The specific qualitative and quantitative dermatoglyphics patterns were analyzed in the obtained traces.

4. RESULTS

The patient (VQ) born in 1978 was guided to the Obstetrics Gynecology Clinic in Prishtina for screening in order to detect cause of her giving birth to a child with Down syndrome and after screening two other spontaneous miscarriages. The patient has had 8 pregnancies in total, two of which resulted in phenotypically healthy children birth, one pregnancy has resulted in twins (gemelar birth), two in spontaneous miscarriages, two others in induced abortions, and the latest pregnancy is still continuing (Fig. 1). Cytogenetic analysis of two

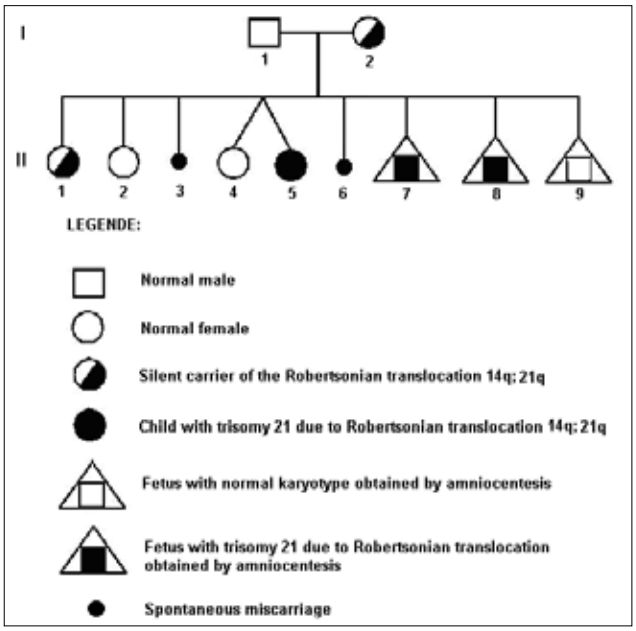

Figure 1. *Family pedigree affected by Robertsonian translocation 14q;21q.*

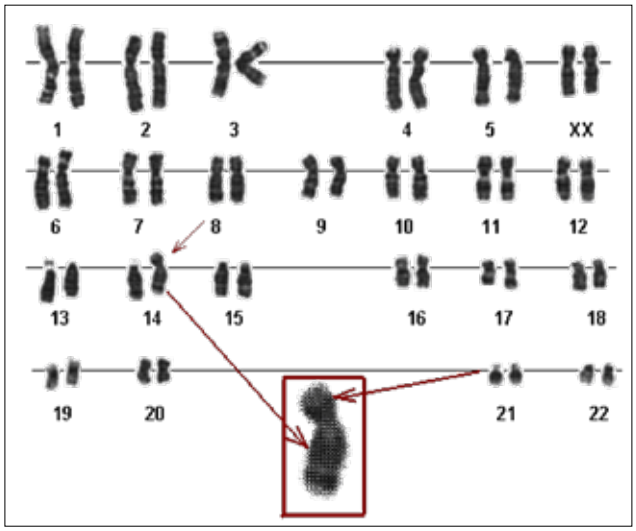

Figure 2. *Child karyotype with trisomy 21 due to Robertsonian translocation: 46, XX, der (14: 21) (q10: q10), +21 mat.*

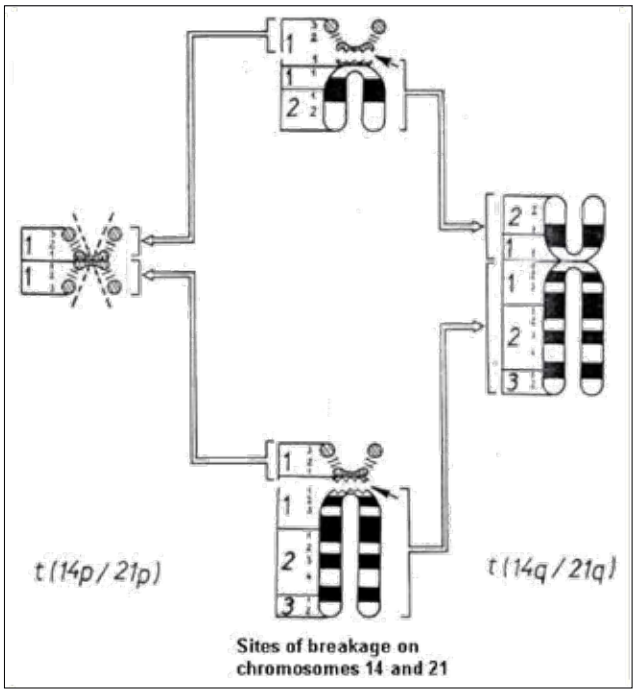

Figure 3. *Schematic representation of the Robertsonian translocation formation between heterologous acrocentric rearrangements involving chromosome 14 and 21.*

miscarriages has not been performed (Figure 1: II_3 and II_6). One twin (Figure 1: $II_{5)}$ had clinical features and characteristic physical signs of a Down syndrome child, and after having performed the cytogenetics analysis it has been established that a child bears unbalanced karyotype: 46,XX,der(14;21)(q10;q10)+21 mat.(Figure 2), having extra genetic material in the long arm of chromosome 21 due to RT between heterologous acrocentric chromosomes 14q and 21q (Figure 3).

To prove whether that child chromosome aberration has occurred *de novo* or it has been inherited from her parents, we performed cytogenetics analysis of both child's parents. Father's karyotype resulted normal (46, XY) and mother: 45,XX,der (14;21)(q10;q10) had a RT involving nonhomologous acrocentric chromosomes 14q and 21q (Figure 4), which is inherited from a mother to a child.

Karyotype of mother with RT was as an indication for

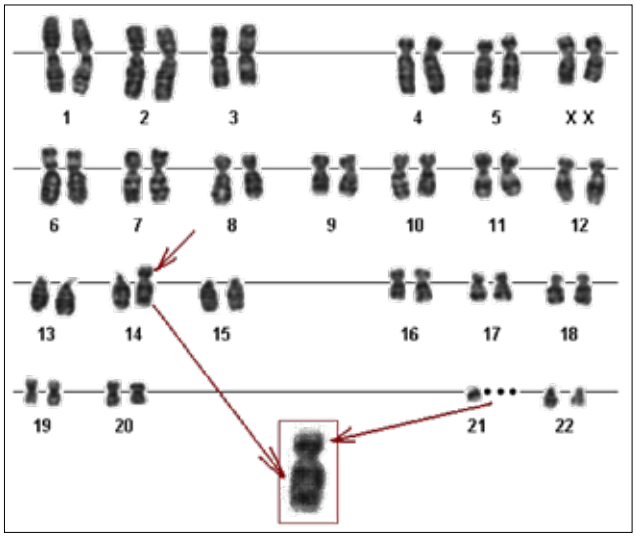

Figure 4. *Karyotype of the silent carrier with Robertsonian translocation: 45, XX, der (14;21) (q10; q10).*

making the cytogenetics diagnosis also on her children. Karyotype: 45,XX,der (14;21) (q10;q10) mat of the first child (Figure 1.II_1) had RT similar to the mother, whereas other 2 children (Figure 1. II_2 and II_4) had normal karyotype. At the age of seven, one of the twins had Down syndrome karyotype (Figure 2), while the other one normal karyotype (Figure 1. II_4), therefore it is shown that between them there are typical differences in height, weight and their intelligence quotient (IQ), (Figure 5). In all three analyzed parameters, the normal karyotype gemel (IQ = 88, body height 120 cm, and 29 kg body weight) showed significant differences compared to the Down syndrome gemel (IQ = 63, body height 105 cm and 18 kg body weight).

Figure 5. *Gemelar girls, at age 7, have fairly large differences in their length and weight as well as and intelligence quotient. (A. Healthy daughter karyotype: 46, XX; B. Down syndrome daughter: 46, XX, der (14; 21) (q10; q10),+21 mat).*

In other words, the Down syndrome child had stagnated in length for 15 cm, weight for 11 kg, and in IQ for 25 units, compared to normal gemel.

Since the mother was at high risk of giving birth to another child with Down syndrome, she has been suggested that in any future pregnancy she should make prenatal cytogenetics diagnosis of her embryos, and through it unbalanced karyotype of embryo was found in her two next pregnancies: 46, XY, der (14; 21) (q10; q10),+21 mat., characteristic for Down syndrome (Figure 1: II_7 and II_8), and they were terminated by artificial abortion. The last pregnancy embryo (Figure 1. II_9) has normal karyotype and pregnancy is still ongoing.

In order to determine the differences in dermatoglyphics between people with normal, balanced and unbalanced karyotype, we performed several qualitative and quantitative dermatoglyphics analysis in all family members (Table 1, 2, and 3). Significant differences in qualitative and quantitative dermatoglyphics patterns were observed in the child with Down syndrome compared to the normal population, as the following:

- Ulnar loops present on all fingertips of both hands (Table 1).
- Simian crease present on the palms of both hands.
- Distal loop on the third inter digital area was present on both palms of hands.
- There were less epidermal ridges on the fingers of hands compared to other family members (Table 2).
- The amount of "atd" angle in right and left hands was

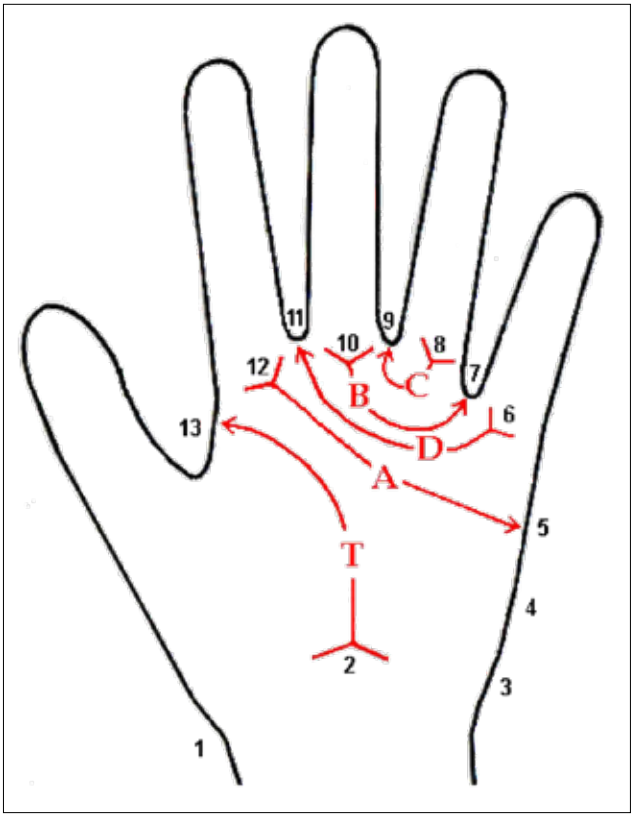

Figure 6. *Terminations of the main lines (A, B, C, D and T) of the child with Down syndrome and of silent Robertsonian translocation carrier 14q;21q.*

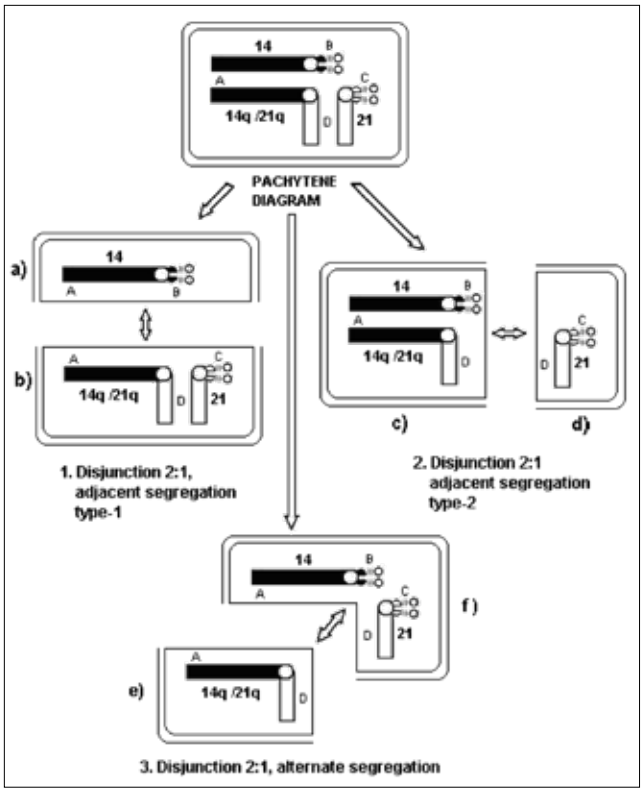

Figure 7. *Chromosomal disjunction and segregation during meiosis (in gametogenesis) in the Robertsonian translocation 14q;21q silent carrier: a) Nullisomic gamete of chromosome 21; b) Disomic gamete of chromosome 21; c) Disomic gamete of chromosome 14 ; d) Nullisomic gamete of chromosome 14 ; e) Balanced gamete with Robertsonian translocation 14q;21q ; and f) Normal gamete with a normal chromosome 14 and 21 .*

No	Studied	Hand	Dermatoglyphic patterns on the fingers of both hands				
			I	II	III	IV	V
	Father (I.Q.) (normal)	Right	W	W	W	W	UL
		Left	W	UL	W	W	UL
	Mother (V.Q.) (RT carrier)	Right	UL	UL	W	UL	UL
		Left	UL	UL	UL	UL	UL
	Child (V.Q.) (RT carrier)	Right	W	RL	W	W	UL
		Left	W	W	W	UL	UL
	Child (B.Q.) (normal)	Right	UL	UL	UL	UL	UL
		Left	UL	RL	UL	UL	UL
	Child (B.Q.) (normal gemel)	Right	W	RL	W	W	UL
		Left	UL	UL	UL	UL	UL
	Child (A.Q.) (Down syndrome gemel)	Right	UL	UL	UL	UL	UL
		Left	UL	UL	UL	UL	UL
	A–Arch						
	L–Loop						
	UL–Ulnar Loop						
	RL–Radial Loop						
	W–Whorl						

Table 1. *Dermatoglyphics traits on the fingers of hands of individuals, belonging to the family affected by Robertsonian translocation 14q;21q.*

No.	Studied	Hand	Number of epidermal ridges on fingers of hands				
			l	ll	lll	IV	V
	Father (I.Q)	Right	20	15	17	16	14
	(Normal)	Left	22	13	14	15	15
1		X	21	14	15.5	15.5	14.5
2	**Mother (V.Q.)** (RT carrier)	Right	20	15	15	16	14
		Left	17	15	17	18	15
		X	18.5	15	16	17	14.5
3	**Child (V.Q.)** (RT carrier)	Right	23	11	13	14	10
		Left	18	11	15	16	12
		X	20.5	11	14	15	11
	Child (B.Q.)	Right	20	4	9	16	8
	(Normal)	Left	14	6	10	13	7
4		X	17	5	9.5	14.5	7.5
5	**Child (B.Q.)** (Normal gemel)	Right	22	14	14	16	13
		Left	11	11	12	17	14
		X	16.5	12.5	13	16.5	13.5
6	**Child (A.Q.)** (Down syndrome gemel)	Right	23	12	15	15	6
		Left	24	13	13	14	6
		X	23.5	12.5	14	14.5	6

Table.2. The *number of epidermal ridges on the fingers of hands in family member individuals affected by Robertsonian translocation 14q; 21q.*

184°, approximately two times greater than in the hands of other family members (Table 3).

- All main lines (A, B, C, D, T) end symmetrically in the same places on the palms
- of the right and left hands. Main line A ends in 5, line B in 7, line C in 9, line D in 11 and T line in 13 (Figure 6).
- The RT silent carriers have some dermatoglyphics patterns related to those of Down syndrome. Those patterns include:
- The mother carrier of translocation has ulnar loop present on 9 fingers of her hands, whereas her daughter translocation carrier had ulnar loop present only on 3 fingers (Table 1).
- Simian crease was present on the palms of both hands of the translocation silent carrier.
- The amount of "atd" angles on right and left hands of mother RT carrier was 100°, whereas of her carrier doughier it was 86° (Table 3).
- Presence of distal loop on the third inter digital area on both palms of hands of RT translocation carriers

Nr.	Patterns (dermato-glyphics variables)	Hand	Father (I.Q.) (Normal)	Mother V.Q.) (RT carrier)	Child (V.Q.) (RT carrier)	Child (B.Q.) (Normal)	Child (B.Q.) (first gemel)	Child (A.Q.) (second gemel)
1	TFRC*		161	162	143	107	144	141
2	a-b rc	Right	33	36	36	40	35	37
		Left	30	36	32	33	37	33
		X	31,5	36	34	36,5	36	35
3	b-c rc	Right	26	34	26	32	31	20
		Left	26	35	27	32	25	23
		X	26	34,5	26,5	32	28	21,5
4	c-d rc	Right	38	40	33	40	36	35
		Left	41	37	34	35	37	36
		X	39,5	38,5	33,5	37,5	36,5	35,5
5	TPRC**		194	218	188	212	201	184
6	Angle atd	Right	43°	51°	43°	46°	53°	95°
		Left	42°	49°	43°	45°	55°	89°
		X	42.5°	50°	43°	45,5°	54°	92°
		ATDT ***	85°	100°	86°	91°	108°	184°

*** TFRC**- Total Finger Ridge Count

**** TPRC**- Total Palmar Ridge Count

*****ATDT**-atd Right+atd Left

Table 3. *The quantitative dermatoglyphic patterns on the palms of hands of family member individuals affected by Robertsonian translocation 14q;21q.*

On the mother and the daughter carrying translocation, all of their main lines (A, B, C, D, T) end symmetrically in the same places on the palms of right and left hands. Main line A ends in 5, B in 7, C in 9, D in 11, and line T ends in 13(Fig. 6).

5. DISCUSSION

The real reproductive condition of our presented case shows all possible reproductive health effects of RT 14q;21q in reproductive abilities of the carrier and in this respect our results are consistent with the results presented by other authors (14).

As presented in our paper, the genetic mechanism of offspring formation with trisomy involving translocated chromosome 21, of silent carrier offspring with RT 14q;21q and of normal offspring can be clarified through meiotic disjunction of chromosomes during gametogenesis of the RT 14q;21q silent carrier. During the anaphase, chromosomes that have formed the pachyten diagram got separated and they moved forwards the opposite poles of a cell (Figure 7). In the RT 14q;21q silent carrier, there are three possibilities of disjunction and movement of chromosome during gametes formation process:

- Disjunction 2:1, adjacent segregation type - 1;

- Disjunction 2:1, adjacent segregation type - 2;
- Disjunction 2:1, alternate segregation.

As a result of these disjunctions, the silent female carrier of 14q;21q RT may produce six types of gametes (Figure 7). After fertilization of these gametes by normal partner gametes, 6 types of embryos with different chromosomal constitution can be created. Three out of six types of embryos can continue embryo developing, be given birth to and live, whereas other embryos types are incompatible with intrauterine life which is also presented in our case report.

Joining of gamete with disomy in chromosome 21 (Figure 6) with normal gamete of the normal partner results in formation of embryo with Down syndrome and of two embryos with trisomy in chromosome 21 by the mother silent carrier for 14q;21q RT (Figure 1. II_5, II_7 dhe II_8). Joining of balanced gamete 14q21q (Figure 6) with normal gamete of a normal partner results in having silent carrier offspring (daughter) with RT 14q;21q, like child's mother is.

Finally, joining of normal gametes (Figure 6) with normal gametes of normal partner genetically and phenotypically normal offspring will be produced.

Three other embryos types have chromosomal constitution incompatible with intrauterine life; therefore they are lost by spontaneous miscarriages.

This study also confirms that silent carriers of RT 14q;21q have increased risk for spontaneous miscarriage and approximately 12-15% chances of giving birth to a child with Down syndrome.

Many authors have shown relation between dermatoglyphics and some chromosomal diseases (15, 16). Dermatoglyphics pattern may serve as screening diagnostic manner of identify suspicious patients (suspects) possible for having Down syndrome which then can be verified by cytogenetics analysis (17). Dermatoglyphics studies of people affected with RT have showed that typical dermatoglyphics patterns present in Down syndrome are also observed in two thirds (2/3) of 15q;21q RT silent carriers (10).

In our study in both RT 14q;21q silent carrier cases, we also found several dermatoglyphics patterns that are characteristic for Down syndrome.

Based on our and others authors study results, we conclude that dermatoglyphics method can be used as screening method for silent carriers detection of RTs 13q;21q, 14q;21q and 15q; 21q in the general population and then it can be verified by cytogenetics analyses.

6. CONCLUSION

After chromosomal and dermatoglyphics analyses of the family presented in our study the conclusions are as follows:

- A women carrying silent RT 14q;21q has high risk (12-15%) for having a child with Down syndrome.
- A Down syndrome child born in this family and two other trisomy 21 foetuses detected through prenatal diagnosis in the same family case studied were a result of gamete formation with disomy in chromosome 21 because of chromosome adjacent-1 segregation due to the segregations of maternal translocated chromosomes (14q;21q) during meiosis and forming zygotes by joining of these gamete with a normal gamete of other partner.
- The daughter carrying silent RT 14q;21q was as a result of gamete formation (in her mother) with balanced translocation 14q;21q due to alternate chromosome segregation during meiosis in her RT 14q;21q silent carrier mother and by union of these gamete with a normal gamete of her father.
- Robertsonian translocation 14q;21q silent carriers have several dermatoglyphics patterns typical for Down syndrome, and can be used in RT 14q;21q silent carriers detection in the general population.

CONFLICT OF INTERESTS: NONE DECLARED.

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