CHROMOSOMAL ABNORMALITIES IN COUPLES WITH TWO OR MORE MISCARRIAGES

Tran Thi Thuy Trang, Ha Thi Minh Thi
Hue University of Medicine and Pharmacy, Vietnam

Abstract

Background: Couples with two and more miscarriages are at increased risk of carrying a chromosomal abnormality, especially a structural chromosome abnormality with balanced karyotype. This study is aimed at (1) Determining the incidence of chromosomal abnormalities in couples with two and more miscarriages and (2) Assessing the relationship between chromosomal abnormalities and some features of miscarriage. **Patients and methods:** One hundred and twenty couples with two and more miscarriages were enrolled for karyotyping. **Results:** The incidence of chromosomal abnormality in couples with two or more miscarriage was found in 5%. Chromosomal abnormalities were reciprocal translocation 50%, Robertsonian translocation 16.7%, inversion 16.7% and numerical abnormalities of sex chromosome 16.7%. The rate of having family history on two and more miscarriage in the group of abnormal chromosome was 75%, but it is only 3.9% in the normal group, $p < 0.0001$. In the group of abnormal chromosome, the rate of 8-12 weeks gestation was the highest, 75%, and only 40% in the normal group, $p = 0.0173$. **Conclusion:** The rate of reciprocal translocation was the highest among chromosomal abnormalities. There was a relationship between chromosomal abnormalities and family history, and gestation.

Key words: Chromosomal abnormalities, miscarriage

1. BACKGROUND

The miscarriage is the common complication of pregnancy in the first trimester. The prevalence of miscarriage is found in 15% among pregnant women. Couples with two and more miscarriages are at increased risk of carrying a chromosomal abnormality, especially a structural chromosome abnormality with balanced karyotype. The incidence of carrier status (Robertsonian translocation, inversion, insertion, reciprocal translocation…) was found in 2.8-5.5% in couples with multiple miscarriages [2], [3], [6, [8]. These couples still have the normal phenotype, but they have high risk of having children with congenital defect or recurrent miscarriages. So detecting chromosomal abnormalities in these couples is the base in order to orient prenatal diagnosis, apply assisted reproductive technology and genetic counseling for improving life quality [1].

Karyotyping technique is only developmented in some health centers in Vietnam, so there are still few researches on chromosomal abnormalities in couples with multiple miscarriages, especially there is no study in Central Vietnam. So this study is aimed at (1) Determining the incidence of chromosomal abnormalities in couples with two and more miscarriages and (2) Assessing the relationship between chromosomal abnormalities and some features of miscarriage.

2. PATIENTS AND METHOD

2.1. Patients

One hundred and twenty couples with two and more miscarriages were enrolled for karyotyping in Department of Medical Genetics, Hue University of Medicine and Pharmacy and Lab of Genetics and Immunology, Hue Central Hospital from 2009 to 2011.

- Corresponding author: Ha Thi Minh Thi, email: haminhthi@gmail.com
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Criteria of exclusion : miscarriages having known causes (medical diseases such as diabetes, heart disease, renal disease…, autoimmune disease, infectious and toxic disease, abnormal uterus, Rh factor, stress, accidence…)

2.2. Methods

Study design: cross-sectional study.

Diagnostic criteria of miscarriage: The spontaneous loss of a fetus before the 20th week of pregnancy or the fetus weight less than 500 gram.

Karyotyping method: Lymphocytes from peripheral blood (anticoagulant by heparine) were cultured in PB-MAX medium (Gibco), then arresting the mitotic cells in metaphase by colcemid. Harvesting cells in metaphase at 72th hour. Making the chromosome slides and G banding. For each patient, 100 metaphases were analyzed according to ISCN 2005.

3. RESULTS

3.1. Chromosomal abnormalities in couples with two and more miscarriages

Table 3.1. The incidence of chromosomal abnormalities

Groups	Number of abnormality	%	p
Wives (n = 120)	3	2.5	p = 0.3894
Husbands (n = 120)	9	7.5	
Sum (n = 240)	12	5	

No significant difference between rates of chromosomal abnormality in wives and in husbands was found. The total incidence of chromosomal abnormality was found in 5%.

Table 3.2. Abnormal karyotypes

Types	Karyotypes	Number	%
Reciprocal translocation	46,XY,t(12;13)	1	50
	46,XY,t(13;20)	1	
	46,XY,t(7;8)	1	
	46,XY,t(5;6)(q33;q15)	1	
	46,XY,t(12;18)(q62;p11.2)	1	
	46,XY,t(2;19)(p16;p12),t(3;7)(q13;q36)	1	
Robertsonian translocation	45,XX,rob(21;21)(q10;q10)	1	16.7
	45,XY,rob(13;14)(q10;q10)	1	
Inversion	46,XY,inv(9)(p11;q12)	2	16.7
Numerical abnormalities of sex chromosome	47,XYY	1	16.7
	47,XXY/46,XY	1	
Sum		12	100

3.2. The relationship between chromosomal abnormalities and some features of miscarriage

Table 3.3. Distribution of chromosomal abnormality in some features of miscarriage

Features		Normal karyotype		Abnormal karyotype		p
Number		%	Number	%	Number	
Number of miscarriage	2 times	139	60.9	5	41.7	$\chi^2 = 1.056$ p = 0.3041
	≥ 3 times	89	39.1	7	58.3	
Family history on two and more miscarriage (*)	No	219	96,1	3	25	$\chi^2 = 73.543$ **p < 0.0001**
	Yes	9	3.9	9	75	
History of abnormal pregnancy	No	60	26.3	4	33.3	$\chi^2 = 0.04$ p = 0.8418
	Yes	168	73.7	8	66.7	
Gestation	< 8 weeks	115	50.4	1	8.3	$\chi^2 = 8.111$ **p = 0.0173**
	8-12 weeks	91	40	9	75	
	> 12 weeks	22	9.6	2	16.7	
Sum		228		12		

NB: (*) including mother, aunts, sisters, sisters in-law, aunts in-law.

4. DISCUSSION

4.1. Chromosomal abnormalities in couples with two and more miscarriages

The result in the table 3.1 showed a total of 12 persons having chromosomal abnormalities (5%).

Table 4.1. Comparison the incidence of chromosomal abnormalities with other studies

Studies	%	p
Our study (n = 240)	5	
Phung Nhu Toan (n = 430)[4]	4.2	p = 0.1 > 0,05
Brumberg (n = 206)[6]	7.4	p = 0.3 > 0,05
Ward (n = 200)[15]	9.3	p = 0.16 > 0,05

No significant different in incidences of chromosomal abnormalities between our study and other authors.

Table 4.2. Distribution of husband/ wife among persons having chromosomal abnormalities

Studies	Husband	Wife	Compare to our study
Our study	9	3	
Phung Nhu Toan [4]	4	14	**p = 0.0131**
Nguyen Van Ha [2]	5	4	p = 0.64
Niroumanesh [13]	5	8	p = 0.1511

The distribution of husband/wife in our study was similar to the results of Nguyen Nhu Ha, Niroumanesh, but different to Phung Nhu Toan.

In general, most studies have found no significant different between husbands and wives. This results had a very important meaning in genetic counseling for couples with recurrent miscarriages, avoiding the attitude of focusing the reason to the wives.

Table 3.2 showed the rate of reciprocal translocations was the highest (50%). This result was similar to results of others such as Phung Nhu Toan (77.8%) [4], Franssen (62%) [9] and Goddijn (63.4%) [10]. The rate of Robertsonian translocation in our study was 16.7%, it was similar to results of Franssen (22.2%) [4] and Goddijn (16%) [10].

However, some authors announed rates different to ours, such as Nguyen Van Ha (the rate of Robertsonian translocation was the highest, 88.9%) [2], Niroumanesh (reciprocal translocation 30.8%, Robertsonian translocation 23%, inversion 30.7%) [13].

All of structural chromosome abnormalities in our study were balanced. These persons have a normal phenotype but they can produce gametes with unbalanced karyotype. For each type of chromosomal abnormality, we have compatible genetic counseling [5], [11].

For reciprocal translocations and Robertsonian translocation rob(13;14), there are three cases:

- Their gamete carries a normal karyotype: fetus is normal in both karyotype and phenotype.

- Their gamete carries a balanced karyotype: fetus is normal in phenotype but has translocation similar to father/mother.

- Their gamete carries an unbalanced karyotype: fetus is abnormal in both karyotype (partial trisomy and partial monosomy) and phenotype (miscarriage or the child with congenital defects)

Many authors studied on F1 generation of couples with reciprocal translocation and showed that the rate of having children with unbalanced karyotype was 11.8% [7]. Neri also announced that the incidence of miscarriage in couples with reciprocal translocation was 50% [12]. About Robertsonian translocation rob(13;14), the risk of having a child with trisomy 13 was 1% [14].

The reciprocal translocations 46,XY,t(2;19)(p16;p12),t(3,7)(q13;q36) in our study is a very rare case, this is a translocation between two pairs of chromosome (2 and 9, 3 and 7). The risk of miscarriage or having children with congenital defects is very high.

We also found a rare Robertsonian translocation, 45,XX,rob(21;21)(q10;q10). This woman never has a normal child, because her gametes either have one Robertsonian chromosome between two chromosome 21 or have no chromosome 21. So she has either miscarriages or children with Down syndrom. Some studies in Europe showed that the rate of having children with Down syndrome in carriers with rob(21;21) was 3%, and the rate of miscarriage was 97% [8].

In this study, we found 2 cases of inversion of chromosome 9, inv(9)(p11;q12). The segment of chromosome 9 from p11 to q12 belongs to polymorphism area. In the past, scientists thought it was not a cause of miscarriage, but now this outlook is changed. This inversion of chromosome 9 can cause repeated miscarriages. Some authors showed that carriers of inversion have the risk of miscarriage in 5.9% [11].

4.2. The relationship between chromosomal abnormalities and some features of miscarriage

We serveyed some features of miscarriage including number of miscarriage, family history on two and more miscarriage, history of abnormal pregnancy, gestation.

Table 3.3 showed that chromosomal abnormalities had a relationship with family history on two and more miscarriage. The rate of having family history on two and more miscarriage in the group of abnormal chromosome was 75%, but it is only 3.9% in the normal group, $p < 0,0001$. Studies of Fitzsimmons and Franssen found a relationship between family history on two and more miscarriage and chromosomal abnormalities, too [8], [9].

Table 3.3 showed the relationship between the gestation and chromosomal abnormalities, too. In the group of abnormal chromosome, the rate of 8-12 weeks gestation was the highest, 75%, while it was only 40% in the normal group, $p = 0,0173$.

Goddijn and Franseen found no significant difference between these rates, but the mean gestation in Goddijn's study was 9 weeks [10] and in Franseen's study was 9.4 weeks [9]. These mean gestations belong to our gestation period.

5. CONCLUSION

5.1. The incidence of chromosomal abnormality in couples with two or more miscarriage was found in 5%. Chromosomal abnormalities were reciprocal translocation 50%, Robertsonian translocation 16.7%, inversion 16.7% and numerical abnormalities of sex chromosome 16.7%.

5.2. A relationship was found between chromosomal abnormalities and family history on two and more miscarriage, and gestation.

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