REVIEW

Chromosomal abnormalities in recurrent miscarriages by conventional karyotyping analysis

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Abstract

Objectives: to describe the prevalence and types of chromosomal abnormalities in couples with recurrent miscarriage and products of conception.

Methods: electronic searches were performed in the PubMed/Medline database and in the Portal Regional da Biblioteca Virtual em Saúde/BVS (Regional Website of the Virtual Library in Health/BVS) using the descriptors "chromosomal abnormalities and abortions and prevalence". After applying the inclusion and exclusion criterias, 17 studies were selected.

Results: 11 studies were conducted in couples with recurrent miscarriage and six in products of conception. The main results of the couples with recurrent miscarriage were: the frequency of chromosomal abnormalities which varied from 1.23% to 12% and there was a predominance alteration of the chromosomal structures (reciprocal translocations, followed by Robertsonian). In products of conception, the results observed were: the frequency of chromosomal abnormality was above 50% in approximately 70% of the studies; there was a predominance alteration of the numerical chromosomal (trisomy - chromosomes 16, 18, 21 and 22, followed by polyploidy and monosomy X).

Conclusions: in summary, cytogenetic alterations represent an importante cause of pregnancy loss and its detection can help couples with genetic counseling. Therefore, the value of knowledge on the prevalence of cytogenetic abnormalities in miscarriage samples is unquestionable, once it is permitted a proper genetic counseling for the couple.

Key words *Miscarriage, Chromosome abnormalities, Cytogenetics, Genetic translocation, Genetic counseling*

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Introduction

Recurrent miscarriage (RM), also referred to as recurrent pregnancy loss (RPL) or habitual abortion (HA), is classically defined by Royal College of Obstetricians and Gynaecologists (RCOG) as the occurrence of three or more consecutive abortions prior to 20 weeks of gestation.[1] However, the American Society of Reproductive Medicine (ASRM) has recently redefined recurrent pregnancy loss as two or more abortions.[2,3]

The RM etiology may be multifactorial and about 40–60% of these patients are non-identifiable causes, in this case the condition is classified as idiopathic or unexplained RM.[4,5]

The main etiological factors related to RM are: 1) genetic abnormalities (parental chromosomal rearrangements and abnormal embryonic karyotypes); 2) endocrine abnormalities; 3) anatomical factors; 4) immune factors; 5) inherited thrombophilic disorders; 6) infective agents; 7) miscellaneous factors (lifestyle and environmental factors); and 8) new risk factors.[6-8]

A recent study described women with RM epidemiologic and obstetric characteristics and some risk factors were identified such as advanced age, consumption of alcoholic beverages and higher body mass index.[9] In this sense, lifestyle modifications should also be implemented to improve reproductive prognosis.[7]

Genetic factors, mainly chromosomal abnormalities, are the most common cause of early miscarriage (50–60%). The chromosomal abnormalities can be divided in two basic groups: numerical and structural abnormalities. These abnormalities can involve one or more autosomal chromosomes, sexual chromosomes and both simultaneously and are identified by using the conventional cytogenetic methods based on light microscopy.[4,5]

Conventional karyotyping is traditionally performed to elucidate the possible causes of fetal loss, indicanting if any chromosomal abnormality was responsible for the miscarriage. The use of the classic cytogenetic to assess the fetal karyotype of the miscarriage material is complicated because the sample may be contaminated by the maternal tissue and the associated risk of false negative results.[10] In addition, products of conception are characterized by a low sample quality that often leads to a cell culture failure.[11,12] In case of culture failure or maternal contamination, molecular techniques may contribute to detect additional chromosome abnormalities in these miscarriage samples in addition to standard karyotyping.[13]

A recent review also summarized a current knowledge on the genetic causes (karyotype abnormalities, recessive diseases carrier status, dominant diseases and thrombophilia) of the RM.[10] Genetic reasons may involve changes in the genetic embryonic/fetal or parental material. Therefore, genetic tests may be performed in both parents as well as in the miscarriage material (fetus or afterbirth).[10]

The presence of karyotype abnormalities in one of the parents is one of the most common known causes of RM. They are most commonly found as balanced rearrangements, i.e. abnormalities cause no clinical symptoms in carriers but possibly induce the production of abnormal reproductive cells containing abnormal amounts of genetic material.[10] In couples with RM, one partner – frequently is the woman - will have a genetically balanced structural chromosome rearranged being the most common balanced translocation (reciprocal followed by Robertsonian). The inversions are much rarer but are also associated to an increased risk of RM.[6]

In products of conception, at least 50% of all miscarriages are associated to numerical chromosome abnormalities - trisomy, polyploidy and monosomy X.[6] Therefore, genetic counselling is important when a genetic factor is identified.[6]

Others genetic factors, such as genetic polymorphisms may contribute for RM.[4,5] A recent systematic review and meta-analysis showed significant associations among RM and 53 genetic polymorphisms of 37 genes. The genetic variants of *HLA-G, IFNG, TNF, IL-6, IL-10, FII, FV, FXIII, ITGB3, MTR, MTHFR, PAI-1, NOS3, KDR, TP53, VEGFA, CYP17, CYP1A1, CYP2D6, ANXA5*, and XCI may serve as RM biological markers.[14] These genetic variants were associated to the immune response, thrombophilia, placental function and hormonal and detoxification system and may contribute to the RM pathogenesis.[15] Although significant associations have been found among many genetic variants and RM, further functional research is needed to establish its role as biomarkers and introduce it into a clinical practice routine.[15]

RM is an important reproductive health issue. Despite various etiologies have been identified, almost half of the cases remain unexplained. Regardless of the cause, a thorough follow-up with an important psychological support can help most couples achieve a successful birth.[7]

Faced with this, the objectives of this present study were to describe the prevalence and types of chromosomal abnormalities in couples with RMs and products of conception.

Methods

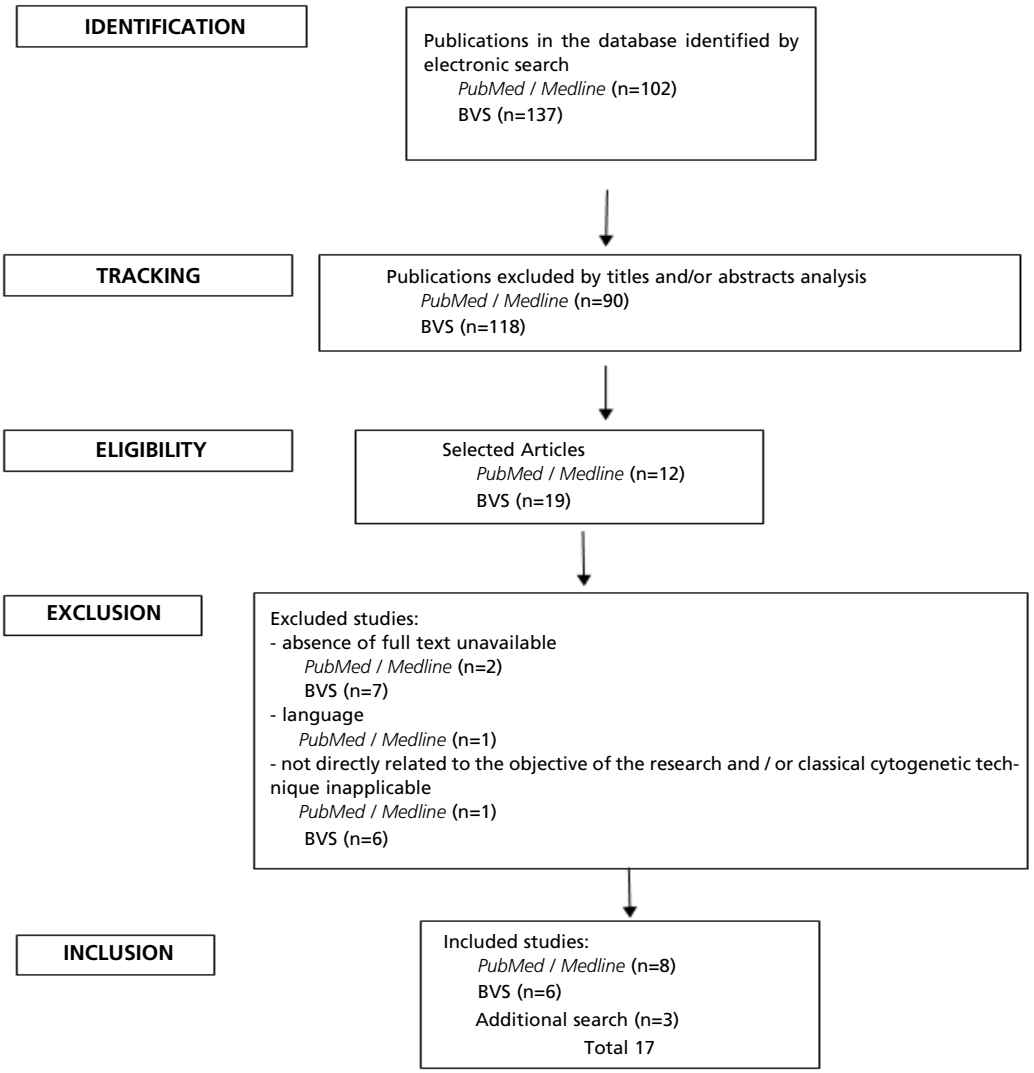
Electronic searches were performed in PubMed/Medline database (available at http://www.ncbi.nlm.nih.gov/pubmed) and in the *Portal Regional da Biblioteca Virtual em Saúde/BVS* (Regional Website of the Virtual Library in Health/BVS) (available at bvsalud.org), in June, 2017. What the descriptors used in both searches were: "*chromosomal abnormalities and abortions and prevalence*". The steps on the electronic search are presented in Figure 1.

The initial screening of the publications was based on the analyses of the titles and/or abstracts. The inclusion criteria were: research articles closely related to the objectives of this research, which used conventional cytogenetic techniques; those published in the last 10 years (that is, between 2007 and 2016), in English, Portuguese and Spanish, which were full text, entirely available and free of charge. The articles that did not fulfill the previous established criteria were excluded.

Conventional karyotyping is defined as the morphological characterization of an individual's

Figure 1

Flow chart illustrating the steps on the electronic search.



complement chromosomal, including number, form and size of the chromosomes. It can detect abnormalities in the entire genome and therefore is used as a standard to detect chromosome abnormalities in miscarriages samples.[13]

From the 102 and 137 articles identified in PubMed / Medline and BVS, eight and six were included, respectively. A further search was performed from the references of the articles identified in the investigated database and three articles[11,12,16] were included, a total of 17 scientific articles.

Results

From the 17 articles included in this literature review, 11 were carried out in couples with RM (Table 1) and six in products of conception (Table 2). The frequencies and types of chromosomal abnormalities in couples with RM and miscarriage material are shown in Tables 1 and 2, respectively.

Some studies have shown higher prevalence of chromosomal abnormalities in couples with larger number of miscarriages.[16,18] According to Ghazaey *et al.*[16] the highest percentage of chromosomal abnormalities was observed in couples with five or more RMs (4.7% - 1 RM, 11% - 2 RMs, 15% - 3 RMs, 15% - 4 RMs and 21.2% - ≥ 5 RMs). Another study showed that chromosome abnormalities were found in 5% of the couples with a history of two miscarriages, in 10.3% with three miscarriages and in 14.3% with four or more miscarriages.[18]

Table 1

Types and prevalence of chromosomal abnormalities in couples with RM.

Study	Sample	Types of chromosomal abnormalities	Prevalence
Ozawa *et al.*[17]	2324 couples had a history of two or more consecutive pregnancy loss	chromosome abnormalities: 114 couples 3.18% (74) reciprocal translocations, 0.99% (23) Robertsonian translocations (17 women, 0.73% and 6 men 0.26%), 0.43% (10) inversions and 0.39% (9) others 14 couples with normal variants (0.6%) and 81 with pericentric inversion 9 (3.49%)	4.91%
Kiss *et al*.[18]	108 couples with history of two or more RMs	chromosome abnormalities: 10 cases (5 women and 5 men) woman-man ratio 1:1 chromosomal analysis (normal results): 46,XX (n=100) and 46,XY (n=103) 5 structural alterations (30% of reciprocal translocation, 20% of Robertsonian translocation, 10% of chromosome inversion) and 5 numerical alterations (50% of mosaicism – sexual chromosomes) in one of the couples, the woman presented two concomitant alterations 3 polymorphisms (1.4%)	9.3%
Pal *et al.*[19]	56 couples who had two or more miscarriages	five couples - chromosomal abnormality in one partner 4 cases - structural alterations (60% reciprocal translocations - women and 20% Robertsonian D/D translocations - men) 1 case - numerical abnormality (20% mosaic of Down syndrome - men) 60% (n=3) occurred in women and 40% (n=2) in men woman-man ratio 1.5:1	8.9%

continue

RMs: recurrent miscarriages.

Table 1 **continued**

Types and prevalence of chromosomal abnormalities in couples with RM.

Study	Sample	Types of chromosomal abnormalities	Prevalence
Dutta *et al.*[20]	1162 couples with recurrent miscarriages	chromosomal anomalies: 78 cases 1.41% (33) structural abnormalities [more frequent: 21 cases of balanced reciprocal translocations and 6 cases of Robertsonian translocations) – women (18 cases) and men (9 cases)] 1.89% (44) polymorphic variants (chromosome 9) 0.05% (1) numerical anomaly (mosaic XY/XXY)	3.35%
Niroumanesh *et al.*[21]	100 couples with two or more miscarriages	chromosome abnormalities: 13 cases chromosomal abnormalities: 8% women and 5% men woman-man ratio 1.6/1 4 (30.8%) balanced reciprocal translocations 3 (23%) Robertsonian translocations (D and G groups) 3 (23%) pericentric inversions (chromosomes 7 and 9) 1 (7.7%) paracentric inversion (chromosome 16) 1 (7.7%) chromosomal marker 1 (7.7%) polymorphism 9qh+ (woman who had a history of eight miscarriages and one live birth) inv(9) – one couple with a similar chromosomal abnormality	12%
Saxena *et al*.[22]	955 couples with recurrent pregnancy loss	chromosomal abnormalities: 49 cases 63.3% (31) reciprocal translocations (18 women and 13 men), 20.4% (10) Robertsonian translocations (7 women and 3 men), 10.2% (5) inversions, 2.04% (1) derivative chromosome, 2.04% (1) aneuploidy sexual chromosome, 2.04% (1) marker chromosome	1.23%
Gonçalves *et al.*[23]	151 women and 94 partners (couples with two or more recurrent first trimester miscarriages)	chromosome abnormalities: 13 cases (11 women and 2 partners) women: 4.7% X-chromosome mosaicism (n=7), 2% reciprocal translocations (n=3) and 0.6% Robertsonian translocations (n=1) men: 1% X-chromosome mosaicism (n=1) and 1% inversions (n=1) 3.65% structural alterations (n=5) and 5.75% numerical alterations (n=8) normal variations in the chromosomes structure: 4.6% (women, n=7) and 6.4% (men, n=6), more frequent: 9qh+ (9 cases)	7.3% (woman) 2.1% (man)
Karatas *et al.*[24]	142 couples with recurrent miscarriage (≥2 pregnancy loss that occurred before the 20th gestational week)	chromosome abnormalities: 33 cases (14 women and 19 men) woman-man ratio 0.7:1 chromosomal analysis (normal results): 46,XX (n=128) and 46,XY (n=123) women: 9 polymorphisms (64.3%), 3 translocations (21.4%) and 2 trisomy X (14.3%) men: 19 polymorphisms (100%) 28 polymorphisms: more frequent 1qh+ (n=9), 9qh+ (n=4) and 16qh+ (n=3)	9.86% (woman) 13.4% (man)

continue

RMs: recurrent miscarriages.

Table 1 **concluded**

Types and prevalence of chromosomal abnormalities in couples with RM.

Study	Sample	Types of chromosomal abnormalities	Prevalence
Ghazaey *et al.*[16]	728 couples with history of miscarriages ranging from 1-7	chromosomal abnormalities: 85 (48 women and 37 men) woman-man ratio 1.3:1 43.5% (37) reciprocal translocations (24 women and 13 men) 9.4% (8) Robertsonian translocations (4 women and 4 men) 8.3% (7) inversions 8.3% (7) numerical abnormalities 52 structural and 7 numerical abnormalities 30.5% (26) polymorphic variants	11.7%
Fan *et al.*[25]	1948 couples with two or more recurrent miscarriages	chromosomal abnormalities: 58 cases (20 men – 34.5% and 38 women – 65.5%) women-men carriers ratio - approximately 2:1 types of structural chromosomal alterations: 72.4% (n=42) reciprocal translocations, 19% (n=11) Robertsonian translocations and 8.6% (n=5) pericentric inversions 42 reciprocal translocations (15 men – 35.7% and 27 women – 64.3% 11 Robertsonian translocations (3 men – 27.3% and 8 women – 72.3%) 5 inversions (2 men – 40% and 3 women – 60%)	2.98% (structural chromosomal alterations) (1.95% woman and 1.03% man)
Sudhir *et al.*[26]	440 couples with at least two consecutive miscarriages	chromosomal abnormalities: 15 cases 53.3% (8) reciprocal translocations, 6.7% (1) Robertsonian translocation, 20% (3) duplications and inversion and 20% (3) polymorphic variants percentage of cases carrying translocations: 78% men and 22% women (man: woman ratio 1.5:1)	3.41%

RMs: recurrent miscarriages.

Table 2

Types and prevalence of chromosomal abnormalities in products of conception.

Study	Sample	Types of chromosomal abnormalities	Prevalence
Teixeira *et al.*[11]	574 miscarriage materials and	Miscarriages 211 (36.76%) – no results 250 (43.55%) – normal karyotype 113 (19.69%) – abnormal karyotype [80 aneuploidias (monosomy X and trisomy 16), 23 euploidies and 10 structural alterations]	19.7% - miscarriages
	197 couples with RMs	Couples 15 (7.6%) - structural alterations in one of the partners (inversion of chromosome 9 and balanced translocations)	7.6% - couples
Rolnik *et al.*[12]	428 miscarriage materials (up to 12 weeks)	46 (10.7%) – there was no cell growth 145 (33.9%) – normal results 237 (55.4%) – abnormal results - more frequent: numerical abnormalities - trisomy 16 (17.3%), triploidy (11.3%), monosomy X (10.9%), tetraploidy (5.4%) and trisomy 15 (5.4%)	55.4%
López *et al.*[27]	120 miscarriage materials	46% (55/120) - normal karyotypes 54% (65/120) - abnormal karyotypes 52.3% (34) trisomy (32.3% - trisomy 16, 23.4% trisomy 22, 11.7% - trisomy 18, 8.8% - trisomy 13 and 5.8% - trisomy 21) 24.6% (16) polyploidy (50% - 69,XXX and 37.5% - 69,XXY) 13.9% (9) monosomy (45,X) 9.2% (6) mosaics	54%
Salazar *et al.*[28]	677 samples of the miscarriage tissues	38.3% (259/677) - normal karyotypes (158 – 46,XX and 101 – 46,XY) 61.7% (418/677) - abnormal karyotypes 63.4% (265) trisomies (34.4% - trisomy 16, 13.6% - trisomy 21 and 12.8% - trisomy 22) 19.8% (83) polyploidy 11.5% (48) monosomy (46 – monosomy X) 5.3% (22) structural abnormalities	61.7%
Boué *et al.*[29]	1498 miscarriages (embryo was less than 12 weeks)	38.5% (577) – normal karyotype 61.5% (921) – anormal karyotype 52% (479) - trisomy (chromosomes of D – n=109 and E groups – n=172) 19.9% (183) – triploidy 15.3% (141) – monosomy (45,X - n=140) 6.2% (57) – tetraploidy 3.8% (35) – translocations 1.7% (16) – double trisomy 1.1% (10) – mosaicism structural abnormalities – only 3.8%	61.5%
Bastos *et al.*[30]	333 recurrent miscarriages and 262 sporadic miscarriages)	(71 72.7% (242/333) - normal karyotype 27.3% (91/333) - abnormal karyotype 92.3% (84/91) numerical alterations, mainly trisomies (65.5%; 55/84); 30.9% (17) - trisomy 16, 21.8% (12) - trisomy 18 and 14.5% (8) trisomy 21 25% (21) - poliploidy 8.3% (7) - monosomy X 7.7% (7) – structural alterations	27.3%

RMs: recurrent miscarriages.

Discussion

RM continues to be a challenging reproductive problem for the patient and clinician. It is a traumatic event for couples and has psychological implications, primarily depression and anxiety, and interferes in the couples' relationship.[31-33] Identifying a cytogenetic cause for a miscarriage can be psychologically important to overcome grief and loss, as well as to decide whether or not to try again.[34]

All the studies included in this review employed the karyotype test, which is the most common technique of conventional cytogenetics. It is laborious technique and requires cell culture and the results can take 10 to 15 days. However, it can detect different types of chromosomal abnormalities. In couples with recurrent miscarriage, a lymphocyte culture was carried out from the peripheral blood, with analyses of approximately 20 to 30 metaphases. In case of miscarriage material, the tissue culture (chorionic villus) is used.

The frequency of chromosomal abnormalities among couples with RMs varied from 1.23% to 12% (Table 1). The results in this present study are similar to those conducted previously (Table 3).

There was a predominance of structural chromosomal abnormalities in couples with recurrent miscarriage.[16,17,19-22,24-26] These findings were in accordance with the literature.[34,35,40-44] Only in two studies had higher frequency of numerical chromosomal alterations[23] or the same percentage of numerical and structural alterations.[18]

Regarding to the type of the structural alteration, the most frequent ones were the reciprocal translocations, followed by the Robertsonians[16-23,25,26] as reported in the literature (Azim *et al.*[35] – 1.6% reciprocal translocations versus 0.6% Robertsonian translocations; Kochhar & Ghosh[42] – 5.9% reciprocal translocations versus 0.7% Robertsonian translocations; Sheth *et al.*[43] – 24.7% reciprocal translocations versus 17.64% Robertsonian translocations). In the reciprocal translocation there is an exchange of two terminal segments from different chromosomes. Robertsonian translocation involves two acrocentric chromosomes with the loss of short arms and their fusion by or near the centromere. Both reciprocal and Robertsonian translocations are balanced rearrangements, that is, individuals with these translocations do not present phenotypic alterations resulting from them. The existing risks are restricted to the offspring, because, depending on the segregation occurred during the gametogenesis there may be chromosomally unbalanced fetuses formation, consequently non-viable.[18] The translocations were more common in women compared to men.[16,17,19,20,22-25] The incidence of translocation is more in women than in men according to the literature.[42,43] Only one study showed that the percentagem of men (78%) carrying translocations was higher than in women (22%).[26] Therefore, the genetic counseling for couples with structural chromosomal abnormalities should consider the gender of the carriers.[25] According to some authors, as men translocations carriers demonstrate reduced fertility.[47,48] A possible explanation for this difference is that the chromosomal abnormalities such as in men carriers of autosomal reciprocal translocations may cause severe meiotic disorders and stoppage of spermatogenic, but the oogenesis usually is conserved and results in production of gametes with a high risk of presenting unbalanced chromosomal abnormalities.[47,48]

It is worth mentioning that most of the studies in Table 1 included the frequency of chromosomal abnormalities of those alterations considered variants of normality (polymorphisms).[16-18,20,21,23,24,26] The frequency of polymorphisms ranged from 0.6%[17] to 100%[24] (Table 1). However, some research has shown a possible association between polymorphic variants and infertility.[49-51] A recent study showed an increase in the frequency of polymorphic variants among infertile patients (19.4% in the study group vs. 13.4% in the control group; $p< 0.01$).[51]

Of the 17 studies included in this review, only six have assessed miscarriage material (Table 2). Two of them referred not having reached the results and the cell culture failure in the cytogenetic analysis (CA).[11,12] The CA of products of conception presents at least two main challenges, cell culture failure and excess of normal woman karyotypes related to maternal cell contamination. Although the CA of abortive material is highly recommended, alternative complementary techniques for CA such as Fluorescence in situ Hybridization / FISH,[52,53] Multiplex Ligation-dependent Probe Amplification / MLPA,[54] Quantitative fluorescent polymerase chain reaction / QF-PCR[55,56] and array Comparative Genomic Hybridization / CGH[57] have been used for genetic testing on miscarriage samples. These techniques do not require cell culture and have been proposed to optimize the genetic results in unsuccessful karyotype. A comparison of classic cytogenetics, molecular cytogenetics, and molecular biology techniques used for the examination of embryonic / fetal material is presented in two reviews, together with the advantages and disadvantages.[10,13]

Table 3

Frequencies of chromosomal abnormalities in previous studies.

Authors	Number of couples	Frequency of chromosomal abnormalities %
Azim *et al.*[35]	300	5.3
Rao *et al.*[36]	160	11.25
Celep *et al.*[34]	645	3.86
Elgehzal *et al.*[37]	1400	6.93
Yuce *et al.*[38]	421	3.68
Meza-Espinoza *et al.*[39]	542	5.7
Goud *et al.*[40]	380	6.84
El Dahtory *et al.*[41]	73	6.1
Kochhar & Ghosh[42]	788 individuals (including 367 couples)	6.8
Sheth *et al.*[43]	4859 individuals (2428 couples and three single mothers)	3.5
Alaraji[44]	61	9.83
Flynn *et al.*[45]	795	3.52
Turki *et al.*[46]	171	6.43

When the cytogenetic studies are successful, the newer techniques may have limited additional clinical use. However, when the tissue culture fails, the molecular techniques are very useful, although it is important to understand the limitations of each tool. In this manner, a combined approach using conventional and molecular methods will elucidate the cause of the miscarriage on almost all the samples. In a clinical setting this would be optimum.[58]

Chromosomal abnormalities in miscarriage material was found above 50% in approximately 70% of the studies.[12,27-29] A frequency of 61% of chromosome abnormalities in products of conception was detected by CA.[55] Other studies using cytogenetics found lower frequencies (33.24% and 48%) of chromosomal abnormalities.[56,59]

Two studies published in 2014 and 2017 employed CA and QF-PCR.[55,56] The first applied CA on 534 miscarriages, 73% (390/534) of them was successful. One hundred and forty-four miscarriages (27%, 144/534) did not grow in culture. A total of 27 cases were analysed by QF-PCR for chromosomes 13, 18, 21, X and Y and 30% (8 of 27 cases) showed a numerical chromosome abnormality by QF-PCR. Two hundred and thirty-seven cases (61%, 237/390) presented chromosomally alterated by CA.[55] The other was conducted in 884 products of conception, 204 of which were analyzed by cytogenetics and 680 by molecular biology based on QF-PCR.[56] Despite using different techniques, the abnormal results were similar (40% by QF-PCR and 48% by cytogenetics).[56] A recent study, using only conventional CA, with 457 products of conception showed that 382 cases were sucessfully karyotyped while 75 cases of cell culture failed (culture failure rate: 16.42%). Cytogenetic abnormalities were detected in 127 of the 382 cases (33.24%).[59]

Unlike the findings presented in Table 1, there was a predominance of numerical chromosomal alterations in the studies about miscarriage material.The frequency of numerical chromosomal alterations was higher than 92%,[28-30] reaching 100%[27] in four of the six studies presented in Table 2. On the other hand, the frequency of structural alterations was lower and ranged from 3.8% to 7.7%.[28-30] In all the studies in Table 2, the structural chromosomal abnormalities were little frequent in products of conception according to the literature.[55,59] When a structural chromosomal alteration is found in the miscarriage material, the karyotype of both parents should be done, in order to assess the inherited nature or the abnormality found in the pregnancy loss.[30]

In general, the trisomy was the most common chromosome abnormality detected in the miscarriage material, followed by polyploidy and monosomy X.[12,27-30] The most frequent trisomy was the 16 [11,12,27,28,30] and others trisomies, especially those involving chromosomes 18, 21 and 22 are also implicated in the miscarriage.[27,28,30] Autosomal trisomies were the predominant chromosomal abnormalities with a frequency of 48.8% (trisomy 16 – 12.6%; trisomy 22 – 7.9%; trisomy 21 – 5.5%; trisomy 13 – 3.1%; trisomy 10 – 3.1%), followed by

poliploidy (18.9% - triploidy and tetraploidy) and 45, X (16.5%). Structural chromossomal abnormalities were rare (9.5%).[59] Trisomy was also the most common chromosome abnormality detected in the miscarriage material, accounting for 63% (232 of 368), followed by polyploidy (18.8%; 69 of 368) and monosomy X (16.6%; 61 of 368).[56] The most frequent trisomy was the 16 (17.4%), followed by trisomy 22 (17.1%).[56] Another study[55] showed that: (1) trisomy was the most common chromosome abnormality and accounted for 53% (125/237) of the abnormal karyotypes; (2) chromosomes 16, 22, 15 and 21 were most frequently involved in the aneuploidies; (3) fifty-four cases (23%, 54/237) with a polyploidy and 7% (16 cases) of monosomy X were also found and (4) individual unbalanced structural chromosome abnormality represented 4% (10/237) of the abnormal karyotypes.[55] Russo *et al.*[53] applied FISH in the interphase of 855 formalin-fixed paraffin embedded miscarriage materials and the aneuploidy rate was detected at 50.3%. The most frequent chromosomal abnormalities were: autosomal trisomies (60%), polyploidies (23.2%), and monosomy X (14%). Among the autosomal trisomies, chromosome 22 was the most frequently involved (33.7%) followed by trisomy of chromosomes 16 (23.3%), 21 (19.4%), 15 (13.3%), 18 (5.34%), and 13 (5.0%).[53]

Two studies[16,18] showed a higher prevalence of chromosomal abnormalities in couples with higher numbers of miscarriages. These findings corrobate previously published data,[41] that was observed in (2/27) = 7.4% of the couples with a history of two miscarriages, in (3/23)=13% with three miscarriages and in (4/23)=17.39% with four or more miscarriages.[41] On the other hand, other studies showed that the prevalence of chromosomal abnormalities does not appear to be related to the number of miscarriages.[37,42]

The present findings also confirm that the chromosomal analysis in couples with RM are an important and necessary part of the etiological investigation in fetal loss. For this sense, it is essential that gynecologists/obstetricians refer to CA couples who had 2 or more recurrent miscarriages in order to confirm or exclude the contribution of chromosomal abnormalities. When a chromosomal abnormality is found in one of the partners and is precisely identified, a more exact prognosis for future pregnancies can be given. The genetic counselling with an option of prenatal diagnosis should be offered to couples with chromosomal abnormalities.[22]

Conclusions

According to the data presented, it can conclude that: (1) chromosomal abnormalities, primarily balanced rearrangements are common in couples with RM; (2) the most common parental abnormalities are the balanced translocations; (3) the most frequent autosomal abnormality observed in products of conception is trisomy 16, followed by other autossomal aneuploidies.

In summary, the cytogenetic alterations represent one of the major cause of pregnancy loss and its detection helps the couple with genetic counseling. Therefore, the value of knowledge on the prevalence of cytogenetic abnormalities in miscarriage samples is unquestionable since it permits the couple for a proper genetic counseling. In addition, researches in miscarriage material, it is appropriate the inclusion of other molecular techniques as a complementation to the conventional CA.

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