AUCTORES
Globalize your Research

Journal of Women Health Care and Issues

Nazdar Raouf *

Open Access

Research Article

Chromosomal Analysis of Pregnancy Tissue from Women with Recurrent Early Pregnancy Loss

Nazdar Raouf [1]*, Hameed Rekani [1], Marwan Zaki [2]

[1] Neonatal Intensive Care Unit/ Hive Pediatrics Teaching Hospital / Duhok, Iraqi Kurdistan

[2] College of science/department of biology

***Corresponding Author:** Nazdar Raouf, Obstetrics and Gynecology Department/ Duhok Obstetrics and Gynecology Teaching Hospital/ Iraqi Kurdistan

Received date: March 09, 2023; **Accepted date:** March 27, 2023; **Published date:** April 04, 2023

Citation: Nazdar Raouf Hameed Rekani, Marwan Zaki (2023), Chromosomal Analysis of Pregnancy Tissue from Women with Recurrent Early Pregnancy Loss, J. *Women Health Care and Issues.* 6(3); DOI:10.31579/2642-9756/145

Abstract

Purpose: This study aimed to determine the cytogenetical distribution of chromosomal disorders in couples after recurrent early pregnancy loss.

Background: One of the most important causes of pregnancy loss found in around half of the first trimester miscarriages is fetal chromosomal abnormalities, the role of fetal chromosomal disorders needs to be better evaluated.

Method: This study was conducted at two hospital and private clinics in Duhok, Iraqi Kurdistan from February 2017 to February 2022, and reviewed retrospectively the study included 150 patients with history of Recurrent Early Pregnancy Loss were admitted for curettage because of miscarriage in early pregnancy Patients were divided in two group.

Results: The study population included a total of 150 fetal tissue specimens obtained during dilation and curettage after the diagnosis of spontaneous miscarriage. Patients were divided in two groups. Group 1 included 95patients with an abnormal embryonic karyotype in the aborted material. Group 2 comprised 55 patients with a normal embryonic karyotype in the aborted products. Patients with a normal embryonic karyotype in the aborted products were significantly younger (p=0.0147).

Conclusion: Young patients suffering from repeated miscarriages have a low probability to find chromosomal disorders the embryonic tissue. Chromosomal analysis should be offered after previous miscarriages before further diagnostic methods are performed.

Key words: chromosomal analysis; recurrent pregnancy loss; pregnancy rate ; pregnancy tissue

Introduction

The normal diploid number of chromosomes in humans is 46. There are 23 pairs of chromosomes with 22 pairs of autosomes and two sex chromosomes, the X and the Y. Human females have two X chromosomes (46,XX), while males have one X and one Y chromosome (46,XY) .The chromosomal aberration or mutation is the process of change in the chromosomes take place either due to the changes in the structure of the chromosomes or due to the abnormality in the chromosome number [1].Aneuploidy, gain or loss of an individual chromosome, is more common, while Polyploidy is the gain of one or more complete set of haploid chromosomes such as (69,XXY). Abnormality of chromosomal structure as shown in figure 1 and 2**,** comprise those changes that are due to one or more breaks in a chromosome. Following a break, the separated fragments are likely to participate in chromosomal rearrangements. Structural chromosomal changes can result in a displacement of chromosomal regions without any loss or duplication of genetic material such as (balanced rearrangements) or they may be unbalanced. This can take several forms: Deletions: A portion of the chromosome is missing or has been deleted, Duplications: A portion of the chromosome has been duplicated, resulting in extra genetic material, Inversions: A portion of the chromosome has broken off, turned upside down, and reattached, therefore the genetic material is inverted, Insertions: A portion of one chromosome has been deleted from its normal place and inserted into another chromosome, Translocations: A portion of one chromosome has been transferred to another chromosome. There are two main types of translocations: Reciprocal translocation: Segments from two different chromosomes have been exchanged. Robertsonian translocation: An entire chromosome has attached to another at the centromere - in humans, these only occur with chromosomes 13, 14, 15, 21, and 22.Rings: A portion of a chromosome has broken off and formed a circle or ring. This can happen with or without the loss of genetic material. Isochromosome: Formed by the mirror image copy of a chromosome segment including the centromere [2].

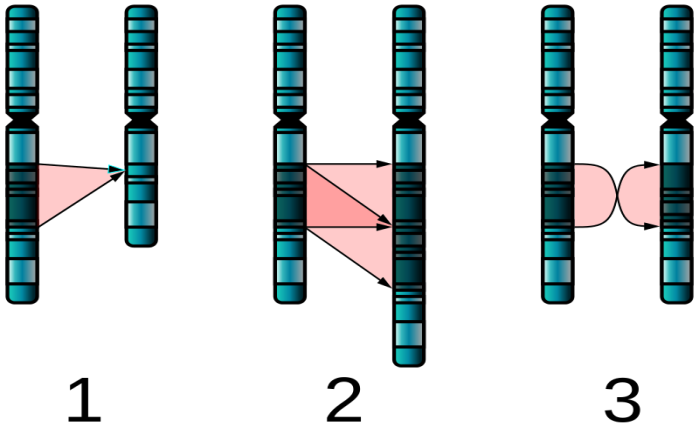

Figure 1: The three major single-chromosome mutations: deletion (1), duplication (2) and inversion (3).

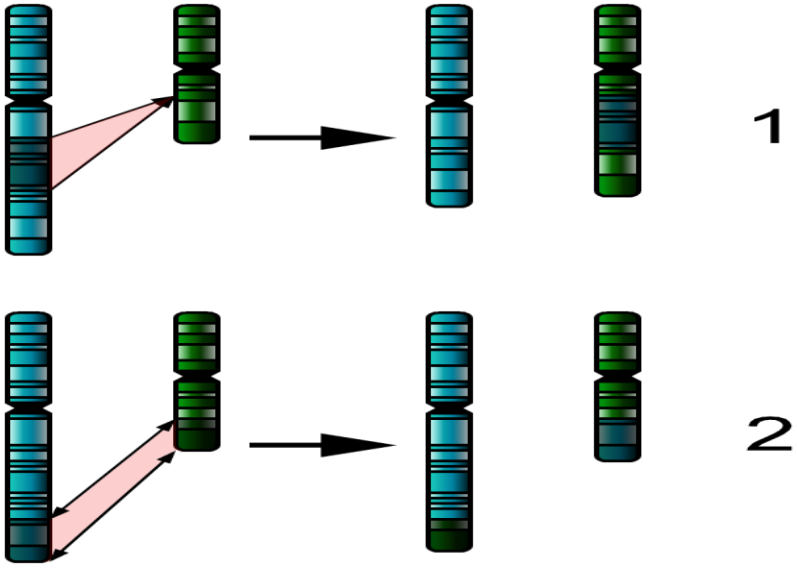

Figure 2: The two major two-chromosome mutations: insertion (1) and translocation **(2).**

Chromosomal mutations lead to abnormalities in the function of the cell and organism, as congenital anomalies, growth deficiency, and intellectual disability are findings often present in individuals with chromosome abnormalities, although some cytogenetic aberrations have little to no clinical effect.Genetic abnormalities of the conceptus are a recognized cause of sporadic and recurrent pregnancy loss (RPL).Cytogenetic abnormalities are more common in spontaneous abortions (50 percent of fetal deaths <20 weeks) than in stillbirths (6 to 13 percent of fetal deaths ≥20 weeks) [3]. It is possible to ascertain whether an early pregnancy loss is due to a genetically abnormal embryo or fetus (aneuploidy) by analyzing the pregnancy or fetal tissue [4]. Published studies have used a variety of genetic techniques (conventional karyotyping, fluorescence *in situ* hybridization [FISH], or array–based comparative genomic hybridization [array-CGH]). Analysis by conventional karyotyping is limited by the failure of tissue culture and the fact that it does not distinguish between maternal contamination and a normal (euploid) female fetus [5]. FISH is limited as it only uses probes for certain chromosomes, and therefore does not necessarily detect the chromosomal cause of the miscarriage. Array CGH is a better technique, and currently preferred technique, looking at all chromosomes and avoiding the limitations associated with karyotype and [4,6].New techniques such as next generation sequencing (NGS) have not yet been extensively investigated in genetic analysis of pregnancy tissue but may be useful in the near future [7].Several authors have suggested a strategy of karyotyping the pregnancy tissue of the second miscarriage and only proceeding to further maternal investigations (for thrombophilia, thyroid dysfunction, uterine malformations) for the cause of the recurrent pregnancy loss if the result is euploid [8,9,10].Aneuploidy is a recognized cause of pregnancy loss, and the frequency of aneuploid early pregnancy losses increases with female age. Aneuploidies occur in comparable frequencies in both women with sporadic and recurrent pregnancy loss. Genetic analysis of pregnancy tissue has the benefit of providing the patient with a reason for the pregnancy loss and may help to determine whether further investigations or treatments are required,but it does not necessarily rule out other underlying conditions.

Methods

Design and Setting

This study was conducted at two hospital and private clinics in Duhok, Iraqi Kurdistan from February 2017 to February 2022, and reviewed retrospectively. the protocols used in the study were approved by the Committee of Scientific research unit of Duhok Obstetrics and Genecology Teaching Hospital. The written informed consent of all the participants was obtained. The study included 150 patients with history of Recurrent Pregnancy Loss were admitted for curettage because of miscarriage in early pregnancy Patients were divided in two groups. Group 1 included those patients with an abnormal embryonic karyotype in the aborted material.

Group 2 included those patients with a normal embryonic karyotype in the aborted products, both groupe were copares.The inclusion criteria included a sonographic presence of a gestational sac and the patient's consent to perform a chromosomal exam.Exclusion criteria were the couple who refuse the procedure Documented parameters included parity, , maternal age gestational age and cytogenetic results.Chromosomal analysis was done by array–based comparative genomic hybridization [array-CGH]) technique.

Statistical analysis

The data were collected and statistically analyzed using a software package, current versions IBM (SPSS) Statistic, descriptive statistics for nominal variables were interpreted as number and percentage(%),while quantitative variables were expressed as mean ± standard deviation. Student's t-test was applied to difference of mean of quantitative variables. Chi-square test was applied to study the difference of frequency. For interpretation of results, p value < 0.05 was considered significant.

Results

During the study period, from February 2017 to February 2022 there were women with history of recurrent pregnancy loss admitted for curettage because of miscarriage in early pregnancy 150 patient was offered a chromosomal examination with determination of the embryonic karyotype. The study population included a total of 150 fetal tissue specimens obtained during dilation and curettage after the diagnosis of spontaneous miscarriage. Patients were divided in two groups. Group 1 included 95patients with an abnormal embryonic karyotype in the aborted material. Group 2 comprised 55 patients with a normal embryonic karyotype in the aborted products.

Patients Characteristics

The characteristics of the patients with history of recurrent pregnancy loss are summarized in Table1.The mean age of patients from Group with abnormal karyotype were (32.24± 5.13) years old and those from Group with normal karyotype were (30.2±4.41), respectively. Patients with a normal embryonic karyotype in the aborted products were significantly younger (p =0.0147). Average parity in patients from Group with abnormal karyotype had 0.75 ± 0.84 while those from Group with normal karyotype were 0.6 ± 1.0 patients. The number of miscarriages in previous pregnancies from group with abnormal karyotypewere 0.34 ± 0.71,while in group with normal karyotypewere 0.46± 0.82, p = 0.3478 The average gestational age in group with abnormal karyotype was 10.43 weeks (± 2.1) comparable to the 10.06 weeks of gestation (± 2.2) found in group with normal karyotype.

CHARACTERISTICS OF PATIENTS	ABNORMAL KARYOTYPE GROUP (95)	NORMAL KARYOTYPE GROUP (55)	P VALUE
Maternal age (years)	32.24± 5.13	30.2±4.41	0.0147
Parity	0.75 ± 0.84	0.6 ± 1.0	0.3278
Number of miscarriages	0.34 ± 0.71	0.46± 0.82	0.3478
Gestational age (weeks)	10.43 weeks (± 2.1)	10.06 weeks(± 2.2)	0.3085

Data are presented as mean ± SD P < 0.05 = Significant, P < 0.001 highly significant

Table 1: Characteristics of patients recurrent pregnancy loss

Cytogenetic findings of the fetal tissue

The Cytogenetic findings of the fetal tissue in patients with history of recurrent pregnancy loss are summarized in Table 2.

Out of 150 aborted products, 55 showed normal karyotypes and 95 were abnormal. The most frequent abnormalities were numeric aberrations 90((94.7%)%)including.5(5.26%) cases showed structural aberrations only.

ABNORMAL KARYOTYPE GROUP	$N = 95$
Numeric aberrations	90(94.7%)
Trisomy 13	34(37.77%)
Trisomy 16	26(28.8%)

Table 2: Cytogenetic findings of the fetal tissue

Data are presented as number (percent)

Discussion

Recurrent pregnancy loss are disaster condition for many couples. Embryonic chromosomal disorders are a frequent cause of early miscarriages. Maternal age is a significant cause for chromosomal aberrations in aborted material. This has been clearly demonstrated in earlier literature as well [11, 12]. Increasing age is associated with a higher aneuploidy rate, especially trisomy risk. [13,14,15].Our finding accords the Scandinavian study of Roepke et al. [16] There are other pathologies like thrombophilia, thyroid dysfunction, parental genetics or uterine malformations which are related to recurrent pregnancy loss and should be taken into account [17]. Since chromosomal aberrations are the most leading cause of miscarriage, the genetic analysis of aborted material is quite indispensable in case of recurrent pregnancy loss, despite the high costs.

Conclusion

The findings of this study revealed that young patients suffering from repeated miscarriages have a low probability to find chromosomal disorders in the embryonic tissue. the effect of maternal age seems to overcome the impact of the abort recurrence itself. Chromosomal analysis should be offered after previous miscarriages before further diagnostic methods are performed.

Competing interests

There are no conflicts of interests to declare

Funding

There was no source of funding for this research.

Authors' contributions

'Not applicable' for that section

Acknowledgement

We would also like to thank all for providing assistance with the manuscript preparation. We also thank everyone involved in the collection and interpretation of data.

References

1. Feuk L, Carson AR, Scherer SW.(2016) Structural variation in the human genome. Nat Rev Genet 7:85.
2. Reddy UM, Page GP, Saade GR. (2012) The role of DNA microarrays in the evaluation of fetal death. Prenat Diagn 32:371.
3. Van den Berg MM, van Maarle MC, van Wely M, Goddijn M. (2012) Genetics of early miscarriage. *Biochim Biophys Acta*1822: 1951-1959
4. Mathur N, Triplett L, Stephenson MD. (2014) Miscarriage chromosome testing: utility of comparative genomic hybridization with reflex microsatellite analysis in preserved miscarriage tissue. *Fertil Steril* 101: 1349-1352.
5. Robberecht C, Schuddinck V, Fryns JP, Vermeesch JR. (2009) Diagnosis of miscarriages by molecular karyotyping: benefits and pitfalls. *Genet Med*;11: 646-654.
6. Kudesia R, Li M, Smith J, Patel A, Williams Z. (2014) Rescue karyotyping: a case series of array-based comparative genomic hybridization evaluation of archival conceptual tissue. *Reprod Biol Endocrinol*12: 19.
7. Shamseldin HE, Swaid A, Alkuraya FS. (2013)Lifting the lid on unborn lethal Mendelian phenotypes through exome sequencing. *Genet Med* 15: 307-309.
8. Bernardi LA, Plunkett BA, Stephenson MD. (2012)Is chromosome testing of the second miscarriage cost saving? A decision analysis of selective versus universal recurrent pregnancy loss evaluation. *Fertil Steril*;98: 156-161.
9. Foyouzi N, Cedars MI, Huddleston HG.(2012)Cost-effectiveness of cytogenetic evaluation of products of conception in the patient with a second pregnancy loss. *Fertil Steril* 98: 151-155.
10. Hogge WA, Byrnes AL, Lanasa MC, Surti U. *(*2003) The clinical use of karyotyping spontaneous abortions. *Am J Obstet Gynecol* 189: 397-400; discussion 400-392.
11. Franasiak JM, Forman EJ, Hong KH et al (2014) The nature of aneuploidy with increasing age of the female partner: a review of 15,169 consecutive trophectoderm biopsies evaluated with comprehensive chromosomal screening.
12. Stephenson MD (2002) Cytogenetic analysis of miscarriages from couples with recurrent miscarriage: a case-control study. Hum Reprod.
13. Cauchi MN, Pepperell R, Kloss M, Lim D (1991) Predictors of pregnancy success in repeated miscarriage. Am J Reprod Immunol 26:72–75.
14. Lund M, Kamper-Jørgensen M, Nielsen HS et al (2012) Prognosis for live birth in women with recurrent miscarriage: what is the best measure of success? Obstet Gynecol 119:37–43.
15. Grande M, Borrell A, Garcia-Posada R et al (2012) The effect of maternal age on chromosomal anomaly rate and spectrum in recurrent miscarriage. Hum Reprod 27:3109–3117.
16. Ogasawara M, Aoki K, Okada S, Suzumori K (2000) Embryonic karyotype of abortuses in relation to the number of previous miscarriages. Fertil Steril 73:300–304.
17. Pandey MK, Rani R, Agrawal S (2005) An update in recurrent spontaneous abortion. Arch Gynecol Obstet 272(2):95–108.

DOI: 10.31579/2642-9756/145