

# Cytogenetics of Fetal Wastage in Bahrain

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## ABSTRACT

A consecutive series of fifty couples with a history of fetal wastage was studied cytogenetically with current banding techniques. Fetal wastage was defined as occurring in couples who had more than two early abortions, still-birth(s) or live-birth(s) or both of infants with multiple congenital anomalies. One couple was found to be balanced reciprocal translocation carriers. One woman was found to have Robertsonian Translocation, another woman was found to be mosaic (46, XX, 47, XXX); and one husband was found to have pericentric inversion of Y chromosome.

We find that parental chromosome abnormalities account for fetal wastage in 8% of couples having such a history.

Cytogenetic studies have shown that numerical and structural chromosome aberrations are important aetiological factors in spontaneous abortions, in still-births and in live-births of infants with multiple anomalies.<sup>1,2,3</sup> A number of studies on spontaneous abortuses<sup>3</sup> have demonstrated that the incidence of chromosomal abnormalities in these abortuses is about 61.5%, most of the anomalies consist of de novo events occurring in the course of meiosis or in early mitotic division. Most chromosomal aberrations occurring in spontaneous abortuses are inheritable.

However, sometimes parents may be carriers for structural rearrangements that, by meiotic segregation, leads to unbalanced gametes and abnormal fetuses. The frequency of balanced structural rearrangements (translocations and inversions) in one parent varies according to sample and according to whether a couple has experienced abortions alone or both abortion and malformed infants. Among parents who have experienced abortions alone, pooled

data indicate that the frequency of translocations is 3.4% in females and 1.6% in males. Among parents who have experienced both abortions and still-born or an anomalous live-born infant, the frequency is 16.4% in females and 4.2% in males<sup>2</sup>. If a structural rearrangement is detected in either parent, subsequent pregnancies should be monitored. Most structural rearrangements are compatible with the production of normal gametes. However, this is not always true, and some women with such translocations should be advised to practice rigorous birth control or consider sterilization.

In order to determine the frequency and types of chromosome aberrations in couples with fetal wastage in Bahrain we designed this study.

## METHODS

During the period of four years 1985-1988 a consecutive series of 50 couples with history of two or more spontaneous abortions, still-birth(s) or live-birth(s) or both with multiple congenital anomalies was studied.

Most of the couples were referred by the obstetrician after other known causes of fetal wastage were ruled out. Blood samples were sent to cytogenetic laboratory in England, banded karyotypes were analysed to search for structural variations.

## RESULT

Results of cytogenetic studies were divided into two groups. Group A are couples with normal karyotype and Group B are couples with abnormal karyotype.

Table 1 classifies the couples according to the history of fetal wastage. We find that 20 couples

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TABLE 1

## Classification of 50 couples with Fetal Wastage

History of Fetal Wastage	No. of couples
Spontaneous first trimester abortions + still-births, or live-births with Multiple Congenital Anomalies	20
> 2 spontaneous abortions with or without normal offspring	30

have spontaneous first trimester abortions + still-births, or live-birth with multiple congenital anomalies and 30 couples have less than two spontaneous abortions with or without normal offspring.

Table 2 shows the results of the cytogenetic study of these couples. We find that 95% have normal karyotypes and 5% have abnormal karyotypes.

TABLE 2

## Results of the Cytogenetic study of 50 couples with Fetal Wastage

Group	No. of Subjects	Percentage
A - Normal Karyotype	95	95%
B - Abnormal Karyotype	5	5%

Table 3 shows the abnormal karyotypes found in these couples.

TABLE 3

## The Abnormal Karyotypes

1. Robertsonian 14/15 Translocation
2. Sex Chromosome Aneuploidy: Mosaicism: 46, XX, 47, XXX
3. Balanced Reciprocal Translocation: 46, XX, t(6;10) (q15;q21.2) Bal.
4. Balanced Reciprocal Translocation: 46, XY, t(6;10) (q15;q21.2) Bal.
5. Pericentric Inversion of Y Chromosome

## DISCUSSION

Each abnormal karyotype case is discussed separately:

## CASE NO. 1

The first patient had a history of six consecutive abortions all within the first three months of gestation. Karyotyping shows that she has Robertsonian Translocation<sup>4</sup> (14/15). These chromosomes belong to the D group.

The D/D translocations are the most common structural rearrangement in man. The frequency of which is 0.72 per 1000 live-births,<sup>4</sup> both males and females heterozygous for D/D translocations show some evidence of diminished reproductive fitness. They show no apparent increased empiric risk of having live-born anomalous offspring. Imbalanced segregants presumably are either never fertilized or lost shortly thereafter. Liveborn progeny are equally likely to inherit the translocation chromosomes or the two normal chromosomes. Antenatal diagnosis and counselling should be offered to couples in which a partner has a D/D translocation.

## CASE NO. 2

The wife is forty years old, she is thin built and has short stature, had menarche at the age of 11,



regular periods, and she is married for the last fifteen years. She got pregnant four times all ended in molar pregnancies, which necessitated curettage twice each time. Cytogenetic analysis showed her to have sex chromosome aneuploidy as she is mosaic 46, XX in 70% of the cell and 47, XXX in the rest which is a rare condition.

There are many types of X chromosome aneuploidy and mosaic<sup>5</sup> 46, XX/47, XXX is one of them. A mosaic is a person who has two or more genetically different types of cells or tissues (chromosome constitution) and it is always the result of mitotic non-disjunction of the fertilized egg, abnormal number of X chromosome is rendered less harmful than an abnormal number of autosomes because of dosage compensation which result in a single active X chromosome irrespective of how many present. It is assumed that they phenotypically resemble 47,XXX females. The incidence of which is 1 in 1000. Females with XXX are physically normal and usually able to bear children, but some have menstrual irregularities and an early onset of menopause and higher incidence of mental retardation. In our case it caused molar pregnancy.

### CASE NO. 3

The patient is twenty five years old and married to her first cousin. She is G4 P3 D2 A1. The first child was normal, the second pregnancy ended in an abortion at three months. The third was macerated still-birth and the fourth was female baby with multiple congenital abnormalities who expired after birth. Cytogenetic studies were done for her and her husband<sup>6,7</sup> which shows that both of them had a similar chromosomal abnormality as shown in Table 3. Both husband and wife have the same balanced reciprocal translocation whilst the risk of chromosome abnormality will be greater than for one partner with a translocation. Normal concepts are still possible. Genetic counselling and amniocentesis are recommended for future pregnancies. Relatives may be at risk and would be advised to have chromosome studies as these chromosomal variants segregate in autosomal dominant fashion.

### CASE NO. 4

This is a young couple married for nearly three years. The wife had one anencephalic macerated

still-birth after seven month gestation. The second pregnancy ended in spontaneous abortion after two month gestation. The husband is normal both phenotypically and mentally but he has pericentric inversion of the Y chromosome. The pericentric inversion of Y chromosome is estimated to be present in 1/1000 males. It has no phenotypic consequences and it segregates<sup>8</sup> in families over several generations. The breaks involved in pericentric inversion may have phenotypic consequences if they occur at critical points such as the regions with the fertility factors SP-2 and SP-3 as exemplified by some rare cases of infertility or subfertility. As the meiotic behaviour of inverted Y chromosomes seems to be normal but there is pairing difficulty between X and Y.<sup>8</sup>

We did not find any couple with deletions and duplications. If the deletions and duplications affect large chromosomal regions they produce severe phenotypic abnormalities. Thus individuals with deletions or duplications rarely reproduce.

### CONCLUSION

**Lukas<sup>9</sup> estimated from review of the literature that one in twenty six couples with fetal wastage carry a balanced translocation. In our study we found that 1/20 of these couples have an abnormal karyotype.**

Although carriers of balanced translocations are usually phenotypically normal, the chance for these individuals to produce chromosomally abnormal gametes is high, owing to unbalanced segregation and non-disjunction of the involved chromosomes. Such an abnormal gamete, if fertilized, will result in either a non-viable or a malformed fetus. Furthermore, carriers of balanced translocations have an apparently increased risk of meiotic non-disjunction of other chromosomes, leading to trisomic offsprings.

Identification of abnormal karyotypes in such cases allows for more precise genetic counselling. It also permits these couples to have subsequent pregnancies monitored by amniocentesis and provides them either with reassurance or with the option to terminate pregnancy with an unbalanced chromosome constitution.

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