**Introduction**

According to some 60-80 million pairs annually has problems with infertility (1). This is so for many reasons, but among other things, the problem of infertility should be sought in the genetic aspect. It is important to detect the problem in time. In cases where genetic disorders in the background of these problems it is essential to assess the risk of transmission of the same. By detecting changes in chromosome or gene, there is a possibility of giving precise genetic information about the risks of inheritance (2). Chromosome aberration represent one of the major reasons and causes of infertility and spontaneous abortions. Female infertility is still a leading cause of infertility. One of the most important causes of infertility in women have polycystic ovary syndrome (PCOS), premature loss of ovarian function (POI), and recurrent miscarriages (RPL). One of the most important causes of repeated miscarriage are aberrant karyotype. Abnormalities in chromosomes affect about 6.3% of infertile patients, and affect both sexes. Compared with the general population infertile couples have a higher level of chromosome aberrations. This is especially true of women. Approximately 2.8% of infertile women have certain numerical abnormalities of sex chromosomes, while 2.1% of them wearer structural changes in autosomes translocation (2).

**Materials and methods**

In our research participated 100 women with reproductive problems (sterility and habitual abortions), 15-46 years of age, with the average value of 36.8 ± 6.75. Research was conducted at the Center for genetics at the Medical faculty of Sarajevo University.

Standard method of 72 hours cultivation of peripheral blood lymphocytes has been applied (3). Cytogenetic analysis has been performed according to instructions and rules given by International System of Human Chromosomal Nomenclature (ISCN) (4). At least 25 G-band technique (GTG) mitotic cells have been analyzed (5), if there was doubt of mosaic karyotype, 50 up to 100 cells have been analyzed. C-band has been applied for confirmation of chromosomal heteromorphy.

The results were analyzed using SPSS 20 (*Statistical Package for the Social Sciences*, IBM, NY, USA) for Windows OS. Chi square test was used for analyzing categorical variables.

**Results**

From a total of 100 women in the study, normal karyotype was observed in 84 and abnormal karyotype in the 16. In order to test whether there is a statistically significant difference between the proportion of normal and abnormal karyotype in the analyzed sample, made the chi-square (χ2) test. The calculated p value was less than 0.05 (p˂0,05), which shows that the difference between the proportion of normal and abnormal karyotype in women with reproductive problems is significant (table 1).

Younger participants was 15 years old, and the oldest 46 years, a mean value of 30.97 years, with a standard deviation of ± 6.9. In the table 2 types are shown recorded chromosome aberrations divided based on the type of aberrant chromosomes (autosomal and sex chromosomes), and their frequency in the analyzed sample

**Discussion**

This study analyzes the frequency of genetic causes in reproductive problems in the population of Bosnian women. In the sample of 100 women, a percentage of chromosomal abnormalities of 16% was recorded. Only major chromosomal abnormalities were cytogenetic analyzed, and chromosome inversion 9 was included in the overall percentage.

From this table shows that the most karyotypes (four) with pericentric inversion of chromosome 9 in a group of autosomal chromosomes. Also in this group were recorded two karyotype with Robertonovom translocation, one karyotype with reciprocal translocation and one karyotype with derivative chromosomes (Figure1). Two respondents in which he found Robertson translocation came to the Center for analysis because they were previously in children found to have translocation. Subjects with a reciprocal translocation had one and the derivative chromosome respondents had three spontaneous abortion history.

In the group with the aberration of sex chromosomes seven karyotypes have shown that it is Turner syndrome. It is six karyotypes had mosaic form (45,X /46,XX; 45,X/46XY), and only one woman had a karyotype without mosaicism, or partial deletion of chromosome X [46,X,delX (q25?)]. Two respondents with mosaic type 45,X/46,XX, as well as two with mosaic type 45,X/46,XY are the Center sent on suspicion of Turner syndrome and / or amenorrhea, and one women with mosaicism 45,X/46,XX for sterility. Subjects with deletion of chromosome X is as diagnosis had oligomenorrhea and women with inversion of chromosome X amenorrhea. An interesting case is a woman with a triple mosaicism [45,X(90)/47,XX,+21(6)/46, XX (4)], which are involved aberration and autosomal sex chromosomes. The women in history had two miscarriages, which is amniocentesis showed that it was a child with Down syndrome (6). The authors of the previous cytogenetic studies have analyzed the incidence of abnormalities of autosomal and sex chromosomes in people with reproductive problems. Therefore, in this study made an analysis in order to determine whether there is a statistically significant difference between the two types of chromosome abnormalities covered by the sample. Of the 16 women with an abnormal karyotype, eight had abnormalities of autosomal chromosomes, seven abnormalities of sex chromosomes, and one woman abnormality and autosomal and sex chromosomes. From the total number of analyzed samples, the percentage of abnormalities of autosomal chromosomes was 8%, 7% sex chromosomes, and 1% by abnormalities of autosomal and sex chromosomes.

In Graph 1 shows the percentages recorded abnormalities of autosomal and sex chromosomes in women in this study and previously published studies.

According to the results of other studies, mostly there is a higher percentage of abnormalities of autosomal chromosomes, rather than sexual. The exception is a study by More et al. (2016) where it is recorded equal to the percentage of 1.49%, and few studies that have reported higher percentages of abnormal sex chromosome abnormalities than autosomal chromosomes. These studies are Radojcic Badinovac et al. (7) have noted that 4.11% of autosomal chromosome abnormalities and 12.60% of sex, Clementine et al. (8), which recorded 0.91% abnormalities of autosomal chromosomes and 1.01% of sex, Azimi et al. (9), which recorded 1.90% abnormalities of autosomal chromosomes and 18.86% of sex, More et al. (10) have noted that 9.09% of autosomal chromosome abnormalities and 15.15% of sex, and Goncalves et al. (11) have noted that 2,65% abnormal autosomal chromosomes and 4,63% sex chromosomes.

The analysis criteria applied for inclusion of subjects in the study it can be concluded that higher percentages of autosomal chromosome abnormalities observed in studies that included subjects with recurrent spontaneous abortions in history, with the exception of the study conducted by Gonçalves et al. (11). Studies that have recorded higher percentage of abnormalities of sex, but autosomal chromosomes had broader criteria included in the study, and that the primary and secondary infertility and sterility.

In this study, as previously stated, the diagnosis on the basis of which the patients sent to the cytogenetic analysis at the Center for Genetics addition miscarriage include other diagnosis. In this case 54% of waste in the diagnosis of spontaneous abortion, or the infertilitas diagnosis, and the remaining 46% of the waste to other diagnosis. For diagnosis infertilitas the largest number of abnormal karyotypes, six, and five on the aberrations of autosomal chromosomes. Other abnormalities were observed in 10 patients with other diagnoses. Given that in this study, 46% of the waste and to other diagnoses, except spontaneous abortions, and that for other diagnoses total recorded higher number of chromosome abnormalities indicated may be the reason that in this study, no statistically significant difference between the proportion of abnormalities of autosomal and sex chromosomes.

The frequency of chromosome abnormalities in this study was 16%, which is a higher percentage than the frequency reported in other studies (12; 13) . If the inversion of chromosome 9 consider normal form karyotype and four recorded inversion exclude such chromosome abnormality, gives a total of 12 abnormal karyotypes recorded in a sample of 100 women, and this percentage is 12%. It is still a higher percentage of the most frequently recorded incidence of the authors of other studies (14). The reason for the high incidence of chromosomal abnormalities may be because in this study cytogenetic analyzes and cases with one or more recurring miscarriages, while most of the studies included cases with two, three or more recurrent miscarriages. In addition to the recorded spontaneous abortion history, in this study included women with other diagnoses, and it Sterilitas primarius and secundaria implying that there was no or maybe it was conception, as well as women with amenorrhea, oligomenorrhea, suspicion of Turner syndrome, and women who have had offspring with abnormal karyotype. So, it is a select group of women who went through many filters including tests of obstretičara / gynecologist, endocrinologist and their suspicion was on chromosomal abnormality when they were sent to the Center for Genetics at the cytogenetic testing. It is possible that all the above (wider criteria inclusion in the study with the involvement and cases with one miscarriage in history, rather select group of respondents, the number of respondents) contributed to the higher percentage of recorded chromosome abnormalities in this study compared to results of other studies.

Conclusen

The final conclusion of this study is that chromosomal abnormalities are more frequent in the population of patients with reproductive problems (sterility and habitual abortions) when compared with general population. This fact should be taken in the consideration in order to estimate true etiology of reproductive problems and it is a valuable information in the process of genetic counseling and decision making in assisted reproductive technology. Once more, the usefulness of classical cytogenetic techniques was shown and confirmed in this study.

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