**Recurrent pregnancy loss study in Uzbekistan**

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**Background**

The problem of infertility in married couples has become increasingly alarming worldwide and requires the close attention of specialists. In Uzbekistan, the number of miscarriages in reproductive woman aged 15-49 has increased over the past ten years by 5% and amounts to 16%. The focus of the current research is to identify genetic variants, associated with recurrent pregnancy loss in Uzbek women, which helps in further development of national reference panel for early diagnosis and preventive screening of recurrent miscarriage in reproductive women.

**Materials and methods**

Peripheral venous blood samples were collected from 400 women with two or more miscarriages and 62 women with stillbirths in several regions of Uzbekistan. As controls, blood samples were taken from 600 women with normal delivery (two or more successful deliveries). Information consent was taken from participants prior data collection. Data was collected from each patient through questionnaire and included 144 items related to general information (9 items), anthropometry (4), external factors (14), reproductive information (18), clinical data (17), information about previous diseases, including COVID-19 (22), as well as information about the spouse and relatives of the parties (60). To date, genomic DNA was extracted from blood samples of 233 individuals with available phenotype data, consisting of 74 cases and 110 controls for further genetic analysis. Genetic screening of 650 000 SNPs was performed using Global Screening Array v.3.0 (Illumina Inc., USA) on DNA microarray scanner iScan (Illumina Inc., USA) according to manufacturer’s protocol. Logistic regression analyses were performed using PLINK v1.90b7.2 on genomic data of 233 females to study associations with recurrent miscarriage.

**Results**

An average miscarriage cases were 2,74 with the minimum and maximum number of miscarriage 2 and 13 respectively. The age of patients at moment of the study varied from 20 to 53 years with an average of 28.58 ±6,45 years. The mean age of patients at the time of miscarriage was 29.16±5,27 years with minimum and maximum age of 17 to 42 years respectively.

In 34,14% of evaluated patients at least one pregnancy ended in childbirth with average of 0,49 successful birth per patient.

All patients were divided into groups by the number of miscarriage events, the mean age distribution in each group as follows: 1-st group - 23,71 ±4,57 years, 2-nd group – 25,62 ±4,91 years, 3-d group – 27,33 ±5,08 years, 4-th group – ±28,65 years, and 5-th group – 30,12 ±6,02 years.

Analysis of the distribution of miscarriage and stillbirth cases across regions of Uzbekistan, revealed that the majority of miscarriages (>5 per patient) happened in women, from Karakalpakstan, Jizzakh and Namangan regions.

Preliminary genetic association study revealed through an additive model, two SNPs (rs4871372 at Chr 8 and rs9967044 at Chr 18) exhibited significant associations with the disease phenotype (p-values of 1.622e-05 and 4.751e-05, respectively). Genotypic analysis imposing a minor allele frequency threshold of 0.05 yielded no statistically significant associations, suggesting potential allelic effects specifically at the identified loci.

**Conclusion**

Additional screening with more samples to be done to expand the number of potential SNPs and significantly associated with recurrent miscarriage. Identified genomic markers rs4871372 and rs9967044 are potential candidate SNPs of recurrent pregnancy loss in Uzbek population.

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