623: Fragile X carrier investigation and Genetic counselling of Premature ovarian insufficiency females in an Indian scenario

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Objective
Fragile X-associated primary ovarian insufficiency (FXPOI), a type of ovarian dysfunction is caused by premutation (PM) expansion mutation (55-200 CGG repeats) in FMR1 gene. It occurs in ~20% of PM females carriers. The risk of having FXPOI in PM female increase with the increase in the number of CGG repeats and is maximum at 80 CGG repeats. Furthermore, 2-6% of women with isolated POI or 14% of women with familial POI are reported to be PM carriers. About 12.6% of women with FXPOI are reported to conceive spontaneously even years after diagnosis. There by suggesting screening of POI females for their CGG repeat expansion status in order to rule out PM as a cause of infertility due to their inherent 50% risk of having Fragile X syndrome (FXS) affected offspring. The study aims for the molecular screening of females POI cohort for presence of PM expanded FMR1 alleles.
Design
Two hundred POI cases were recruited from the Department of Medical Genetics, SGPGIMS, Lucknow, India during the period from 2015 to 2019.
Materials and Methods
A previously validated laboratory-developed test using triplet-primed polymerase chain reaction (TP-PCR) was used to identify PM alleles in POI females. Genomic DNA was extracted from 200 POI females and subjected to TP- PCR amplification. The amplicons were subjected to fragment analyses and results were documented. Genetic counseling and extended family screening was offered to identified PM positive cases.
Results
Triple-primed- polymerase chain reaction (TP-PCR) screening of 200 POI females identified 5 of 200 subjects with (Grey zone) GZ allele and 7 subjects with PM allele. Genetic counselling and extended family screening was done in carriers.
Conclusions
The frequency of PM carriers identified in this study was significant and in concordance with previous studies carried worldwide. PM carrier identification among POI subjects will serve dual purpose of recognizing cause for ovarian dysfunction and in getting genetic counselling that will help carriers in taking reproductive decisions.
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Authors have no conflict of Interest.