

MOLECULAR EVALUATION:

BRCA1 & *BRCA2* targeted gene sequencing was performed with validated clinical assay that provides 100% exomic coverage, including flanking intronic sequences with high average depth of coverage. For the proband (here affected individual), Percent reads on target was 97.52% with a 99.68% Target base coverage at 100X. For asymptomatic family members - *BRCA1* gene targeted mutation analysis was performed by Polymerase Chain Reaction (PCR) followed by DNA sequencing and the raw data obtained was subsequently analyzed for the presence or absence of mutation at the hot spot region. .

RESULTS:

In affected individual sample, we got positive report for heterozygous variant c.4508C>A (p.Ser1503Ter) in *BRCA1* gene. The risk of developing cancer in a sibling who inherits the familial *BRCA1* or *BRCA2* pathogenic variant depends on numerous variables including the penetrance of the pathogenic variant and the sex and age of the heterozygous sibling. Here we have no information on affected individual's deceased sibling. (2) Post an elaborate counselling session with family members by trained genetic counselors, mutation specific testing (MST) was recommended in four children (3 females, 1 male) for segregation analysis of the detected variant. Reports for 2 females were positive for variant and 1 male and 1 female was negative. Hence, 50 % of the children are predisposed to c.4508C>A (p.Ser1503Ter) variant putting them at high risk for HBOC, pancreatic, endometrial and other cancer related with *BRCA1* gene mutation. In post-test genetic counselling session pattern of inheritance, penetrance and expression of *BRCA1* gene variant in individuals; risk reduction surgical options were explained to asymptomatic carriers completed with/without child bearing process with its pros and cons. Regular breast screening, mammograms followed by MRI were explained and advised to undergo based on their individual risk in counselling session. Benefits of self-breast examination with periodic check was explained to them in case where they do not have an immediate access to healthcare professional. Basic knowledge of symptoms of HBOC was given to children to be monitored on a regular basis and to visit a clinician if symptoms exaggerated.