HEREDITARY BREAST AND OVARIAN CANCER SYNDROME: FREQUENCY AND DISTRIBUTION OF BRCA1/2 PATHOGENIC VARIANTS IN SICILIAN POPULATION

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Background:
Hereditary breast and ovarian cancer syndrome (HBOC) is caused by germline mutations in BRCA1/2 genes. These genes are wide and their mutations are heterogeneous among different ethnic and geographical regions. However, in some restricted population specific mutations have been found, some of them with higher frequency have an impact on the management of families affected by HBOC, with an improvement in the cost-efficiency ratio. Purpose of our study is to describe the mutation spectrum and frequencies in the BRCA1-2 carriers in Sicilian population with HBOC.
Patients and Methods: Since 2002, 903 patients of both sexes, with breast and/or ovarian cancer, have been screened in our reference regional center in order to detect the mutational status of BRCA1/2 genes on blood samples. This analysis was performed using Ion torrent NGS platform and sanger sequencing for validation of pathogenic variants (PVs).
Results: Our analysis showed that the frequency of PVs of BRCA1/2 genes in Sicilian population was 22% (197/903 patients). Among all of them, 195 had point mutations and 2 rearrangements detected by MLPA; 110 were carriers of a pathogenic alteration in BRCA1 and 85 in BRCA2.
The 22% (20/110 patients) BRCA1 PVs had c.4964_4982del19 and 20 % (18/110) had c.514delC. The most represented alterations in BRCA2 were c.1238delT (10%, 12/85), c.5851del4 (6%, 7/85) and c.631G>A (6%, 7/85).
Conclusions: The frequency of BRCA PVs in Sicilian patients with suspected HBOC was 22%. The most frequent variants were c.4964_4982del19, an Italian founder of Sicilian origin, and c.514delC both in BRCA1. The Sicilian founder mutation c.4724delC still remains less frequent.
In BRCA2 the most frequently detected PVs were c.1238delT, c.5851del4 and c.631G>A, while the Italian founder mutation c.6174delT was not found.