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Prevalence of pathogenic mutations in BRCA genes in patients with HBOC Syndrome in Brazil: a meta-analysis.

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Introdução

Hereditary Breast and Ovarian Cancer syndrome (HBOC) is a genetic condition associated with an increased risk for developing breast, ovarian, and other cancers. This genetic predisposition syndrome can be caused by germline mutations in DNA repair genes, such as Breast Cancer genes (named BRCA1 and BRCA2). Mutations in BRCA genes increase the chance of developing breast cancer by up to 80% and ovarian cancer by 50% over a lifetime. Patients diagnosed with HBOC Syndrome are more likely to develop breast or ovarian cancer when compared to families that do not have such mutations. In addition, they present the cancer at a younger age, with a greater chance of having more than one primary tumor at the same time. In these cases, genetic testing is the best way to confirm the clinical diagnosis and/or provide early prevention measures for these patients.

Casuística e Métodos

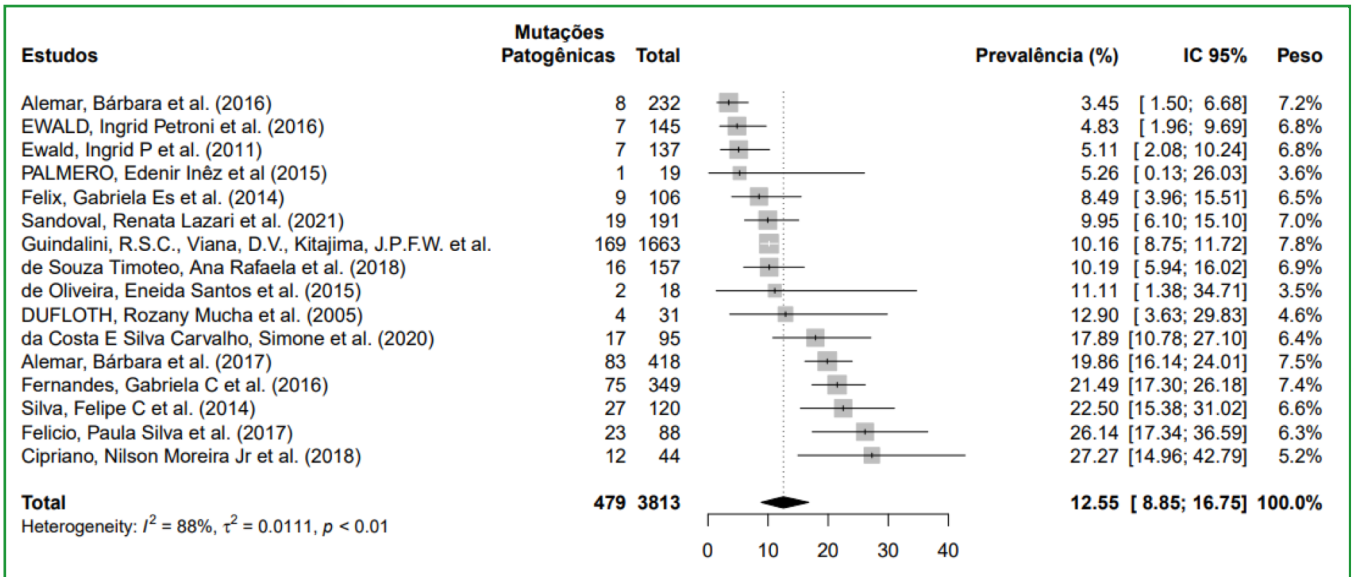
The aim of the study was to perform a meta-analysis of Brazilian studies that have described the prevalence of mutations in BRCA1 and BRCA2 genes in patients with risk factors for HBOC. The aim is to add the prevalence of pathogenic mutations that are more frequent in Brazilian HBOC patients.

The systematic review and meta-analysis was designed according to the protocols indicated by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Medline (via Pubmed) and Scielo databases were used to identify articles published in English and/or Portuguese until May 10, 2022. The search terms were: “BRCA” and “Brazil” or “Brazilian”, “HBOC” and “Brazil” or “Brazilian”. The variables extracted were: author, total sample size, sample size of patients diagnosed with HBOC, type of genetic test used to determine mutations, database used, criteria for identifying the clinical diagnosis for patients with HBOC, year and location of publication. Statistical analyzes were performed using RStudio version 4.1 software. The random effects model was used, with the DerSimonian and Laird method. The transformation method used was the Freeman-Tukey double arcsine to stabilize the variances.

Resultados

A total of 5,170 articles were found after searching databases. Of these, 16 articles were included for analysis of BRCA1 and BRCA2 mutations in patients with a clinical diagnosis of HBOC syndrome. The total number of patients included in this study was 3,813. We found 176 different pathogenic mutations reported in the analyzed studies, however, only 54 mutations appeared in more than one patient. The frequency found of pathogenic mutations in these genes, taking into account only studies that included both genes in the search, was 65.9% for the BRCA1 gene and 34.1% for the BRCA2 gene. Approximately 67% of the mutations occurred in the BRCA1 gene and 33% in the BRCA2 gene. The most common pathogenic mutation in the study, *c.5266dupC* in BRCA1, with a 20.8% prevalence, followed by the *c.3331_3334del* mutation, detected in 6.6% of patients. In the BRCA2 gene, the most prevalent mutation was *c.2808_2811del*, described in 3.4% of HBOC patients.

HGVS name	Mutated Gene	Mutation Effect	Patients	Prevalence
c.5266dupC (p.Gln1756Profs)	BRCA1	Frameshift	91	20,8%
c.3331_3334del (p.Gln1111fs)	BRCA1	Frameshift	29	6,6%
c.2808_2811del (p.Ala938Profs)	BRCA2	Frameshift	15	3,4%
c.156_157insAlu	BRCA2	Splice Donor	12	2,7%
c.1687C>T (p.Gln563Ter)	BRCA1	Nonsense	11	2,5%
c.6405_6409del (p.Asn2135fs)	BRCA2	Frameshift	9	2,1%
c.2T>G (p.Met1Arg)	BRCA1	Missense	8	1,8%
c.211A>G (p.Arg71Gly)	BRCA1	Missense	8	1,8%
c.5173_5176GAAA[1] (p.Arg1726fs)	BRCA1	Frameshift	6	1,4%
c.8488-1G>A	BRCA2	Splice Acceptor	6	1,4%
c.1138del (p.Ser380fs)	BRCA2	Frameshift	5	1,1%
c.9382C>T (p.Arg3128Ter)	BRCA2	Nonsense	5	1,1%
c.6656C>G (p.Ser2219Ter)	BRCA2	Nonsense	5	1,1%
c.4829_4830del (p.Val1610fs)	BRCA2	Frameshift	4	0,9%
c.5059GTT[1] (p.Val1688del)	BRCA1	In Frame Deletion	4	0,9%
c.4675+1G>A	BRCA1	Splice Donor	4	0,9%
c.3598C>T (p.Gln1200Ter)	BRCA1	Nonsense	4	0,9%
c.4183C>T (p.Gln1395Ter)	BRCA1	Frameshift	4	0,9%
c.4484G>T (p.Arg1495Met)	BRCA1	Missense	4	0,9%



Conclusões

It was possible to observe that have many different BRCA mutations prevalence in Brazil. As Brazilian population is highly mixed, it is expected that there is great genetic diversity. Meanwhile, it was possible to identify some mutations that are more prevalent in HBOC patients

Contato

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