Genetic Mutations in a Young Population in Chile with Breast Cancer

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Introduction

Approximately 5–10% of breast cancer cases are linked to genetic predisposition, primarily involving pathogenic germline variants in BRCA1 and BRCA2, which confer a lifetime risk of 80–90% and 60–85%, respectively. Other genes like CHEK2, BRIP1, and PALB2 are associated with moderate risks (20–40%). While pathogenic variants can predispose to triple-negative breast cancer, most cases occur without these mutations. High-risk patients may opt for genetic screening and prophylactic mastectomy, which reduces breast cancer risk and improves disease-free survival, though it does not eliminate risk or increase overall survival.

Objective

This study aims to analyze genetic mutations and variants of uncertain significance in breast cancer cases treated at Clínica Alemana, Santiago, over the past ten years, and compare them with global data. It also examines how these findings influence clinical management, including prophylactic mastectomy.

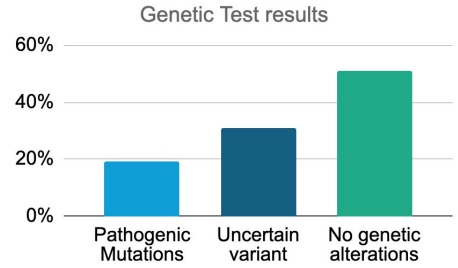
Methods and materials

Retrospective descriptive study of genetic mutations in 200 women aged ≤40 with breast cancer over 10 years at Clínica Alemana, Santiago, Chile.

Pathogenic Mutations	Population	Prophylactic mastectomy
BRCA 1	5	3
BRCA 2	3	2
PALB2	2	1
MUTYH	2	0
ATM	2	0
APC	1	0
MSH2	1	0
LIN	1	0
TP53	1	0
None	174	18

Results

In this study, 47.4% of patients received genetic counseling and all underwent testing. Pathogenic mutations were found in 18 patients, mostly in BRCA1/2, while 28 had variants of uncertain significance, primarily in CHEK2.



Discussion

Genetics are implicated in about 10% of breast cancer cases, consistent with our finding of 9.4% positive genetic tests. Variants of uncertain significance (VUS) occur in 2–7% of BRCA1/2-only tests and up to 10–41% in multigene panels; our study found 14.6% VUS after multigene testing. BRCA1/2 pathogenic variants were present in 4.2% of cases, aligning with reported rates of 3–4%. Prophylactic mastectomy rates vary between 40–80% in carriers of high-penetrance mutations, and are lower for moderate-penetrance genes. In our cohort, 63% of BRCA1/2 carriers and 10% with moderate-risk gene mutations underwent prophylactic mastectomy.