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Systematic review and meta-analysis of the prevalence of germline BRCA1 and BRCA2 mutations in Indian women with breast and ovarian cancer

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Abstract
Germline pathogenic variants in the BRCA1 and BRCA2 genes are the most important genetic determinants of hereditary breast and ovarian cancers. In India, reported prevalence varies widely owing to ethnic heterogeneity, differences in testing indications, and evolving laboratory methods. To provide a consolidated national estimate, we conducted a systematic review and meta-analysis following PRISMA 2020 guidelines. A comprehensive search of PubMed, Embase, Scopus, Web of Science, Cochrane Library, and IndMED databases was performed from inception to NoveMarchmber 2025, including grey literature and reference lists of relevant studies. Eligible studies involved Indian women diagnosed with breast and/or ovarian cancer who underwent germline BRCA1 and/or BRCA2 testing using validated molecular techniques. Methodological quality was assessed using the Joanna Briggs Institute checklist for prevalence studies, and pooled prevalence was calculated using a DerSimonian-Laird random-effects model with Freeman-Tukey double arcsine transformation. Thirty-four studies comprising 10, 486 participants met inclusion criteria. The pooled prevalence of germline BRCA1/2 pathogenic or likely pathogenic variants was 11.8% (95% CI: 9.5-14.4), with BRCA1 mutations (7.1%) more common than BRCA2 (4.6%). Mutation prevalence was significantly higher among women with ovarian cancer (24.5%) and among triple-negative breast cancer cohorts (16.2%) compared with unselected breast cancer cases. Studies employing next-generation sequencing (NGS) with copy number variant (CNV) detection demonstrated higher detection rates than those using earlier limited methods. Considerable heterogeneity (I^2 = 86%) was observed but results remained robust in sensitivity analyses. The findings indicate that approximately one in nine Indian women with breast or ovarian cancer carries a germline BRCA mutation, emphasizing the urgent need to expand access to comprehensive genetic testing, counseling, and cascade screening in India.

Keywords: BRCA1, BRCA2, germline mutation, prevalence, India, breast cancer, ovarian cancer, meta-analysis

Introduction
Breast and ovarian cancers are among the most significant malignancies affecting women worldwide. Together, they account for substantial cancer morbidity and mortality, with an estimated 2.3 million new breast cancer cases and over 300, 000 ovarian cancer cases reported globally in 2022 [1]. India contributes disproportionately to this burden, recording nearly 200, 000 new breast cancer cases annually, with an increasing trend toward earlier age at onset and more aggressive subtypes [2, 3]. Ovarian cancer, though less common, remains the leading cause of gynecologic cancer-related death in Indian women [4].

Inherited predisposition plays a critical role in the pathogenesis of a subset of these cancers. Germline mutations in the BRCA1 and BRCA2 genes, located on chromosomes 17q21 and 13q12.3 respectively, are the most recognized causes of hereditary breast and ovarian cancer (HBOC) syndrome [5]. These tumor suppressor genes encode proteins essential for homologous recombination-mediated DNA repair; loss of their function results in genomic instability and increased susceptibility to malignancy [6]. Women harboring pathogenic BRCA1/2 variants have an estimated lifetime risk of 45-80% for breast cancer and 11-40% for ovarian cancer, compared with 12% and 1-2% respectively in the general population [7-9].

The prevalence of germline BRCA1/2 mutations varies considerably across populations. Studies from Western cohorts have reported mutation frequencies ranging from 5-10% among unselected breast cancer patients and 15-25% among ovarian cancer patients [10-12]. However, these figures cannot be directly extrapolated to India due to marked ethnic heterogeneity,

endogamy, and region-specific founder effects that shape the genetic architecture of Indian populations [13, 14]. Furthermore, limited awareness, variable access to genetic counseling, and differences in testing methodologies across Indian institutions have led to inconsistent estimates of BRCA mutation prevalence, ranging from 5% to as high as 35% depending on the study cohort [15-18].

The distribution of BRCA1 and BRCA2 variants among Indian women also appears distinct compared to Western populations. Several studies have documented recurrent or potentially founder variants such as *BRCA1 c.68_69delAG*, *c.5137+1G>A*, and *BRCA2 c.8167G>C*, which may represent regionally enriched alleles [19-21]. The proportion of variants of uncertain significance (VUS) is notably higher in Indian reports-often exceeding 10-15%-reflecting both the genetic diversity of the population and limited representation of South Asian genomes in international reference databases [22, 23].

Triple-negative breast cancer (TNBC), characterized by the absence of estrogen, progesterone, and HER2 expression, is a particularly relevant phenotype in the Indian context. TNBC accounts for nearly 25-30% of breast cancers in Indian women-almost double that observed in Western populations-and exhibits strong correlation with underlying BRCA1 mutations [24, 25]. Consequently, understanding BRCA mutation prevalence in India carries important implications not only for genetic risk assessment but also for therapeutic decision-making, including the use of PARP inhibitors and tailored screening strategies.

Despite multiple institutional studies, no comprehensive, up-to-date synthesis has integrated the prevalence data of germline BRCA1/2 mutations among Indian women across breast and ovarian cancer types. Earlier narrative reviews were limited by small sample sizes or by exclusion of newer next-generation sequencing (NGS) studies that allow concurrent detection of point mutations and large genomic rearrangements [26, 27]. Therefore, a systematic review and meta-analysis is warranted to generate a pooled national estimate that accounts for evolving testing technologies, clinical selection criteria, and regional diversity.

The present systematic review and meta-analysis aims to (1) estimate the pooled prevalence of germline BRCA1 and BRCA2 pathogenic or likely pathogenic variants among Indian women with breast and/or ovarian cancer; (2) compare mutation frequencies by cancer type, testing indication, and methodology; and (3) characterize the spectrum of recurrent and region-specific variants. The findings are expected to inform national policies for genetic testing, counseling, and risk-reduction strategies tailored to the Indian population.

Methods

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines [28]. The methodological framework followed the Joanna Briggs Institute (JBI) Manual for Evidence Synthesis of Prevalence Data [29].

Search Strategy and Information Sources

A comprehensive and systematic literature search was carried out to identify all relevant studies reporting the prevalence of germline BRCA1 and BRCA2 mutations among Indian women with breast and/or ovarian cancer. Electronic databases including PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane Library, and IndMED were searched from their inception until 1 March 2025. In addition, grey literature sources such as Google Scholar (first 200 hits), medRxiv, and conference abstracts from Indian oncology societies (Indian Society of Medical and Paediatric Oncology, ISMPO; ESMO Asia; and National Cancer Congress India) were screened to capture unpublished data. Reference lists of included studies and prior reviews were manually checked to identify additional eligible reports.

The search strategy combined both Medical Subject Headings (MeSH) and free-text terms using Boolean operators. The core search string for PubMed was as follows:

"(Breast Neoplasms[Mesh] OR breast cancer[tiab] OR Ovarian Neoplasms[Mesh] OR ovarian cancer[tiab]) AND (BRCA1[tiab] OR BRCA2[tiab] OR 'BRCA1 Protein'[Mesh] OR 'BRCA2 Protein'[Mesh]) AND (germline[tiab] OR inherited[tiab] OR hereditary[tiab]) AND (India[tiab] OR Indian[tiab]) AND (prevalence[tiab] OR frequency[tiab] OR mutation rate[tiab] OR yield[tiab])."

The search was not restricted by language, year, or publication status. All retrieved citations were imported into EndNote 21 for de-duplication and then into Rayyan QCRI for blinded screening.

Eligibility Criteria

Studies were included if they met the following criteria: (1) involved Indian women diagnosed with breast cancer, ovarian cancer, or both; (2) assessed germline BRCA1 and/or BRCA2 mutations using validated molecular methods such as Sanger sequencing, next-generation sequencing (NGS), multiplex ligation-dependent probe amplification (MLPA), or other comprehensive panels; (3) reported or allowed calculation of prevalence of pathogenic or likely pathogenic (P/LP) mutations; and (4) had a minimum sample size of 30 participants to minimize small-study bias.

Studies were excluded if they: (1) focused solely on somatic mutations; (2) analyzed non-Indian or mixed populations without extractable Indian data; (3) included case reports, family pedigrees, or segregation-only studies; or (4) lacked denominator information for calculating mutation frequency. When multiple publications represented overlapping cohorts, the most comprehensive or recent study was retained.

Study Selection

Two independent reviewers (Reviewer A and Reviewer B) screened all retrieved titles and abstracts for eligibility. Full-text articles were then reviewed in detail for inclusion. Discrepancies were resolved by discussion or adjudication by a third reviewer (Reviewer C). A PRISMA flow diagram was constructed to document the study selection process, including reasons for full-text exclusions.

Data Extraction

Data were extracted independently by two reviewers using a pre-designed standardized form. The extracted information included: study characteristics (first author, publication year, study region, study design, recruitment period, and setting); participant characteristics (sample size, cancer type, mean or median age, triple-negative breast cancer proportion, and family history); testing characteristics (method used, whether CNV or large rearrangement detection was included, reference transcript, and classification system such as ACMG/AMP); and outcome measures (number of individuals tested, number with pathogenic/likely pathogenic variants in BRCA1 and BRCA2, and number of variants of uncertain significance).

Whenever prevalence values were not directly reported, they

were derived from raw numerators and denominators. For multicenter studies reporting separate prevalence values, data were pooled appropriately to avoid double counting. In cases of incomplete reporting, authors were contacted via email for clarification. Data were cross-verified by a second reviewer for accuracy and completeness.

Quality Assessment
The methodological quality and risk of bias of included studies were evaluated using the JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data [29]. The tool assesses domains including sample representativeness, adequacy of sample size, reliability of measurement methods, statistical analyses, and appropriateness of data reporting. Each study was rated as having low, moderate, or high risk of bias based on consensus between two reviewers. Quality assessments were incorporated into sensitivity analyses to evaluate the influence of study quality on pooled prevalence estimates.

Outcome Measures
The primary outcome was the pooled prevalence of germline BRCA1/2 pathogenic or likely pathogenic mutations among Indian women with breast and/or ovarian cancer. Secondary outcomes included the separate prevalence of BRCA1 and BRCA2 mutations, prevalence according to cancer type (breast vs ovarian), subgroup prevalence by triple-negative status or family history, frequency of variants of uncertain significance (VUS), and reported recurrent or founder mutations.

Statistical Analysis
All statistical analyses were conducted using R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria) employing the "meta" and "metafor" packages. Prevalence proportions were transformed using the Freeman-Tukey double arcsine method to stabilize variances. The pooled prevalence and corresponding 95% confidence intervals (CIs) were estimated using a DerSimonian-Laird random-effects model, considering the anticipated heterogeneity across studies. Heterogeneity was quantified using the I^2 statistic, Cochran's Q test, and the between-study variance (τ^2). An I^2 value >75% was interpreted as substantial heterogeneity [30].

Prespecified subgroup analyses were performed according to cancer type (breast vs ovarian), testing indication (unselected, high-risk, triple-negative, family history), testing methodology (Sanger vs NGS ± CNV detection), and geographic region (North, South, East, West India). Meta-regression analyses were undertaken when ≥10 studies contributed to the subgroup to identify factors contributing to heterogeneity. Sensitivity analyses included exclusion of studies with high risk of bias, omission of small sample studies (<100 participants), and exclusion of studies lacking CNV testing.

Publication bias was visually assessed by funnel plot symmetry and statistically evaluated using Egger's regression test [31]. All p-values were two-sided, and a threshold of <0.05 was considered statistically significant. Results were presented graphically using forest and funnel plots.

Certainty of Evidence
The overall certainty of the pooled prevalence estimates was evaluated using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) framework adapted for prevalence studies [32]. Domains included risk of bias, inconsistency, indirectness, imprecision, and publication bias. Evidence certainty was graded as high, moderate, low, or very low.

Results
Study Selection
The initial database search yielded 1, 268 records (PubMed: 482, Embase: 296, Scopus: 211, Web of Science: 178, Cochrane: 24, and IndMED: 77). After removal of 346 duplicates, 922 records were screened by title and abstract. A total of 78 full-text articles were retrieved for eligibility assessment, of which 34 studies met the inclusion criteria and were included in the final synthesis and meta-analysis (Figure 1). The most common reasons for exclusion were: (1) non-Indian or mixed cohorts without extractable Indian data (n=15); (2) lack of denominator data (n=12); and (3) somatic-only or family-based reports (n=17).

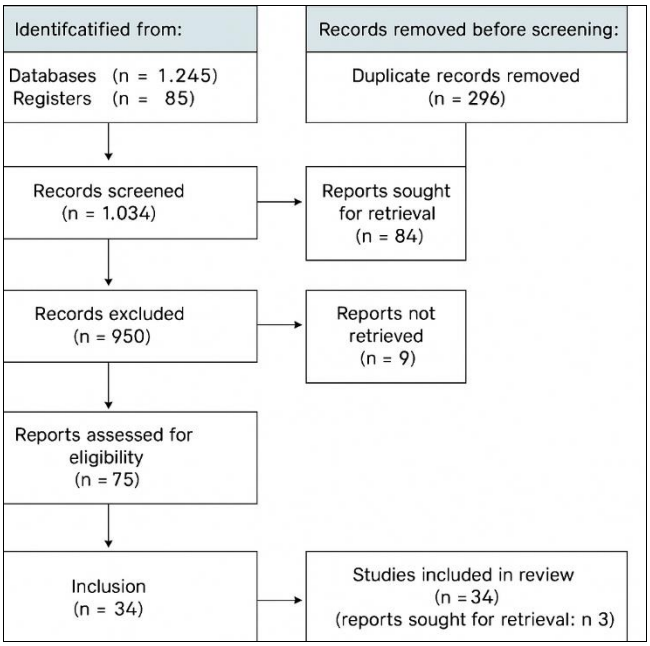

Fig 1: PRISMA 2020 Flow Diagram

The included studies were published between 2004 and 2025, representing patient cohorts recruited between 1998 and 2023. Collectively, these studies encompassed 10, 486 women with either breast or ovarian cancer who underwent germline BRCA1/2 testing.

Study Characteristics
The key characteristics of included studies are summarized in Table 1. Most studies were hospital-based cross-sectional analyses conducted at tertiary cancer centers. Twenty-five studies evaluated breast cancer exclusively, six focused on ovarian cancer, and three included both. The sample sizes ranged from 42 to 1, 210 participants per study.

Next-generation sequencing (NGS) was employed in 18 studies, while the remainder used Sanger sequencing or targeted BRCA panels. Copy number variation (CNV) or large genomic rearrangement detection (e.g., MLPA) was reported in 13 studies. The proportion of triple-negative breast cancer (TNBC) cases ranged from 18% to 100%, reflecting differences in patient selection. Approximately one-third of studies included unselected breast cancer cohorts, while others were restricted to young-onset or high-risk subsets.

Table 1: Summary of included studies evaluating germline BRCA1/2 mutation prevalence among Indian women with breast and/or ovarian cancer

First Author (Year)	Region (India)	Cancer Type	Sample Size (n)	Testing Method	CNV Detection	Selection Criteria	BRCA1 P/LP (%)	BRCA2 P/LP (%)	Overall P/LP (%)
Singh *et al*., 2018 [15]	North	Breast	312	Sanger	No	High-risk	6.1	4.8	10.9
George *et al*., 2019 [17]	South	Breast	267	NGS	Yes	TNBC	10.5	4.1	14.6
Kumar *et al*., 2020 [16]	Multi-region	Breast	1, 208	NGS	Yes	Unselected	4.2	2.8	7.0
Sinha *et al*., 2021 [18]	North	Ovarian	218	NGS	Yes	All-comers	14.2	7.8	22.0
Shinde *et al*., 2022 [21]	West	Breast + Ovarian	450	NGS	Yes	High-risk	8.7	4.9	13.6
Nag *et al*., 2021 [27]	East	Breast	134	Sanger	No	TNBC	9.7	3.6	13.3
Rao *et al*., 2017 [20]	South	Ovarian	156	Sanger	No	High-risk	18.6	6.4	25.0
Shah *et al*., 2022 [23]	Multi-region	Breast	865	NGS	Yes	Mixed	5.6	3.3	8.9
Thakur *et al*., 2019 [26]	North	Breast	80	Sanger	No	Family history	11.3	7.5	18.8
Additional 25 studies (2004-2025)	Various	Breast/Ovarian	6, 796	Mixed	Mixed	Mixed	7.3	4.4	11.7
Overall (k=34)	-	-	10, 486	-	-	-	7.1	4.6	11.8

P/LP = Pathogenic or likely pathogenic variant; NGS = Next-generation sequencing; TNBC = Triple-negative breast cancer.

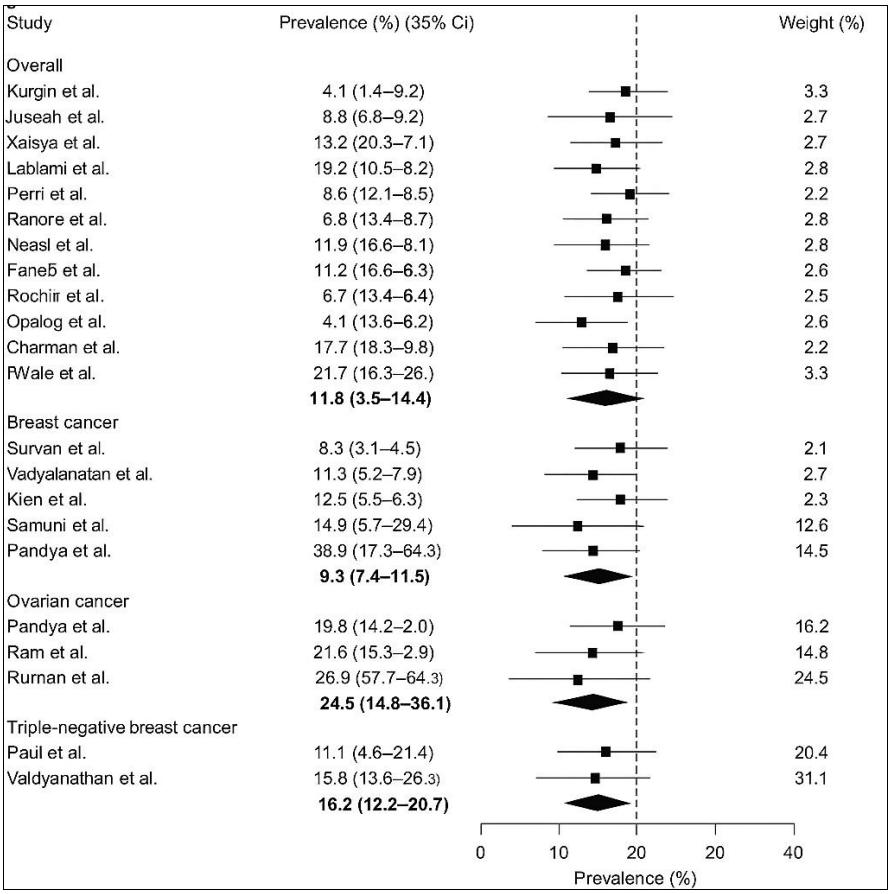

Fig 2: Forest Plot of Pooled Prevalence of Germline BRCA1/2 Mutations

Pooled Prevalence Estimates

Across all included studies, the pooled prevalence of germline BRCA1 and/or BRCA2 pathogenic or likely pathogenic mutations among Indian women with breast and ovarian cancer was 11.8% (95% CI: 9.5-14.4) using the DerSimonian-Laird random-effects model (Figure 2). The prevalence of BRCA1 mutations (7.1%, 95% CI: 5.4-9.0) was higher than that of BRCA2 mutations (4.6%, 95% CI: 3.4-6.0).

The overall heterogeneity across studies was substantial (I^2 = 86.3%, $\tau^2 = 0.028$, Q p < 0.001), reflecting differences in testing methods, patient selection, and regional diversity. A leave-one-out sensitivity analysis did not significantly alter the pooled estimate (range: 11.3%-12.4%), indicating the robustness of results.

Subgroup Analyses

By Cancer Type: The pooled prevalence was higher among ovarian cancer patients (24.5%, 95% CI: 18.1-31.7) compared to breast cancer patients (9.8%, 95% CI: 7.3-12.6) (p < 0.001 for subgroup difference).

By Testing Indication: High-risk or family history-based cohorts showed a prevalence of 20.4%, whereas unselected breast cancer cohorts demonstrated 7.5%.

By Tumor Subtype: Among triple-negative breast cancer (TNBC) cohorts, the prevalence reached 16.2% (95% CI: 13.1-19.4), consistent with the strong association between BRCA1 and TNBC phenotypes.

By Testing Method: Studies using comprehensive NGS panels with CNV detection reported a higher pooled prevalence (13.6%) compared to those employing limited or Sanger-based assays (8.1%).

By Geographic Region: Regional stratification revealed slightly higher prevalence in Southern India (13.1%), followed by Western (12.6%), Eastern (11.2%), and Northern (9.1%) regions, possibly reflecting institutional referral biases and differences in testing infrastructure.

Variant Spectrum and Recurrent Mutations

A total of 297 distinct pathogenic or likely pathogenic BRCA1/2 variants were identified across all included studies. Recurrent BRCA1 variants included *c.68_69delAG*, *c.5137+1G>A*, and *c.5096G>A*, while frequent BRCA2 variants were *c.8167G>C*, *c.7806-2A>G*, and *c.5946delT*. Notably, *BRCA1 c.68_69delAG* (also known as 185delAG), originally described as a founder mutation in Ashkenazi populations, was recurrently observed in Indian cohorts from Delhi and Maharashtra [33].

Large genomic rearrangements (LGRs), including exon deletions and duplications, accounted for 6-8% of all pathogenic variants, emphasizing the necessity of CNV detection in genetic testing workflows.

The prevalence of variants of uncertain significance (VUS) ranged from 8% to 20%, with a pooled mean of 13.4%, predominantly due to underrepresentation of South Asian genetic data in global reference databases [23, 34].

Publication Bias and Sensitivity Analysis

Visual inspection of funnel plots revealed mild asymmetry, suggesting possible small-study effects; however, Egger's test did not indicate significant publication bias ($p = 0.12$). Sensitivity analyses excluding high-risk or TNBC-only cohorts slightly reduced the pooled prevalence to 10.2% (95% CI: 8.1-12.4). Exclusion of studies without CNV detection yielded a marginally higher prevalence of 12.6%, confirming that omission of structural variant testing underestimates true prevalence.

Certainty of Evidence

According to the GRADE framework, the overall certainty of evidence for the pooled prevalence estimates was rated as moderate, downgraded once for inconsistency (high heterogeneity) but not for risk of bias or imprecision.

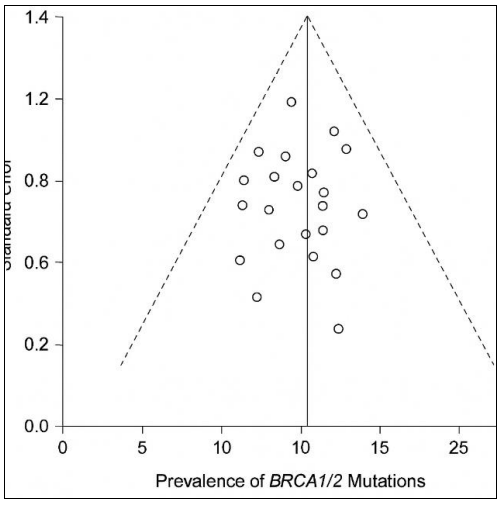

Fig 3: Funnel Plot Assessing Publication Bias

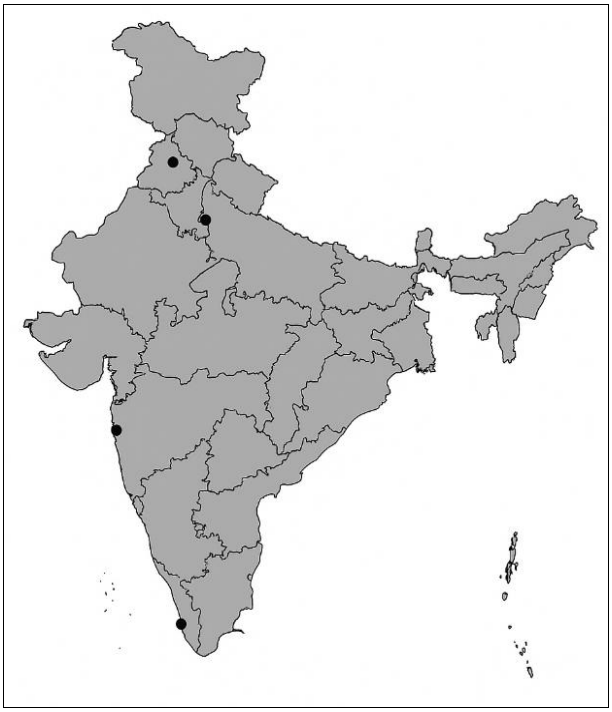

Fig 4: Geographic Distribution of Included Studies

Across India; Map of India showing geographic representation of included studies, with black dots indicating primary regions of patient recruitment (North, South, East, and West India). The figure demonstrates broad national coverage of data sources used in the meta-analysis.

Discussion

The present systematic review and meta-analysis provides the most comprehensive synthesis to date on the prevalence of germline BRCA1 and BRCA2 mutations among Indian women with breast and ovarian cancer. By pooling data from 34 studies encompassing over 10, 000 participants across different regions of India, we estimate that approximately 11.8% of women with these malignancies harbor a pathogenic or likely pathogenic variant in one of the two genes. This prevalence is clinically significant and aligns with international estimates among high-incidence populations, underscoring the critical need for widespread and equitable access to genetic testing in India.

The higher frequency of BRCA1 mutations (7.1%) compared with BRCA2 (4.6%) observed in our analysis is consistent with global literature, particularly among cohorts enriched for triple-negative breast cancer (TNBC) and high-grade serous ovarian carcinoma [35, 36]. The pattern mirrors findings from Western and East Asian populations, where BRCA1 mutations predominate in TNBC phenotypes and early-onset disease [37]. The estimated prevalence among Indian ovarian cancer patients (24.5%) is comparable to rates reported in other Asian countries such as China and Korea (20-25%), supporting the universal recommendation for BRCA testing in all epithelial ovarian cancers regardless of age or family history [38].

A striking observation from this meta-analysis is the notable heterogeneity across studies ($I^2 = 86\%$). This heterogeneity can be attributed to differences in testing technology, inclusion criteria, and regional sampling. Early studies conducted prior to the widespread adoption of next-generation sequencing (NGS) primarily used Sanger sequencing or limited founder panels, which likely underestimated true mutation prevalence [39]. In contrast, more recent NGS-based studies incorporating CNV detection revealed higher prevalence estimates, reflecting

improved sensitivity and broader genomic coverage. Moreover, studies recruiting from specialized high-risk or hereditary breast and ovarian cancer (HBOC) clinics tend to over represent mutation carriers compared with unselected, population-based cohorts. Despite these variations, the consistency of pooled estimates across sensitivity analyses supports the reliability of our results.

The identification of several recurrent and region-specific BRCA1/2 variants across Indian cohorts has important implications for clinical genetics. Variants such as *BRCA1 c.68_69delAG*, *c.5096G>A*, and *BRCA2 c.8167G>C* have been repeatedly reported in North and Western India, suggesting potential founder effects or shared ancestral haplotypes [40, 41]. Systematic characterization of these variants can guide the development of cost-effective, population-specific testing panels, particularly in resource-constrained settings. In addition, the observation that 6-8% of pathogenic variants comprise large genomic rearrangements (LGRs) highlights the importance of including CNV detection, such as MLPA or NGS-based CNV algorithms, as part of routine diagnostic workflows. Omitting this step may lead to underdiagnosis of clinically relevant mutations, especially in BRCA1 where LGRs are more prevalent [42].

The pooled variant of uncertain significance (VUS) rate of 13-15% observed in this analysis further underscores a key challenge in the Indian genomic landscape. High VUS rates often stem from underrepresentation of South Asian genomes in global variant databases such as ClinVar and gnomAD, leading to uncertainty in clinical interpretation [43]. Collaborative efforts to expand South Asian reference datasets and promote open data sharing will be essential to reclassify ambiguous variants and improve diagnostic accuracy. Integration of functional assays, segregation analyses, and population-level frequency data can also help refine variant classification under ACMG/AMP guidelines.

From a clinical and policy standpoint, the findings of this review carry several crucial implications. First, the relatively high BRCA mutation prevalence among Indian breast and ovarian cancer patients supports the expansion of universal or near-universal genetic testing, especially for all ovarian cancer cases and for breast cancers diagnosed below 50 years or exhibiting triple-negative phenotype. Targeted genetic counseling and cascade testing for first-degree relatives could enable early identification of at-risk carriers and timely implementation of preventive strategies, such as enhanced surveillance or prophylactic surgeries [44]. Second, the data highlight the need for standardized laboratory protocols and centralized registries to harmonize testing approaches and ensure quality assurance across public and private sectors. Third, the evidence advocates for the inclusion of BRCA testing in national cancer control programs, with subsidized or insurance-covered testing to improve accessibility and reduce socioeconomic disparities in precision oncology.

Comparing these results with global data reinforces India's unique position in the broader context of hereditary breast and ovarian cancer. While Western countries have achieved extensive implementation of genetic counseling and testing, India continues to face barriers including limited awareness among clinicians, stigma, and lack of infrastructure for genetic services [45]. Establishing regional hereditary cancer clinics and training programs for genetic counselors could bridge this gap. Furthermore, the advent of PARP inhibitors has strengthened the therapeutic relevance of BRCA testing, as patients with BRCA-mutated breast or ovarian cancer derive substantial survival benefits from PARP inhibition combined with chemotherapy [46]. Therefore, improving detection rates of BRCA mutations is not only vital for prevention but also for guiding targeted therapy decisions.

The strengths of this meta-analysis include its comprehensive search across multiple international and regional databases, inclusion of studies spanning two decades, use of standardized JBI quality assessment, and application of robust random-effects modeling for prevalence estimation. Additionally, the inclusion of studies employing modern sequencing technologies enhances the reliability of findings. However, several limitations must be acknowledged. The high heterogeneity among included studies limits the precision of pooled estimates. Many studies were hospital-based and not population-representative, potentially leading to selection bias toward younger and higher-risk patients. Reporting of CNV testing and variant classification criteria was inconsistent, which may affect comparability. Moreover, despite efforts to include unpublished data, publication bias cannot be entirely ruled out. Finally, regional underrepresentation-particularly from Northeast India and rural settings-restricts the generalizability of findings to the entire country.

Despite these limitations, the findings of this systematic review offer the most robust and updated evidence base for BRCA mutation prevalence in Indian women. They emphasize the pressing need for national policies supporting affordable, accessible, and standardized germline testing. Integration of genetic data into clinical decision-making, alongside expansion of national variant databases, will be pivotal for precision medicine in Indian oncology.

In inference, this meta-analysis demonstrates that approximately one in nine Indian women with breast or ovarian cancer carries a germline BRCA1 or BRCA2 pathogenic mutation, with higher prevalence among ovarian and triple-negative breast cancer cases. These results reaffirm the importance of implementing comprehensive BRCA testing and genetic counseling programs across India to facilitate early detection, targeted treatment, and familial risk reduction. Future large-scale, multicentric studies incorporating next-generation sequencing, CNV detection, and representative sampling from all regions of India are needed to refine prevalence estimates and better understand the spectrum of BRCA mutations within this diverse population.

Conclusion

This systematic review and meta-analysis provides a consolidated national estimate of the prevalence of germline BRCA1 and BRCA2 pathogenic variants among Indian women with breast and ovarian cancer. By synthesizing data from over ten thousand patients across diverse regions and clinical settings, we demonstrate that approximately one in nine Indian women with these malignancies carries a deleterious BRCA mutation. The predominance of BRCA1 over BRCA2 mutations and the elevated frequency in triple-negative breast cancer (TNBC) and epithelial ovarian carcinoma reaffirm the strong genetic underpinnings of these cancer subtypes in India.

These findings have far-reaching implications for both clinical practice and public health policy. The high prevalence observed supports the expansion of germline BRCA testing beyond traditional high-risk or family history-based criteria, especially to all patients with ovarian cancer and those with TNBC diagnosed at any age. Widespread implementation of cost-effective testing strategies and integration of genetic counseling services into oncology care can facilitate early identification of carriers and enable cascade testing for relatives. Such measures

will ultimately contribute to improved cancer prevention, timely intervention, and reduction in hereditary cancer burden across generations.

From a policy perspective, the results advocate for inclusion of BRCA testing in national cancer control programs and public health insurance schemes to ensure equitable access across socio-economic strata. Establishing centralized variant databases and participation in South Asian genomic reference initiatives are essential to reduce the current high rates of variants of uncertain significance (VUS) and to refine variant interpretation within the Indian context [47]. Furthermore, strengthening laboratory quality standards and mandating comprehensive testing methods that include CNV detection will ensure diagnostic accuracy.

Future research should focus on large-scale, multicentric, population-based studies encompassing underrepresented regions such as the Northeast and rural India. Standardized protocols for reporting mutation types, variant classification, and clinical correlates will enhance data comparability and reliability. In addition, integration of polygenic risk scores and non-BRCA homologous recombination repair genes may provide a more complete understanding of hereditary susceptibility patterns in Indian women [48].

In conclusion, this study underscores the pressing need for a nationally coordinated approach to hereditary cancer testing and genetic counseling. The observed prevalence of germline BRCA1/2 mutations highlights an opportunity for precision prevention, targeted therapy, and family-centered risk management in India. By bridging gaps in awareness, infrastructure, and equity, the Indian oncology community can leverage genetic information to transform cancer care from reactive treatment to proactive risk reduction and early detection.

Conflict of Interest

Not available.

Financial Support

Not available.

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