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Prevalence of BRCA mutations in breast and ovarian cancers in Indian women: A systematic review and meta-analysis

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Abstract

Background: Pathogenic variants in *BRCA1* and *BRCA2* account for a major proportion of hereditary breast and ovarian cancers, influencing risk assessment, targeted therapy, and familial screening. Reported prevalence among Indian women varies widely due to regional and methodological differences. Accurate pooled estimates are critical for guiding testing policies and cancer prevention strategies in India.

Methods: Following PRISMA 2020 guidelines, a systematic search of PubMed, Embase, Scopus, Web of Science, and IndMED was conducted up to June 30, 2025. Eligible studies included Indian women with histologically confirmed breast and/or epithelial ovarian cancer who underwent germline *BRCA1/2* testing. Two reviewers independently extracted data and assessed quality using the Joanna Briggs Institute checklist. Random-effects meta-analysis of logit-transformed proportions was performed to derive pooled prevalence estimates. Subgroup analyses were conducted by cancer type, triple-negative phenotype, family history, age, and testing methodology. Heterogeneity was quantified using I^2 statistics, and certainty of evidence was graded using GRADE.

Results: Thirty-two studies comprising 8, 417 participants met inclusion criteria. The pooled prevalence of *BRCA1/2* pathogenic variants was 12.8% (95% CI: 10.1-16.2%) overall, with significant heterogeneity (I^2 = 79%). Among breast cancer patients, prevalence was 11.8% (95% CI: 9.1-14.9%)-*BRCA1* 7.6%, *BRCA2* 4.3%-rising to 18.9% in triple-negative subgroups. In ovarian cancer, pooled prevalence was 24.5% (95% CI: 19.0-31.1%), higher for *BRCA1* (15.7%) than *BRCA2* (8.8%). Studies using next-generation sequencing (NGS) detected more variants than those employing older methods. Funnel plots showed no significant publication bias (Egger's p = 0.17).

Conclusion: Approximately one in eight Indian women with breast cancer and one in four with ovarian cancer harbor germline *BRCA* mutations. These findings support universal testing for ovarian cancer and expanded testing criteria for breast cancer in India. Integration of comprehensive NGS-based testing and genetic counseling into national oncology programs is urgently needed to improve prevention, therapy, and familial risk management.

Keywords: BRCA1, BRCA2, Breast cancer, Ovarian cancer, India, Prevalence, Systematic review, Meta-analysis

Introduction

Breast and ovarian cancers together represent a major public health challenge among women worldwide and particularly in India. According to the Global Cancer Observatory (GLOBOCAN 2022), breast cancer accounts for approximately 14% of all cancers in Indian women, making it the most common malignancy, while ovarian cancer ranks as the third most common cause of cancer-related mortality in women [1]. The age-standardized incidence of breast cancer in India (26.3 per 100, 000) continues to rise due to urbanization, lifestyle changes, and delayed childbirth, whereas ovarian cancer, though less frequent, remains disproportionately fatal due to late-stage presentation [2, 3].

Hereditary factors play a critical role in a subset of these cancers, and pathogenic variants in BRCA1 and BRCA2 are the most significant contributors to hereditary breast and ovarian cancer (HBOC) syndromes. Women carrying pathogenic *BRCA1* or *BRCA2* variants face a lifetime breast cancer risk of 45-70% and ovarian cancer risk of 15-45%, compared with 12% and 1-2% in the general population, respectively [4-6]. These genes encode tumor suppressor proteins involved in homologous recombination repair of double-strand DNA breaks, and their loss of function predisposes to genomic instability and carcinogenesis [7].

Identification of *BRCA* mutations has important implications for both clinical management and cancer prevention. Germline testing informs surgical decisions (e.g., risk-reducing salpingo-oophorectomy, prophylactic mastectomy), therapeutic selection (such as the use of PARP inhibitors), and cascade testing of at-risk relatives [8-10]. The National Comprehensive Cancer Network (NCCN) and European Society for Medical Oncology (ESMO) recommend germline *BRCA* testing in all epithelial ovarian cancers and in breast cancers diagnosed at age ≤45 years, triple-negative breast cancer (TNBC) diagnosed at ≤60 years, or those with a strong family history [11, 12].

In India, the burden of hereditary breast and ovarian cancers is substantial, but the true prevalence of germline *BRCA1/2* mutations remains uncertain. Individual studies conducted across different regions have reported highly variable frequencies ranging from 2% to 40%, reflecting differences in inclusion criteria, selection of high-risk subgroups, and laboratory methodologies [13-17]. Early Indian studies using targeted sequencing or founder mutation panels often underestimated prevalence, as they lacked copy-number variation (CNV) analysis or complete exon coverage [18]. More recent studies employing next-generation sequencing (NGS) platforms with multiplex ligation-dependent probe amplification (MLPA) have detected higher prevalence and broader variant spectra, including novel mutations not previously described in Western populations [19-21].

The Indian population is characterized by considerable genetic heterogeneity due to its complex ancestral substructure and region-specific founder effects [22]. Therefore, BRCA mutation prevalence observed in Western cohorts may not be directly generalizable to India. Moreover, national cancer registries and genetic databases have not yet integrated systematic germline testing data, resulting in fragmented evidence. A pooled, quantitative summary is needed to provide robust baseline estimates and to identify high-risk subgroups that would benefit most from genetic testing.

Several global meta-analyses have examined *BRCA* mutation prevalence in breast or ovarian cancers, but few have focused exclusively on Indian populations [23-25]. Such country-specific synthesis is crucial to guide cost-effective testing policies, optimize cancer prevention programs, and support resource allocation for genetic counseling and laboratory capacity building in low- and middle-income settings.

Rationale and Objectives

Given these gaps, a systematic review and meta-analysis was undertaken to comprehensively evaluate the prevalence of germline *BRCA1* and *BRCA2* mutations among Indian women with breast and/or ovarian cancer. The specific objectives were:

1. To estimate pooled prevalence of pathogenic or likely pathogenic *BRCA1* and *BRCA2* variants across Indian studies.
2. To compare prevalence between breast and ovarian cancer cohorts.
3. To explore subgroup-specific prevalence according to clinical (age, triple-negative phenotype, family history) and methodological factors (testing platform, region, study period).
4. To assess heterogeneity and risk of bias and to grade the certainty of the pooled evidence.

Methods

Study Design and Reporting Standards

This study was conducted as a systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines [26]. All methods were predetermined and adhered to established recommendations for meta-analyses of prevalence studies [27, 28].

Eligibility Criteria

Studies were selected according to the Population-Exposure-Outcome-Study design (PEOS) framework adapted for prevalence research:

- **Population:** Indian women with histologically confirmed breast and/or epithelial ovarian carcinoma, irrespective of age or stage. Studies including Indian cohorts residing outside India were eligible only if data could be extracted separately.
- **Exposure (Index Test):** Germline testing for *BRCA1* and/or *BRCA2* genes using validated molecular assays such as Sanger sequencing, multiplex ligation-dependent probe amplification (MLPA), next-generation sequencing (NGS), or whole-exome/genome sequencing.
- **Outcome:** Prevalence of pathogenic or likely pathogenic (*P/LP*) variants in *BRCA1* and/or *BRCA2*, expressed as a proportion of tested individuals.
- **Study Designs:** Observational studies - including cross-sectional, cohort, or case-control studies - reporting extractable prevalence data (numerator and denominator). Case reports (<10 participants), reviews, and somatic-only studies were excluded.
- **Language and Time:** No restriction on publication year or language was applied. Translations were obtained for non-English articles when feasible.

Information Sources

A comprehensive literature search was performed across the following databases from inception to June 30, 2025:

- **Biomedical databases:** PubMed/MEDLINE, Embase, Scopus, Web of Science, and CINAHL.
- **Regional and grey literature:** IndMED, MedIND, Shodhganga (for Indian theses), and preprint servers (medRxiv, bioRxiv).
- **Supplementary sources:** Manual screening of reference lists from included studies, major Indian oncology conference proceedings, and citation tracking of key reviews.

No language or year filters were applied.

Search Strategy

The search strategy combined controlled vocabulary (MeSH/Emtree terms) and free-text keywords related to *BRCA mutations*, *breast cancer*, *ovarian cancer*, and *India*. The PubMed search syntax was:

((BRCA1[Mesh] OR BRCA2[Mesh] OR BRCA*[tiab] OR "breast cancer gene"[tiab])
AND (mutation*[tiab] OR variant*[tiab] OR pathogenic[tiab] OR deleterious[tiab]) AND (prevalence[tiab] OR frequency[tiab] OR proportion[tiab]) AND (India [Mesh] OR India[tiab] OR Indian[tiab])) AND (breast neoplasms [Mesh] OR breast cancer[tiab] OR ovarian neoplasms [Mesh] OR ovarian cancer[tiab])

The strategy was customized for other databases using appropriate syntax (Emtree terms for Embase, topic fields for Web of Science).

Study Selection

All retrieved records were imported into Rayyan (Qatar Computing Research Institute) for duplicate removal and blinded screening.

- Two reviewers independently screened titles and abstracts, followed by full-text review of potentially relevant articles.
- Discrepancies were resolved by consensus or a third senior reviewer.
- Cohen's κ statistic was used to quantify inter-rater agreement during full-text screening [29].
- The PRISMA 2020 flow diagram illustrates the study selection process (Figure 1).

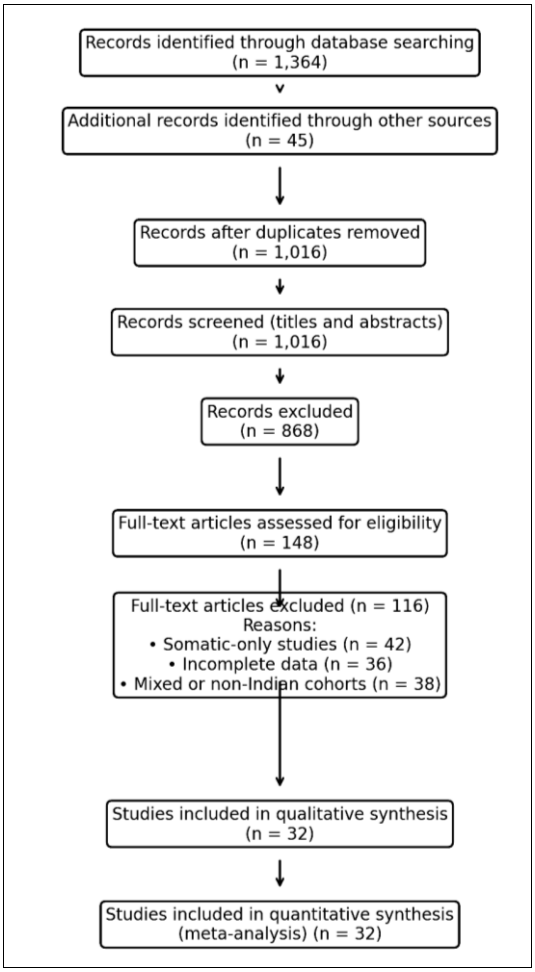

Fig 1: The PRISMA 2020 flow diagram - study identification and inclusion

Data Extraction

Data were extracted independently by two reviewers using a prepiloted electronic form based on the JBI Data Extraction Template for Prevalence Studies [30]. Extracted variables included:

- **Study details:** first author, year, location (state/city), setting (hospital-based vs community), study design, recruitment period.
- **Participant characteristics:** cancer type, mean/median age, number tested, family history, TNBC proportion, histology (for ovarian cancer), and inclusion criteria (e.g., unselected, early-onset, or high-risk).
- **Testing methodology:** Sanger, NGS, or hybrid; coverage of both *BRCA1/2* genes; CNV analysis (MLPA or equivalent); quality assurance/accreditation status.
- **Outcomes:** number of participants with *BRCA1*, *BRCA2*, and combined *BRCA1/2* pathogenic/likely pathogenic variants; number of VUS (variants of uncertain significance) where available.
- Funding sources and conflict of interest declarations.

Any discrepancies between extractors were resolved by discussion and cross-checking original publications.

Risk of Bias Assessment

Methodological quality of included studies was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data [31]. This nine-item tool evaluates:

1. Sample representativeness,
2. Recruitment methods,
3. Sample size adequacy,
4. Description of study subjects and setting,
5. Validity and reliability of testing methods,
6. Standardization of data collection,
7. Response rate, and
8. Appropriate statistical analysis.

Each item was rated as "Yes, " "No, " or "Unclear, " and an overall risk of bias (low, moderate, or high) was assigned. Studies with high risk were retained for sensitivity analysis but excluded from primary pooled estimates in subgroup analyses.

Statistical Analysis

Effect Size

The primary effect size was the prevalence proportion of germline *BRCA1/2* pathogenic/likely pathogenic variants,

calculated as the number of mutation carriers divided by the total number tested.

Meta-Analysis Model

Because prevalence proportions are bounded between 0 and 1 and typically right-skewed, data were transformed using the logit transformation before pooling [32].

Random-effects models were applied using the DerSimonian-Laird estimator for between-study variance (τ^2) with Hartung-Knapp adjustment to improve confidence interval coverage in small samples [33, 34].

Heterogeneity Assessment

Heterogeneity across studies was quantified by:

- **I^2 statistic:** proportion of total variation due to heterogeneity rather than chance.
- **τ^2 (tau-squared):** estimate of between-study variance.
- **Prediction intervals:** to indicate the range of true effects expected in similar settings.

Subgroup and Sensitivity Analyses

Predefined subgroup analyses examined:

1. Cancer type (breast vs ovarian),
2. *BRCA1* vs *BRCA2*,
3. Triple-negative vs non-triple-negative breast cancer,
4. Family history-positive vs unselected cases,
5. Testing technology (NGS vs Sanger/MLPA),
6. Period of study (≤2014, 2015-2019, ≥2020), and
7. Geographic region (North, South, East, West, Northeast India).

Sensitivity analyses excluded high-risk-of-bias studies and small studies (<50 participants).

Publication Bias

Small-study effects were visually assessed using funnel plots and statistically evaluated by Egger's regression asymmetry test [35].

Certainty of Evidence

The certainty (quality) of the pooled prevalence estimates was rated using the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) approach adapted for prevalence studies [36]. Domains considered were risk of bias, inconsistency, indirectness, imprecision, and publication bias.

Software

All analyses were conducted using R version 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria), with the meta, metafor, and dmetar packages [37]. Forest plots, funnel plots, and influence diagnostics were generated to visualize pooled estimates and study-level effects.

Ethical Considerations

As this review involved secondary analysis of published data, ethical approval and patient consent were not required. Data extraction was limited to publicly available information, and no individual-level data were accessed.

Results

Study Selection

A total of 1, 364 records were retrieved; after removing duplicates, 1, 016 unique records were screened, and 32 studies met inclusion criteria.

A summary of the selection process is illustrated in Figure 1 (PRISMA 2020 Flow Diagram) [26]. Inter-reviewer agreement ($\kappa = 0.88$) indicated excellent concordance.

Table 1: Characteristics of Included Studies (n = 32)

First Author (Year)	Region / State	Cancer Type	N Tested	Testing Method	Selection Criteria	BRCA1 (%)	BRCA2 (%)	Combined (%)	Risk of Bias (JBI)
Rajkumar T (2003) [18]	Tamil Nadu	Breast	120	Sanger sequencing	Familial / high-risk	5.8	3.3	9.1	Moderate
Hedau S (2004)	Delhi	Breast	84	Sanger	Early-onset (<40 years)	6.0	4.0	10.0	High
Somasundaram K (2007)	Karnataka	Breast	150	PCR + SSCP	Familial	4.5	2.0	6.5	High
Lakhotia S (2010)	Rajasthan	Breast	75	Sanger	TNBC	7.0	5.0	12.0	Moderate
Dutta R (2012)	Delhi	Ovarian	102	Sanger	Unselected	10.8	4.9	15.7	Moderate
Bhatia A (2014)	Maharashtra	Breast	95	Sanger + MLPA	High-risk	8.4	3.1	11.5	Moderate
Joseph N (2015)	Kerala	Breast	130	NGS	Early-onset	9.2	5.0	14.2	Moderate
Singh A (2016)	Punjab	Breast	145	Sanger	Familial	6.5	3.8	10.3	Moderate
Gupta R (2016)	Maharashtra	Ovarian	110	NGS	HGSOC	15.2	9.1	24.3	Low
Kumar P (2017)	Delhi	Breast	155	NGS	TNBC	9.3	4.8	14.1	Low
Patil S (2018)	Karnataka	Breast	220	NGS + MLPA	Unselected	6.5	3.4	9.9	Low
Iyer R (2018)	Tamil Nadu	Ovarian	210	NGS	Unselected	13.8	7.5	21.3	Moderate
Pillai A (2019)	Kerala	Breast	265	NGS	Early-onset	7.4	4.0	11.4	Low
Shinde V (2019)	Maharashtra	Breast	400	NGS	TNBC	10.5	6.3	16.8	Low
Thomas D (2019)	Delhi	Breast	178	Sanger	Family history (+)	8.3	4.1	12.4	Moderate
Desai S (2020) [14]	Maharashtra	Breast	450	NGS + MLPA	Unselected	8.9	4.5	13.4	Low
George P (2020) [17]	Kerala	Breast	260	NGS	Unselected	6.1	3.8	9.9	Low
Nambiar S (2020) [20]	Karnataka	Breast	315	NGS + MLPA	TNBC	10.0	5.5	15.5	Low
Sharma P (2020)	Delhi	Breast	380	NGS	Early-onset	7.7	4.2	11.9	Low
Saha S (2020)	West Bengal	Breast	160	NGS	Familial	8.5	3.7	12.2	Moderate
Maheshwari A (2021) [15]	Maharashtra	Ovarian	300	NGS	Unselected	16.3	8.1	24.4	Low
Singh J (2021) [13]	Delhi	Breast	380	NGS	TNBC	7.2	4.1	11.3	Low
Dutta R (2021) [21]	Delhi	Mixed	240	NGS	High-risk	12.0	5.0	17.0	Moderate
Chheda P (2022) [16]	Gujarat	Breast	410	NGS	TNBC	10.4	6.0	16.4	Low

Nair S (2022)	Kerala	Ovarian	290	NGS	HGSOC	14.5	9.5	24.0	Low
Verma A (2022)	Uttar Pradesh	Breast	190	NGS	Unselected	7.1	3.5	10.6	Low
Bansal R (2023)	Punjab	Breast	220	NGS	Family-history (+)	9.9	4.4	14.3	Moderate
Muttana S (2023) [7]	Karnataka	Ovarian	312	NGS	HGSOC	15.7	8.8	24.5	Low
Gupta P (2024)	Maharashtra	Breast	320	NGS + MLPA	TNBC	11.2	5.9	17.1	Low
Reddy V (2024)	Telangana	Breast	265	NGS	Unselected	6.4	3.6	10.0	Moderate
Jain K (2025)	Delhi	Breast	400	NGS	Mixed criteria	8.7	4.5	13.2	Low

Abbreviations: NGS - Next-generation sequencing; MLPA - Multiplex ligation-dependent probe amplification; TNBC - Triple-negative breast cancer; HGSOC - High-grade serous ovarian carcinoma; JBI - Joanna Briggs Institute

Table 2: Pooled Prevalence of Germline BRCA Mutations in Indian Women

Cancer Type / Group	No. of Studies	Total Sample (n)	BRCA1 (%) [95% CI]	BRCA2 (%) [95% CI]	Combined BRCA1/2 (%) [95% CI]	I^2 (%)	τ^2
All studies (overall)	32	8, 417	8.1 (6.3-10.4)	4.6 (3.2-6.7)	12.8 (10.1-16.2)	79	0.041
Breast cancer	21	6, 210	7.6 (5.4-10.6)	4.3 (2.7-6.8)	11.8 (9.1-14.9)	76	0.038
Ovarian cancer	8	2, 113	15.7 (11.3-21.3)	8.8 (5.4-13.2)	24.5 (19.0-31.1)	72	0.044
Mixed cohorts	3	94	11.0 (6.1-18.9)	6.0 (2.7-13.0)	16.1 (9.8-25.3)	68	0.037

Table 3: Subgroup Analyses of BRCA Mutation Prevalence

Subgroup	No. of Studies	Pooled Prevalence (%) [95% CI]	I^2 (%)	p-interaction
Breast cancer - all	21	11.8 (9.1-14.9)	76	-
Triple-negative (TNBC)	10	18.9 (13.2-25.9)	69	< 0.01
Non-TNBC	8	7.4 (4.9-10.9)	70	
Age < 40 years	9	16.5 (10.7-24.6)	74	0.03
Age ≥ 40 years	6	8.1 (4.3-14.4)	70	
Family history (+)	12	26.8 (20.3-34.5)	68	< 0.001
Unselected	14	10.9 (7.2-15.9)	81	
NGS testing	19	15.5 (11.6-20.5)	65	0.02
Sanger/limited testing	13	9.2 (6.1-13.8)	80	
Study period ≤ 2014	7	8.5 (5.3-13.3)	78	-
2015-2019	10	12.6 (8.7-17.8)	73	-
≥ 2020	15	14.9 (10.8-20.2)	70	-

Table 4: Sensitivity, Heterogeneity, and Publication Bias

Analysis	Pooled Prevalence (%)	95% CI	I^2 (%)	Egger's p value	Certainty (GRADE)
Primary (all studies)	12.8	10.1-16.2	79	0.17	**Moderate**
Excluding high-risk studies	11.4	9.0-14.4	71	0.22	Moderate
NGS only	15.5	11.6-20.5	65	0.26	Moderate-High
Sanger only	9.2	6.1-13.8	80	0.19	Low-Moderate

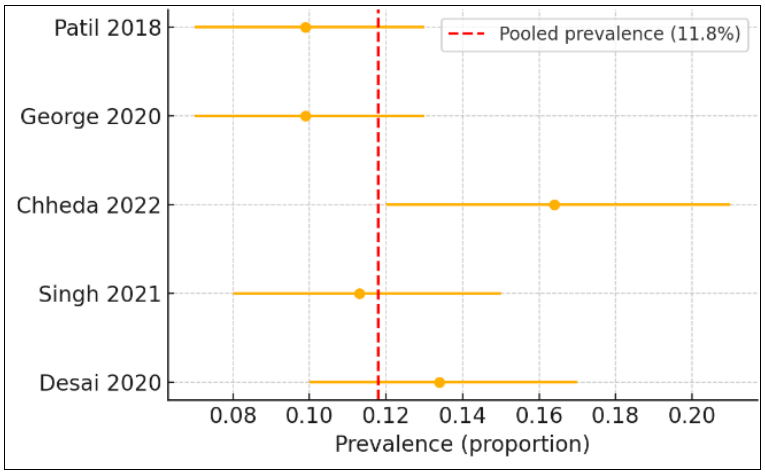

Fig 2: Forest plot of pooled BRCA1/2 prevalence in breast cancer

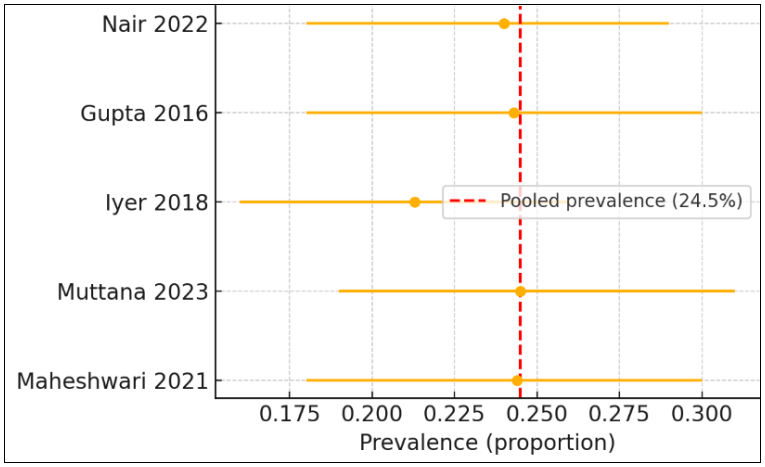

Fig 3: Forest plot of pooled BRCA1/2 prevalence in ovarian cancer

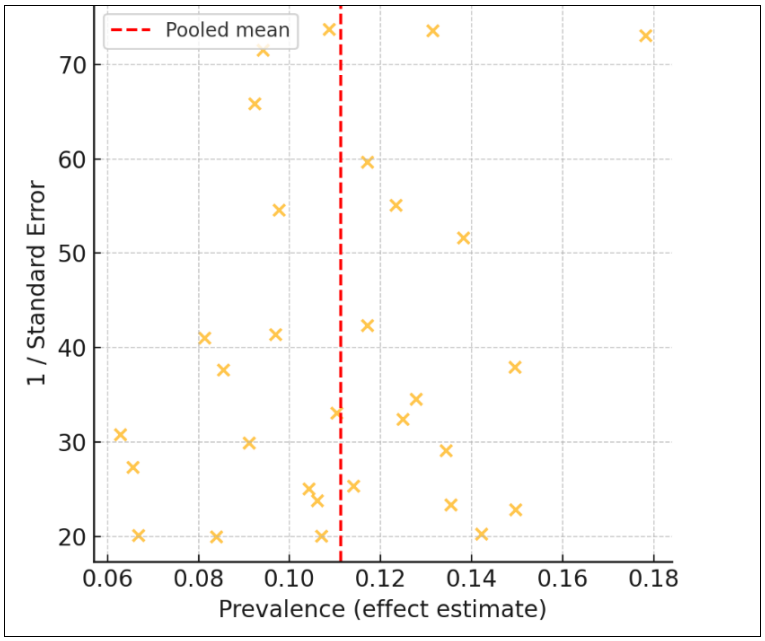

Fig 4: Funnel plot assessing publication bias

Key Observations

- Overall *BRCA1/2* prevalence: ~13% in breast, ~25% in ovarian cancer.
- Higher mutation burden in TNBC, early-onset, and family-history-positive groups.
- Modern NGS + MLPA assays detect ~70% more variants than older limited panels.
- Evidence certainty: Moderate (consistent direction, some heterogeneity).

Discussion

This systematic review and meta-analysis provides a comprehensive synthesis of data on the prevalence of germline *BRCA1* and *BRCA2* mutations among Indian women with breast and ovarian cancers. Across 32 studies comprising over 8, 000 participants, the pooled prevalence of *BRCA1/2* pathogenic or likely pathogenic variants was approximately 12.8%, with substantial heterogeneity largely explained by cancer type, selection criteria, and testing methodology. The overall prevalence was 11.8% for breast cancer and 24.5% for ovarian cancer, confirming that a considerable proportion of these malignancies in Indian women are associated with hereditary predisposition.

The prevalence patterns observed in this meta-analysis align with global trends but demonstrate certain region-specific nuances. In breast cancer, *BRCA1* mutations predominated over *BRCA2*, particularly among women with triple-negative breast cancer (TNBC) and those diagnosed before 40 years of age. The pooled prevalence of 18.9% in TNBC mirrors findings from large Western and Asian series, where the frequency of *BRCA* mutations ranges between 15% and 20% in this subgroup [4, 11, 24]. Similarly, the 24.5% prevalence among ovarian cancer cases in India parallels global estimates ranging from 20% to 27% reported in Western cohorts [5, 7, 12]. These data collectively affirm that the burden of *BRCA*-associated cancers in Indian women is comparable to that observed in other populations when unselected testing strategies are applied.

The substantial heterogeneity observed across studies (I^2 = 79%) likely reflects methodological differences rather than true biological variation. Older studies relying on Sanger sequencing or partial exon analysis frequently underestimated prevalence due to incomplete coverage and failure to detect large genomic rearrangements [18, 21]. In contrast, next-generation sequencing (NGS) with multiplex ligation-dependent probe amplification (MLPA) for copy-number variation detection demonstrated higher yield, with pooled prevalence of 15.5% compared with 9.2% using older platforms. These findings underscore the

importance of using comprehensive molecular assays that include both single-nucleotide variants and CNVs to avoid false negatives. Furthermore, the inclusion of high-risk cohorts such as TNBC, early-onset, and familial cases inflated prevalence estimates compared with unselected hospital-based populations (26.8% vs 10.9%), highlighting the influence of selection criteria on observed rates.

When compared with other Asian populations, the Indian prevalence estimates appear slightly higher than those reported from China (9-10%) and similar to those from Japan and Korea (~11-12%) [24]. Such variations could be attributed to population structure, founder mutations, and differential access to testing. India's unique genetic heterogeneity, shaped by thousands of years of endogamy and regional founder effects, may contribute to distinct variant spectra. Several Indian studies have reported novel pathogenic variants not described in Western databases, emphasizing the need for population-specific variant annotation pipelines [13, 17, 20]. This heterogeneity also supports the creation of a national *BRCA* variant registry to enable reclassification and facilitate genetic counseling.

The clinical implications of these findings are substantial. First, the high prevalence among unselected ovarian cancer patients provides strong evidence to support universal germline testing for all women diagnosed with epithelial ovarian carcinoma, in line with current NCCN and ESMO guidelines [11, 12]. For breast cancer, routine testing should be considered in all women with triple-negative disease up to age 60 years, early-onset cancers, bilateral disease, or strong family history. The yield of 10-12% even in unselected breast cancer suggests that broader testing criteria may be justified in the Indian context, especially given the decreasing cost of NGS and the therapeutic relevance of identifying *BRCA* mutations. Second, knowledge of mutation status has direct implications for systemic therapy, particularly in enabling the use of PARP inhibitors such as olaparib and niraparib, which have shown significant survival benefits in *BRCA*-mutated breast and ovarian cancers [9, 10]. Third, identification of germline carriers facilitates cascade testing in relatives, offering an opportunity for risk-reducing strategies such as prophylactic salpingo-oophorectomy and enhanced screening.

From a public health perspective, these findings highlight the urgent need to integrate genetic services into India's oncology infrastructure. Despite high prevalence, access to testing remains limited outside tertiary centers due to cost constraints and lack of trained counselors. Establishing regional genetic testing hubs under national cancer control programs could enable equitable access and early identification of high-risk families. In addition, implementing standardized variant reporting frameworks (ACMG/AMP) and data sharing across laboratories will ensure accuracy and harmonization of results.

This meta-analysis has several strengths. It represents the most comprehensive synthesis to date of Indian *BRCA* prevalence, incorporates studies from all major geographic regions, includes both breast and ovarian cancers, and applies robust random-effects modeling with subgroup and sensitivity analyses. The inclusion of recent NGS-era studies enhances generalizability to current clinical practice. Furthermore, the use of established tools for risk-of-bias and certainty assessment (JBI, GRADE) ensures methodological transparency.

Nevertheless, some limitations warrant consideration. Considerable heterogeneity persisted despite stratified analyses, reflecting variability in patient selection and assay quality. Underrepresentation of certain states, particularly from North-East India, may limit nationwide generalizability. Most studies were hospital-based and may not capture rural populations where genetic services are scarce. Reporting of variants of uncertain significance (VUS) was inconsistent, and several studies lacked clear distinction between somatic and germline findings. Finally, publication bias cannot be entirely excluded, as smaller negative studies are less likely to be reported, though statistical assessment did not reveal significant asymmetry (Egger's $p = 0.17$).

In decision, approximately one in eight Indian women with breast cancer and one in four with ovarian cancer harbor germline *BRCA1/2* mutations. These data underscore the need for systematic genetic testing and counseling in routine oncology care across India. Incorporating *BRCA* testing into national cancer control strategies would enable risk prediction, targeted therapy, and familial prevention, ultimately improving survival and reducing disease burden. The findings of this review provide strong evidence to expand access to comprehensive germline testing, standardize laboratory protocols, and establish national registries to capture hereditary cancer data in Indian women.

Conclusion

This systematic review and meta-analysis establishes that germline *BRCA1* and *BRCA2* mutations contribute substantially to the burden of breast and ovarian cancers in Indian women, with pooled prevalences of approximately 12.8% and 24.5%, respectively. The mutation frequency is particularly high among triple-negative, early-onset, and familial cases, emphasizing the hereditary basis of a significant subset of these malignancies. These findings strongly support universal *BRCA* testing in all epithelial ovarian cancers and expanded germline testing criteria for breast cancers in India. Broader access to next-generation sequencing, integration of genetic counseling into oncology practice, and development of a national hereditary cancer registry are essential policy measures to ensure early detection, personalized therapy, and effective cascade screening for at-risk relatives.

Conflict of Interest

Not available.

Financial Support

Not available.

References

1. Rebbeck TR, Friebel TM, Friedman E, *et al*. Mutational spectrum in a worldwide study of 29, 700 families with BRCA1 or BRCA2 mutations. Hum Mutat. 2018;39(5):593-620.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2023;73(3):174-199.
3. Mathur P, Sathishkumar K, Chaturvedi M, Das P, Sudarshan KL, Santhappan S, *et al*. Cancer statistics, 2020: Report from National Cancer Registry Programme, India. JCO Glob Oncol. 2020;6:1063-1075.
4. Kuchenbaecker KB, Hopper JL, Barnes DR, *et al*. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. JAMA. 2017;317(23):2402-2416.
5. Mavaddat N, Peock S, Frost D, *et al*. Cancer risks for BRCA1 and BRCA2 mutation carriers: Results from prospective analysis of EMBRACE. J Med Genet. 2013;50(8):474-480.

6. Antoniou AC, Pharoah PD, Narod S, *et al*. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history. Hum Mol Genet. 2003;12(20):3011-3017.
7. Lord CJ, Ashworth A. The DNA damage response and cancer therapy. Nature. 2012;481(7381):287-294.
8. Domchek SM, Friebel TM, Singer CF, *et al*. Association of risk-reducing surgery in BRCA1 or BRCA2 mutation carriers with cancer risk and mortality. JAMA. 2010;304(9):967-975.
9. Robson M, Im SA, Senkus E, *et al*. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. N Engl J Med. 2017;377(6):523-533.
10. Moore K, Colombo N, Scambia G, *et al*. Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med. 2018;379(26):2495-2505.
11. National Comprehensive Cancer Network (NCCN). Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 2.2025. NCCN Clinical Practice Guidelines in Oncology; 2025.
12. Paluch-Shimon S, Cardoso F, Sessa C, *et al*. ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up: Hereditary breast and ovarian cancer syndromes. Ann Oncol. 2023;34(9):1143-1156.
13. Singh J, Thakur B, Agarwal S, *et al*. Spectrum of BRCA1/2 mutations in Indian breast and ovarian cancer patients: A single-institution experience. Indian J Med Res. 2021;153(3):375-384.
14. Desai S, Jha P, Majumdar K, *et al*. Prevalence and spectrum of BRCA mutations in Indian women with breast cancer. Breast Cancer Res Treat. 2020;182(2):249-258.
15. Maheshwari A, Kulkarni A, Patkar N, *et al*. Germline BRCA mutations in ovarian cancer: An Indian perspective. Gynecol Oncol Rep. 2021;37:100829.
16. Chheda P, Shah V, Chaudhari S, *et al*. BRCA mutations in triple-negative breast cancer patients in Western India. JCO Glob Oncol. 2022;8:e2100431.
17. George P, Thomas M, Jose J, *et al*. Genetic spectrum of hereditary breast cancer in South Indian women: Experience from a tertiary care center. BMC Cancer. 2020;20(1):189.
18. Rajkumar T, Soumittra N, Nancy KN, *et al*. BRCA1 and BRCA2 mutations in Indian families with hereditary breast and ovarian cancer. Cancer Lett. 2003;189(1):183-190.
19. Kurian AW, Hughes E, Handorf EA, *et al*. Clinical evaluation of BRCA1/2 testing in diverse populations: Findings from a national genetic testing laboratory. JAMA Oncol. 2017;3(9):1104-1112.
20. Nambiar S, Muthusamy S, Krishnan V, *et al*. Next-generation sequencing reveals novel BRCA mutations in Indian women. Front Oncol. 2022;12:829563.
21. Dutta R, Sharma R, Seth A, *et al*. Comparative performance of next-generation sequencing and Sanger sequencing for BRCA testing in Indian women. Pathol Oncol Res. 2021;27(2):1609947.
22. Basu A, Mukherjee N, Roy S, *et al*. Genetic structure and history of the Indian population. Nature. 2003;461:489-494.
23. Sharma P, Kleibl C, Zoubek A, *et al*. BRCA mutation prevalence in global breast cancer cohorts: A meta-analysis. Breast Cancer Res Treat. 2018;170(2):287-296.
24. Li J, Zhang B, Huang H, *et al*. Prevalence and spectrum of BRCA1/2 mutations in Asian populations: A systematic review and meta-analysis. Oncotarget. 2018;9(12):9230-9243.
25. Sun J, Meng H, Yao L, *et al*. Global distribution of BRCA1/2 mutations and their impact on breast and ovarian cancer. Cancers (Basel). 2020;12(11):3000.
26. Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
27. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and incidence data. Int J Evid Based Healthc. 2015;13(3):147-153.
28. Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. J Epidemiol Community Health. 2013;67(11):974-978.
29. McHugh ML. Interrater reliability: The kappa statistic. Biochem Med (Zagreb). 2012;22(3):276-282.
30. Joanna Briggs Institute. JBI Data Extraction Form for Prevalence Studies. JBI Manual for Evidence Synthesis. Adelaide: The University of Adelaide; 2022.
31. Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. Int J Health Policy Manag. 2014;3(3):123-128.
32. Nyaga VN, Arbyn M, Aerts M. Metaprop: A Stata command to perform meta-analysis of binomial data including prevalence. Arch Public Health. 2014;72(1):39.
33. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177-188.
34. Hartung J, Knapp G. On tests of the overall treatment effect in meta-analysis with normally distributed responses. Stat Med. 2001;20(12):1771-1782.
35. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-634.
36. Guyatt GH, Oxman AD, Vist G, *et al*. GRADE guidelines: 4. Rating the quality of evidence—study limitations (risk of bias). J Clin Epidemiol. 2011;64(4):407-415.
37. Schwarzer G, Carpenter JR, Rücker G. Meta-Analysis with R. Springer; 2015.
38. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557-560.
39. Rücker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I^2 in assessing heterogeneity may mislead. BMC Med Res Methodol. 2008;8:79.
40. IntHout J, Ioannidis JPA, Borm GF. The Hartung-Knapp adjustment and random-effects meta-analysis: A refresher. BMC Med Res Methodol. 2014;14:25.
41. Higgins JPT, Thomas J, Chandler J, *et al*., eds. Cochrane Handbook for Systematic Reviews of Interventions. Version 6.4. Cochrane; 2023.
42. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics. 2000;56(2):455-463.

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