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Systematic Review and Meta-analysis

Epidemiology, Risk Factors, Health Literacy and Emerging Diagnostic Approaches of Breast Cancer in Sri Lanka: A Systematic Review

Wanasinghe MHBSM*, Wijesuriya PASL, Jayewardene KLTD

Department of Medical Laboratory Science, Faculty of Allied Health Sciences, University of Peradeniya, Sri Lanka

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***Corresponding author:**
Wanasinghe, MHBSM
Tel: +94 716558654
Email:
sandunisithara256@gmail.com
sitharaw@ahs.pdn.ac.lk

Abstract

A thorough grasp of epidemiology and screening techniques is required due to the increasing incidence of breast cancer in Sri Lanka. This review aims to study breast cancer epidemiology, health literacy and screening methods in Sri Lanka. A systematic search was conducted in Medline, Embase, PUBMED, and AMED databases with studies conducted in Sri Lanka up to 2024. Two independent researchers identified 149 studies, from which data were extracted from 27 eligible studies by the PRISMA guidelines. The quality of the studies was evaluated using the quality assessment tools in the National Institute of Health. The available epidemiological data on breast cancer in Sri Lanka are limited. Contributing factors to the high mortality rate include low health literacy, barriers to care, and delays in diagnosis and treatment. The awareness about breast cancer is low, especially regarding diagnosis and breast self-examination (BSE). The practice of BSE is rare. Health education appears to improve health literacy. Notable breast cancer risk factors are menopause, abortions, passive smoking, age (>45), early menarche (<12 years), late menopause (>55 years), no children, oral contraceptives, alcohol and tobacco use, diabetes, family history, radiation, obesity, and prolonged breastfeeding. The screening and diagnosis tests are mammography, breast self-examination, clinical breast examination, molecular detection, and histology. The limited resources allocated for screening and diagnostic services in Sri Lanka present a significant challenge for early detection and management of diseases. The future paths for the diagnosis are considering genetic variations with advanced molecular methods. Considering the high incidence and limited awareness, the adoption of highly accurate screening and diagnosis techniques, with nationally accessible educational programs about breast cancer awareness is necessary.

***Keywords**: Breast cancer, Epidemiology, Health literacy, Screening, Diagnosis*

Introduction

Breast cancer stands as a formidable global health challenge, affecting millions of women and, to a lesser extent, men [1-7]. Women are a risk of developing breast cancer at any age after puberty, and the risk increases with age [7]. In most nations, this disease pattern is common.

Breast cancers are an expansion of the epithelial cells that line the glandular tissue of the lobules (15%) or ducts (85%) of the breast. In situ refers to the initial confinement of the malignant development to the duct or lobule and usually presents with no symptoms and minor metastasis changes. Yet, over time, these in situ (stage 0) tumors may develop into regional metastasis (invade neighboring lymph nodes) or may develop into distant metastasis as invasive breast cancer (invade the breast tissue around). Extensive metastasis is the frequent cause of death due to the breast cancers in women [4,7].

The disease of breast cancer is not contagious. There are no known viral or bacterial infections linked to the development of breast cancer, in contrast to several cancers that have infection-related origins, such as human papilloma virus infection and cervical cancer [7].

Worldwide, 1.5 million women, or about 25% of all cancer patients, receive a breast cancer diagnosis each year [2,5]. Globally, 2.3 million women had a breast cancer diagnosis in 2020, and 685,000 deaths were attributed to the disease. Among Asian women, breast cancer is the most common cancer. In 2017, a huge number of new cases has been reported among women [6]. Male breast cancer accounts for approximately 0.5% to 1% of all breast cancer cases worldwide. Despite the biological and clinical differences, men are generally diagnosed, treated, and managed same as female breast cancer patients. [7].

A thorough grasp of the epidemiology of the diseases and screening methods within Sri Lanka, a country in central Asia, is desperately needed as the country struggles with an increasing number of breast cancer cases [1, 8-11]. Over time, breast cancer has become more common in Sri Lanka. Data from the National Cancer Registry reveals a doubling of breast cancer cases from 4.6 per 100,000 women in 1985 to 9.8 in 2005, highlighting a substantial and alarming increase. This surge in cases poses a significant public health challenge and also underscores the urgency of understanding the underlying factors contributing to this trend. Previous studies provide glimpses into the prevalence landscape; nevertheless, a systematic review is warranted to synthesise and critically appraise the existing literature, identifying gaps and opportunities for further exploration [1,8].

More than half of the women diagnosed with breast cancer had no known risk factors for the disease, except for age and female gender [1,7]. Some important known risk factors for breast cancer include aging (over 40), obesity, alcohol consumption, family history, reproductive history, including the age of the first pregnancy and menstruation, radiation exposure, tobacco use, and postmenopausal hormone therapy [1,7]. The female gender is considered the major risk factor [1,7]. Early detection remains a cornerstone in mitigating the impact of breast cancer [12,13]. In Sri Lanka, however, challenges in access to care,

knowledge gaps, and delays in screening, diagnosis, and treatment have contributed to a relatively low survival rate [9,14-17]. Understanding the efficacy of existing strategies and potential barriers to their implementation is pivotal in designing targeted interventions that can enhance early detection rates and, subsequently, survival outcomes.

The role of health literacy in breast cancer awareness, prevention, and early detection cannot be overstated. According to some previous studies, Sri Lanka grapples with disparities in health literacy, which can impact the effectiveness of screening programs and overall disease understanding [9,14-17]. Worldwide, mammography, breast MRI, and breast self-examination are recommended breast cancer screening methods. Although breast cancer is the most common cancer in Sri Lanka, limited resources prevent a nationwide mammography program. Mammography is available in 18 public hospitals and some private facilities, but breast self-examination is promoted as an alternative [18-20]. Globally, advanced diagnostic techniques such as MRI, flow cytometry, ultrasound, RT-qPCR, and hybridization methods are used, but molecular diagnostics in Sri Lanka are largely limited to the Medical Research Institute [18-20].

This systematic review explores breast cancer in Sri Lanka, focusing on its prevalence, risk factors, and the effectiveness of current screening and diagnostic methods. By comparing local practices with global standards, the review aims to inform public health strategies and improve early detection and outcomes for the readers. A key component is assessing community health literacy on breast cancer. By identifying knowledge gaps, future researchers can develop targeted educational initiatives that empower individuals to make informed decisions, reduce risk, and better navigate healthcare systems through improved awareness and understanding of prevention and early detection.

Methods

The protocol for the current systematic review, considering the study design, was registered on September 22, 2022, in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42022359600). The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocol served as the basis for the methodology of the current systematic review (Figure 01) [1, 21].

Any studies published in English were considered. All the full paper articles that assessed breast cancer diagnosis conditions in adult humans that were conducted only in Sri Lanka were eligible to be included in the review. Studies that were in other languages, not conducted in Sri Lanka, were excluded. Conference papers, review papers, commentaries, research notes, reports, or editorials were also excluded. The systematic review was conducted at the Department of Medical Laboratory Science, Faculty of Allied Health Sciences, University of Peradeniya.

Data up to 2024 were searched using Medline, Embase, Google Scholar, PUBMED, and AMED databases. The search strategy used key terms related to breast cancer in Sri Lanka: epidemiology, health literacy, screening, diagnosis, and risk factors.

Studies assessing epidemiological data (prevalence, incidence, mortality rates, and survival rates) of breast cancer in Sri Lanka were extracted. Potential risk factors for breast cancer, screening, and diagnosis methods, and the level of health literacy of the community about breast cancer in Sri Lanka were also eligible for the final inclusion. Future directions regarding study on breast cancer were also noted. Two reviewers separately extracted the data and inspected the whole text, abstract, and titles. A third reviewer was involved if there were any disagreements.

The data were extracted directly into the COVIDENCE software and then exported into an Excel sheet for further analysis. The publication details (Supplementary Materials; Table 01), the data regarding the people with breast cancer, and details about the outcomes were extracted. Data were narratively synthesised, and the findings were tabulated and graphically summarised to address the research objectives appropriately.

The epidemiology of breast cancers in Sri Lanka, including their prevalence, incidence, mortality, and survival rates, was the primary outcome measure. Any quantitative and qualitative outcome measures were used to measure outcomes. As the secondary outcome measures, potential risk factors for breast cancer, screening, and diagnosis methods, and the level of health literacy of the community about breast cancer in Sri Lanka, including patients, healthcare workers, and school children, were assessed. Any quantitative and qualitative outcome measures were used to measure secondary outcomes.

The quality of the included studies was evaluated using quality assessment tools for observational cohort and cross-sectional studies, controlled intervention studies, systematic review and meta-analysis, and case-control studies in the National Heart, Lung and Blood Institute [22]. Although not all quality assessment criteria were fully met, all 27 studies were included due to the limited number of articles available in Sri Lanka, particularly on breast cancer epidemiology.

Results

A total of 149 citations were found in the preliminary literature search. The duplicates were removed, and the inclusion and exclusion criteria were applied. Of these, 27 studies were found to need additional examination (Figure 01).

When considering the quality of the studies included in the review, almost all studies have clearly stated the research questions or objectives. Predetermined inclusion and exclusion criteria were not reported in over half of the investigations. The exposure and outcome measurements in the majority of the research were well-defined, legitimate, and trustworthy. However, the majority of studies did not report the sample size rationale. The following criteria did not apply in most studies: follow-up after baseline ≤20%, adjustment for potential confounding variables, adequate time frame, exposure(s) of interest measured before the outcome(s), exposure(s) measured more than once over time, and outcome assessors blinded to the exposure status (Supplementary materials -Figure 01).

Epidemiology of breast cancer in Sri Lanka

There were only 10 studies that provided information on epidemiology (Table 01). However, it lacked some necessary information,

particularly about the prevalence, mortality, and morbidity rates of breast cancer in Sri Lanka.

In one study on breast cancer in Sri Lanka, two-thirds of patients were diagnosed at stages I and II at the time of diagnosis. Approximately 72% of patients tested positive for estrogen receptor (ER)/progesterone receptor (PR), while 22% tested positive for human epidermal growth factor receptor 2 (HER-2) [11, 19, 23-25]. Fifty-three (24%) of the tumors were triple-negative [19]. Diabetes mellitus and hypertension were common co-morbidities [11]. The incidence of female breast cancer in Sri Lanka has risen from 17.3 per 100,000 in 2001 to 24.7 per 100,000 in 2010. This increase has been steady but considerable [8]. Furthermore, the age group of 75 and older had the highest incidence of male breast cancer (3.38 per 100,000 people) [8]. In the included studies, the survival rates were around 70-90% (acceptable 5-year survival rates without breast cancer). Patients with localised cancer had a 1.6% median overall survival rate, whereas patients with metastatic disease had a 30-month median survival rate [17, 20, 26, 27]. The mortality rate was 9% [20].

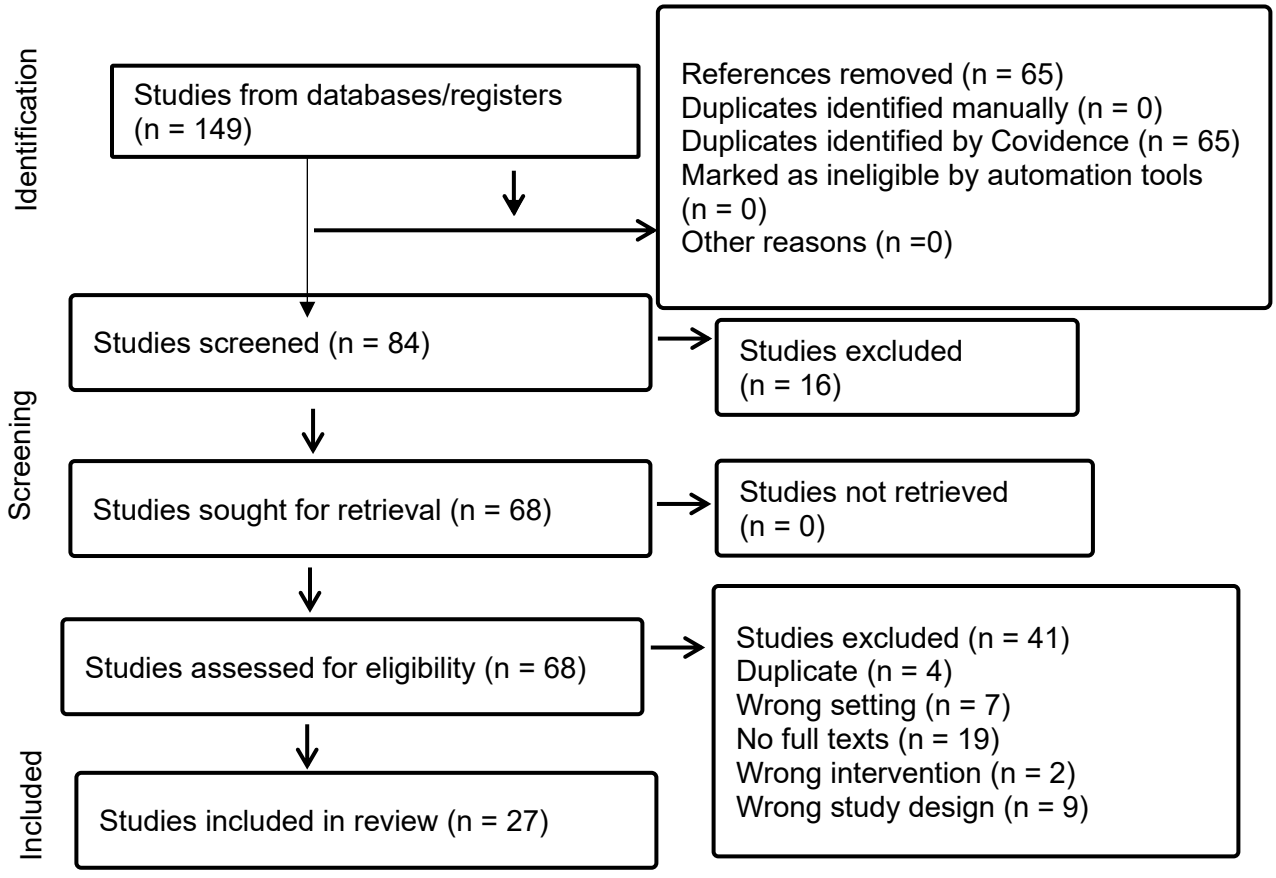

Figure 01: Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram.

Sri Lankan health literacy concerning breast cancer

Nine studies offered health literacy related to breast cancer in Sri Lanka (Table 01).

Inadequate health information about breast cancer was found in eight of the nine investigations, especially about diagnosis and breast self-examination (BSE) [14, 15, 18, 28-33]. Women's awareness was marginally higher than men's [15]. Effective health education programs have been shown to raise health literacy in the population [18, 32, 33]. Even though health literacy is higher in one study, participants' clinical breast inspection and self-examination practices are very poor [32].

Table 01 Main findings of epidemiology, health literacy, risk factors, screening, diagnosis, and future directions of breast cancer in Sri Lanka

No. of participants	Sex	Mean age (years)	Outcome	Sources
>2000	Female	52	The acceptable 5-year survival rate is 71% breast cancer.	[17]
73		34.5	In the BRCA2 hotspot locations, the prevalence of pathogenic and potentially pathogenic mutations was 6.3% and 23%, respectively.	[23]
19,755	98% were females and 2% were males.	53.1	The percentage of female breast cancer in Sri Lanka has gradually increased (17.3 per 100,000 in 2001 (95% confidence interval (CI) to 24.7 per 100,000 in 2010 (95% CI).	[8]
713	Female	NI	Recurrence-free survival (RFS) was Low-risk (LR) -85%, intermediate-risk (IR) -84%, and high-risk (HR) -65%, and five-year breast cancer-specific survival was LR-100%, IR-91%, HR-66%.	[26]
944	Female	NI	The breast cancer-specific survival after five years = 78.8%.	[27]
233	Female	55	94% of malignancies are ductal carcinoma.	[24]
124	Female	NI	Global studies indicate that the rates of ER, PR, and Her/2neu amplification in breast cancer were comparable among Sri Lankans.	[25]

5181	Female	56	At the time of diagnosis, two-thirds (66%) of the malignancies were in stages I and II.	[11]
221	Female	56.25	Fifty-three (24%) of the overall tumors were triple-negative (95% CI=18.37%–29.63%).	[19]
208	Female	56.39	19 (9%) People died, leaving 174 (82.9%) disease-free. With metastases, 13 (6.2%) and 4 (1.9%) of the survivors experienced recurrences.	[20]
865	Female	55.5	Insufficient understanding and knowledge about breast cancer (odds ratio 1.7; 95% confidence interval 1.1-2.7)	[28]
			Poor knowledge	[29]
400	Female	27-76	Insufficient knowledge about diseases, treatments, diagnosis, and physical screenings, particularly among younger (age ≤37) and more educated (p<0.0001) women.	[30]
1500	Male-725 Female-775	37.21	Inadequate health literacy for early detection and screening (screening and early diagnosis).	[31]
219	Female	<35=104 (47.5) 35-45=48 (21.9) 46-55= 50 (22.8) >55=17(7.8)	More than 98% were aware of breast self-exams. 84.1% of people practiced it, although only 47.9% did so every month. Of those surveyed, 94.1% were aware of clinical breast exams and 64.3% were aware of mammograms, while 94.1% were aware of clinical breast exams. Of them, 19.2% had had a clinical breast examination within the previous year, and 3.6% had ever had one.	[32]
859	Female	NI	Inadequate knowledge of health. (In particular, inadequate understanding of breast self-examination). Out of the entire sample, 17.1% were able to self-examine their breasts.	[14]
260	Female	43	Inadequate literacy before the intervention in health education.	[33]
38- Intervention Group (IG) 47-Control Group (CG)	Female (Public Health Midwives)	IG- 42.5 CG- 43.0	Inadequate reading comprehension before the health education program.	[18]

282 (n-282, 564 individuals) couples	Male and female-775	Females: 43.05 Males: 44.83	Both sexes had a low level of health literacy for all cancers. Women's awareness was marginally higher than men's.	[15]
100	Female	36-64	Menopause and abortion, and passive smoking.	[1]
944	Female	NI	Premenopausal status, big tumors with positive lymph nodes, and a family history of breast cancer	[27]
859	Female	NI	Greater age (>45), early menarche (<12 years), late menopause (>55 years), no children, more than five children, late age at first childbirth, radiation, breastfeeding, alcohol, tobacco, diabetes, prior history of breast lumps, oral contraceptive, and a positive family history	[14]
700	Female	cases -60 controls -74	Common postmenopausal Sri Lankan women.	[12]
260	Female	43	Obesity, long-term use of hormone replacement therapy or oral contraceptives, early menarche, late menopause, not having children, genetic, first pregnancy beyond 30 years, breast cancer in the past or family history, extended breastfeeding, and having more children	[33]
38	Female	IG- 42.5 CG- 43.0	Obesity, long-term use of oral contraceptives or hormone replacement therapy, early menarche, late menopause, nulliparous women, first pregnancy beyond age 30, ovarian cancer in the family, and a history of breast cancer in the past.	[18]
NI	NI	NI	Screening test- Clinically and Histologically (mammographic screening, breast self-examination, clinical breast examination. Diagnostic test- Histology and Molecular diagnosis	[33]
742	Female	NI	Screening test- Clinically and Histologically. Diagnostic test- Histology-It is a simple and	[34]

			inexpensive tool in the prognostication of breast cancers.	
130	Male and Female	Familial breast cancer patients-46.97, Sporadic breast cancer patients-47.37, risk Individuals-40.51	In disease, the BRCA1 gene has nineteen sequencing variations identified. In diagnosis, Single conformation analysis and hetero-duplex analysis were used to screen exon 11. Sequencing was done on polymerase chain reaction (PCR) products that displayed aberrant patterns in SSCP. The 11th exon was sequenced directly.	[35]
48	Female	NI	In diagnosis, thirty-one variations demonstrated genome-wide suggestive heterogeneity, logarithm of odds. While linkage studies have been used to identify variants linked to cancer worldwide, little is known about their role in non-BRCA1/2 persons in Sri Lanka.	[36]
149	NI	familial breast cancer patients-47.76±9.55 sporadic breast cancer patients-47.60±10.49	In disease, when compared to earlier findings for the BRCA1 gene, Sri Lankan family breast cancer patients had higher frequencies of pathogenic and potentially pathogenic mutations in the BRCA2 gene. In diagnosis, direct sequencing (exon 11) and sequencing of aberrant bands following screening with single-strand conformation polymorphism (remaining exons).	[37]
73	NI	34.5	In the disease, thirty-six sequence variants were found. It consists of two intronic variants of unknown relevance, two variants of questionable significance, seven pathogenic and two likely pathogenic variants, and 23 benign variants.	[23]
105	NI	47.76 ± 9.55 -familial breast cancer patients	In the disease, an unclear loss was found in exon 6 of the BRCA1 gene in one patient with familial breast cancer. The unclear region's whole sequencing was used to diagnose multiplex ligation-	[38]

			dependent probe amplification and to validate MLPA results.	
865	Female	55.5	In the disease, only 34 patients with occult metastasis	[28]
92	Male and Female	patient cohort- 59.24 Breast Cancer- 60.29, Colorectal cancer- 48.9, healthy female controls, and healthy male controls- 49.01	In disease, twenty-seven sequence variants were discovered, several of which were unique in the TP53 gene. In diagnosis, PCR and direct sequencing are used to determine the TP53 mutant status.	[39]

NI-Not Indicated

Risk factors of breast cancer in Sri Lanka

In Sri Lanka, risk factors include menopausal, abortions, passive smoking, age above 45, having early menarche (before the age of 12), late menopause (beyond the age of 55), no children, more than five children, oral contraceptive, alcohol and tobacco use, diabetes, prior history of breast lumps, family history of breast cancer, radiation, obesity, prolonged breastfeeding, and first pregnancies after age 30 [1, 12, 14, 18, 27, 33].

Screening and diagnostic methods of breast cancer in Sri Lanka

Mammography screening, breast self-examination, and clinical breast examination are examples of screening tests that are performed both clinically and histologically. Histology and molecular diagnosis are confirmatory tests which considered diagnostic methods. Histo-pathological diagnosis has aided in the precise Molecular diagnosis of complex malignancies, which is crucial for the choice of the most suitable course of treatment [29, 34].

Future directions of research related to breast cancer in Sri Lanka

Future directions for the diagnosis of breast cancer will be more towards advanced molecular techniques [35-39]. Examples include the use of multiplex ligation-dependent probe amplification (MLPA), single-strand conformation analysis (SSCP), hetero-duplex analysis, PCR, direct sequencing (exon 11), and sequencing of aberrant bands following screening with single-strand conformation polymorphism (remaining exons) [23, 35-39]

Discussion

The current systematic review addresses the epidemiology, health literacy, risk factors, screening and diagnostic methods, and future research directions for breast cancer in Sri Lanka. This is the most common cancer in Sri Lanka [1, 8, 9]. However, there is a lack of comprehensive epidemiological data with the above other details in Sri Lanka. The current study also faced limitations in obtaining specific data on prevalence, mortality, and morbidity rates.

In terms of epidemiology, our research revealed that there are a few details on the prevalence of ER and PR positivity, which are consistent with previous studies [11, 16, 17, 19, 25]. Additionally, triple-negative tumors accounted for 24% of all cancers in this study [19]. Despite limited published articles, it is evident that breast cancer prevalence is significant in Sri Lanka, particularly among females, according to the epidemiological data of the country [10]. Compared to most populations investigated in West and East Asia, the prevalence of breast cancer is higher in Sri Lanka [18-20].

It is predicted that among elderly women, the incidence of breast cancer will increase. This is common, especially those who are also more likely to have co-morbidities with diabetes mellitus or hypertension, and a worse probability of surviving breast cancer [6]. Sri Lanka shows an increase in the incidence of female breast cancer, demonstrating a steady but significant rise [8, 10]. This sharp increase in cases has raised severe public health concerns [1, 11]. In contrast, the incidence among men has remained relatively stable [8]. In line with other countries, our research revealed that the age range of 75 and above has the highest prevalence of male breast cancer. Breast cancer is a rare condition in the male population (around 0.5–1%). The reason for the low incidence is its comparatively small quantity of breast tissue in men, and the differences in their hormonal milieu account for the low incidence rate. Men have less breast tissue than women do, but the elements that affect malignant alterations are similar [18-20].

The breast cancer survival rate was very low in Sri Lanka [9, 14-17, 20, 26, 27]. Nevertheless, in other countries, current findings regarding survival rates are different. For instance, in the United States, women have high survival rates. When considering the relative survival rate from breast cancer, compared to white women, black women had a 9% lower level [18-20]. It indicates that, in Sri Lanka, the survival rate for breast cancer is also relatively low due to several factors, such as a lack of knowledge about the disease, a lack of cancer-related literacy, a lack of access to care, and a delay in diagnosis and treatment [9, 14-17]. The reported death rate of breast cancer is 9% in the included studies[20]. This rate is 2.5% globally [18-20]. Hence, the death rate is also high in Sri Lanka.

The current study discovered a lack of health awareness regarding breast cancer, primarily about diagnosis and BSE [14, 15, 18, 28-33]. Results of health literacy are similar to those in some nations, for example, a more extensive study conducted in Northern Saudi Arabia likewise revealed low general awareness of BSE and breast cancer [18-20]. The current study shows that men and women had slightly different levels of awareness (slightly lower levels in men) [15]. Regrettably, other countries also experience the same situation [18-20]. In communities where males dominate gender roles, more awareness of men may encourage women to use screening facilities. Thus, there is a mandatory awareness among men regarding female cancer. Despite higher health literacy, the clinical breast inspection and self-examination habits of the participants in this study are very rare [32]. Effective health education can raise health literacy, according to two studies [18,32,33]. Comparable outcomes have been reported in

previous literature regarding educational initiatives to improve BSE for medical professionals and women in communities throughout the Asia-Pacific area [18-20]. Nonetheless, research has indicated that higher general literacy rates have a positive impact on breast cancer prevention practices [18-20]. Therefore, it might also require appropriate training for students and the community (both males and females). Hiring well-trained public health nurses and midwives, the community's front-line healthcare providers, could be a solution, as the current study found that healthcare staff's awareness of BSE and breast cancer is also somewhat lacking [18]. Similarly, in other countries, the knowledge of health care providers, like midwives, is low regarding breast cancer prevention.

The risk factors for breast cancer identified in our study include menopause, abortions, exposure to secondhand smoke, age >45, early menarche (<12 years), late menopause (>55 years), having no children or more than five children, oral contraceptive, alcohol and active tobacco use, diabetes, history of breast lumps, family history of breast cancer, radiation exposure, obesity, prolonged breastfeeding, and first pregnancies after age 30 [1, 12, 14, 18, 27, 33]. Overall, the risk factors for breast cancer in other nations are the same [7, 14, 26]. Thus, any special risk factors were not found in Sri Lanka.

Guidelines for the early detection and referral of seven prevalent malignancies in Sri Lanka were recently published by the National Cancer Control Program [10]. The BSE, clinical breast examination, and mammography screening are a few examples of screening tests, and molecular diagnostics and histology are confirmatory diagnostic tests in our study. The accurate diagnosis of complicated cancers, which is essential for selecting the best course of treatment, has been made possible by molecular diagnosis [29,34]. Worldwide, mammography, breast magnetic resonance imaging, and breast self-examination are the recommended methods for screening for breast cancer [18-20]. Even though breast cancer is the most prevalent cancer in Sri Lanka, the government does not have the resources or personnel to launch a nationwide mammography screening program. Although 18 public hospitals and a few private sector facilities do mammography screening, breast self-examination is advised as a substitute [2, 10]. Numerous imaging and molecular biotechnology-based diagnostic techniques have been developed worldwide for definitive disease diagnosis. Such examples include magnetic resonance imaging (MRI), flow cytometers (FCM), mammography (MG), ultrasound (US), and real-time fluorescence quantitative PCR (RT-qPCR), protein hybridization (PHS), and nucleic acid hybridization (NAHS) [18-20]. Molecular diagnostics in Sri Lanka, however, is severely restricted to the Medical Research Institute (MRI), Sri Lanka [29]. Taking advantage of these positive features might also offer an opportunity to exert control over the handful of native healers who practice Ayurveda medicine and assert their ability to treat cancer [29].

The results of our study, along with those of several other studies, have indicated important avenues for future research in the areas of breast cancer and the discovery of related genetic variations. The greater frequency of pathogenic

and possibly pathogenic mutations in the BRCA2 gene among individuals with familial breast cancer from Sri Lanka is one of our study's most notable findings. This pattern deviates from earlier research that focused on a higher incidence of BRCA1 mutations, suggesting a potential genetic predisposition that is specific to a region or community [23, 35-39].

These results highlight the need for more thorough investigations and the creation of specialised treatment plans that are adapted to the distinct genetic characteristics seen in particular communities. It is anticipated that developments in molecular genetic technologies, which provide increased sensitivity and specificity in mutation identification, will propel the field of breast cancer diagnostics in the future. For example, methods like multiplex ligation-dependent probe amplification (MLPA) are essential for identifying significant genomic rearrangements that traditional sequencing might overlook. Furthermore, heteroduplex analysis and single-strand conformation polymorphism (SSCP) are useful techniques for screening mutations, especially when paired with polymerase chain reaction (PCR) amplification techniques to increase detection efficiency [23, 35-39].

Furthermore, a more thorough examination of the BRCA1 and BRCA2 genes is made possible by the direct sequencing of exon 11, an area known to contain common mutations, and the sequencing of abnormal bands discovered while screening the remaining exons using SSCP. These techniques make it possible to find both common and uncommon variations that could raise the chance of developing hereditary breast cancer [23,35-39].

When combined, these molecular techniques not only help detect breast cancer earlier and more precisely, but they also open the door to customised care, in which a patient's genetic composition informs therapy and surveillance plans. The incorporation of state-of-the-art diagnostic technologies will be crucial in enhancing clinical outcomes and directing public health initiatives as research continues to identify new variants and molecular pathways linked to breast cancer, especially in genetically diverse and underrepresented populations like those in Sri Lanka.

Conclusion

Though the published articles is less, the incidence, prevalence, low survival rate, and death rate are significant in our country, particularly among females. These are caused by several issues, including a lack of awareness about the illness both in the community and the healthcare system, illiteracy regarding cancer, difficulty accessing care, and a delay in diagnosis and treatment. The practice of BSE is rare. The risk factors among the Sri Lankan population are mainly menopause, abortions, passive smoking, age (>45), early menarche (<12 years), late menopause (>55 years), no children, oral contraceptives, alcohol and tobacco use, diabetes, family history, radiation, obesity, and prolonged breastfeeding. In Sri Lanka, the screening and diagnosis tests are mammography, breast self-examination, clinical breast examination, molecular detection, and histology. However, there is an issue with the

nation's limited resources for screening and diagnosis.

These findings underscore the urgent need for improved breast cancer awareness, early detection, and treatment strategies in Sri Lanka. Future research should focus on addressing the gaps in epidemiological data and exploring effective interventions to reduce the burden of breast cancer in the country. It can be observed that both health literacy and screening/diagnosis mechanisms need to be on par with the modern technology available in the world. It should be vital to establishing nationally accessible educational programs about breast cancer awareness among men and women.

Limitations

Lack of published articles, especially regarding the epidemiology of breast cancer, was the main limitation.

List of abbreviations

AMED databases - Allied and Complementary Medicine Database
EMBASE - Excerpta Medica data BASE
NIH - National Heart, Lung, and Blood Institute
BSE - Breast self-examination
PRISMA - Preferred Reporting Items for Systematic Reviews AND Meta-Analysis
MLPA - Multiplex Ligation-Dependent Probe Amplification
SSCP - Single-Strand Conformation Analysis
NI - Not indicated
CI - Confidence Interval
IG - Intervention Group
CG - Control Group
BC - Breast Cancer
CRC - Colorectal Cancer
RFS - Recurrence-free survival
LR - Low-Risk
IR - Intermediate-Risk
HR - High-risk
PCR - Polymerase Chain Reaction
ER - Estrogen Receptor
PR - Progesterone Receptor
HER-2 - Human Epidermal Growth Factor Receptor 2

Declaration of conflicting interest

The authors declare no conflict of interest.

Author contribution

Concept/design was done by WMHBS, WPASL, JKLTD and Data acquisition and analysis was done by WMHBSM, WPASL**.** Final Drafting and revision were done by WMHBSM, JKLTD.

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References

1. De Silva M, Senarath U, Gunatilake M, Lokuhetty D. Prolonged breastfeeding reduces risk of breast cancer in Sri Lankan women: A case–control study. *Cancer Epidemiology.* 2010;34(3):267-273 https://doi.org/10.1016/j.canep.2010.02.012

2. WHO. World Health Statistics 2014; https://www.who.int/news/item/15-05-2014-world-health-statistics-2014. Accessed 02 Jan, 2023.

3. Collaboration GBoDC. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2017: a systematic analysis for the global burden of disease study. *JAMA oncology.* 2019

4. Sun YS, Zhao Z, Yang ZN, et al. Risk Factors and Preventions of Breast Cancer. *International Journal of Biological Sciences.* 2017;13(11):1387-1397 https://doi.org/10.7150/ijbs.21635

5. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA: A Cancer Journal for Clinicians.* 2018;68(1):7-30 https://doi.org/10.3322/caac.21442

6. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. *International Journal of Cancer.* 2015;136(5):E359-E386 https://doi.org/10.1002/ijc.29210

7. WHO. WHO Results report 2020-2021. 2021; https://www.google.com/search?client=firefox-b-d&q=WHO.2021. . Accessed 05 Jan, 2024.

8. Fernando A, Jayarajah U, Prabashani S, Fernando EA, Seneviratne SA. Incidence trends and patterns of breast cancer in Sri Lanka: an analysis of the national cancer database. *BMC Cancer.* 2018;18(1):482 https://doi.org/10.1186/s12885-018-4408-4

9. Jayasinghe R, Fernando A, Jayarajah U, Seneviratne S. Post treatment quality of life among Sri Lankan women with breast cancer. *BMC Cancer.* 2021;21(1):305 https://doi.org/10.1186/s12885-021-08055-5

10. Program NCC. Cancer Incidence Data : Sri Lanka Year 2001-2005.National Cancer Control Programme. https://www.nccp.health.gov.lk/ Accessed 05 Jan, 2024.

11. Wijeratne DT, Gunasekera S, Booth CM, Promod H, Jalink M, Jayarajah U, Seneviratne S. Demographic, tumour, and treatment characteristics of female patients with breast cancer in Sri Lanka; results from a hospital-based cancer registry. *BMC Cancer.* 2021;21(1):1175 https://doi.org/10.1186/s12885-021-08929-8

12. Sirisena ND, Adeyemo A, Kuruppu AI, Neththikumara N, Samaranayake N, Dissanayake VHW. Genetic determinants of sporadic breast cancer in Sri Lankan women. *BMC Cancer.* 2018;18(1):180 https://doi.org/10.1186/s12885-018-4112-4

13. Sirisena ND, Adeyemo A, Kuruppu AI, Samaranayake N, Dissanayake VHW. Genetic variants associated with clinicopathological profiles in sporadic breast cancer in Sri Lankan women. *Journal of breast cancer.* 2018;21(2):165-172 https://doi.org/10.4048/jbc.2018.21.2.165

14. Ranasinghe HM, Ranasinghe N, Rodrigo C, Seneviratne RDA, Rajapakse S. Awareness of breast cancer among adolescent girls in Colombo, Sri Lanka: a school based study. *BMC Public Health.* 2013;13(1):1209 https://doi.org/10.1186/1471-2458-13-1209

15. Witharana C, Wijesiriwardhana P, Jayasekara K, Kumari P, Rodrigo C. Awareness of female malignancies among women and their partners in Southern Sri Lanka and implications for screening: a cross sectional study. *BMC Public Health.* 2015;15(1):1179 https://doi.org/10.1186/s12889-015-2531-6

16. Mudduwa L, Peiris H, Liyanage T, Gunasekera S, Ranawaka N. Trends in clinico-pathological and risk factor profile of breast cancer; 10-year experience at a single center in Sri Lanka. *Journal of Diagnostic Pathology.* 2019;14(2):5-12 https://doi.org/10.4038/jdp.v14i2.7772

17. Balawardena J, Skandarajah T, Rathnayake W, Joseph N. Breast Cancer Survival in Sri Lanka. *JCO Global Oncology.* 2020(6):589-599 https://doi.org/10.1200/jgo.20.00003

18. Vithana PVSC, Ariyaratne MAY, Jayawardana PL. Effectiveness of an Educational Intervention among Public

Health Midwives on Breast Cancer Early Detection in the District of Gampaha, Sri Lanka. *Asian Pacific Journal of Cancer Prevention.* 2015;16(1):227-232 http://dx.doi.org/10.7314/APJCP.2015.16.1.227

19. Wijesinghe HD, Fernando J, Senarath U, Wijesinghe GK, Lokuhetty MDS. A clinicopathological study of triple-negative breast carcinoma in a patient cohort from a tertiary care center in Sri Lanka. *Indian Journal of Pathology and Microbiology.* 2020;63(3) https://doi.org/10.4103/IJPM.IJPM_657_19

20. Wijesinghe HD, Thuvarakan P, Samarasekera A, S. Lokuhetty MD. Prognostic indices predictive of short-term disease-free survival of breast carcinoma patients receiving primary surgical treatment in Sri Lanka. *Indian Journal of Pathology and Microbiology.* 2018;61(4):505-509 https://doi.org/10.4103/IJPM.IJPM_321_17

21. Green S, Higgins JP, Alderson P, Clarke M, Mulrow CD, Oxman AD. Introduction. In: *Cochrane Handbook for Systematic Reviews of Interventions.*2008:1-9.

22. National Heart L, and Blood Institute. Study Quality Assessment Tools. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools Accessed 10 Feb, 2023.

23. De Silva S, Tennekoon KH, Dissanayake A, De Silva K, Jayasekara L. Novel and reported pathogenic variants in exon 11 of BRCA2 gene in a cohort of Sri Lankan young breast cancer patients. *Familial Cancer.* 2017;16(3):329-338 https://doi.org/10.1007/s10689-016-9962-9

24. Rajasooriyar C, Sritharan T, Chenthuran S, Indranath K, Surenthirakumaran R. The role of staging Computed Tomography on detection of occult metastasis in asymptomatic breast cancer patients. *Cancer Reports.* 2020;3(3):e1247 https://doi.org/10.1002/cnr2.1247

25. Ratnatunga N, Liyanapathirana LVC. Hormone receptor expression and Her/2neu amplification in breast carcinoma in a cohort of Sri Lankans. *The Ceylon medical journal.* 2007;52(4):133-136 https://doi.org/10.4038/cmj.v52i4.916

26. Peiris H, Mudduwa L, Thalagala N, Jayatilake K. Validity of St Gallen risk categories in prognostication of breast cancer patients in Southern Sri Lanka. *BMC Women's Health.* 2018;18(1):30 https://doi.org/10.1186/s12905-018-0524-1

27. Peiris HH, Mudduwa LK, Thalagala NI, Jayatilaka KA. Do Breast Cancer Risk Factors Affect the Survival of Breast Cancer Patients in Southern Sri Lanka? *Asian Pac J Cancer Prev.* 2017;18(1):69-79 https://doi.org/10.22034/apjcp.2017.18.1.69

28. Athanasiou P, van Dongeren A, Giardino A, Vousdoukas MI, Ranasinghe R, Kwadijk J. Uncertainties in projections of sandy beach erosion due to sea level rise: an analysis at the European scale. *Scientific Reports.* 2020;10(1):11895 http://doi.org/10.1038/s41598-020-68576-0

29. Jayarajah U, Abeygunasekera AM. Cancer services in Sri Lanka: current status and future directions. *Journal of the Egyptian National Cancer Institute.* 2021;33(1):13 10.1186/s43046-021-00070-8

30. Kuruppu DC, Wijeyaratne CN, Gunawardane N, Amarasinghe I. Assessment of Information Needs of Patients with Breast Cancer: A Hospital-Based Study in Sri Lanka. *Asia-Pacific Journal of Oncology Nursing.* 2020;7(4):375-381 https://doi.org/10.4103/apjon.apjon_23_20

31. Kuruppu DC, Wijeyaratne CN, Gunawardena N, Amarasinghe I. Perceived Importance of Information Needs on Breast Cancer among Adults: a Population-Based Survey in the District of Colombo, Sri Lanka. *Asian Pac J Cancer Prev.* 2018;19(8):2247-2253 https://doi.org/10.22034/apjcp.2018.19.8.2247

32. Nilaweera R, Perera S, Paranagama N, Anushyanthan A. Knowledge and practices on breast and cervical cancer screening methods among female health care workers: a Sri Lankan experience. *Asian Pacific Journal of Cancer Prevention.* 2012;13(4):1193-1196

https://doi.org/10.7314/APJCP.2012.13.4.1193

33. Chiranthika V, P.V.S , Ariyaratne, M.A.Y , Jayawardana PL. Educational Intervention on Breast Cancer Early Detection: Effectiveness among Target Group Women in the District of Gampaha, Sri Lanka. *Asian Pacific Journal of Cancer Prevention.* 2015;16(6):2547-2553

34. Peiris H, Mudduwa L, Thalagala N, Jayatialake K. The value of Nottingham grade in breast cancer re-visited in the Sri Lankan setting. *Malaysian Journal of Pathology*. 2017;39(2):141-148

35. De Silva W, Karunanayake EH, Tennekoon KH, Allen M, Amarasinghe I, Angunawala P, Ziard MH. Novel sequence variants and a high frequency of recurrent polymorphisms in BRCA1gene in Sri Lankan breast cancer patients and at risk individuals. *BMC Cancer.* 2008;8(1):214 https://doi.org/10.1186/1471-2407-8-214

36. Wijesiriwardhana P, Musolf AM, Bailey-Wilson JE, Wetthasinghe TK, Dissanayake VHW. Genome-wide linkage search for cancer susceptibility loci in a cohort of non BRCA1/2 families in Sri Lanka. *BMC Research Notes.* 2022;15(1):190 https://doi.org/10.1186/s13104-022-06081-5

37. De Silva S, Tennekoon KH, Karunanayake EH, De Silva W, Amarasinghe I, Angunawela P. Novel sequence variants and common recurrent polymorphisms of BRCA2 in Sri Lankan breast cancer patients and a family with BRCA1 mutations. *Exp Ther Med.* 2011;2(6):1163-1170 https://doi.org/10.3892/etm.2011.337

38. De Silva S, Tennekoon KH, Karunanayake EH, Amarasinghe I, Angunawela P. Analysis of BRCA1 and BRCA2 large genomic rearrangements in Sri Lankan familial breast cancer patients and at risk individuals. *BMC Research Notes.* 2014;7(1):344 https://doi.org/10.1186/1756-0500-7-344

39. Manoharan V, Karunanayake EH, Tennekoon KH, et al. Pattern of nucleotide variants of TP53 and their correlation with the expression of p53 and its downstream proteins in a Sri Lankan cohort of breast and colorectal cancer patients. *BMC Cancer.* 2020;20(1):72 https://doi.org/10.1186/s12885-020-6573-5