International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 7, July 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.7.2024.139

ORIGINAL RESEARCH

Exploring Interconnections: Ovary Removal, Hormone Replacement Therapy, and Familial Factors in Breast Cancer Dynamics

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Received Date: 22 May, 2024 Accepted Date: 25 June, 2024

ABSTRACT

Background: Breast cancer is a pervasive and impactful malignancy, causing substantial global mortality. This study explores the association between ovary removal, hormone replacement therapy (HRT), and familial factors in the context of breast cancer, aiming to unravel the intricate mechanisms influencing its etiology and prognosis. **Methods:** This prospective study was executed at Sher-i-Kashmir Institute of Medical Sciences, Soura. Rigorous data collection employed a meticulously crafted questionnaire, validated through expert reviews and pre-testing. Data on ovary removal patterns, HRT usage, and familial breast cancer history were collected across various districts. Statistical methods were employed to determine frequencies and percentages, providing a nuanced understanding of these interrelated factors. **Results:** The compiled data, when considered across all districts, indicated an overall frequency of one ovary removal at 1.77%, notably contrasting with a significantly higher frequency of 98.23% for individuals who did not undergo any oophorectomy. Familial factors play a significant role, with 13.27% reporting a positive history, emphasizing the need for tailored screening. HRT usage was low (0.88%), influenced by historical events and aligned with reduced breast cancer risk post-HRT discontinuation. **Conclusion:** The comprehensive analysis of ovary removal patterns, familial breast cancer history, and HRT usage provided nuanced insights into breast cancer management dynamics. Oophorectomy aligns with historical trends, familial factors underscore the need for tailored strategies, and low HRT usage resonates with reduced breast cancer risk post-discontinuation. These observations contribute to a holistic understanding, guiding targeted healthcare interventions in breast cancer prevention and treatment.

Keywords: Breast cancer, ovary removal, hormone replacement therapy (HRT), familial factors

INTRODUCTION

Breast cancer, a prevalent and formidable malignancy affecting women globally, claimed approximately 570,000 lives in 2015, underscoring its substantial impact on public health. An annual diagnosis rate of 1.5 million women, constituting 25% of all female cancer cases, accentuates the widespread occurrence of this disease.[1,2] In the United States, breast cancer accounts for an estimated 30% of new cancer cases among women in 2017, totaling 252,710 instances.[3]Various risk factors, encompassing sex, age, estrogen exposure, familial predisposition, genetic mutations, and lifestyle choices, contribute to the heightened susceptibility to breast cancer.[4] Of particular relevance is the association between ovarian removal, hormone replacement therapy (HRT), and family history in the context of breast cancer. The association between ovary removal, hormone replacement therapy (HRT), and familial factors in individuals diagnosed with breast cancer is a complex and multifaceted aspect of oncological research.[5-7] Oophorectomy, the surgical removal of one or both ovaries, is often undertaken for various medical reasons, including the management or prevention of conditions such as ovarian cancer and other reproductive health issues. However, the implications of this procedure extend beyond its immediate objectives, as it may have a profound impact on hormonal balance due to the cessation of estrogen production. Concurrently, the use of hormone

DOI: 10.69605/ijlbpr_13.7.2024.139

replacement therapy, designed to supplement declining hormone levels following ovary removal, introduces an additional dimension to the breast cancer narrative. The relationship between HRT and breast cancer risk has been a subject of considerable investigation, with studies exploring the potential influence of exogenous hormones on tumor development and progression. Moreover, familial factors, encompassing genetic predispositions and familial clustering of breast cancer cases, contribute substantially to the intricate web of variables influencing breast cancer outcomes. Understanding the interplay between ovary removal, hormone replacement therapy, and familial influences is paramount for elucidating the intricate mechanisms underlying breast cancer etiology and prognosis.

MATERIALS AND METHODS

In the pursuit of primary data, a meticulously curated questionnaire, bespoke to the unique requirements of this study, served as the principal instrument for data collection, its content rigorously validated through expert scrutiny. Prior to the commencement of actual data acquisition, the questionnaire underwent a meticulous field pre-test to optimize its efficacy. The self-administered questionnaire, thoughtfully structured for respondents, encompassed a demographic background section, probing into age, age at menarche and menopause, marital status, number of children, educational attainment, parity, and other salient factors.

The methodology unfolded in a tripartite fashion: firstly, the conceptualization of the self-administered questionnaire in collaboration with medical experts; secondly, a pre-testing phase designed to validate content and resolve any potential ambiguities; and thirdly, the execution of data analysis employing SPSS version 17, facilitated by graphical representations and pre-charts to enhance the depth of interpretation. Safeguarding the quality of primary data involved meticulous strategies such as articulating the questionnaire in lucid language, validation by a singular investigator, fostering rapport during interviews, upholding confidentiality, maintaining detailed record-keeping, and thoroughly documenting the entire analytical process.Conversely, secondary data was procured from diverse reputable sources, with PubMed—an open-access database predominantly interfacing with the MEDLINE database—serving as a primary conduit. This encompassed archival references, records for articles pre-indexing with Medical Subject Headings (MeSH), and access to comprehensive full-text books. The Indian Journal of Cancer, established in 1963, assumed a pivotal role as an invaluable resource, indexed with databases such as MEDLINE, Index Medicus, and EMBASE. The National Cancer Registry Programme, instigated by the Indian Council of Medical Research (ICMR) in 1981, played a pivotal role in generating reliable cancer data and contributing substantively to epidemiological studies, augmenting the comprehensive scope of secondary data collection in this study.

Statistical Methods

The acquired data underwent meticulous consolidation and entry into a spreadsheet using Microsoft Excel, subsequently transposed to the data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA) for further analysis. Continuous variables were articulated as Mean±SD, while categorical variables were succinctly summarized as percentages. The presentation of data was executed graphically through the adept utilization of bar and pie diagrams for enhanced visual representation.

RESULTS

The primary dataset, derived from a cohort comprising 113 patients, underwent a meticulous categorization process aimed at systematically extracting pertinent information pertaining to distinctive characteristics and risk factors. This methodical approach to data collection was employed with the utmost objectivity, aligning with the study's objectives to investigate the interplay between ovary removal, hormone replacement therapy, and familial influences in the underlying etiology and prognosis of breast cancer.

Table 1: Distribution of Ovary Removal Across Districts among studied patients

District	Frequency (%)		
	Yes, one removed	Yes, both removed	No
Srinagar	0	0	25(22.12%)
Budgam	1(0.88%)	0	18(15.92%)
Ganderbal	1(0.88%)	0	7(6.19%)
Anantnag	0	0	21(18.58%)
pulwama	0	0	8(7.07%)
Kulgam	0	0	3(2.65%)
Shopian	0	0	2(1.76%)
Baramulla	0	0	12(10.61%)
Kupwara	0	0	13(11.5%)
Ramban	0	0	2(1.76%)
Overall	**2 (1.77%)**	0	**111 (98.23%)**

DOI: 10.69605/ijlbpr_13.7.2024.139

Table 1 presents the distribution of the studied population with a focus on the removal of ovaries. The data categorizes the respondents across various districts, delineating the frequency and percentage distribution for each district based on the removal status of one or both ovaries. In Srinagar, none of the observed cases involved the removal of one ovary, with 22.12% of individuals not undergoing any ovary removal. Similarly, in Budgam, 0.88% of individuals had one ovary removed, while 15.92% did not undergo any removal. Ganderbal exhibited a parallel trend, with 0.88% having one ovary removed and 6.19% not undergoing any removal. In Anantnag, none of the observed cases involved the removal of one ovary, and 18.58% of individuals did not undergo any ovary removal. Pulwama recorded no instances of one ovary removal, with 7.07% not undergoing any removal. Kulgam, Shopian, Baramulla, Kupwara, and Ramban demonstrated a complete absence of oophorectomy cases, as outlined in Table 1. Within these districts, varying percentages of individuals were observed not to have undergone any removal procedure. The compiled data, when considered across all districts, indicated an overall frequency of one ovary removal at 1.77%, notably contrasting with a significantly higher frequency of 98.23% for individuals who did not undergo any oophorectomy. These discerning observations offer nuanced insights into the prevalence of ovary removal within specific districts, thereby contributing substantively to a comprehensive understanding of this characteristic within the studied population.

Table 2: Distribution of Studied Population Based on Breast Cancer History in the Family Across Districts

District	Frequency (%)		
	Yes	No	Don't know
Srinagar	0	25(22.12%)	0
Budgam	5(4.42%)	14(12.38%)	0
Ganderbal	1(0.88%)	7(6.19%)	0
Anantnag	2(1.76%)	19(16.81%)	0
Pulwama	2(1.76%)	6(5.53%)	0
Kulgam	1(0.88%)	2(1.76%)	0
Shopian	0	2(1.76%)	0
Baramulla	2(1.76%)	10(8.84%)	0
Kupwara	2(1.76%)	11(9.73%)	0
Ramban	0	2(1.76%)	0
Overall	15 (13.27%)	98 (86.72%)	0

Table 2 provides an insightful distribution of the studied population based on the presence or absence of a history of breast cancer within their families. The characteristics, frequencies, and corresponding percentages are meticulously detailed for respondents affirming a positive history, confirming the absence of familial breast cancer, or expressing uncertainty.In Srinagar, none of the observed cases reported a familial history of breast cancer, with 22.12% of individuals acknowledging the absence of such history. No respondents indicated uncertainty regarding their family's breast cancer history. Moving to Budgam, 4.42% of individuals reported a positive history of breast cancer in their families, while 12.38% affirmed the absence of familial breast cancer history. No respondents expressed uncertainty about their family's breast cancer history. Similarly, in Ganderbal, 0.88% of individuals reported a history of breast cancer in their families, with 6.19% affirming the absence of such history. No respondents were uncertain about their family's breast cancer history. In Anantnag, 1.76% of individuals reported a positive history of breast cancer in their families, and 16.81% acknowledged the absence of familial breast cancer history. No respondents expressed uncertainty about their family's breast cancer history. Pulwama recorded 1.76% of individuals reporting a history of breast cancer in their families, with 5.53% affirming the absence of familial breast cancer history. No respondents were uncertain about their family's breast cancer history. For Kulgam, Shopian, Baramulla, Kupwara, and Ramban, varying percentages of individuals reported a positive history of breast cancer in their families, and varying percentages affirmed the absence of such history. No respondents in these districts expressed uncertainty about their family's breast cancer history. Overall, across all districts, a cumulative 13.27% of the studied population reported a positive history of breast cancer in their families. A substantial 86.72% of individuals affirmed the absence of familial breast cancer history, and no respondents indicated uncertainty regarding their family's breast cancer history. These detailed observations contribute significantly to the understanding of familial breast cancer prevalence within the studied population.

DOI: 10.69605/ijlbpr_13.7.2024.139

Table 3: Distribution of Studied Population Based on Hormone Replacement Therapy across Districts

District	Frequency (%)	
	Yes	No
Srinagar	0	25(22.12%)
Budgam	0	19(16.8%)
Ganderbal	0	8(7.07%)
Anantnag	1(.88%)	20(17.7%)
pulwama	0	8(7.07%)
Kulgam	0	3(2.65%)
Shopian	0	2(1.76%)
Baramulla	0	12(10.6%)
Kupwara	0	13(11.5%)
Ramban	0	2(1.76%)
Overall	**1 (0.88%)**	**112 (99.12%)**

Table 3 presents a comprehensive overview of the distribution of the studied population based on their engagement with hormone replacement therapy (HRT). The table outlines characteristics, district-wise frequencies, and corresponding percentages, categorizing individuals according to their utilization or non-utilization of HRT.In Srinagar, none of the observed cases reported the utilization of hormone replacement therapy, with 22.12% of individuals abstaining from such treatment. Similarly, in Budgam, none of the individuals opted for hormone replacement therapy, with 16.8% choosing not to undergo this form of treatment. Ganderbal exhibited a similar trend, with no individuals reporting the use of hormone replacement therapy and 7.07% choosing not to undergo it. In Anantnag, 0.88% of individuals reported the use of hormone replacement therapy, while 17.7% opted not to undergo such treatment. Pulwama mirrored the trend observed in Srinagar and Budgam, with none of the individuals choosing hormone replacement therapy and 7.07% opting out of this treatment. For Kulgam, Shopian, Baramulla, Kupwara, and Ramban, none of the individuals reported engaging in hormone replacement therapy, with varying percentages abstaining from it as reflected in table 3. Overall, the aggregated data indicates that 0.88% of the studied population reported the use of hormone replacement therapy, while a significant majority, comprising 99.12% of individuals, did not partake in this form of treatment. These detailed observations contribute to a nuanced understanding of the prevalence of hormone replacement therapy within specific districts, providing valuable insights into the healthcare choices of the studied population.

DISCUSSION

The comprehensive analysis of ovarian removal patterns within the studied population aligns with the historical context and evolution of oophorectomy as a therapeutic approach in breast cancer treatment. The overarching trend of a relatively infrequent occurrence of one ovary removal (1.77%) and a significantly higher frequency (98.23%) of individuals opting against oophorectomy resonates with the historical shifts in the perception and utilization of this medical intervention. The historical trajectory, underscores the long-standing recognition of the relationship between ovarian function and breast cancer. Pioneering figures such as Thomas William Nunn, Albert Schinzinger, and George Thomas Beatson laid the foundation for understanding the potential role of oophorectomy in breast cancer treatment.[8-10] The initial hesitation and limited popularity of the procedure in the early 20th century, attributed to high morbidity, echo the observed infrequency in the contemporary context as reflected in the studied population. The mid-20th century marked a turning point with Charles Huggins and Thomas Dao popularizing oophorectomy, bringing it back to the mainstream of breast cancer therapy.[11] Large randomized trials in the latter half of the century, particularly the overviews published by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG), provided substantial evidence in favor of oophorectomy.[12,13] This historical context aligns with the discerning observation in the studied population, where the procedure remains relatively rare (1.77%). The advancements in breast cancer treatment, such as alternate methods for ovarian ablation/suppression, the detection of estrogen receptors, and the use of chemotherapy and tamoxifen, have contributed to a diversified landscape of therapeutic options. This broader context sheds light on the complexity of medical decision-making and the nuanced considerations surrounding oophorectomy, as reflected in the low frequency observed in the contemporary demographic. In essence, the observed patterns in the studied population resonate with the historical trajectory of oophorectomy, providing contemporary insights into the prevalence of this medical intervention. The discerning observation contributes to the broader discourse on reproductive health and medical decision-making, aligning with historical shifts in the utilization of oophorectomy in the context of breast cancer treatment.

The comprehensive analysis of familial breast cancer history within the studied population, as revealed

DOI: 10.69605/ijlbpr_13.7.2024.139

across all districts, provides a valuable context for understanding the broader implications of family-related risks in the context of breast cancer. The data analysis underscores pertinent insights into the familial aspects of breast cancer within the studied population. Specifically, 13.27% of individuals report a positive history of breast cancer in their families, underscoring the substantial impact of familial factors on this health aspect. Conversely, a significant majority, comprising 86.72% of the studied population, affirms the absence of familial breast cancer history, shedding light on the prevalence of non-familial factors within this demographic. These findings align with a wealth of existing studies, reinforcing the established notion that approximately 5–15% of newly diagnosed patients with breast cancer or ovarian cancer have a family history of these malignancies.[14-16] The observed patterns are also consistent with broader statistical insights indicating that nearly a quarter of all breast cancer cases are related to family history, a trend that resonates with the outcomes of our study.[17,18] Furthermore, the study aligns with the research conducted by Liu L et al, where 7.4% of the entire patient cohort had a family history of breast/ovarian cancer.[14] This finding, consistent with results from other studies, further corroborates the prevalence of familial factors in a broader patient population. Brewer HR et al in their study reported that the susceptibility to breast cancer in women with affected relatives, as highlighted by a cohort study of over 113,000 women in the UK, further supports the significance of familial factors in breast cancer risk.[15] The study's finding that women with one first-degree relative with breast cancer have a 1.75-fold higher risk, and the risk becomes 2.5-fold or higher with two or more affected relatives, echoes the patterns identified in the studied population.[15] Moreover, the interconnection between breast cancer and ovarian cancer, both being female hormone-responsive cancers, is highlighted. It has been reported that approximately 5–10% of newly diagnosed breast cancer patients with a family history of breast or ovarian cancer suggest the role of genetic or non-genetic inheritance.[19.20] The inherited susceptibility to breast cancer, attributed in part to mutations in genes like BRCA1 and BRCA2, further emphasizes the genetic component in familial breast cancer risk.[20] These shared observations contribute significantly to the body of knowledge on familial breast cancer history, offering valuable insights that can inform future research, public health initiatives, and targeted healthcare interventions. Understanding the prevalence of familial breast cancer risks within specific regions is crucial for tailoring effective health strategies, promoting awareness, and implementing preventive measures. By correlating the regional data with broader epidemiological trends, these findings contribute to a comprehensive understanding of the multifaceted factors influencing breast cancer susceptibility. This holistic perspective supports evidence-based decision-making in healthcare planning and underscores the importance of considering familial history as a key determinant in breast cancer risk assessment and prevention strategies.

The outcomes of our study, revealed that only 0.88% of the studied population reported utilizing hormone replacement therapy (HRT), exhibit alignment and complementarity with the findings observed in a study conducted by Liu J et al. The study by Liu et al illustrated that HRT users did not demonstrate a pre-existing higher breast cancer hazard ratio (HR) compared to non-users during the initial three years of follow-up.[21] This concurrence between our study and the research by Liu et al underscores the consistency in results across distinct populations, strengthening the validity of our observations. Additionally, our observation that a significant majority (99.12%) opted not to engage in HRT resonates with broader studies suggesting that past HRT users experienced a lower risk of breast cancer compared to current users. This diminished risk is ascribed to the dissipation of risk following the discontinuation of HRT use, a phenomenon substantiated by previous research.[22-24]The alignment of our results with studies demonstrating a lower risk post-HRT discontinuation contributes to the accumulating evidence supporting the temporal influence of HRT on breast cancer risk. Moreover, our study's identification of a notably low incidence (0.88%) of breast cancer among Hormone Replacement Therapy (HRT) users is intricately linked to historical dynamics. The discernible reduction in HRT utilization following the release of the Women's Health Initiative (WHI) results in 2002, which brought to light more detrimental than beneficial effects of HRT, offers a plausible rationale for the observed low incidence.[25] The widespread dissemination of adverse study outcomes and subsequent adjustments in medical guidance for HRT prescription likely exerted a substantial influence on patterns of HRT usage, thereby contributing to the diminished incidence among breast cancer patients who opted for HRT.

CONCLUSION

The comprehensive examination of ovarian removal, familial breast cancer history, and hormone replacement therapy (HRT) usage in the studied population illuminates the intricate landscape of breast cancer management. Notably, oophorectomy, reflecting historical treatment shifts, was relatively uncommon at 1.77%. The substantial influence of familial factors, with 13.27% reporting positive histories, underscores the necessity for personalized screening and preventive measures. Moreover, the low prevalence of HRT usage (0.88%), intertwined with historical events, aligns with decreased breast cancer risk post-discontinuation. These findings collectively enhance our understanding of breast cancer dynamics, providing valuable insights for

DOI: 10.69605/ijlbpr_13.7.2024.139

tailored healthcare interventions and shaping the trajectory of breast cancer management strategies.

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