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Research Article

ASSESSMENT OF PREVALENCE OF BREAST CANCER IN PATIENTS WITH OBESITY AND EVALUATING BENEFITS OF STATIN THERAPY IN BREAST CANCER TREATMENT

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ABSTRACT

Objective: Assessing the prevalence of breast cancer and evaluating the feasibility of statins as adjunct therapy in breast cancer management as well as their effectiveness in reducing recurrence.

Methods: A bi-directional study was conducted over 6 months at Parul Sevashram Hospital, India, involving 102 breast cancer patients. Data on demographics, body mass index (BMI), cancer subtypes, statin usage (type, dose, duration), adjuvant therapy integration, and recurrence were collected through medical records and organized discussions. Analytical methods comprised of Pearson-Chi square tests to assess associations between statin continuation and recurrence.

Results: Among 102 patients, 46.07% (n=47) possessed a normal BMI, whereas 53.66% (n=55) were pre-obese/obese (BMI≥25). Invasive ductal carcinoma (65%, n=63) was the most prevalent subtype. Of 83 patients assessed for statin use, 38.55% (n=32) were prescribed statins (atorvastatin: 62.5%, rosuvastatin: 31.25%, simvastatin: 6.25%), primarily for hypercholesterolemia (71.87% obese patients). Among statin users, 71.87% (n=23) continued therapy as adjuvant treatment. Recurrence occurred in 21.74% (n=5) of statin-continuation patients versus 66.67% (n=6) in the discontinuation group (χ^2=3.97, p=0.046). Lipophilic statins (atorvastatin, simvastatin) showed stronger recurrence reduction (78.26% non-recurrence) compared to discontinuation (33.33%).

Conclusion: Statin continuation as adjuvant therapy significantly reduced breast cancer recurrence, particularly in obese patients, with lipophilic statins (e.g., atorvastatin) demonstrating notable efficacy. The study highlights statins' potential dual role in managing hyperlipidemia and cancer outcomes, emphasizing their integration into breast cancer care for high-BMI populations. Further large-scale trials are needed to validate optimal dosing, duration, and long-term survival benefits.

Keywords: Breast cancer, Prevalence, Statins, Body mass index, Invasive ductal carcinoma, Atorvastatin, Rosuvastatin, Recurrence.

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INTRODUCTION

Breast cancer is the most prominent form of malignancy across the globe, inclusive of India, where it is a culprit of posing life-hampering disabilities and heavy life losses [1]. According to a report by GLOBOCAN, it has overshadowed cervical cancer to become the leading type of malignancy among Indian women, contributing to approximately 14% of all new cancer cases in the country [2]. The rising incidence is attributed to various factors, including heredity, hormonal dysregulation, as well as ecological influences. Breast cancer is the leading cause of cancer-related deaths worldwide [3].

Several diagnosis techniques are available for detecting breast cancer. CA-125 may serve as a neoplastic indicator in individuals with breast carcinoma for assessment purposes, with salivary specimens proving equally efficient as blood serum samples, while also being simpler and safer to collect [4]. The high sensitivity of fourier transform infrared spectroscopy to biomolecular alterations is utilized to differentiate between non-cancerous and cancerous breast tissues [5].

There already are several pharmacological options that are viable for treatment. Nanotechnology-based approaches, including SEDDS, quantum dots, and carbon nanotubes, offer promising therapeutic solutions for containing CA in the near future [6].

Statins, a class of medications initially developed to manage high cholesterol levels and prevent cardiovascular diseases (CVDs), have been widely used for over two decades. Their efficiency in lowering cardiovascular mortality is well established [7]. These drugs function primarily by inhibiting the enzyme hydroxy methyl glutaryl-coenzyme A reductase (HMGCR), a key player in the cholesterol production pathway [8]. However, beyond their role in lipid regulation, statins have been found to influence several other metabolic activities, leading to a range of additional therapeutic effects known as pleiotropic effects. Among these pleiotropic effects, their potential anti-cancer properties are being investigated thoroughly [9].

Mechanisms of statin-induced anti-neoplastic effects

Statins exert their anti-neoplastic effects through multiple mechanisms. One major pathway involves the inhibition of farnesyl pyrophosphate (FPP) and geranylgeranyl pyrophosphate (GGPP), crucial in cholesterol synthesis. These molecules are crucial for the post-translational modification of small signaling proteins, pivotal in the viability, and multiplication of malignant tissues. Second, statins lower the levels of 27-hydroxycholesterol (27HC), a metabolite that acts as a selective estrogen receptor (ER) modulator, contributing to the proliferation of hormone-dependent malignancies, such as ER-positive breast cancer. Third, they inhibit the epithelial-mesenchymal transition (EMT), which allows primary tumor units to become more invasive and metastatic [10].

The primary target of these moieties, HMGCR, is an endoplasmic reticulum-based membrane-mediated glycoprotein. This enzyme regulates cholesterol production, steroid-based hormones, as well

as non-sterol isoprenoids. Inhibiting HMGCR in liver cells results in decreased intracellular amounts of cholesterol, which significantly results in the augmentation of low-density lipoprotein cholesterol (LDL-C) receptors to facilitate cholesterol uptake from the bloodstream. This process helps maintain cellular function and reduces LDL-C levels, thereby lowering the risk of CVDs [11].

Despite the strict feedback mechanisms that regulate cholesterol amounts in cells and HMGCR action, extracellular cholesterol concentrations in the serum can vary significantly. Along with lowering LDL levels, inhibiting this metabolic pathway prevents the formation of GGPP and FPP. These molecules are crucial for the iso-prenylation of proteins that are involved in cellular signaling, including oncogenes such as Ras, Rac, and Rho. By blocking these modifications, statins interfere with cancer-related processes such as proliferation, migration, and angiogenesis [12].

Cholesterol metabolism and cancer progression

Rapidly dividing cancer cells require increased cholesterol synthesis to support the formation of new lipid bilayer membranes. In normal cells, cholesterol synthesis is tightly regulated; however, in cancer cells, this regulation is often disrupted. There is growing evidence suggesting that HMGCR functions as a metabolic oncogene. Alterations in the mevalonate pathway may contribute to the oncogenic transformation of various tissues. Elevated expression of HMGCR can result in worsened prognosis in individuals suffering from malignancy of mammary glands.

The pathway is particularly relevant for cancers with aberrations in the TP53 gene. It is crucial for tumor suppression by instigating DNA restoration, inhibiting the proliferation of cells, and apoptosis to contain genomic damage [13]. Mutant p53, however, has been linked to sterol gene promoters and plays a significant role in regulating the mevalonate pathway. In malignant cells, mutant p53 upregulates genes involved in cholesterol biosynthesis, leading to aberrant cell morphology and aggressive tumor behavior. Reducing mutant p53 expression has been shown to restore normal cell morphology, highlighting its role in tumor progression.

Notably, treatment with statins, particularly simvastatin, has demonstrated a significant inhibitory effect on malignant cell proliferation, inducing cellular death as well as restoring standard cellular activity in several malignant mammary tissues. However, these actions are diminished when FPP and GGPP, outputs of the mevalonate pathway, are supplemented in the culture medium approving statin's mevalonate inhibition. Furthermore, p53 in this process appears to be modulated by sterol regulatory element binding proteins (SREBPs) and the YAP/TAZ effectors of the Hippo signaling pathway. Since Rho GTPases regulate YAP/TAZ activity and rely on prenylation, this highlights a complex interplay between p53, SREBPs, mevalonate pathway genes, and YAP/TAZ transcriptional regulators. As a result, overexpression of these genes may serve as potential biomarkers for identifying breast cancers that are responsive to statin therapy [14].

Lessened cholesterol levels inside the cells may result in a decrease in the production of hormones within the tumor itself. This is because cholesterol is necessary for the synthesis of all steroid hormones. Statin treatment has been demonstrated to reduce 27HC levels, which is particularly important for hormone-responsive disorders, such as ER-positive breast cancer. Significantly, 27HC functions as an ER ligand, promoting the development of tumors that are dependent on ER [11] The development and survival of cancer cells are strongly dependent on cholesterol, making the reduction of cholesterol production an attractive technique for fighting cancer. It is crucial to acknowledge that cancer cells that multiply quickly have a higher need for cholesterol to aid in the production of cell membranes. The reduction in plasma levels of cholesterol and 27HC leads to a decrease in their availability for cancer cells to use. Furthermore, the statins directly inhibit HMGCR, resulting in the reduction of isoprenoid levels within tumors. Isoprenoids control growth as well as the spread of cancer cells. Present researches are seeking to provide more clarity on the specific functions of cholesterol, cholesterol metabolites, and statins in the proliferation of breast cancers [15].

Statins and metastasis

The ability of cancerous cells to transition between different phenotypic states is critical for tumor progression, therapy resistance, and metastatic potential. One of the key processes in this regard is EMT, which facilitates tumor cell dissemination. Once metastatic cells reach distant organs, they undertake mesenchymal-to-epithelial transition, enabling them to establish new tumor colonies. Collectively, these dynamic transitions are referred to as epithelial-mesenchymal plasticity, a process that significantly influences cancer development, progression, and treatment response [16].

Researchers discovered that treatment with statin reduces the metastatic potential of cancer cells. Animal models have shown that administering statins results in a significant lowering of the quantity of metastatic lesions in pre-existing tumors. This suggests that statins impair cellular plasticity, thereby limiting the ability of cancer cells to transition into a metastatic state. Moreover, pre-treating cancer cells with statins before seeding further reduces their ability to form colonies. These findings indicate that statins not only inhibit EMT but also prevent the re-establishment of metastatic tumor cells in secondary sites [17].

Statins and cancer recurrence

Among different types of statins, lipophilic statins have demonstrated a greater potential in reducing breast cancer recurrence compared to hydrophilic statins. Studies indicate that individuals with breast cancer staged 2 and 3 who were administered with lipophilic statins experienced a 10% concession in the appearance of secondary tumors (re-occurrence), independent of the primary treatment modality used [18].

Statin suppression of cancer cell growth

Statins, by instigating cell cycle halt, inhibits key signaling pathways, and modulating gene expression. They do so specifically by regulating cyclin-dependent kinases and increasing the expression of CDK inhibitors, such as p21 and p27. Furthermore, statins suppress the activation of Ras, Rac, and Rho GTPases while upregulating PTEN, resulting in P13K course blocking. In addition, statins influence gene transcription by inhibiting clamping of nuclear transcription elements, such as NF-κB and AP-1 to DNA as well as alleviating DNA methylation levels [19].

Statins and apoptosis

Several studies have demonstrated that statins instigate programmed cell death of various malignancies, mainly prostate, breast, and colorectal. This occurs through multiple mechanisms, first, by augmentation of Bax, Bad, Bim (factors inducing apoptosis), and second, by the suppression of Bcl-2 and Bcl-Xl (factors inhibiting apoptosis). Statins also enhance caspase activation, increase reactive oxygen species production, together with triggering calcium-dependent apoptosis. However, the pro-apoptotic effects of statins are typically observed at doses much higher than those used in clinical practice [20].

Statins and angiogenesis

Statins, at low doses, promote angiogenesis by activating PI3K as well as eNOS pathways. In contrast, at higher concentrations, statins inhibit angiogenesis by suppressing RhoA activity. Statins, at high doses, also promote programmed cell death in endothelial cells, lower pro-angiogenic molecules' production, together with limiting VEGF binding to the extracellular matrix by inhibiting MMP-9 activity. Notably, the anti-tumor effects of statins correspond to their anti-angiogenic activity [21].

Present treatment approaches

In the field of oncology diagnostics, visualization, and treatment, nanocarrier-mediated drug transport systems have garnered significant

attention due to their favorable characteristics and potential to improve treatment efficacy [22]. Various other methods are being researched and considered. One such is ablation therapy, which has emerged as a minimally invasive technique that destroys tumors by freezing or heating them, eliminating the need for traditional open surgery [23].

METHODS

We affirm the approval from the IEC of Parul Sevashram Hospital alongside the IEC no. – PUIECHR/PIMSR/00/081734/6516.

The research took place at Parul Sevashram Hospital, Waghodia, Vadodara, with a sample size of 102 breast cancer patients. Data were collected through a patient profile form with additional support from the Medical Record Department. The inclusion criteria encompassed women diagnosed with breast cancer who were willing to participate and provided dated informed consent. Exclusion criteria included patients unwilling to give written consent or participate in the study. A specifically designed and validated data collection form was utilized in ensuring accurate data from the Medical Record Department. It captured key details such as the patient's age, gender, dates of admission and discharge, reason for admission, medical history, social history, and treatment history, along with dosage, route, frequency, and other relevant treatment information. The collected data were systematically tallied and subjected to statistical analysis, with figures, tables, and graphs used to present the data visually. Word documents and Excel spreadsheets were organized for analysis. Statistical parameters such as means were calculated for quantitative variables, while percentages were computed for categorical variables. A Pearson Chi-square test of independence was employed in examining the relationships between variables. Graphical tools, such as bar graphs and pie charts were generated to convey trends, patterns, and correlations, making the statistical findings easier to understand.

RESULTS

Distribution of patients as per the body mass index (BMI) (kg/m^2)

The collected data show that 46.07% (n=47) of patients possessed a normal BMI whereas 16.66% (n=17) were pre-obese and 37% (n=38) were under obesity class 1. Such a distribution reveals a notable portion of females falling into the obese category portion attributing increased prevalence of breast cancer among pre-obese and obese females validating the idea that BC runs with obesity. The data evaluation is provided in Table 1 and its graphical representation is illustrated in Fig. 1.

Distribution of patients as per prevalence of CA subtype

65% of the patients were affected with Invasive ductal carcinoma making it the most prevalent subtype, followed by ductal carcinoma with an incidence rate of 22%, whilst fibroadenoma was the least prevalent subtype with an incidence rate of 13% in the sample of patients. The data evaluation is provided in Table 2 and its graphical representation is illustrated in Fig. 2.

Distribution of patients as per the usage of statins

Result suggest that a definite quantity of female patients (38.55%, n=32) were having statin therapy prescribed for certain co-morbidities and conditions, while a substantial percentage of patients under the study were non-statin users (61.44%, n=51). The data evaluation is provided in Table 3 and its graphical representation is illustrated in Fig. 3.

Distribution of patients as per the indication of statin usage

Data signifies that a greater percentage of obese female patient (71.87%, n=23) were prescribed with statin in contrast to pre-obese female patients (28.12%, n=9). Amidst pre-obese females, statin was mainly prescribed for high cholesterol (77.78%, n=7) along with the smaller percent of cardiovascular (11.11% n=1) and hypertriglyceridemia

Table 1: Distribution of patients as per the BMI (kg/m^2)

BMI (Kg/m^2)	Number of patients	Percentage of patients
18.5–24.9	47	46.07
25.0–29.9	17	16.66
30.0–34.9	38	37

Values represent BMI classifications. Estimated mean BMI=26.66±4.89 kg/m^2 (standard deviation). BMI: Body mass index

Table 2: Distribution of patients as per prevalence of CA subtype

Cancer subtypes	Number of patients	Percentage of patients
Invasive ductal carcinoma	63	65
Ductal carcinoma	21	22
Fibroadenoma	13	13

Values represent cancer type. Mean number of patients=32.33±21.93 (standard deviation)

Table 3: Distribution of patients as per usage of statins

Past use of statin therapy	Number of patients	Percentage of patients
Yes	32	38.55
No	51	61.44

Values represent the presence of statin therapy. Mean number of patients=41.5±9.5 (standard deviation)

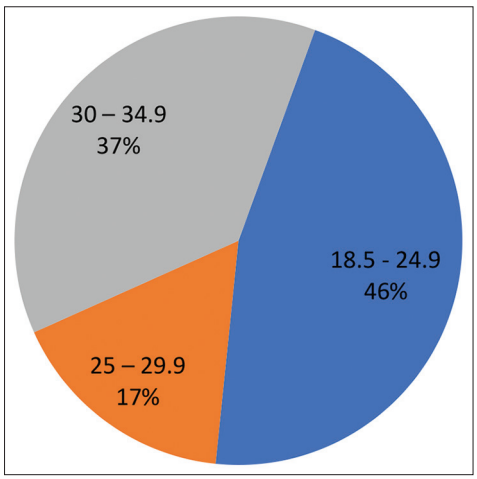

Fig. 1: Distribution of patients as per the body mass index (kg/m^2)

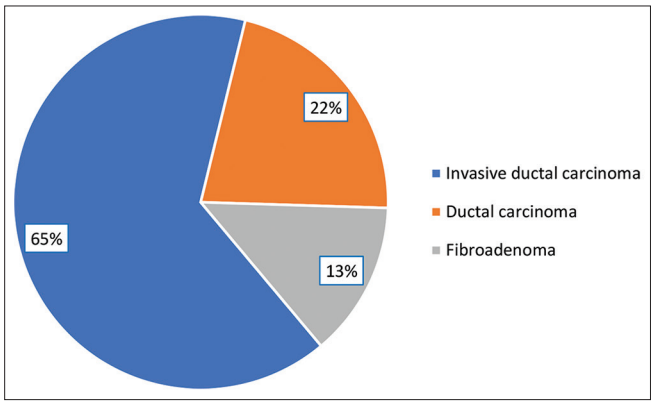

Fig. 2: Distribution of patients as per prevalence of CA subtype

Table 4: Distribution of patients as per the indication of statin usage

Body mass index kg/m²	Indication of statin usage					Total
	CVD	High cholesterol	High Cholesterol, CVD	Hypertriglyceridemia	Stroke	
25.0–29.9	1	7		1		9
Percentage	11.11	77.78		11.11		100
30.0–34.9	3	9	3	6	2	23
Percentage	13.04	39.13	13.04%	26.08	8.69	100

Values represent statin usage. Mean number of patients per statin indication=6.4±5.08 (standard deviation). CVD: Cardiovascular disease

Table 5: Distribution of patients as per the statin prescribed and their doses

Statins	Dosage of statins				Total number of patients	Percentage of patients
	5 mg	10 mg	20 mg	40 mg		
Atorvastatin	1	12	5	2	20	62.5
Rosuvastatin	3	5	2		10	31.25
Simvastatin			2		2	6.25

Values represent patients per statin. Mean number of patients=10.67±7.36 (standard deviation)

Table 6: Distribution of patients as per statins prescribed as an adjuvant therapy and its indications

Indications of statin usage	Statin continued as an adjuvant therapy?	
	Yes	No
CVD	3	1
High cholesterol	9	7
High CHOLESTEROL, CVD	2	1
Hypertriglyceridemia	7	
Stroke	2	

Values represent patients per statin (adjuvant). Mean number of patients=4.6±2.87 (standard deviation)

Table 7: Distribution of patients as per statin therapy continuation and recurrence of breast cancer

Statin therapy	Recurrence of breast cancer		Total
	Yes	No	
Statins continued in adjuvant therapy	5	18	23
Percentage	21.74	78.26	100
Statins discontinued in adjuvant therapy	6	3	9
Percentage	66.67	33.33	100

Values represent recurrence per statin therapy. Mean number of patients=16±5 (SD)

Table 8: Distribution of patients as per statin therapy continuation and recurrence of breast cancer

Statin therapy	Recurrence of breast cancer		Total
	Yes	No	
Statins continued in adjuvant therapy	5	18	23
Statins discontinued in adjuvant therapy	6	3	9

(11.11% n=1). For obese females, high cholesterol (39.13%, n=9) and hypertriglyceridemia (26.08%, n=6) being the dominant reason, statin prescriptions were also distributed for other pronounced conditions, such as CVD co-existing with high cholesterol (13.04%, n=3), cardiovascular disorder itself (13.04%, n=3), and stroke (8.69%, n=2). The data evaluation is provided in Table 4 and its graphical representation is illustrated in Fig. 4.

Distribution of patients as per the statin prescribed and their doses

As data demonstrates that pre-obese and obese females are linked to a higher percentage of cardiovascular risk factors, high cholesterol, hypertriglyceridemia, 32 females with higher BMI were prescribed statins with the majority receiving atorvastatin (62.5%, n=20) and smaller section receiving rosuvastatin (31.25%, n=10) and simvastatin (6.25%, n=2). Sorting the statin according to the doses involved atorvastatin at 5 mg (n=1), 10 mg (n=12), 20 mg (n=5) and 40 mg (n=2), rosuvastatin at 5 mg (n=3), 10 mg (n=5) and 20 mg (n=2) and simvastatin at 20 mg (n=2). The data evaluation is provided in Table 5 and its graphical representation is illustrated in Fig. 5.

Distribution of patients as per statins prescribed as an adjuvant therapy and its indications

In regard to 32 female patients prescribed with statin and considering individualized treatment decisions according to the specific patient factors and health professional decisions, 71.87% (n=23) had statin continued as part of their adjuvant therapy for breast cancer in the comprehensive treatment plan and 28.12% (n=9) did not have statins in their adjuvant therapy. The data evaluation is provided in Table 6 and its graphical representation is illustrated in Fig. 6.

Distribution of patients as per statin therapy continuation and recurrence of breast cancer

Evaluating the potential relation between statin therapy continuation and reduced possibility of secondary tumor occurrence in breast cancer patients, among 23 female subjects who had statin therapy continued in their adjuvant breast cancer therapy, 78.26% (n=18) did not encounter any recurrence in the form of secondary tumor of breast cancer, while in 21.74% (n=5) of subjects had secondary tumors. Contrary to 9 females who had statin therapy discontinued in adjuvant therapy, 33.33% (n=3) had no secondary tumors, alongside 66.67% (n=6) had recurrence. The data evaluation is provided in Table 7 and its graphical representation is illustrated in Fig. 7.

Statistical analysis

Chi-square test of independence (Statin therapy continuation versus Recurrence of breast cancer)

The data for carrying out the Chi-square test are clubbed and provided in Table 8

H_0=Statin therapy continuation is not associated with breast cancer recurrence.

Chi-square statistic (χ^2): 3.97

p=0.0464

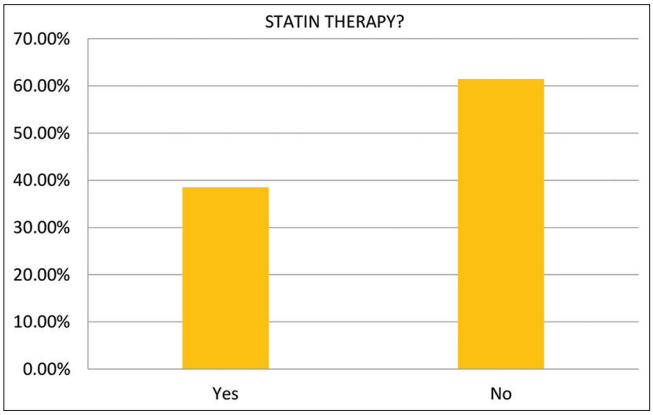

Fig. 3: Distribution of patients as per usage of statins

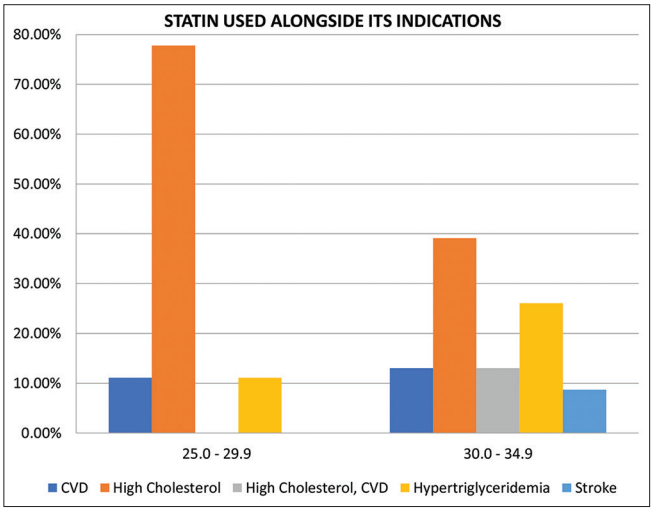

Fig. 4: Distribution of patients as per the indication of statin usage

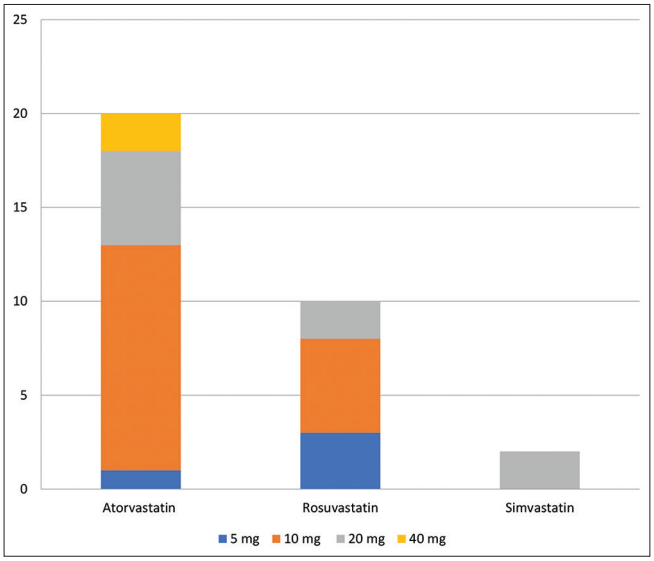

Fig. 5: Distribution of patients as per the statin prescribed and their doses

Interpretation

Since the p-value (0.0464) is <0.05, we reject the null hypothesis at the 5% significance level. This suggests that there is a statistically significant association between statin therapy continuation and breast cancer recurrence.

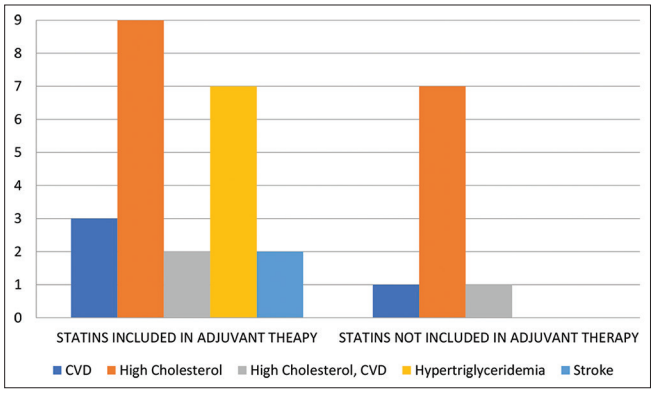

Fig. 6: Distribution of patients as per statins prescribed as an adjuvant therapy and its indications

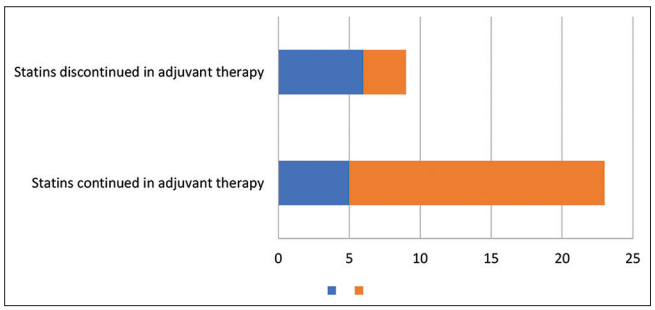

Fig. 7: Distribution of patients as per statin usage and recurrence of breast cancer

CONCLUSION

There is a statistically significant association between statin therapy continuation and recurrence of breast cancer. Out of 23 patients who continued statin therapy, 18 patients did not encounter any recurrence of secondary tumors whilst 5 had. On the other hand, out of 9 patients who discontinued the use of statins, 6 patients encountered recurrence and 3 patients did not.

DISCUSSION

The study sample classifies females based on BMI, revealing that 46.07% had a normal BMI, 37% were categorized as obese, and 16.66% fell into the pre-obese category. This highlights a relationship between elevated BMI and breast cancer occurrence, reinforcing the consideration of obesity as a risk factor for developing this ailment. This association was advocated by Pati *et al*. in a study conducted in 2023 [24].

While assessing the prevalence of breast cancer, we found that 65% of the patients were affected by Invasive ductal carcinoma, making it the most prevalent subtype. A significant proportion of pre-obese and obese females presented with co-morbidities, including hypertriglyceridemia (21.85%, n=7), hypercholesterolemia (50%, n=16), stroke (6.25%), cardiovascular disorders with hypercholesterolemia (9.37%, n=3), and CVD alone (12.50%), necessitating the use of statins for management. Consequently, 38.55% (n=32) of females were prescribed statins, while a substantial 61.44% (n=51) were classified as non-statin users.

Among the 32 statin users, atorvastatin was the most frequently prescribed (62.5%), followed by rosuvastatin (31.25%) and simvastatin (6.25%). The prescriptions were tailored to individual patient needs, particularly for cholesterol management and cardiovascular risk reduction in higher BMI groups thereby bringing in a vast variety of doses in the regimen.

Of the 32 females prescribed statins, 71.87% continued statin therapy as part of their adjuvant breast cancer treatment. In contrast, 28.12% discontinued statin use due to individual risk assessments, patient preferences, or contraindications.

The findings suggest a significant link between continued statin utilization and a lower likelihood of breast cancer recurrence. Among those 23 females who continued statins as part of their adjuvant therapy, 78.26% (n=18) did not experience secondary breast cancer malignancies, whereas 21.74% (n=5) developed secondary tumors despite statin use. A Chi-square test of independence (p=0.0464) confirmed a statistically significant association between statin continuation and reduced breast cancer recurrence. This aligns with previous findings, suggesting that statins may help inhibit EMT, potentially explaining the observed differences in disease recurrence based on tumor location. Similar conclusions were drawn in a study conducted in 2021 [25].

CONCLUSION

The findings emphasize the relationship between BMI, statin therapy, contraindications, and breast cancer recurrence. Obesity was identified as a significant risk factor for breast cancer, with 37% of females classified as obese and 16.66% as pre-obese. Invasive ductal carcinoma was found to be the most prevalent subtype. A notable proportion of these individuals exhibited co-morbidities such as hypertriglyceridemia (21.85%), hypercholesterolemia (50%), stroke (6.25%), cardiovascular disorders with hypercholesterolemia (9.37%), and CVD alone (12.50%), necessitating statin therapy.

Among the 32 females prescribed statins (38.55%), the majority received atorvastatin (62.5%), followed by rosuvastatin (31.25%) and simvastatin (6.25%). The distribution of dosages varied based on patient needs: Atorvastatin was prescribed at 5 mg (3.12%), 10 mg (37.5%), 20 mg (15.62%), and 40 mg (6.25%), while rosuvastatin was administered at 5 mg (9.37%), 10 mg (15.62%), and 20 mg (6.25%). Simvastatin, though less frequently used, was prescribed at 20 mg (6.25%).

Despite potential benefits, 28.12% of patients did not continue statins in their adjuvant therapy due to contraindications, patient preferences, or risk assessment. However, among those who continued statins, a significant association (p=0.0464) was found between statin use and reduced breast cancer recurrence, suggesting a possible protective effect. 78.26% of statin users did not experience secondary tumors, further supporting the hypothesis that statins may play a role in reducing breast cancer recurrence, potentially through the inhibition of EMT.

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AUTHOR CONTRIBUTIONS

Zainab Lokhandwala – Drafting of manuscript, verifying results, creating figures and graphs, refining research data and scrutinizing the end results, designing the research idea and conceptualization.

Fahim Khan – Data collection, maintaining research data, data modeling, statistical analysis.

SP Srinivas Nayak – Developing the experimental design, mentoring junior researchers, revising the manuscript critically for content, clarity, or accuracy.

Gunosindhu Chakraborthy – Overseeing the research activity, acquiring ethical permission, and precepting the entire group of researchers.

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CONFLICT OF INTEREST

The authors declare no possibility of any conflict of interest for this article.

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