<u>**Original Research Article**</u>

Assessment of Factors Influencing Medication Adherence among Breast Cancer Patients

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Abstract:

Introduction: Breast cancer (BC) is a complex tumor that is characterized by different molecular and biological types. Currently, there are therapeutic agents available to treat some variants of breast cancer. However, there is no universally available treatment strategy to manage different types of BC. The major concern, however, is the awareness of BC, its prevalence, awareness of symptoms, treatment and preventive measures, and medication adherence that could potentially contribute to improved quality of life and better outcomes. This study was carried out to assess the knowledge, perception, and practice of medication and identify the factors that affect medication adherence among BC patients.

Methods: This prospective questionnaire-based study was carried out among 51 women who were diagnosed with BC. The subjects were assessed for various factors that influenced adherence. The factors assessed included family type, reaction to the diagnosis, treatment place, co-morbidities, following instructions, who reminded of taking medication, feeling after medication, taking medication while traveling, who was accompanied on follow-up, asking doubts, feeling like stopping treatment due to cost, felt like stopping treatment due to travel constraints, communication from/with the hospital.

Results: Of the total 51 women included in the study, the age was 51.47±11.76 years. More than half (58.2%) of the BC women in this study showed medication adherence. Among the variables assessed for their influence on adherence, feeling after taking medication (p=0.010), medication while traveling (p=0.001), cost associated with medication (p=0.001), and travel-associated factors (p=0.001) significantly influenced medication adherence.

Conclusions: Despite the availability of medication, women diagnosed with BC face several difficulties in following the treatment schedules. Medication adherence was greatly influenced by the positive effects of treatment and the cost associated with treatment and travel.

Keywords: Breast Cancer, Quality of Life, Medication Adherence.

Introduction

Breast cancer (BC) is a cancer of the breast tissue wherein the cells demonstrate abnormal multiplication leading to lumps and tumors. More than half a million deaths were attributed to BC in the year 2020 according to the data available at World Health Organization (WHO). Interestingly, BC appears to show no specific predisposing factors except the age and sex of the affected person. However, some of the factors that could influence the development of BC include obesity, genetic predisposition, mutations in the genes (BRCA1, BRCA2, PALB-2), alcoholism,

consumption of tobacco, exposure to radiation, and hormonal therapy among others.

Besides, BC is prevalent globally and doesn't have geographical influences. Breast cancer follows different stages that include stage I (tumor confined to breast tissue), stage II (tumors in the breast), stage III (tumor cells spread to nearest lymph nodes), and stage IV (tumor cells spread/disseminated to other body parts like brain, lung, and liver).

There are different forms of BC like the estrogen receptor-positive (ER+ve), progesterone receptor positive (PR+ve), hormone receptor negative (HR-ve), and human epidermal growth factor receptors (HER2)/neu oncogene/HER-2 positive BCs. All these BCs are treatable with hormone therapies and monoclonal antibodies [1]. Triple-negative breast cancer (TNBC) has also been identified wherein the patients in this type are negative for ER, PR, and HER-2 receptors [2].

BC management has shown a significant transformation from the times when only surgical excision was the choice of treatment to the availability of modern and effective treatment strategies. Despite the advancement of therapeutic strategies, there are several limitations that need to be addressed for improved diagnosis, management, and prevention of BC. A majority of BCs, when identified at early stages are completely treatable. However, the major drawback appears to be the knowledge of BCs among people. Since BCs show some symptoms at the initial stages, awareness of these could contribute to early diagnosis [3].

Additionally, the treatment of BCs involves financial constraints and treatment-related factors like medication adherence that influence the disease outcomes [4]. A previous study from India observed that women in India have lower cancer literacy rates that were independent of socioeconomic status and educational qualifications. This study opined that there is an urgent need to implement sensitization programs to improve public awareness about various aspects of BC [5].

A significant number of Indian people living in tribal/forest areas have been found to be suffering from BC. The majority of BC cases may be missing due to a lack of awareness and infrastructural and diagnostic facilities that carry out screening and diagnosis of BC [6]. In recent studies, it was observed that age, presence of co-morbidities, adverse effects of medication, and time of initiation of treatment significantly influenced medication adherence [7, 8]. In this study, we carried out a prospective, questionnaire-based study to assess the factors that influence medication adherence among BC patients.

Materials and Methods

This prospective, questionnaire-based study included 51 women who were diagnosed with BC. The patients included in this study were those attending MVR Cancer and Research Institute, Kozhikode, Kerala, India. The study was approved by the Institutional Ethics Committee of MVR Cancer and Research Institute, Kozhikode. Informed consent was obtained from all the study participants.

Inclusion and exclusion criteria

Female patients aged between 18-65 years who were diagnosed with BC and those who were on oral anti-cancer medications and patients who were willing to participate in the study and were permanent residents of the area were included in the study. Patients with debilitating illness that make it difficult to respond, and those who had other constraints to participate in the study were excluded.

The patient's responses regarding medication adherence were collected through a pre-validated questionnaire. The subjects were assessed for various factors that influenced adherence. The factors assessed included family type, reaction to the diagnosis, treatment place, co-morbidities, following instructions, who reminded of medication, feeling after medication, taking medication while traveling, who was accompanied on follow-up, asking doubts, feeling like stopping treatment due to cost, felt like stopping treatment due to travel constraints, communication from/with hospital **(Annexure)**.

Statistical analysis: The data were systematically entered into Microsoft Excel sheets. Analysis of the association of the factors with adherence was carried out by Chi square test.

Results

Of the total 51 women included in the study, the age was 51.47±11.76 years. More than half (58.2%) of the BC women in this study showed medication adherence. Among the variables assessed for their influence on adherence, feeling after taking medication (p=0.010), medication while traveling (p=0.001), cost associated with medication (p=0.001), and travel-associated factors (p=0.001) significantly influenced medication adherence. The details of the variables and their influence on the adherence and non-adherence of medication are presented in **Table 1**.

Table 1:

Variables	Categories	Adherence (total n=51)		
		Adherence (n)	Nonadherence (n)	p-value
Family type	Nuclear	21	11	
	Joint	10	9	0.200
Reaction to diagnosis	Sad but overcome	10	7	
	Sad	20	14	0.700
Treatment type	Allopathy	22	16	
	Allopathy + ayurvedha	8	5	0.818
Co morbidities	Yes	14	11	
	No	16	10	0.688
Follow instruction	Yes	12	9	
	Sometimes	18	12	0.838
Who reminds for medication	Self	12	9	
	Family members	18	12	0.838
Feel after medication	Normal	21	7	
	Sick	9	14	0.010*
Take medication while travel	Yes	22	5	
	No	8	16	0.001*
Who accompany on follow up	Family members	23	17	
	Relatives	5	3	
	Neighbor	2	1	0.928
Ask doubts	Yes	19	14	
	No	11	7	0.806
Felt stop treatment due to cost	Yes	7	24	
	No	14	6	0.001*
Felt stop treatment due to travel	Yes	7	17	
	No	23	4	0.001*
Communication from hospital	Yes	21	17	
	No	9	4	0.377

p-value was derived from Chi-square test (x^2). P-value<0.05 is considered statistically significant

Discussion

BC is the fifth most common cause of cancer-related deaths affecting women throughout the world [9]. Prevalence of BC and deaths associated with it has increased significantly in the past three decades [10]. Additionally, cancer prevalence is expected to increase among people living in low and middle-income countries due to Westernization, changing lifestyles, and eating habits among others [11]. The risk factors for BC include both unmodifiable and modifiable components. The unmodifiable risk factors for the development of BC include female sex, old age, family history, race, mutations, reproductive history, and radiation exposure. Exposure to certain drugs/chemicals, lifestyle, body mass index, alcoholism, tobacco consumption, vitamin deficiency, and diet are some of the modifiable risk factors [12].

The Food and Drug Administration (FDA) approved BC preventive and treatment drugs are available in the market. The BC preventive drugs include Evista (Raloxifene Hydrochloride) Raloxifene Hydrochloride, Soltamox (Tamoxifen Citrate), and Tamoxifen Citrate. Drugs approved to treat BC include Abemaciclib, Abraxane (Paclitaxel Albumin-stabilized Nanoparticle Formulation), Cyclophosphamide, 5-FU (Fluorouracil Injection), and several others [13].

Despite the availability of medications, there is significantly lower usage of anticancer drugs due to the lack of cancer awareness among people. Additionally, cancer diagnosis needs to be emphasized in order to increase cancer detection rates. Medication adherence could become crucial to the prognosis of the disease and its outcome. The results of this study identified factors like feeling after taking medication (p=0.010), medication while traveling (p=0.001), cost associated with medication (p=0.001), and travel-associated factors (p=0.001) that significantly influenced medication adherence.

Therefore, it is essential to identify the factors that contribute to medication adherence and non-adherence. A recent report evaluated the potential drug adverse effects that could be evaluated before prescribing to BC patients [14].

A recent study from Uruguay observed that only 19% of BC patients were nonadherent to therapy and older age patients were more adherent to

medication. The high adherence noticed in this study may be attributed to the fact that the medicine was distributed free of charge [15]. These points to the fact that subsidizing the cost of medicine could improve medication adherence. Also, it is essential to evaluate different factors that could interfere with or facilitate medication adherence. It must be noted that Nonadherence to medication could lead to worse treatment outcomes as evidenced by the results of a recent study. This study's results confirm that there is less chance of event-free survival among the non-medication adherent group [hazard ratio (HR) of 1.26 (95% CI, 1.11-1.43) to 2.18 (95% CI, 1.99-2.39)] [16].

Adverse reactions related to medication were assessed for their influence on medication adherence among female breast cancer patients who were treated as outpatients [17]. This study emphasizes the need to understand patient factors that interfere with medication adherence. Enlightening/educating patients about the benefits of medication, and identifying and eliminating factors that interfere with compliance to medication must be carried out by the healthcare professionals [18].

Since a significant number of BC patients are prescribed oral anti-cancer agents, it is the responsibility of oncologists to devise effective strategies to ensure compliance/adherence to medication [19, 20].

Conclusions

The results of the present study suggest that more than half of the study participants adhered to BC medication. The factors that significantly influence medication adherence includes factors like feeling after taking medication, medication while traveling, cost associated with medication, and travel-associated factors. Since BC treatment is essential to improve the quality of life and reduce the morbidity and mortality associated with the disease, it is essential to evaluate the factors that contribute to or interfere with medication adherence.

Limitations:

As this was a single center study with a comparatively short sample size, results of this study cannot be generalized. Generalization requires the support of results from similar large studies

Ethical statement:

Institutional ethical committee accepted this study. The study was approved by the institutional human ethics committee, the Institutional Ethics Committee of MVR Cancer and Research Institute, Kozhikode, Kerala, India. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and the voluntary nature of participation were explained to the participants before obtaining consent. The confidentiality of the study participants was maintained.

Authors' contributions:

Author's contribution: **Reshma V** and **Prakashiny S** - conceptualization, data curation, investigation, methodology, project administration, visualization, writing—original draft, writing—review and editing; **Nithyapriya M** and **Shahina Khan** - conceptualization, methodology, writing—original draft, writing—review and editing; **Durgesh kumar** and **Madhuram** - conceptualization, visualization, supervision, writing—original draft; **NK warrier** and **Uma shanker**- methodology, writing—original draft, writing, review and editing. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. All authors have read and agreed to the published version of the manuscript**.**

Data Availability:

All datasets generated or analyzed during this study are included in the manuscript.

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