Complementary and Alternative Medicine Use and Its Impact on the Delayed Presentation and Advanced Stage of Breast Cancer in Newly Diagnosed Indian Women

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Abstract

Introduction   Complementary and alternate medicine (CAM) use is highly prevalent among Indian cancer patients. However, such studies from the perspective of Indian patients with breast cancer (BC) are lacking.

Objective   The aim of this study was to evaluate the incidence of CAM use and its impact on the presentation of patients with BC.

Materials and Methods   This retrospective study was performed in the Department of Radiation Oncology over a period of 6 months (January to June 2019) and involved review of hospital-record of 229 newly-diagnosed patients with BC. Univariate and multivariate binary logistic regression analysis was done to evaluate the association of CAM use with the BC stage and various clinicodemographic variables.

Results   Of 229 patients, 96 (41.92%) used CAM. The CAM use was significantly associated with rural residence (odds ratio [OR]: 4.092; 95% confidence interval [CI]: 2.27–7.35), illiteracy (OR: 6.417; 95% CI: 1.83–22.45), delayed presentation by 3 to 6 (OR: 12.964; 95% CI: 2.94–57.00) and more than 6 months (OR: 40.667; 95% CI: 9.26–178.46), and advanced stage at diagnosis (OR: 10.786; 95% CI: 5.15–22.58). Similarly, advanced stage at diagnosis was significantly associated with rural residence (OR: 2.78; 95% CI: 1.59–4.84), illiteracy (OR: 7.20; 95% CI: 1.86–22.79,), and delayed presentation by 3 to 6 (OR: 6.41; 95% CI: 2.81–14.61) and more than 6 months (OR: 17.55; 95% CI: 7.26–42.45).

Conclusions   CAM use was highly prevalent among the patients with BC and significantly associated with advanced stage at diagnosis. Moreover, both CAM use and advanced stage at diagnosis were significantly associated with rural residence, low educational status, and delayed presentation.

Keywords
► advanced stage
► alternative therapies
► breast cancer
► complementary therapies
► India

Introduction

Globally, breast cancer (BC) is the leading cancer to be diagnosed and is the leading cause of cancer-related mortality in women.[1] Following the global trend, BC is the most frequent cancer in Indian women. Its incidence is rising, with the highest burden reported from the metropolitan areas.[2] The current healthcare system in India is insufficient to cater to the rising incidence of cancer with just 9.28 doctors per

10,000 patients, as compared to 26.04 in United States and 58.23 in United Kingdom.[3] This problem is further compounded by disproportionate distribution of healthcare services and lack of trained healthcare workers. In a National Sample Survey, 56.4% health workers were found to be unqualified, including 42.3% practitioners of conventional medicine. Among all qualified workers, 77.4% catered to the needs of patients in urban areas.[4]

In India, majority of the patients with BC have high attrition toward the quacks and the complementary and alternative medicine (CAM).[5] The lack of healthcare services in rural areas makes the CAM a feasible option. It is observed that the prevalence of CAM use among Indian cancer patients ranges from 34.3 to 46.2%.[6–8] The reasons that make CAM popular among patients in rural areas are their easy availability and economical nature. Moreover, most of the patients perceive that CAM is more effective and safer relative to the conventional therapy.[9] The patients with cancer prefer CAM due to the risk of death, surgery-associated long-term morbidity, and adverse effects associated with conventional therapy.[10]

Despite advances in diagnosis and management, around 57% patients with BC are diagnosed in the locally advanced stage.[2] The CAM use is associated with delays in presentation and diagnosis.[11] A recent study reported that patients residing in rural areas are diagnosed at an advanced stage and have higher death rate relative to those residing in urban areas.[12] Another study compared the income and educational background of patients with BC and reported that patients with low-income and lower educational status were diagnosed at later stage, underwent less relevant investigations, and had lower rates of treatment.[13] Thus, coupled with low-income and higher illiteracy rate, patients with BC residing in rural areas are at disadvantage and have fewer options than to choose CAM. However, the association of CAM use with delayed presentation and stage at diagnosis in patients with BC has not been evaluated from the perspective of Indian patients. Thus, we assessed the incidence of CAM use, its impact on the presentation of patients with BC, and association with various clinicodemographic characteristics.

Materials and Methods

Study Design and Setup
This retrospective, hospital-record based study was performed in the department of radiation oncology of a tertiary care institute. Ours is the only government hospital in the region with treatment facility for patients with cancer that caters to around 3,000 newly-diagnosed cancer patients annually.

Selection and Description of Patients
A total of 229 patients with BC diagnosed between January and June 2019 were included in the study. The record files were scanned manually, and following characteristics were collected: Demographic details (age, literacy level, and area of residence), history and type of CAM use, baseline investigations (chest X-ray, abdominal ultrasonography,

fine-needle aspiration cytology or biopsy, and mammography and/or positron emission tomography scan, if required), and clinical details (delay in presentation and BC stage). For the purpose of analysis, stage I to II and stage III to IV of BC were considered as early and late, respectively. CAM use suggested indulgence in any products and methods that are not a part of conventional medicine prior to the diagnosis. The time to presentation was calculated from the time point the patient noticed the symptom to the time lump was evaluated and diagnosed. Presentation delay suggested the duration between symptom onset to initial presentation of more than 3 months.

Inclusion Criteria
All newly diagnosed, histopathologically confirmed patients with BC were included in the study.

Exclusion Criteria
Patients with recurrent or operated BC, those already receiving chemo- or radiotherapy, and incomplete data on files were excluded.

Primary Outcome
Incidence of CAM use among newly diagnosed patients with BC.

Secondary Outcome
Impact of CAM use on the presentation of patients with BC and its association with various clinicodemographic characteristics.

Statistical Analyses
SPSS (IBM, Armonk, New York, United States) version 23.0 for Windows was used to analyze the data. The data was depicted as frequency (percentages). CAM use and BC stage were divided into dichotomous outcome: "Yes" or "No" and "Early" or "Late," respectively. The association between categorical variables and dependent variables (CAM use and BC stage) was assessed with chi-squared test. The association of CAM use with BC stage was assessed with multivariate binary logistic regression analysis. The findings are represented as odds ratio (OR) with 95% confidence interval (95% CI). A two-tailed p-value less than 0.05 was regarded as significantly significant.

Ethics
The Institutional Ethics Committee, Government Medical College, Nagpur (Dated 17/12/2018, Letter no. 2018/418) approved the study protocol. In this study, all procedures performed in the human subjects followed the ethical standards of the institutional research committee and the 1964 Helsinki Declaration (and subsequent amendments).

Results

Among 229 patients, more than half (51.97%) patients were aged less than 50 years. Most of the patients resided in the rural areas (58.52%) and presented in advanced stage

Table 1 Univariate analysis of association between CAM use and patient characteristics

Parameters	CAM use		Total n (%)	p-Value
	Yes [n = 96 (%)]	No [n = 133 (%)]		
Age (years)				
<50	51 (53.13)	68 (51.13)	119 (51.97%)	0.828
≥50	45 (46.87)	65 (48.87)	110 (48.03%)	
Area of residence				
Rural	74 (77.08)	60 (45.11)	134 (58.52%)	<0.0001
Urban	22 (22.92)	73 (54.89)	95 (41.48%)	
Stage of cancer				
Early	10 (10.42)	74 (55.64)	84 (36.68%)	<0.0001
Late	86 (89.58)	59 (44.36)	145 (63.32%)	
Educational status				
Illiterate	22 (22.92)	6 (4.51)	28 (12.23%)	<0.0001
Primary	10 (10.42)	31 (23.31)	41 (17.90%)	
Secondary	56 (58.33)	82 (61.65)	138 (60.26%)	
Graduate	8 (8.33)	14 (10.53)	22 (9.61%)	
Delay in presentation (months)				
<3	2 (2.08)	44 (33.08)	46 (20.08%)	<0.0001
3–6	33 (34.38)	56 (42.11)	89 (38.86%)	
>6	61 (63.54)	33 (24.81)	94 (41.05%)	

Abbreviation: CAM, complementary and alternative medicine.

(63.32%). Most of the patients had higher secondary education (60.26%) and delay in presentation for more than 6 months (41.05%). Finally, 41.92% patients accepted CAM use. Predominantly used CAM, in the decreasing order, were ayurvedic [30 (31.25%)], ayurvedic + spiritual therapy [17 (17.71%)], spiritual therapy + homeopathy [10 (10.42%)], ayurvedic + yoga [8 (8.33%)], ayurvedic + meditation [8 (8.33%)], spiritual therapy [6 (6.25%)], homeopathy [5 (5.21%)], naturopathy [4 (4.17%)], spiritual therapy + naturopathy [4 (4.17%)], meditation [3 (3.13%)], and homeopathy + meditation [1 (1.04%)].

Univariate analysis revealed significant association between CAM use and area of residence ($p < 0.0001$), educational status ($p < 0.0001$), delay in presentation ($p < 0.0001$), and BC stage ($p < 0.0001$; ►**Table 1**). Similarly, significant association was observed between BC stage and area of residence ($p < 0.0001$), educational status ($p = 0.024$), and delay in presentation ($p < 0.0001$; ►**Table 2**).

On multivariate binary logistic regression analysis, area of residence, BC stage, educational status, and delay in presentation were significantly associated with CAM use. Moreover, the odds of CAM use among patients residing in rural areas and those presenting with advanced-stage BC were found to be 4.1 (OR: 4.092; 95% CI: 2.27–7.35, $p < 0.0001$) and 10.7 times (OR: 10.786; 95% CI: 5.15–22.58, $p < 0.0001$) higher than patients residing in urban areas and those with early-stage cancer, respectively. Illiterate patients had 6.4 (OR: 6.417; 95% CI: 1.83–22.45, $p = 0.004$) times higher chances of CAM use than the graduates. Finally, the odds of CAM use

were 12.9 (OR: 12.964; 95%CI: 2.94–57.00, $p = 0.001$) and 40.6 (OR: 40.667; 95%CI: 9.26–178.46, $p < 0.0001$) times higher among patients with delay in presentation for 3 to 6 and more than 6 months, respectively, than those with delay in presentation for less than 3 months. However, age of the patient did not predict CAM use in patients with BC (►**Table 3**).

Similarly, area of residence, educational status, and delay in presentation were significantly associated with the BC stage. The odds of patient presenting with advanced-stage cancer were 2.7 (OR: 2.78; 95% CI: 1.59–4.84, $p < 0.0001$) times higher in those residing in rural areas than urban areas. The odds of patient presenting with advanced-stage cancer were 7.2 (OR: 7.20; 95% CI: 1.86–22.79, $p = 0.004$) times higher in illiterates than the graduates. Finally, the odds of patient presenting with advanced-stage cancer were 6.4 (OR: 6.41; 95% CI: 2.81–14.61, $p < 0.0001$) and 17.5 (OR: 17.55; 95% CI: 7.26–42.45, $p < 0.0001$) times higher among patients with delay in presentation for 3 to 6 and more than 6 months, respectively, than those with delay in presentation for less than 3 months. However, age of the patient did not predict BC stage (►**Table 4**).

Discussion

In the developed world, around 50% patients with cancer survive, while this proportion is only 20% among patients from developing part of the world. In India, among a million newly diagnosed cancer patients each year, more than 50%

Table 2 Univariate analysis of association between stage of cancer and patient characteristics

Parameters	Stage of cancer		Total	p-Value
	Early [n = 84 (%)]	Late [n = 145 (%)]	n (%)	
Age (years)				
<50	39 (46.43)	80 (55.17)	119 (51.97%)	0.202
≥50	45 (53.57)	65 (44.83)	110 (48.03%)	
Area of residence				
Rural	36 (42.86)	98 (67.59)	134 (58.52%)	<0.0001
Urban	48 (57.14)	47 (32.41)	95 (41.48%)	
Educational status				
Illiterate	4 (4.76)	24 (16.55)	28 (12.23%)	0.024
Primary	17 (20.24)	24 (16.55)	41 (17.90%)	
Secondary	51 (60.71)	87 (60.00)	138 (60.26%)	
Graduate	12 (14.29)	10 (6.89)	22 (9.61%)	
Delay in presentation (months)				
<3	36 (42.86)	10 (6.89)	46 (20.08%)	<0.0001
3–6	32 (38.09)	57 (39.32)	89 (38.86%)	
>6	16 (19.05)	78 (53.79)	94 (41.05%)	

patients die within 1 year following diagnosis, while another million demonstrate cancer progression within 5 years of diagnosis. Moreover, among 1.5 million patients who require palliative therapy, less than 0.1 million are catered by the current facilities.[8] Thus, majority of the patients use CAM.

Recently, Hill et al found a high CAM use among patients with cancer in developing part of the world (54.5%),

Table 3 Multivariate binary logistic regression analysis of association between CAM use and patient characteristics

Parameters	CAM use		OR	95% CI	p-Value
	Yes	No			
Age (years)					
<50	51	68	1.083	0.64–1.83	0.765
≥50	46	65	1.00	Reference	–
Area of residence					
Rural	74	60	4.092	2.27–7.35	<0.0001
Urban	22	73	1.00	Reference	–
Stage of cancer					
Early	10	74	1.00	Reference	<0.0001
Late	86	59	10.786	5.15–22.58	–
Educational status					
Illiterate	22	6	6.417	1.83–22.45	0.004
Primary	10	31	0.565	0.18–1.73	0.319
Secondary	56	82	1.195	0.47–3.03	0.708
Graduate	8	14	1.00	Reference	–
Delay in presentation (months)					
<3	2	44	1.00	Reference	–
3–6	33	56	12.964	2.94–57.00	0.001
>6	61	33	40.667	9.26–178.46	<0.0001

Abbreviations: CI, confidence interval; CAM, complementary and alternative medicine; OR, odds ratio.

Table 4 Multivariate binary logistic regression analysis of association between stage of cancer and patient characteristics

Parameters	Stage of cancer		OR	95% CI	p-Value
	Early	Late			
Age (years)					
<50	39	80	1.42	0.83–2.44	0.203
≥50	45	65	1.00	Reference	–
Area of residence					
Rural	36	98	2.78	1.59–4.84	<0.0001
Urban	48	47	1.00	Reference	–
Educational status					
Illiterate	4	24	7.20	1.86–22.79	0.004
Primary	17	24	1.69	0.59–4.81	0.322
Secondary	51	87	2.05	0.83–5.07	0.122
Graduate	12	10	1.00	Reference	–
Delay in presentation (months)					
<3	36	10	1.00	Reference	–
3–6	32	57	6.41	2.81–14.61	<0.0001
>6	16	78	17.55	7.26–42.45	<0.0001

Abbreviations: CI, confidence interval; OR, odds ratio.

including India.[14] In patients with BC, higher CAM use may be due to severe adverse effects with conventional therapy and a relatively younger women consider that conventional therapy may hamper their future plans and capacity for child care.[15]

CAM Use

We observed a high prevalence of CAM use among the patients with BC (41.92%). Though some of the authors have evaluated the prevalence of CAM use in Indian patients with cancer,[6–8] there is absence of specific data regarding the CAM use in those with BC. Shreyamsa et al pointed out that 41.2% patients with BC use CAMs, mainly due to fear of conventional therapy, claims of no adverse effects, and easy/cheap availability.[16] Studies from Malaysia (46.5%) and Europe (44.7%) have reported comparable CAM use in patients with BC.[11,17] However, studies from United States (60.2%), Germany (62.5%), and Korea (67%) have reported higher prevalence.[18–20] These distinct findings could be due to differences in BC stage, educational status, economic background, type of CAM used, number of patients evaluated, and time point of the CAM use.

We observed that ayurvedic (31.25%), ayurvedic + spiritual therapy (17.71%), and spiritual therapy + homeopathy (10.42%) were most common CAMs used. Other studies from India reported ayurvedic remedies as the most commonly used CAM.[6–8] However, CAM use depends on the local preference and several other factors. Natural products, dietary supplements, and yoga and exercise were the most common CAM used in developed world.[18–20] In this study, all the patients were newly diagnosed, and most had low educational level. However, in other studies, patients were known cases of BC and had higher educational level.[18–20] This might have resulted in higher prevalence of CAM use.

Association of CAM Use with Clinicodemographic Characteristics

We observed that CAM use was significantly associated with rural residence, lower educational status, longer delay in presentation, and advanced stage at diagnosis. Similarly, Maghous et al reported that CAM use was significantly associated with rural residence and absence of primary and tertiary cancer care, thereby resulting in delayed diagnosis.[21] Moreover, Hwang et al found that lower educational status and longer duration following diagnosis were significantly associated with CAM use.[20] Contrarily, McLay et al reported that higher education was associated with significantly increased CAM use.[22] This could be attributed to higher awareness and ability to find specific information regarding CAM.

Mohd Mujar et al found that CAM use was associated with significantly greater risk of delayed presentation, advanced stage at diagnosis, and delayed treatment initiation.[11] Moreover, Tautz et al demonstrated that patients with advanced-stage BC generally use CAM to a significantly higher degree.[23] This suggests that patients with advanced stage are more likely to look for further treatment options beyond conventional medicine.

Association of BC Stage with Clinicodemographic Characteristics

We found that advanced stage at diagnosis was significantly associated with the rural residence, lower educational status, and longer delay in presentation. Liu et al reported that

educational status was significantly associated with the BC stage and significantly greater proportion of uneducated patients had advanced stage at diagnosis than those with education of university and above.[13] Similarly, a study from South India reported that patients with illiterate/primary school educational status had significantly higher chances of being diagnosed with advanced BC.[24] Thus, diagnosis of BC in early stage is possible if women are educated about the screening and diagnostic techniques.

Foroozani et al reported that rural residence was significantly associated with delayed diagnosis and higher chances of being diagnosed with end-stage BC.[25] These findings can be ascribed to the fact that well-educated individuals prefer to reside in developed cities and thus, have a greater likelihood of undergoing screening investigation for BC and being diagnosed at an early stage.

Delay on the part of patient to seek medical attention following self-discovery of a potential BC symptom is linked to advanced stage at diagnosis. Foroozani et al demonstrated that longer delay in diagnosis (>3 months) was significantly linked to higher chances of being diagnosed with end-stage BC.[25] We observed that around 57% patients had a delayed presentation for more than 3 months in seeking the medical attention. Other studies from North, South, and Central India reported that nearly 62, 54, and 48.3% of women with BC had a delay of more than 3 months, respectively.[26–28] Thus, our findings are consistent with those conducted in other parts of India.

We observed that age did not predict CAM use. Similarly, Chin et al suggested that age was not related to the CAM use.[29] Contrarily, Hwang et al reported that young patients had significantly higher CAM use.[20] This could be due to higher literacy rate among younger patients and better access to information related to CAM use. We further observed that age was not significantly associated with the BC stage. Contrarily, Foroozani et al[25] and Gangane et al[26] reported that old age is significantly associated with longer delay resulting in advanced stage at diagnosis. These contradictory findings could be attributed to difference in number of patients evaluated and different distribution of patients according to age groups.

Strengths

First, this is the initial study from India to assess the CAM use in newly diagnosed patients with BC. Second, findings of this study add to the sparsely published literature related to CAM use in Indian patients with BC and its effect on the delayed presentation and stage at diagnosis. Third, we tried to assess the association of CAM use with several demographic factors that result in advanced stage of cancer at diagnosis. Finally, diverse population of Central India makes the findings generalizable to other patients with BC.

Limitations

First, the available medical records did not have economic background of the patients and thus, we could not assess the association of CAM use with economic status. Second,

retrospective nature of study did not allow us to assess the factors responsible for CAM use.

Conclusion

This study suggests high prevalence of CAM use in Indian women with BC. The CAM use was significantly associated with rural residence, low educational status, delayed presentation, and advanced stage at diagnosis. Similarly, advanced stage at diagnosis was significantly associated with residence in rural areas, low educational status, and delayed presentation. The findings of the present study suggest assessment of current BC care and their accessibility, as poor access is very likely to promote CAM use. Further studies are needed to support our findings. Moreover, further studies evaluating various causes of delay in presentation, both patient- and system-related, need to be carried out.

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