

Factors associated with attrition in patients with breast cancer: A retrospective study

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ABSTRACT

Background. Attrition in follow up is a key limitation of longitudinal studies, especially in cancer patients in developing countries. We did a retrospective analysis of possible factors that resulted in attrition of patients with breast cancer during follow up.

Methods. This study is a comparison between patients who came for a follow up regularly to our clinic with those who did not but could be contacted on phone or by post. A computerized grouped database was constructed with the following parameters: age, religious community, other co-morbid conditions if present, distance from place of residence to our city, residence in city/village, initial stage of the disease, type of treatment and disease relapse or death.

Results. Using binary logistic regression, disease relapse was found to be the most important cause of non-compliance. The odds ratio for irregularity or loss to follow up of patients with disease relapse was 2.53 (95% CI: 1.17–5.46; $p=0.02$) for patients who were alive with disease relapse and 6.18 (95% CI: 3.47–11.02; $p<0.001$) for patients who had died due to the disease compared with those who were alive and free of disease. The age and place of residence in a village were other significant factors. The odds of attrition due to age were 1.03 (95% CI: 1.01–1.05; $p=0.04$) for each year of increase in age and that of residence in a village was 1.85 (95% CI: 1.02–3.36; $p=0.04$).

Conclusion. Age, disease relapse and residing in a village are important causes of attrition during follow up of patients with breast cancer in India.

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INTRODUCTION

Attrition in follow up of patients recruited for clinical trials is a key reason for incomplete data in longitudinal studies. In patients with malignancies, disease progression can be an important cause of attrition, i.e. patients may fail to return because they have suffered exactly those events which are of interest to the investigators; for example, they died or had a relapse of disease. Conversely, patients who feel entirely healthy may also not return for evaluation because it is not their priority any more.¹ The assumption that the data are missing at random is usually unjustified in the setting of cancer clinical trials and recommendations have

been made to minimize missing data and document reasons for the same.² Therefore, it is important to identify the possible predictors of, and identify groups at high risk for attrition, and find methods to prevent this.

Breast cancer is the second most common cancer in Indian women and is fast emerging as the most common cancer among women in metropolitan cities in India. In the absence of effective screening programmes for early detection of breast cancer, it is important to institute appropriate methods of treatment with early identification and treatment of relapse, which has been suggested to improve the outcome of such patients.^{3,4} However, attrition is often high and remains a key drawback in the treatment and follow up of patients in India.

Few studies have evaluated factors that affect the rates of attrition in patients with breast cancer,^{5–7} but we found no study from India in the indexed literature. As challenges related to recruitment and retention in cancer trials vary by geographical location and among ethnic groups,^{5,8} it is important to identify subgroups with the highest risk of attrition in a given area or community. In India, the diverse socioeconomic, cultural and ethnic backgrounds can have a bearing on attrition.

We did this study to identify the potential causes of attrition in the follow up of patients with breast cancer treated at a tertiary care centre in India.

METHODS

This is a retrospective study of patients who received treatment for breast cancer during 1994–2003 in a single surgical unit at the All India Institute of Medical Sciences and made at least one follow up visit to the clinic. Patients were counselled regarding the disease, available treatment options, chances of disease relapse and the importance of regular follow up. After completion of therapy they were advised to come for a follow up every 3 months for the first 2 years, every 6 months for the next 3 years and yearly thereafter. Detailed information regarding the initial clinical history, findings at examination, investigations, treatment received as also of clinical and investigative observations at follow up evaluations of breast cancer patients enrolled in the clinic are recorded in individual patient files maintained by the unit and data from these files were used for the purpose of the study.

Follow up data were categorized into 2 groups, i.e. for patients who complied with the above-mentioned recommendations and those who did not. The following categories of patients were considered as compliers:

1. Those who completed the treatment and came for at least 5 years for follow up.
2. Those who did not come to the clinic, but their relatives informed us about their status.

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3. Those who missed a few visits in between but subsequently followed up regularly on their own.
4. Those with terminal illness at the time of last follow up.
5. Those who died before the recommended next follow up visit.

Efforts were made to contact those patients who did not comply with telephone calls and letters to know the potential causes of attrition in this group.

Statistical analysis was done using the SPSS software. A computerized grouped database was created using the above information and the following statistical tests were done.

1. Chi-square tests
2. Mann–Whitney U tests
3. Binary logistic regression

In multivariate analysis, the dependent variable was compliance to regular follow up (0 compliers, 1 non-compliers) and the independent variables analysed were: (i) age; (ii) religious community; (iii) presence of other co-morbid illnesses; (iv) distance from city of residence to Delhi calculated with distance calculator between cities; (v) place of residence (city or village); (vi) marital status; (vii) the initial stage of the disease; (viii) surgical therapy; (ix) whether adjuvant systemic therapy was given and the type of such therapy; (x) radiotherapy received; (xi) disease progression, relapse or death due to disease. The variable of sex was not included in the analysis due to the low incidence of breast cancer in men. Socioeconomic factors, literacy rates and psychological factors could not be included due to difficulty in assessing these variables retrospectively.

RESULTS

Three hundred and seventy-five patients who had completed therapy were followed up during the study period. There were 370 women and 5 men. Of these, 353 patients (94%) could be contacted on phone, by post or came on their own for follow up; 22 patients (6%) who could not be contacted and their current status could not be ascertained were not included in the analysis.

Sixty-two per cent (219/353) came for follow up visits regularly and 38% (134/353) were tracked with phone calls or letters. The median follow up of the entire group was 35.8 months.

The mean (SD) age of the study group was 47.34 (10.75) years, median 46 years, range 25–80 years. Table I shows the descriptive variables studied with respect to their proportion in compliers and non-compliers. The proportion of patients with disease relapse was significantly higher in the group of non-compliers. A higher number of patients were from cities (270) than from villages (83); the difference though was not significant. In multivariate analysis using binary logistic regression and forward selection, disease relapse was found to be the most important cause of non-compliance. The odds ratio for attrition of patients with disease relapse was 2.53 (95% CI: 1.17–5.46; $p=0.02$) for patients who were alive with disease relapse and 6.18 (95% CI: 3.47–11.02; $p<0.001$) for patients who had died due to the disease (Tables II and III) compared with those who were alive and free of disease. Age and place of residence in a village were also significant but at lower odds. The odds ratio for each year increase in age was 1.03 (95% CI: 1.01–1.05; $p=0.04$) and for place of residence in a village it was 1.85 (95% CI: 1.02–3.36; $p=0.04$).

TABLE I. Comparison of variables between compliers and non-compliers

Variable	Categories	Compliers (n=219)	Non-compliers (n=134)	p value
Place of residence	City	175	95	0.053
	Village	44	39	
Marital status	Married	213	130	1.00
	Single	6	4	
Stage of disease	1	13	5	0.216
	2 and 3	185	109	
	4	21	20	
Co-morbid conditions	Absent	198	118	0.484
	Present	21	16	
Disease outcome	Alive without disease	167	59	<0.0001
	Alive with disease	20	19	
	Died due to disease	32	56	
Religious community	Hindus	184	113	0.812
	Muslims	23	12	
	Christians and others	12	9	
Definitive surgical therapy	Received	198	113	0.070
	Not received	21	21	
Systemic therapy (chemo- and hormone therapy)	Received both	155	92	0.084
	Either	62	38	
	Neither	2	4	
Radiotherapy	Received	106	63	0.859
	Not received	113	71	
Distance categories	Residents of Delhi	109	67	0.223
	Within a radius of 50 km	40	16	
	Beyond a radius of 50 km	70	51	
Mean (SD) age (in years)		47.37 (10.82)	44.08 (9.39)	0.077
Mean (SD) distance (km)		264 (342)	258 (310)	0.44

TABLE II. Univariate analysis of the variables studied

Variable	Categories	Odds ratio (95% CI)	p value
Place of residence	City	1 (reference category)	0.17
	Village	1.61 (0.81–3.22)	
Marital status	Married	1 (reference category)	0.77
	Single	1.26 (0.27–5.82)	
Stage of disease	1	1 (reference category)	0.51
	2 and 3	0.82 (0.44–1.50)	
	4	0.80 (0.26–2.45)	
Co-morbid conditions	Absent	1 (reference category)	0.69
	Present	1.18 (0.52–2.68)	
Disease outcome	Alive without disease	1 (reference category)	0.02
	Alive with disease	2.75 (1.21–6.28)	
	Died due to disease	7.94 (4.01–15.752)	
Religious community	Hindus	1 (reference category)	0.86
	Muslims	1.09 (0.43–2.74)	
	Christians and others	1.60 (0.56–4.36)	
Definitive surgical therapy	Received	1 (reference category)	0.48
	Not received	0.70 (0.26–1.89)	
Systemic therapy (chemo- and hormone therapy)	Received both	1 (reference category)	0.517
	Either	0.82 (0.45–1.50)	
	Neither	1.70 (0–13)	
Radiotherapy	Received	1 (reference category)	0.92
	Not received	1.03 (0.58–1.81)	
Distance	Resident of Delhi	1 (reference category)	0.34
	Within a radius of 50 km	0.68 (0.31–1.50)	
	Beyond a radius of 50 km	1.40 (0.72–2.73)	
Age (in years)	–	1.03 (1.00–1.05)	0.05

Table III. Significant factors in binary logistic regression using step-wise selection

Variable	Categories	Odds ratio (95% CI)	p value
Disease outcome	Alive without disease	1 (reference category)	0.021
	Alive with disease	2.53 (1.17–5.46)	
	Died due to disease	6.18 (3.47–11.02)	
Age (in years)	–	1.03 (1.01–1.05)	0.04
Residence	City	1 (reference category)	0.04
	Village	1.85 (1.02–3.36)	

Among 134 patients who did not comply, 59 (44%) had no disease relapse while 75 (56%) had disease relapse or had died due to disease progression. Ninety-one per cent of the latter group (68/75) had disease at last follow up, i.e. at the time when they stopped coming to the clinic.

DISCUSSION

Most studies evaluating causes of attrition report a non-random pattern of data loss with identifiable factors related to the characteristics of the general population, healthcare delivery systems and disease.^{5,7,9–18} In our study disease relapse was the most important predictor of attrition in the follow up of patients treated for breast cancer. Death, severity of illness and ill health have been identified to be important risk factors for attrition.^{8,12,13} High initial symptoms with advanced cancers in palliative settings, depression related to ill health and treatment failure are other causes that have been proposed for the attrition in follow up of patients with cancer.^{8,11,18,20} In our study, over 90% of patients with disease relapse made at least one follow up visit to the clinic after disease relapse but discontinued

thereafter. Though depression, nihilism, lack of social support in patients with disease relapse could have been possible factors, we feel that economic constraints of affording costlier second-line treatment regimens prescribed to some of the patients may be a reason for attrition in Indian patients.

We found increasing age to be a risk factor for attrition in follow up. Age of the patient has been reported to be independently responsible for a decreased survival in patients with breast cancer in all stages.²¹ Also, it has been shown that limitations due to co-morbid conditions and lack of social support, especially in single elderly people, result in a poorer outcome in patients with cancer.^{22,23} Age has also been shown to be a factor for non-response to mailed clinical questionnaires.^{7,12,17}

Our observations also suggest that patients residing in villages were more likely to not come back for follow up visits. This was despite the relatively smaller number of patients from villages in our study. The place of residence reflects, to an extent, the socio-economic and literacy status of the patients, work habits, difficulties related to travel and support, and access to alternative healthcare options.^{24–26} In a study assessing the needs of rural women and women from remote areas travelling to a city for treatment of breast cancer, lack of social and logistical support largely related to lack of financial assistance were identified as prime concerns.²⁵

We did not find the distance to be travelled for follow up to be an independent cause for attrition even though it has been reported to be responsible for non-attendance in breast cancer screening programmes,^{15,17} and in determining the treatment options²⁷ in patients with breast cancer. While a precise cut-off value beyond which travel distance can be incriminated is not established, a travel time of >2 hours has been shown to influence attendance in

breast cancer screening and treatment programmes. In addition, the availability of transport and timing of the day during which an interview was scheduled have been shown to affect attendance in screening clinics. Others have suggested a role of motivation or socioeconomic factors rather than travel distance as a risk factor resulting in attrition among patients who live far away from the healthcare facility.^{15,16}

The initial stage at presentation, the religious community to which the patient belonged, presence of co-morbid conditions and type of therapy administered (locoregional or systemic therapy) were not significant factors for attrition in follow up in our study. Women, minority communities and certain ethnic groups have been previously identified to have a higher dropout rate.^{5,7,10,13,18} The association between co-morbid conditions and disease outcome has been variably reported. The presence of co-morbid conditions has been observed to negatively affect prognosis, stage of disease and treatment.²⁸ Some influence on the early detection, both positive and negative, has been suggested. In addition, co-morbid conditions can influence treatment options as well as affect the attendance at a follow up clinic. Social status, wealth and literacy are other reasons cited for attrition in the literature.^{10,13,15,18} The inability to analyse socioeconomic and literacy status is a limitation of our study. However, patients attending our clinic generally belong to the lower socioeconomic strata.

Community-based educational intervention programmes related to awareness of breast diseases have been shown to be effective in improving the public attitude in screening for cancers.²⁹ However, such interventions in assessing follow up of treated breast cancer patients have not been studied. We specifically advised our patients about the necessity for regular follow up visits at the time of initial therapy.

Interference with work, lack of time, misinformation regarding the usefulness of the procedure, difficulty in rescheduling appointments, lack of flexibility and change in the place of residence have been also cited as reasons for non-compliance in varied situations.^{6,8,13,14,16} It is interesting that though there was an initial high rate of dropout (about one-third of patients failed to come for a follow up) in our study, efforts at reaching patients by phone calls and letters were successful in a large number. Only 6% of our patients could not be contacted despite letters and phone calls. The success of data collection with telephone interviews has been found to be effective in certain situations though a follow up at the clinic is better and a combined strategy of follow up may be beneficial in reaching out to different population groups.^{30,31} In a study assessing clinical follow up by mailed self-reported questionnaires in breast cancers, 16% were non-responders and 4% were not contactable.⁷

In conclusion, in patients with breast cancer, disease relapse, increasing age and residing in a village are important risk factors for attrition in follow up. Focusing on these groups may help decrease the rates of attrition.

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