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ORIGINAL ARTICLE

Secondary and Quaternary Delays in the Diagnosis of Breast Cancer: Are the Physicians Responsible too?

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Abstract

Causes of delay in presentation of breast cancer has been categorised into 'Primary Delay' (delay by the patient or her family); 'Secondary Delay' (delay by the doctors in the first contact — family physician or quacks/alternative medicine practitioners); 'Tertiary Delay' (delay in the system in a specialist breast care unit e.g. waiting list, delayed reporting, doctors on leave, strikes); and 'Quaternary Delay' (e.g. patient hopping from one competent breast cancer specialist to another or mid-course attrition to alternative treatments). In India, many patients have blind belief and high attrition towards the quacks and alternative medicine practitioners. Our study was to assess whether these 'Secondary and Quaternary Delays', particularly the attrition towards the alternative non-modern medical practitioners, have any effect on the delayed presentation and advancement of the overall anatomical staging among the breast cancer patients. We performed a retrospective observational study, based on 'Triple Assessment' and pre-structured Questionnaire. All pathologically confirmed female breast cancer patients admitted from 02/2017 to 08/2018 in the department of General Surgery in our Institute were included. Male breast cancer, histopathologically unconfirmed/inconclusive breast lumps, patients with previous breast surgery/radiotherapy/chemotherapy were excluded. Data from 267 patients was analysed. The mean age at presentation of breast cancer was 47.54 years. The average delay between the onset of the first symptom and the histological diagnosis was $13.76 \pm$ SD 13.08 months. About half (50.2%) of our patients visited the non-modern medical practitioners at least once during their disease. The mean delay in diagnosis was significantly higher ($p < 0.0001$) among them. The average 'Secondary Delay' was significantly higher among those who visited the non-modern medical practitioners ($9.7 \pm$ SD 9.38 months). The average delay between the visit to the first doctor and the histological diagnosis was also significantly higher among them (18.35 ± 14 months). Patients with attrition to non-modern medical practitioners also were diagnosed in higher cT stages: cT4a (66.67%, 2 of 3) and cT4b (60%, 33 of 55). Most (56.9%) of stage IIIB patients visited the non-modern medical practitioners before their diagnosis. Patients who visited the non-modern medical practitioners had significantly more delay in the diagnosis of breast cancer. The 'Secondary and Quaternary Delays' form the major portion in the overall delay and lead to advancement of the anatomical staging of the disease. Creating public awareness, proper training and 'continued medical education' for primary care physicians, and the AYUSH practitioners are required. Further population-based studies are advised.

Keywords Breast Cancer · Delay in diagnosis · Secondary delay · Tertiary delay · Alternative medicine · Non-modern medicine · Homeopathy · Ayurveda · AYUSH

Introduction

The delayed presentation of the breast cancer patients is a complex psycho-social phenomenon. This 'Delay' has been classified as the following:

1. Primary Delay: due to patient and family factors.
2. Secondary Delay: time taken by the consulting family physician or the caregiver in the first contact, including the quacks or alternative medicine practitioners not equipped to treat breast cancer.
3. Tertiary Delay: time taken by the competent breast cancer specialists/units due to waiting list, false negative biopsies, doctors on leave, strikes etc.

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4. Quaternary Delay: due to patient hopping from one competent breast cancer specialist to another or mid-course attrition to alternative treatments [1, 2].

In a specialised breast cancer management set-up, primary, secondary, and quaternary causes are most important contributors for the overall delay in diagnosis [3]. Majority of the patients in India have high attrition towards the quacks and the alternative non-modern medical practitioners e.g. Homeopathy, Ayurveda, Unani, Siddha, Tantra, Exorcism, Astrology, and Palmistry.

Our study was to assess whether these 'Secondary and Quaternary Delays', particularly the attrition to the non-modern medical practitioners, result in the delay in diagnosis and advancement of the overall anatomical staging among the breast cancer patients.

Materials and Methods

We performed a retrospective observational study in the Department of General Surgery, IPGMER & SSKM Hospital, Kolkata, India from February 2017 to August 2018. All women admitted with biopsy proven newly diagnosed breast cancers were included in the study. Male breast cancer, any histopathologically unconfirmed/inconclusive cases of breast lump, patients too sick to participate in the study, any history of previous admission with breast cancer, patients with history of previous breast surgery/radiotherapy/chemotherapy were excluded.

Permission was taken from the Institutional Ethical Committee. Proper informed consent was taken, and the patients were assessed with history and relevant clinical examinations, imaging, and biopsy of the suspected lesion. Staging of the disease was done according to the American Joint Committee on Cancer (AJCC) Cancer Staging 8th Edition (2016) [4]. Data was collected in a pre-structured printed questionnaire. Continuous variables (e.g. age) with a normal distribution were reported as mean ± standard deviation (SD). Variables with a non-normal distribution (e.g. delay in presentation) were reported as medians with range. Categorical variables were expressed with the use of frequencies. We used the chi-square test and Fisher's exact test for categorical variables, and Student's unpaired '*t*' test and Mann–Whitney's test for continuous data to analyse and compare the study groups. *P*-value of less than 0.05 was considered statistically significant. All analyses were performed in consultation with a Statistician using Microsoft Office Excel 365 and IBM SPSS Statistics, v25 (IBM Corp. N.Y.).

Results

We found 281 patients eligible for the study. Fourteen patients were excluded due to critical illness, non-availability of pathology reports or refusal to participate; and 267 patients were finally analysed.

The mean age of the patients at diagnosis was 47.54 (SD 10.85, 95% CI: 46.23 to 48.85) years. Seventy three percent ($n = 196$) of patients were from the rural area and 27% ($n = 71$) were from the urban area. The mean age at presentation of patients from the urban area was 51.07 (SD 11.3) years, and from the rural area was 46.26 (SD 10.44) years.

For their first consultation, 47.19% ($n = 126$) went to the Homoeopaths, 30% ($n = 80$) went to the Surgeons and 11% ($n = 30$) attended the General Practitioners (GPs). Among the others, only 6% ($n = 17$), attended the Gynaecologists, 5% ($n = 12$) consulted the General Medicine Specialists and 1% ($n = 2$) consulted the Oncologists. While comparing the visit to the modern medicine, overall, 57.75% of patients from the urban area and 51.02% of patients from the rural area visited Modern Medicine Practitioners ($p = 0.4$, not significant).

The proportion of patients attending the modern and non-modern medical practitioners (either for first consultation or subsequent visits) are given in Table 1.

The average delay between the detection of the breast problem by the patient herself and the definite histological diagnosis was 13.76 (SD 13.08) months.

The mean 'delay' till histological diagnosis among the patients presenting for first consultation to the modern medical practitioners and non-modern medicine practitioners was 6.43 (SD 1.99) months and 21.1 (SD 15.36) months, respectively (p-value = < 0.001, significant).

The average duration of history of presenting complaints of patients before attending different medical practitioners are presented in Table 2.

Table 1 Proportion of the patients presenting to different modern and non-modern medical practitioners (for either first consultation or subsequent visits)

Type of medical practitioners	*N*	Percentage
Modern medicine practitioners only	133	49.8%
Non-modern medicine practitioners	134	50.2%
Homoeopaths	134	50.2%
Ayurvedic practitioners	10	3.7%
Only to Ayurvedic or other non-modern medical practitioners	0	0

All the patients visiting non-modern medical practitioners visited the modern medical practitioners later. All the patients attending Ayurvedic practitioners also attended the Homoeopathic consultants

The average 'Primary Delay' was 4.42 (SD 6.02) months. The average primary delay of patients presenting to the different medical practitioners are given in Table 3.

The average delay in between the visit to first doctor and the visit to the surgeons (Secondary and Tertiary Delay) are presented in Table 4.

The average overall delay (in months) between visit to the first doctor and the histological diagnosis of the breast cancer is presented in Table 5.

Overall, the most common cT stage on presentation was cT2 disease (39%, $n=103$) followed by cT3 (35%, $n=94$), cT4b (21%, $n=55$), cT1 (3.7%, $n=10$), cT4a (1.1%, $n=3$) and cTis (0.7%, $n=2$). Most common cT staging of patients who consulted non-modern medical practitioners were cT4a = 66.67% (2 out of 3), cT4b = 60% (33 out of 55), cTis = 50% (1 out of 2), cT3 = 48.94% (46 out of 94), cT2 = 47.57% (49 out of 103) and cT1 = 30% (3 out of 10). The result is represented in Fig. 1.

Overall, the most common cN status was cN1 = 51% ($n=135$) followed by cN0 = 41% ($n=110$) and cN2 = 8.2% ($n=22$). We found no cN3 disease during our study period. The most common nodal status of the patients who visited the non-modern medical practitioners were: cN2 = 72.73% (16 out of 22), cN0 = 49.09% (54 out of 110) and cN1 = 47.41% (64 out of 135).

Five patients (1.9%) had cM1 disease. Among the patients presenting with metastatic disease, 40% (2 out of 5) had visited the Non-Modern Medical Practitioners. About half (50.38%, 132 out of 262) of the patients presenting with cM0 disease had visited the Non-Modern Medical Practitioners.

Overall, the most common anatomical stage on diagnosis was Stage IIB (25.09%, $n=67$), followed by Stage IIIA and IIA (each 23.59%, $n=63$), Stage IIIB (21.72%, $n=58$)

Table 2 Average duration of history of presenting complaint before presenting to doctor for first consultation (p significant if <0.01)

First doctor attended by patient	*N*	Average duration of history of presenting complaints (months)	Standard deviation (months)	*p*-value
Surgeon	80	6.95	4.79	< 0.0001
Gynaecologist	17	5.29	2.80	
Medicine	12	9.75	5.14	
Oncologist	2	2.00	0	
GP	30	8.17	5.13	
Modern Medicine (overall)	141	6.43	1.99	
Homoeopath	126	21.10	15.36	

Table 3 Delay due to patient factors among patients before visiting different practitioners for first consultation (significant if $p<0.05$)

First doctor consulted by the patients	*n*	Average delay before consultation (in months)	SD	*p*-value
Surgeon	80	3.14	3.70	< 0.0001
Gynaecologist	17	1.89	1.95	
Medicine	12	5.48	3.97	
Oncologist	2	0.17	0.09	
GP	30	3.35	3.65	
Modern Medicine (overall)	141	2.80	1.47	
Homoeopath	126	5.80	7.71	

Table 4 Average delay in between the first visit to any doctor and visit to the surgeons (significant if $p<0.05$)

First doctors visited by the patients	*n*	Average gap between the first visit to doctor and the visit to surgeons (in months)	± SD	*p*-value
Surgeon	80	Not applicable (NA)	NA	< 0.0001
Gynaecologist	17	0.48	0.36	
Medicine	12	1.74	2.82	
Oncologist	2	1.37	1.23	
GP	30	1.72	2.62	
Modern Medicine (overall)	141	1.74	1.22	
Homoeopath	126	9.72	9.38	

Table 5 Average delay between the first visit to any doctor and the histological diagnosis (in months) (significant if $p < 0.05$)

First doctors visited by patients	*n*	Average delay between the first visit to doctor and the histological diagnosis (in months)	± SD	*p*-value
Surgeon	80	5.48	4.06	< 0.0001
Gynaecologist	17	3.94	2.41	
Medicine	12	8.10	4.80	
Oncologist	2	1.58	0.12	
GP	30	6.71	4.75	
Modern Medicine (overall)	141	5.16	1.78	
Homoeopath	126	18.35	13.9	

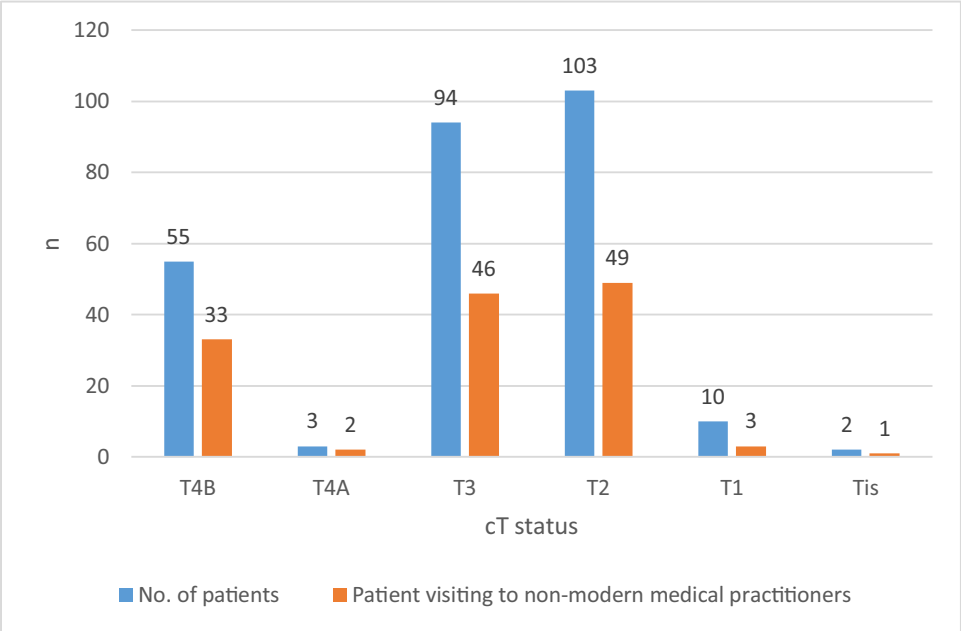

Fig. 1 Distribution of the patients visiting the non-modern medical practitioners according to cT stages

Table 6 Distribution of patients who visited non-modern medical practitioners according to the different anatomical stages of disease

Anatomical stage	Number of patients ($N = 267$)	No. of patients visiting the non-modern medical practitioners	Percentage
IV	5	2	40%
IIIC	0	0	
IIIB	58	33	56.9%
IIIA	63	30	47.6%
IIB	67	28	41.79%
IIA	63	31	49.2%
IB	0	0	
IA	9	1	11.11%
0	2	1	

and Stage IV (1.87%, $n = 5$). Distribution of patients who visited the non-modern medical practitioners according to the stage of the disease on diagnosis is presented in Table 6.

Discussion

The aim of our study was to find out whether visiting the different modern and non-modern medical practitioners by the breast cancer patients had any effect on the delayed diagnosis and presentation in advanced stage of the disease.

The mean age at presentation of breast cancer patients in our study was 47.54 (SD 10.85) years, which is much younger than its western counterpart [5]. Our result corroborates with the ICMR data, which shows that the peak incidence of breast cancer in Indian women is 45 to 49 years in all registries, except in north-eastern registries where the peak is seen in the age group 35 to 39 years [6–8].

In our study, urban women had older mean age at presentation (51.07 ± SD 11.3 years), compared to the rural women (46.26 ± SD 10.44 years). We performed Mann–Whitney's 2-tailed *U* test which revealed the

difference to be significant (p-value 0.004). Nagrani et al. [9] opined that living the first 20 years of life in a rural area reduces the risk of breast cancer. In another study in Kolkata, eastern India, Das et al. (2012) [10] concluded that the urban residence is a significant protective factor, probably due to a westernized lifestyle in urban areas. We could not find any other literature explaining why rural women have relatively younger age at presentation. This result remains a matter of debate and further research.

In our study, 47.19% of patients visited the Homoeopaths for their first consultation, whereas only 30% presented to Surgeons for the same. Overall, 50.2% of patients visited non-modern medicine practitioners (Homoeopathic or Ayurvedic Medical Practitioners) at least once during their course of treatment. We did not ask the patients the reasons behind presenting to different doctors. However, presenting to the non-modern medical practitioners for consultation may be contributed by multiple factors like financial constraints, illiteracy, lack of knowledge about disease, being critical and sceptical about the efficacy of modern medicine, past ill experience with modern medicine, non-availability of modern healthcare facility and blind belief on non-modern medicine..

The mean delay between onset of the first symptom and the definite histological diagnosis was 13.76 (SD 13.08) months in our study. A recent Brazilian study showed an average delay of 3 to 6 months due to various factors [11]. Two Indian studies showed the average delay in presentation to be 3 to 13 months [12] and 10.9 months [13], respectively. Though detailed population-based data is lacking, this delay is higher compared with data from other developing countries.

The mean duration of history of presenting complaints before first consultation among the patients visiting the non-modern medical practitioners was significantly higher ($21.1 \pm$ SD 15.36 months, $p = < 0.001$) in our study. If we consider only the patients visiting the modern medical practitioners for first consultation, this duration is much lesser ($6.43 \pm$ SD 1.98 months) and is comparable to the studies from Brazil [14] and Delhi [13] we quoted before. An Iranian study showed that the average delay in diagnosis to be 10.90 months [15]. This delay may be due to secondary and quaternary causes, including patients' ignorance to follow the advice of the doctors, inability of the physician to diagnose the disease and delayed referral.

The average 'Primary Delay' was also significantly higher among the patients visiting to the GPs and the General Medicine Practitioners for first consultation. Multiple psychosocial factors including ignorance, illiteracy, lack of health seeking behaviour, non-adherence to doctor's advice, fear of approaching to a surgeon ("they often suggest cutting the tumour, rather than giving medicines!"). On the contrary, patients presenting to the Gynaecologists and Oncologists had significantly early presentation, probably due to knowledge and attitude of this patient population — who knew about the disease and outcome but did not know whom to consult. Some studies opined that this 'Primary Delay' or 'delay due to patient factor' is responsible as the major cause for delayed presentation, followed by system delay ('secondary, tertiary or quaternary delays') [16]. Factors like lack of awareness, ignorance, posteriority, social stigma financial constraints, beliefs like "cutting on a cancer" may cause it to spread, herbal remedies, over-the-counter medications, chiropractic regimens, prayer, and reliance on God to heal the disorder, residence in rural area, older age, fear, embarrassment and shyness about breast as a private organ, posteriority and social stigma are some of the other significant patient factors responsible for delayed presentation [10, 17–19].

The 'Secondary Delay' may occur due to delay or failure of the first consultant to diagnose the disease, or due to delayed referral to the specialist surgeon. On the other hand, the delay in between the first visit to a doctor and the histological diagnosis of cancer is attributed by both the 'Tertiary' and 'Quaternary Delays'. Causes of 'Tertiary Delay' includes different system factors like delay in getting reports of investigations, repeated investigations due to previous erroneous/suspicious/inconclusive reports and delay in admission due to long waiting list.

In our study, the average *Secondary Delay* was significantly higher among patients visiting to the non-modern medicine practitioners ($9.7 \pm$ SD 9.38 months). The average *delay in between visit to the first doctor and the histological diagnosis* was significantly higher among the patients visiting to the non-modern medicine practitioners ($18.35 \pm$ SD 14 months). This delay was attributed by the *Secondary and Quaternary Delays*. On the other hand, patients visiting the modern medicine practitioners experienced lesser delay till histological diagnosis, causes being only attributed by the *Tertiary Delay* ($5.16 \pm$ SD 1.8 months). Patients presenting to the GPs and the Medicine Specialists also had slightly higher delay in histological diagnosis compared with average ($6.7 \pm$ SD 4.75 months and $8.1 \pm$ SD 4.8 months, respectively). False promise by some quacks and unethical medical practitioners to heal the cancer with medicine only, inability to identify the disease early by untrained doctors, lack of referral, non-adherence to doctor's advice by patients, financial constraints, distance to healthcare facilities etc. may be the contributing factors behind 'Secondary Delays'. In our study, the patients presenting to the Gynaecologists ($3.94 \pm$ SD 2.41 months) and Oncologists ($1.58 \pm$ SD 0.12 months) had significantly lower delay in histological diagnosis, probably due to the prompt referral by the doctors and adherence of advice by the patients, which significantly reduced the 'Tertiary Delay'.

In our study, visiting the non-modern medical practitioners was associated with higher stage of the disease at

diagnosis. Most commonly, they presented with cT4b disease (60%, 33 out of total 55 cT4b patients). The results for cT4a and cTis may be considered statistically insignificant due to the small sample size (may be co-incidental).

Similarly, our study showed that visiting the non-modern medical practitioners were related significantly with higher nodal status (72.73% i.e. 16 out of 22 patients with cN2 disease visited non-modern medical practitioners, followed by 49.09% of cN0 disease and 47.41% of cN1 diseases. This progression is probably due to the amount of precious time lost during those visits before definitive histopathological diagnosis could be achieved.

We found only 5 cases (1.9%) with metastatic disease. Nigam et al. (2014) reported 5.5% of patients having metastatic disease [20]. This lower percentage of metastatic disease in our study may be a sampling error (very few metastatic breast cancer patients get admitted in a Surgical Ward). Two out of 5 patients with metastatic disease visited the non-modern medical practitioners before the histological diagnosis was made.

Visiting the non-modern medical practitioners was significantly associated with increased anatomical staging of the disease in our study (56.9% of stage IIIB patients visited the non-modern medical practitioners before their diagnosis). This result was followed by Stage IIA (49.2%), Stage IIIA (47.6%), Stage IIB (41.79%), Stage IV (40%) and Stage IA (11.11%). The result of stage 0 disease is inconclusive due to the small sample size ($n=2$) and may be co-incidental.

Stagewise overall survival (OS) data in breast cancer shows nearly 100% 5-year OS with Stage I disease, 60–80% with locally advanced disease and about 20% in Stage IV diseases [21–23]. The importance of diagnosis of breast cancer at early stage cannot be overemphasized. Any factor leading to advancement of staging decreases the survival of the patient.

Our study provides evidence that, 'attrition to the non-modern medical practitioners' is an important contributing factor behind the 'Secondary' and 'Quaternary' delays in presentation of breast cancer and advancement of staging on diagnosis. About half of the patients visited the non-modern medicine practitioners at any point of time during their course of the disease. The interval between the first symptom and the definite histological diagnosis is much higher in the Indian population compared to other developing and developed countries. Total duration of history before definitive histological diagnosis, the 'Primary Delay', and the 'Secondary Delay' are higher among the patients with attrition to the non-modern medical practitioners. The patients consulting the non-modern medical practitioners also have higher cTNM staging on diagnosis.

Our study was a retrospective observational study. Further large population-based studies are required to establish the conclusions of our study. Sample size, which was adequately powered for this observational study, was underpowered to establish the correlations between the different factors of delayed presentation and staging. Other risk factors of early progression of breast cancer like Family History and Genetics were not included in our study. Only admitted patients in the surgery ward were considered.

For further studies, multicentric population-based study with larger sample size may be done. Follow-up may be done to this cohort to assess the outcome and the prognosis of the patients visiting the modern versus non-modern medical practitioners.

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Declarations

Conflict of Interest The authors declare no competing interests.

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