Original Research Article

Factors ~~C~~contributing to d~~D~~elayed b~~B~~reast c~~C~~ancer presentation: A prospective study at Parirenyatwa ~~Group~~ group of ~~Hospitals~~hospitals, Harare, Zimbabwe 2010-2013.

Abstract

Background: Breast cancer is one of the most common female cancers in Zimbabwe. A considerable proportion of patients delay ~~in~~ presentation, leading to ~~a~~ high morbidity and mortality. Delay in presentation can either be provider or patient delay. Survival is related to the stage at presentation. Delayed presentation is associated with lower survival. Understanding the reasons for delay may ~~in breast cancer presentation helps~~ help in ~~shortening~~ reducing ~~the~~ delays and ~~reduction in~~ morbidity and mortality. ~~It is for this reason that this study was carried out.~~ This study addresses these concerns.

Aim: To~~The study was carried out to~~ determine factors contributing to delayed breast cancer presentation at Parirenyatwa Group of Hospitals

Methods: A prospective observational study of ~~on~~ patients with the clinical and histological diagnosis of breast cancer~~. Participants were patients~~ attending Surgical Outpatient clinics ~~with a diagnosis of breast cancer~~ and awaiting surgery, or operated on from ~~the period~~ January 2010 to December 2013 were included.~~inclusive~~. Patients were interviewed and specific questions relating to breast cancer risk and delay factors recorded~~Interviews were carried out on each patient to answer specific questions on the data collection sheet.~~ Relevant investigations, including Human Immuno Deficiency Virus (HIV) testing, were done and recorded. Patients were prospectively followed up from admission until they were operated upon. Final histology results were collected from Histopathology Department, analyzed and recorded. In addition to chi-square test for associated factors of delay and proportionate z test for percentage differences, the researchers validated the observed factors using discriminant analysis. Discriminant analysis was used to model the reasons and delay period with a cut-off point 3 months (< 3 months / > 3 months).

Results: Seventy three patients were enrolled in the study. Forty nine (62.1%) were of rural domicile. Time to ~~The delay in~~ breast cancer presentation ranged from 1 to 52 months. The most common reason for delay ~~(66%) of patients)~~ was ignorance and the secondly ~~commonest cause (18%) of patients) was~~ poverty. Fifty three ~~(72.6%) of~~ patients~~)~~ were unemployed (p<0.05). Primary school ~~education~~ was the highest level of education ~~in~~ 23 patients (31.5%), with 38 (52.1%) having attained secondary level education. Fifty~~-~~ seven ~~57~~(78.1%) patients presented with an ulcerated mass (p<0.05%) with pain occurring in 29 (39.7%) of patients. Fifty four patients (74%) had no knowledge of self-breast examination and 37 (51%) of these patients were of rural domicile (p<0.05). Of the 37 rural patients with no knowledge of self- breast examination 35 (94.5%), had primary level education (p<0.005). Fifty one (69.9%) patients consented to HIV testing, ~~44(86.3%) were HIV negative and~~ 7 (13.7%) were HIV positive. A ~~Low~~ low- level of education, ignorance ~~and~~ poor socio-economic status, rural residence and lack of knowledge of breast self examination (BSE) were important predictors of breast cancer ~~presentation~~ delay to presentation~~. Lack of knowledge of self-breast examination was a predictor of delay. Rural domicile was a major positive predictor of delayed presentation. Urban domicile was a negative predictor of delayed presentation.~~ Age, HIV status, level of education and family history were major reasons associated with breast cancer presentation delay.

Conclusion: ~~An~~ The overwhelming majority of breast cancer patients attending Parirenyatwa Group of Hospitals presented with advanced disease. These patients were mostly of low socio-economic status. Current health education campaigns seem ~~not~~ to be ineffective in improving breast cancer awareness. Strategies to reduce delays in presentation, through various interventions focused on education and poverty alleviation need to be formulated.

Key words: breast cancer, presentation, delay, factors, developing countries

Introduction

~~Worldwide -~~ Bbreast cancer is the most common malignancy in females worldwide. It is the leading cause of cancer related mortality [1]. Over 1-2 ~~one to two~~ million cases are diagnosed every year, affecting 10 to 12% of the female population, and accounting for more than 500,000 deaths per year worldwide [2, 3]. The Zimbabwe National Cancer Registry 2012 Report [3] highlighted that 11% of cancer deaths were due to breast cancer, with an incidence of 7%. ~~In general,~~ breast cancer mostly af-

fects women and only a very small percentage of men. [2,3] Factors contributing to ~~D~~delayed b~~B~~reast c~~C~~ancer presentation **have been** ~~were~~ studied elsewhere but not in Zimbabwe, despite the ~~huge deaths numbers~~ large number of deaths due to breast cancer. ~~Figures 1, 2 and 3, show pictures of a women with delayed breast cancer presentation seen at Parirenyatwa Group of Hospitals during the study period.~~

Patients who present late ~~as shown in~~ (figures 1~~-3-~~) have ~~a~~ lower survival rates [4]. ~~Research evidence established an~~An association between stage at diagnosis and survival has been established [4]. Delayed patient presentation refers to a prolonged interval between the discovery of initial symptoms and evaluation by a service provider. Delayed presentation is typically defined as an interval greater than 12 weeks [5]. ~~The delay could be provider or patient related. In~~ provider delay is when patients are referred late. This could either be due to wrong diagnoses being made or to failures ~~encountered~~ in the referral system, as commonly experienced in developing countries like Zimbabwe. In Zimbabwe general medical practitioners and local clinics refer cases of breast cancer directly to central hospitals ~~directly~~. A proportion of ~~these~~ patients are delayed at this level. In provider delay, patients who present early are managed late thereby worsening their outcome. In patient delay, for various reasons patients procrastinate so ~~and~~ by the time they ~~decide to~~ seek medical help, the disease may ~~will~~ be advanced. Patient delay plays a major role in breast cancer related morbidity and mortality [5]. Patients with delays of 3 to 6 months have worse survival rates than those with delays of less than 3 months [6].

During the patient delay process [6], the time from the individual detecting the symptom until they seek medical attention is termed "appraisal delay" [7] or "passive detection"[8].The time from the individual recognizing the symptom to seeking help is called "action appraisal [9], or behavioral delay[7]. Negative attitudes towards healthcare providers are among the determinants of behavioral delay [10, 11]. Knowledge of breast cancer symptoms and self breast examination have been associated with less appraisal and behavioral delays [8,12, 13]. Patient delay may be related to poor socioeconomic status, cultural beliefs, ~~and~~ level of education, ignorance and accessibility ~~of~~ to healthcare facilities [14-22]~~,~~ among other factors.

The Zimbabwe National Cancer Registry (2012) report showeds ~~that~~ on average 1, 800 women are affected annually by breast cancer. Approximately 1, 200 ~~of these cancer affected women~~ die from this disease annually.[2, 3] In Zimbabwe, breast cancer affects one in every 10 women.[3] This study was carried out to provide scientific data on factors associated with delayed breast cancer presentation in Zimbabwe. The aim was to identify possible strategies to shorten these delays thus reducing breast cancer mortality in Zimbabwe.

AIM: This study aimed to determine the factors associated with ~~delayed~~ delay- to- breast cancer presentation

Objectives:

To determine the magnitude and reasons for delayed breast cancer presentation at Parirenyatwa Group of Hospitals

To determine any association between level of education and delay in presentation

To determine the stage at presentation of breast cancer

To determine the presenting symptoms

To determine any association between HIV infection and advanced breast cancer

Study design: A prospective observational study

Sampling Procedure and Sample Size

Sample Size Estimation

The minimum sample size n was obtained using the formula developed by Cochran (year 2006) was used in populations that are large:

$$n = \frac{z^2 p(1-p)}{\varepsilon^2}$$

Where,

p = Proportion of breast cancer patients who delayed for more than three months, p = 94%, calculated from a proportion of breast cancer patients delayed for more than three months in a study done by Muguti *et al.*, (1993) in Zimbabwe

ε = margin of error set at 6 %

Z= standard normal deviate set at 1.96 for 95% confidence level

n= Population size = 61

Materials and Methods

All patients with a clinical and histological diagnosis of breast cancer attending Surgical Outpatient Department clinics, admitted~~, patients in general surgical wards with a diagnosis of breast cancer admitted patients~~ awaiting surgery or operated on from ~~the period~~ January 2010 to December 2013 were included in the study. ~~Interviews~~ Patients were interviewed and specific questions relating to breast cancer risk and delay factors recorded ~~were carried out on each patient to answer specific questions on the data collection sheet. Data were collected and recorded on data collection sheets.~~ Relevant investigations including HIV testing were done and recorded. Patients were prospectively followed up from admission until they were operated upon. Final histology results were collected ~~from Histopathology Department,~~ analyzed and recorded. Delayed patient presentation was defined as a prolonged interval between the ~~discoveries~~ discovery of the initial symptom to presentation to a provider, typically ~~-~~greater than 12 weeks (3 months).[5,21,22] Discriminant analysis was used to model delay period with a cut-off point 3 months (< 3 months / > 3 months).

Inclusion Criteria:

All female patients with a clinical and histological diagnosis of breast cancer ~~with~~ over 15 years age~~above~~ attending clinics or admitted ~~at~~ to Parirenyatwa University Teaching Hospital

Exclusion Criteria:

~~All~~ ~~male~~Male patients with breast cancer

Patients with breast cancer ~~<below the age of~~ 15 years

Patients who did not have histological confirmation of breast cancer

Statistical analysis

All data ~~were~~ was entered in Epidata Entry version 3.1 software and cleaned before analysis. Statistical analysis was carried out by SPSS version 16 statistical package. Discriminant analysis was used to model the reasons for delay in months. Descriptive statistics; means, standard deviations, canonical discriminant parameters were determined as discriminant analysis procedure. The significance levels used to indicate effect size were $p < 0.05$.

Model validation

Among other diagnostics parameters used were Wilk's lambda (preferred the smallest value), and Box's M. We used a 50% Bernoulli (0.5) random sampling of the 73 patients to create a discriminant analysis model, setting the remaining (50%) patients aside to validate the analysis. We then used the model to classify the 50% of the patients as delayed or not delayed. Checking for other assumptions see table 5

Ethics statement

Ethical approval was sought from Parirenyatwa and College of Health Sciences Joint Research (JREC). Written c~~C~~onsent to participate ~~to~~ in the study and ~~to~~ publish ~~the inserted~~ pictures ~~were~~ was ~~sought from the patients~~obtained ~~in both written and verbal form.~~

Conflict of Interest

The authors declare no conflict of interest. The study was self-funded.

Results

Descriptive analysis

In this study, 53(72.6%) patients presented with advanced breast cancer, 23 (31.5%) were ~~in~~ stage 3 and~~whilst~~ 30 (41.1%) were stage 4 ~~(figure 4). Figure 5 show that 43~~ Forty-three ~~(59%)~~ patients (59%) self-delayed ~~to~~ in seeking breast cancer treatment whilst only 30 (41%) were treated within the recommended period (within 3 months from the first symptom onset) [5, 21, 22]. Most patients 37 (50.7%), $p = 0.05$ (insignificant) with advanced breast cancer (stage 3 to 4) were from rural area compared to 16 (21.9%) from urban. Of the ~~Out of~~ 73 study patients, ~~enrolled in the study~~ 49

(62.1%) were of rural ~~domicile -~~and 24 (32.9%) urban domicile (figure 6). Time to ~~The delay in~~ breast cancer presentation ranged from 1 to 52 months. ~~Figure 9, show that the~~ The most common reason for delay ~~in –~~(48 patients, ~~(~~66%) ~~patients~~ was ignorance and ~~the~~ secondly poverty ~~commonest cause in~~ (13 patients (18%)) ~~patients was poverty~~.Other reasons were…….. Fifty three, ~~53 -~~(72.6%) ~~of~~ patients were unemployed;~~,~~ unemployment was associated with delay (p<0.05), table 6. Patients whose highest level of education was primary education were 23 (31.5%) and 38 (52.1%) had secondary level education as their highest level (figure 8). The presenting symptom in~~Table 5 show that~~ 57 (78.1%) patients ~~presented with~~was ~~an ulcerated~~a mass (p<0.05%) and pain occurred in 39.7% of patients (Table 5). Table 2 show that 74 (54%) of patients had no knowledge of self- breast examination and 37 (51%) of these patients were of rural domicile, thus there was a significant relationship (p<0.05). Of the 37 rural patients with no knowledge of self- breast examination 35 (94.5%) patients had primary education (p<0.005), significant relationship. Generally more patients 20 (27.4%) were within an age range of 51-60 years followed by 15 (20.5%), aged between 41-50 years (figure 7). ~~Out of 73 patients, 51~~ Fifty-one patients (69.9%) consented to HIV testing, of which ~~whilst 22 (30.1%) declined. Among the HIV tested patients only~~ 7 (13.7%) were positive~~.~~.~~and 44 (86.3%) were negative~~.

Discriminant analysis

~~In table 8, the coefficients for *HIV Status* and *Level of education* are the first 2 highly scored reasons in the classification function, which means that the~~ *HIV positive ~~Status~~ status* and a low level of education or ignorance (“a lack of knowledge, understanding, or education”)Webster dictionary reference ~~contributes more~~are among the main reasons ~~of~~ for breast cancer treatment delay (table 8). The Webster's Learner's Dictionary defines ignorance as “a lack of knowledge, understanding, or education”. The findings in Figure 9 therefore confirms that lack of education tops the indicated reasons. Thus ignorance or “a lack of knowledge, understanding, or education” is another major reason of breast cancer presentation delay.

~~Table 8 show~~In standardized factor mean scores and standard deviations, the higher the mean score the ~~higher~~ greater the factor contributes in categorizing the dependent variable. Small standard deviations are preferred. ~~Thus, table 8 show the preferred small standard deviations showing good variance of measurement. The total numbers of 73 observations represents 100% of the observations have been grouped for the Discriminant Analysis. Table 10 show the distribution of~~ observations ~~into 2 different groups. In the present study we have~~ were categorized by presentation ~~presentation delay into two groups vis a vis~~as "delayed" (~~as~~ 1) and "not delayed" ~~as (~~ 0'). ~~Preferably for all the reasons, group means are associated with smaller group standard deviations~~.

~~In table 8-10, the researchers compare variables measured on different scales using standardized coefficients.~~ Coefficients with large absolute values correspond to variables with greater discriminating ability as ~~reasons of~~factors associated with patients who had delayed presenatation ,~~breast cancer delay~~ namely ~~Age~~ age at first pregnancy (Coefficient; 1.061), HIV status (Coefficient; 0.89), level of education (Coefficient; 0.679), and family history (Coefficient; 0.221) (table 10)~~.~~

Discussion

Breast cancer is a common health problem in our environment and patients present late. Factors causing delayed presentation are both patient and system related. In our study the major reasons for patient delay were ~~Age~~age, HIV status, and low level of education~~.~~.~~are respectively main patient-mediated reasons resulting in increased time to presentation~~. In this study 43 (59%) ~~were as a result of patient delays~~of delays were patient related.. This correlates with other studies which looked at reasons for patient delay [6, 17, 30]. A large proportion of our patients were of low socioeconomic background and had the least educational background [14-22]. Knowledge of self-breast examination is lacking. It is recommended that~~Education~~ campaigns must be directed at this population group with a view to provide education regarding the early signs and symptoms of breast cancer so as to change and improve their health seeking behavior [8, 12, 13]. Burgess et al [11] concluded in their study that patients presenting late had competing demands and priorities, fears about cancer treatments

and anxieties about 'bothering the doctor'[11]. These psychosocial factors were noted in our study and need to be addressed in health education campaign programmes. Although only ~~Though a~~ small ~~proportion~~ percentage of patients ~~consented to~~were HIV ~~testing~~positive, the majority of ~~HIV-positive patients~~these presented with advanced breast cancer. ~~HIV infection besides being a health problem on its own has a double negative effect in breast cancer patients in this study. It increases the aggressiveness and progression of the disease and~~ the stigmata associated with HIV~~it~~ is a risk factor for delayed presentation. This correlates with Brazilian studies.~~The association between breast cancer and HIV infection correlate~~ [39, 40, and 41] ~~very well with similar study as one done by de Andrade *et al*., in Rio de Janeiro, Brazil~~ [40, 41, 42]. ~~This study looked at~~ which reviewed breast cancer in a cohort of HIV ~~human immunodeficiency virus (HIV)~~ infected women. The median age at diagnosis was 46 years. The m~~M~~edian survival after breast cancer diagnosis was 12 months and b~~.~~ ~~B~~reast cancer diagnosis was made within 2 to 15 years of HIV-infection diagnosis. All patients were diagnosed late with breast cancer and thus ~~suffered~~ had a~~from~~ worse prognosis [40,41,42].

Most Breast cancer patients attending Parirenyatwa Group of Hospitals present with advanced disease. Current health education campaigns seem not to be interdisciplinary and effective in improving breast cancer awareness; People living with HIV are suffering stigma and eventually delay due to low self-esteem. It is our collective responsibility to reduce this delay through various interventions focused on education and poverty alleviation. Follow-up studies regarding management of these patients need to be done so as to recommend and formulate local guidelines

Conclusion

Factors causing delayed presentation are both patient and system related. In our study the major reasons for delay were ~~Age~~age, HIV status, and low level of education ~~are~~ respectively. ~~-~~Most were patient delays. ~~In this study 43 (59%) were as a result of patient delays~~. ~~A large proportion of our patients were~~ with~~of~~ low socioeconomic background and ~~had the least~~low educational back-ground. Knowledge of self-beast examination is lacking. Education campaigns must be directed at this population group with a view to provide education regarding the early signs and

symptoms of breast cancer so as to change and improve their health seeking behavior. ~~Though a small proportion of patients consented to HIV testing,~~ tThe majority of HIV-positive patients presented with advanced breast cancer and HIV infection was~~.~~ ~~HIV infection besides being a health problem on its own has a double negative effect in breast cancer patients. It increases the aggressive-ness and progression of the disease and the stigmata associated with it is~~ a risk factor for delayed presentation.

Current health education campaigns seem not to be inter-disciplinary and effective in improving breast cancer awareness; People living with HIV suffering stigma and eventually delay due to low self-esteem. It is our collective responsibility to reduce this delay through various interventions focused on education and poverty alleviation.

Recommendations

Focused public health campaigns aimed at raising breast cancer awareness must target rural communities. Self-breast examination must be taught to women at all levels. Rural communities need to be encouraged to advance their education. Communities need to be empowered economically in order to improve their health seeking behaviour with special emphasis on breast cancer. Patients presenting late have competing demands and priorities, fears about cancer treatments and anxieties about 'bothering the doctor. These psychosocial factors need to be addressed in health education campaign programs. Follow-up studies regarding management of these patients need to be done so as to recommend and formulate local guidelines

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Figure 1: Patient 1 advanced breast cancer (Stage 4)

Figure 2: Patient 2 advanced ulcerated breast cancer (stage 4)

Figure 3: Patient 3 advanced ulcerated breast cancer (stage 4)

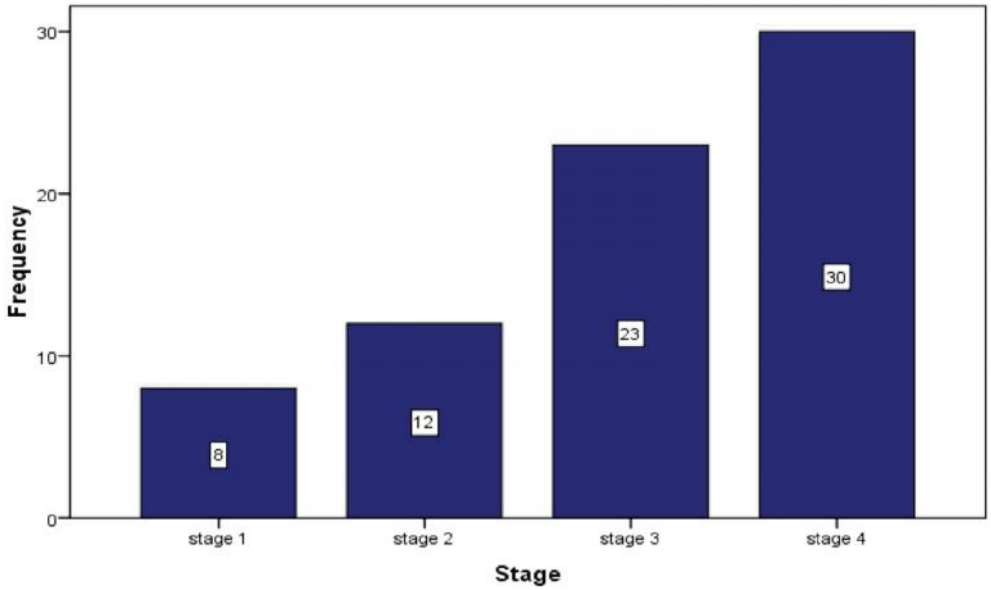

Figure 4: Stage of the disease and frequency

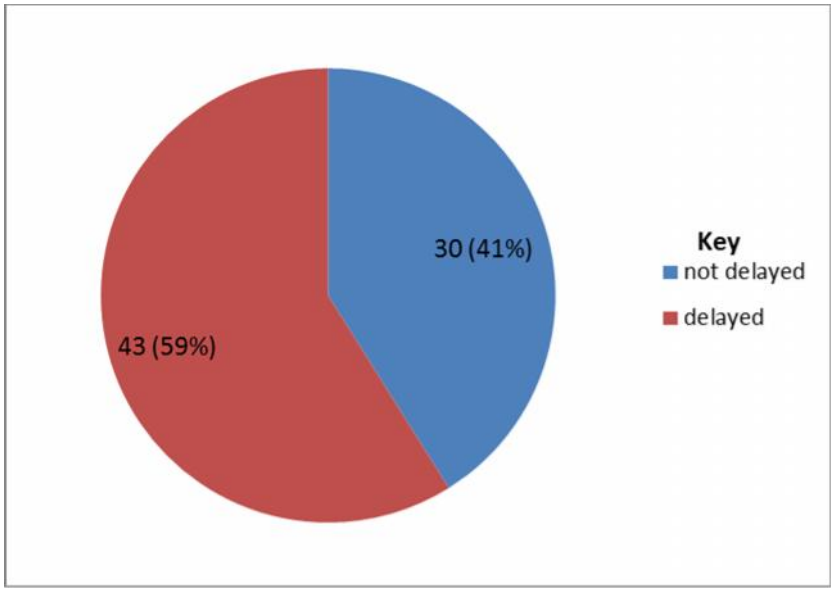

Figure 5: Prevalence of self-delay

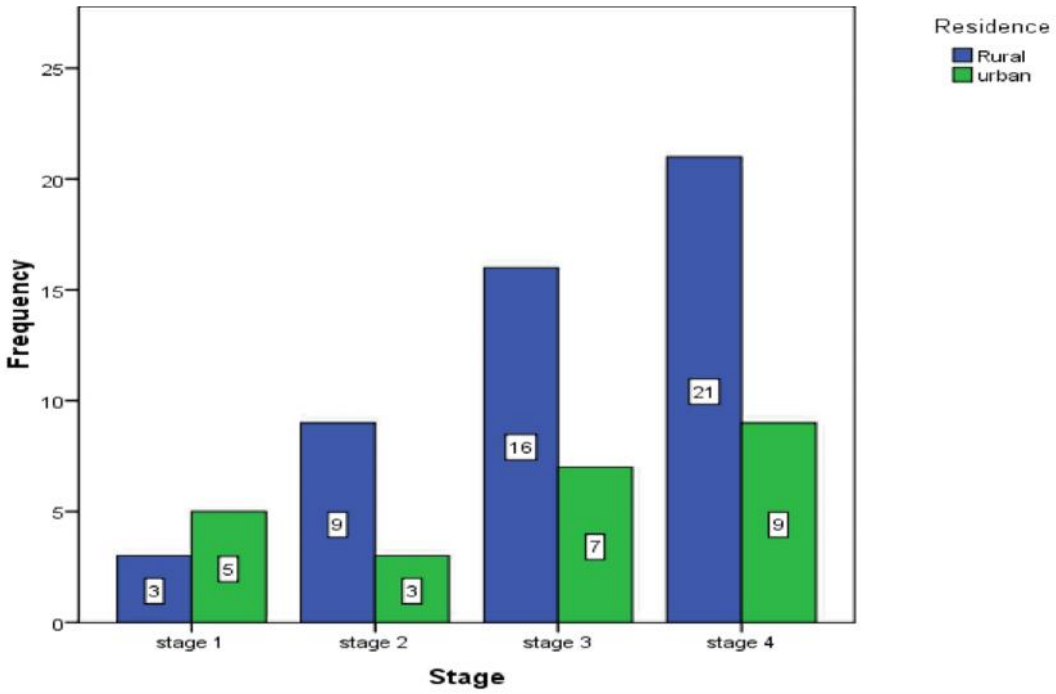

Figure 6: Clinical Stage vs Domicile

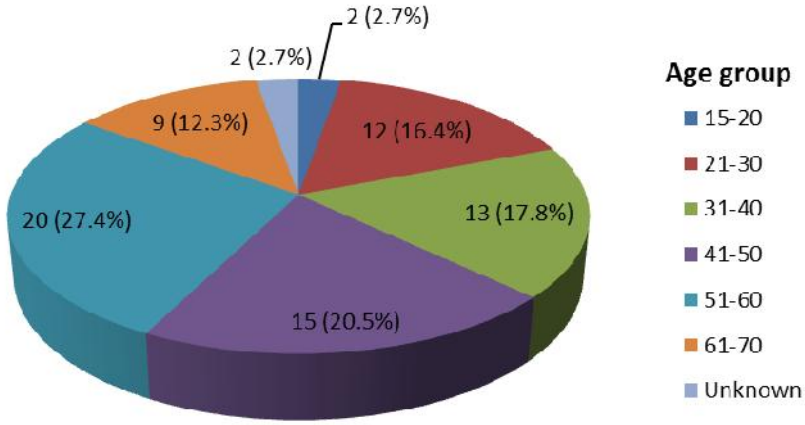

Figure 7: Breast cancer-age distribution

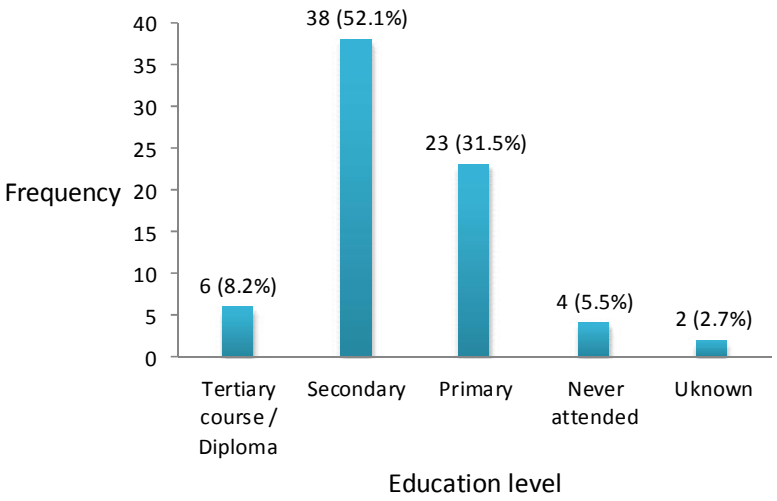

Figure 8: Highest level of education

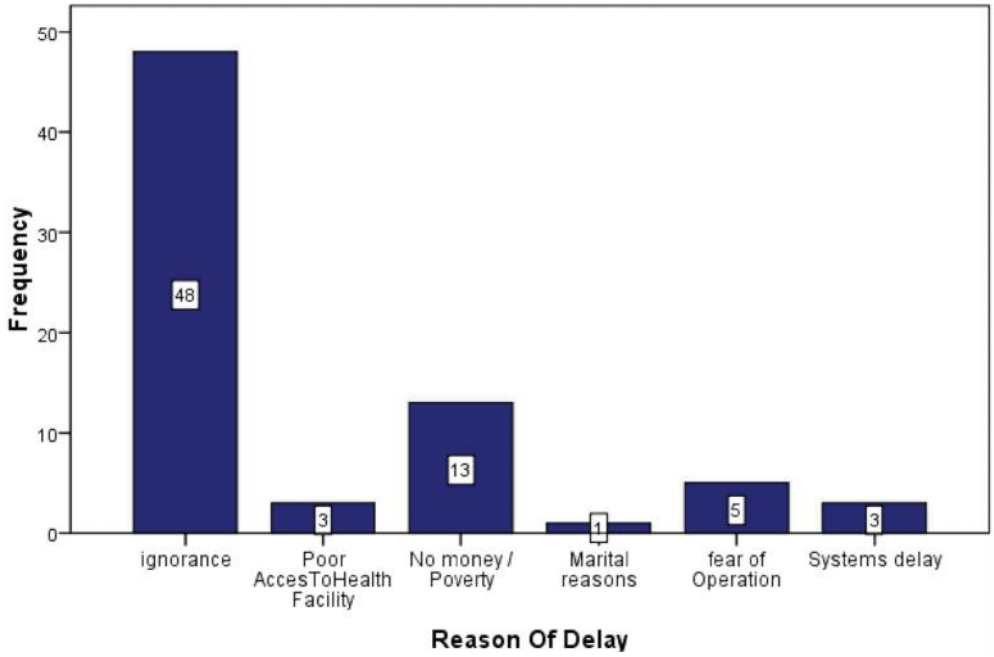

Figure 9: Frequency distribution of reasons for delay

Table 1: Knowledge of self- breast examination and Residence

Residence	Knowledge of Self Breast Examination		Total
	Yes (%)	No (%)	
Rural	12 (16.4)	37 (50.7)	49 (67.1)
Urban	7 (9.6)	17 (23.3)	24 (32.9)
Total	19 (26.0)	54 (74.0)	73 (100.0)

Note: p < 0.05 ,Statistically significant association

Table 2: Knowledge of self- breast examination

Knowledge of Self Breast Examination

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	19	26.0	26.0	26.0
	no	54	74.0	74.0	100.0
	Total	73	100.0	100.0	

Table 3: Knowledge of self- breast examination and Domicile

		Knowledge of Self Breast Examination		Total
		yes	no	
Residence	Rural	12	37	49
	urban	7	17	24
Total		19	54	73

(p < 0.05 ,Statistically significant)

Table 4: Relationship between knowledge of self-breast examination and age group

		Knowledge of Self Breast Examination		Total
		yes	no	
Age Group	11-20	1	1	2
	21-30	3	9	12
	31-40	5	8	13
	41-50	3	12	15
	51-60	4	16	20
	61-70	2	7	9
Total		18	53	71

(p > 0.05, Not statistically significant)

Table 5: Symptoms

Symptom	Frequency	Percent
Mass	57	78.1
Nipple Discharge	12	16.4
Nipple Retraction	8	11
Pain	29	39.7
Ulcer	13	17.8

Table 6: Relationship between delay and employment status

		Delay									
		0-6 months	7-12 months	13-18 months	19-24 months	25-30 months	31-36 months	37-42 months	43-48 months	49 and above	Total
Employed	yes	3	2	1	1	2	4	3	1	2	19
	no	8	12	2	8	5	8	3	0	7	53
Total		11	14	3	9	7	12	6	1	9	72

(p < 0.05, Statistically significant)

Table 7: Relationship between Knowledge of self-breast examination and level of education

Knowledge of Self Breast Cancer		Level of Education				Total
		Tertiary course / Dip-loma	Second-ary	Primary	Never attended	
	no	0 (0%)	14 (20.9%)	10 (14.9%)	2 (3.0%)	26 (38.8%)
	yes	6 (9.0%)	22 (32.8%)	12 (17.9%)	1 (1.5%)	41 (61.2%)
Total		6 (9.0%)	36 (53.7%)	22 (32.8%)	3 (4.5%)	67 (100.0%)

***Note**: p < 0.05, Statistically significant association*

Table 8: Contributions of specific reasons to delayed breast cancer presentation

Reasons	Delayed presentation score	
	No	Yes
HIV Status	20.240	24.526
Age at First Pregnancy	6.169	7.406
Early Menarche	-1.521	-2.525
Family History	.055	.148
Late Menopause	7.697	4.812
Level of Education	5.269	8.898
(Constant)	-91.994	-115.295
Note: *Classification Function Coefficients determined by Fisher's linear discriminant functions*		

Table 9: Standardized discriminant Coefficients by reason

Reason	Function
	1
HIV Status	.890
Age at First Pregnancy	1.061
Early Menarche	-.524
Family History	.221
Late Menopause	-.424
Level of Education	.679

Table 10: Group means and standard deviations

Delay		Mean	Std. Deviation	N	
				Unweighted	Weighted
Delayed (≥ 3 months)	HIV Status	1.33	0.58	3	3
	Age at First Pregnancy	18.67	2.52	3	3
	Early Menarche	13.00	1.00	3	3
	Family History	1.67	0.58	3	3
	Late Menopause	2.00	0.00	3	3

	Level of Education	1.67	0.58	3	3
	Knowledge of Self Breast Examination (BE)	1.33	0.58	3	3
	Health Worker of first Contact	2.67	1.16	3	3
	Duration of Symptoms in Months	2.67	2.08	3	3
	Marital Status	2.00	1.00	3	3
	Age Group	5.00	1.00	3	3
	Employed	1.00	0.00	3	3
Not delayed (< 3 months)	HIV Status	2.00	0.63	6	6
	Age at First Pregnancy	21.83	2.56	6	6
	Early Menarche	14.17	1.72	6	6
	Family History	5.17	8.25	6	6
	Late Menopause	1.67	0.52	6	6
	Level of Education	2.50	0.55	6	6
	Knowledge of Self (BE)	1.17	0.41	6	6
	Health Worker of first Contact	2.33	0.82	6	6
	Duration of Symptoms in Months	2.17	1.60	6	6
	Marital Status	2.50	0.55	6	6
	Age Group	5.17	0.75	6	6
	Employed	1.67	0.52	6	6
Total	HIV Status	1.78	0.68	9	9
	Age at First Pregnancy	20.78	2.86	9	9
	Early Menarche	13.78	1.56	9	9
	Family History	4.00	6.76	9	9
	Late Menopause	1.78	0.44	9	9
	Level of Education	2.22	0.67	9	9
	Knowledge of Self (BE)	1.22	0.44	9	9
	Health Worker of first Contact	2.44	0.88	9	9
	Duration of Symptoms in Months	2.33	1.66	9	9
	Marital Status	2.33	0.71	9	9
	Age Group	5.11	0.78	9	9

	Employed	1.44	0.53	9	9

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