

Factors Contributing to Delayed Breast Cancer presentation: A prospective study at Parirenyatwa Group of 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 in breast cancer presentation helps in shortening the delays and reduction in morbidity and mortality. It is for this reason that this study was carried out.

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

Methods: A prospective observational study on patients with clinical and histological diagnosis of breast cancer. Participants were patients attending Surgical Outpatient clinics with a diagnosis of breast cancer awaiting surgery from the period January 2010 to December 2013 inclusive. Interviews were carried out on each patient to answer specific questions on the data collection sheet. Relevant investigations including Human Immuno Deficiency Virus (HIV) test 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. 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 second 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 in 23 patients (31.5%), with 38 (52.1%) having attained secondary level education. Fifty seven (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. Low level of education, ignorance and poor socio-economic status were important predictors of breast cancer presentation delay. 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 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 be effective in improving breast cancer awareness. Strategies to reduce delays in

52 presentation, through various interventions focused on education and poverty alleviation need to be formulated.

54
55 **Key words:** breast cancer, presentation, delay, factors, developing countries

56 57 **Introduction**

58 Worldwide breast cancer is the most common malignancy in females. It is the leading cause of cancer related mortality¹. Over 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 Report³ highlighted that 11% of cancer deaths were due to breast cancer, with incidence of 7%. In general, breast cancer mostly affects women and a very small percentage of men.^{2,3} Factors contributing to Delayed Breast Cancer presentation were studied elsewhere but not in Zimbabwe, despite the huge deaths numbers 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.

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70 Patients who present late as shown in figures 1-3 have a lower survival rate⁴. Research evidence established an association between stage at diagnosis and survival⁴. Delayed patient presentation refers to a prolonged interval between the discovery of initial symptoms and evaluation by service provider. Delayed presentation is typically defined as an interval greater than 12 weeks⁵. The delay could be provider or patient related. In provider delay 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 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 the outcome. In patient delay, for various reasons patients procrastinate and by the time they decide to seek medical help, the disease will be advanced. Patient delay plays a major role in breast cancer related morbidity and mortality⁵. Patients with delays of 3 to 6 months have worse survival rates than those with delays of less than 3 months⁶.

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86 During the patient delay process⁶, 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 delay⁷. 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 healthcare facilities¹⁴⁻²², among other factors.

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96 The Zimbabwe National Cancer Registry (2012) report shows 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

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101 was to identify possible strategies to shorten these delays thus reducing breast cancer mortality in Zimbabwe.

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

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Objectives:

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

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

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To determine the stage at presentation of breast cancer

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To determine the presenting symptoms

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To determine any association between HIV infection and advanced breast cancer

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Study design: A prospective observational study

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Sampling Procedure and Sample Size

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Sample Size Estimation

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

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

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Where,

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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

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ε = margin of error set at 6 %

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

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n= Population size = 61

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Materials and Methods

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All patients with 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 from the period January 2010 to December 2013 were included in the study. Interviews 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 test 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 of the initial symptom to presentation to a provider, typically greater than 12 weeks (3 months).^{5,21,22}

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Discriminant analysis was used to model delay period with a cut-off point 3 months (< 3 months / > 3 months).

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Inclusion Criteria:

150 All female patients with a clinical and histological diagnosis of breast cancer with 15
151 years above attending clinics or admitted at Parirenyatwa University Teaching Hos-
152 pital
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154 **Exclusion Criteria:**

155 All male patients with breast cancer

156 Patients with breast cancer below the age of 15 years

157 Patients who did not have histological confirmation of breast cancer
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159 **Statistical analysis**

160 All data were entered in Epidata Entry version 3.1 software and cleaned before anal-
161 ysis. Statistical analysis was carried out by SPSS version 16 statistical package.

162 Discriminant analysis was used to model the reasons for delay in months. Descrip-
163 tive statistics; means, standard deviations, canonical discriminant parameters were
164 determined as discriminant analysis procedure. The significance levels used to indi-
165 cate effect size were $p < 0.05$.
166

167 **Model validation**

168 Among other diagnostics parameters used were Wilk's lambda (preferred the smal-
169 lest value), and Box's M. We used a 50% Bernoulli (0.5) random sampling of the 73
170 patients to create a discriminant analysis model, setting the remaining (50%) patients
171 aside to validate the analysis. We then used the model to classify the 50% of the pa-
172 tients as delayed or not delayed. Checking for other assumptions see table 5
173

174 **Ethics statement**

175 Ethical approval was sought from Parirenyatwa and College of Health Sciences Joint
176 Research (JREC). Consent to participate to in the study and to publish the inserted
177 pictures were sought from the patients in both written and verbal form.
178

179 **Conflict of Interest**

180 The authors declare no conflict of interest. The study was self-funded.
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182 **Results**

183 **Descriptive analysis**

184 In this study, 53(72.6%) patients presented with advanced breast cancer, 23 (31.5%)
185 were in stage 3 whilst 30 (41.1%) were stage 4 (figure 4). Figure 5 show that 43
186 (59%) patients self-delayed to seek breast cancer treatment whilst only 30 (41%)
187 were treated within the recommended period (within 3 months from the first symptom
188 onset)^{5, 21, 22}. Most patients 37 (50.7%), $p = 0.05$ (insignificant) with advanced breast
189 cancer (stage 3 to 4) were from rural area compared to 16 (21.9%) from urban. Out
190 of 73 patients enrolled in the study 49 (62.1%) were of rural domicile and 24(32.9%)
191 urban domicile (figure 6). The delay in breast cancer presentation ranged from 1 to
192 52 months. Figure 9, show that the most common reason for delay in 48 (66%) pa-
193 tients was ignorance and the second commonest cause in 13 (18%) patients was
194 poverty. Fifty three, 53 (72.6%) of patients were unemployed, unemployment was
195 associated with delay ($p < 0.05$), table 6. Patients whose highest level of education
196 was primary education were 23 (31.5%) and 38 (52.1%) had secondary level educa-
197 tion as their highest level (figure 8). Table 5 show that 57 (78.1%) patients presented
198 with an ulcerated mass ($p < 0.05$) and pain occurred in 39.7% of patients. Table 2
199

200 show that 74 (54%) of patients had no knowledge of self- breast examination and 37
201 (51%) of these patients were of rural domicile, thus there was a significant relation-
202 ship ($p < 0.05$). Of the 37 rural patients with no knowledge of self- breast examination
203 35 (94.5%) patients had primary education ($p < 0.005$), significant relationship. Gen-
204 erally more patients 20 (27.4%) were within an age range of 51-60 years followed by
205 15 (20.5%), aged between 41-50 years (figure 7). Out of 73 patients, 51 (69.9%)
206 consented to HIV testing whilst 22 (30.1%) declined. Among the HIV tested patients
207 only 7 (13.7%) were positive and 44 (86.3%) were negative.

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210 Discriminant analysis

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212 In table 8, the coefficients for *HIV Status* and *Level of education* are the first 2 highly
213 scored reasons in the classification function, which means that the *HIV Status* and
214 low level of education contributes more among the reasons of breast cancer treat-
215 ment delay. The Webster's Learner's Dictionary defines ignorance as "a lack of
216 knowledge, understanding, or education". The findings in Figure 9 therefore confirms
217 that lack of education tops the indicated reasons. Thus ignorance or "a lack of know-
218 ledge, understanding, or education" is another major reason of breast cancer pres-
219 entation delay.

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221 Table 8 show standardized factor mean scores and standard deviations, the higher
222 the mean score the higher the factor contribute in categorizing the dependent varia-
223 ble. Small standard deviations are preferred. Thus, table 8 show the preferred small
224 standard deviations showing good variance of measurement. The total numbers of
225 73 observations represents 100% of the observations have been grouped for the
226 Discriminant Analysis. Table 10 show the distribution of observations into 2 different
227 groups. In the present study we have categorized presentation delay into two groups
228 *vis a vis* "delayed" as 1 and "not delayed" as 0. Preferably for all the reasons, group
229 means are associated with smaller group standard deviations.

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231 In table 8-10, the researchers compare variables measured on different scales using
232 standardized coefficients. Coefficients with large absolute values correspond to va-
233 riables with greater discriminating ability as reasons of breast cancer delay namely
234 Age at first pregnancy (Coefficient; 1.061), HIV status (Coefficient; 0.89), level of
235 education (Coefficient; 0.679), family history (Coefficient; 0.221).

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237 Discussion

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239 Breast cancer is a common health problem in our environment and patients present
240 late. Factors causing delayed presentation are both patient and system related. In
241 our study the major reasons for delay were Age, HIV status, and low level of educa-
242 tion are respectively main patient-mediated reasons resulting in increased time to
243 presentation. In this study 43 (59%) were as a result of patient delays. This corre-
244 lates with other studies which looked at reasons for patient delay^{6, 17, 30}. A large pro-
245 portion of our patients were of low socioeconomic background and had the least
246 educational background¹⁴⁻²². Knowledge of self-breast examination is lacking. Edu-
247 cation campaigns must be directed at this population group with a view to provide
248 education regarding the early signs and symptoms of breast cancer so as to change
249 and improve their health seeking behavior^{8, 12, 13}. Burgess et al¹¹ concluded in their

250 study that patients presenting late had competing demands and priorities, fears
251 about cancer treatments and anxieties about 'bothering the doctor'¹¹. These psy-
252 chosocial factors were noted in our study and need to be addressed in health educa-
253 tion campaign programs. Though a small proportion of patients consented to HIV
254 testing, the majority of HIV-positive patients presented with advanced breast cancer.
255 HIV infection besides being a health problem on its own has a double negative effect
256 in breast cancer patients in this study. It increases the aggressiveness and progres-
257 sion of the disease and the stigmata associated with it is a risk factor for delayed
258 presentation. The association between breast cancer and HIV infection correlate ^{39,}
259 ^{40, and 41} very well with similar study as one done by de Andrade *et al.*, in Rio de Ja-
260 neiro, Brazil ^{40, 41, 42}. This study looked at breast cancer in a cohort of human immu-
261 nodeficiency virus (HIV)-infected women. The median age at diagnosis was 46
262 years. Median survival after breast cancer diagnosis was 12 months. Breast cancer
263 diagnosis was made within 2 to 15 years of HIV-infection diagnosis. All patients were
264 diagnosed late with breast cancer and thus suffered from worse prognosis ^{40,41,42}.

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

273 274 **Conclusion**

275 Factors causing delayed presentation are both patient and system related. In our
276 study the major reasons for delay were Age, HIV status, and low level of education
277 are respectively. In this study 43 (59%) were as a result of patient delays. A large
278 proportion of our patients were of low socioeconomic background and had the least
279 educational back-ground. Knowledge of self-beast examination is lacking. Education
280 campaigns must be directed at this population group with a view to provide educa-
281 tion regarding the early signs and symptoms of breast cancer so as to change and
282 improve their health seeking behavior. Though a small proportion of patients con-
283 sented to HIV testing, the majority of HIV-positive patients presented with advanced
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285 negative effect in breast cancer patients. It increases the aggressive-ness and pro-
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288
289 Current health education campaigns seem not to be inter-disciplinary and effective in
290 improving breast cancer awareness; People living with HIV suffering stigma and
291 eventually delay due to low self-esteem. It is our collective responsibility to reduce
292 this delay through various interventions focused on education and poverty allevia-
293 tion.

294 295 **Recommendations**

296 Focused public health campaigns aimed at raising breast cancer awareness must
297 target rural communities. Self-breast examination must be taught to women at all le-
298 vels. Rural communities need to be encouraged to advance their education. Com-
299 munities need to be empowered economically in order to improve their health seek-

ing 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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424 rospective study of Brazilian and U.S. *clinical cohorts Infectious Agents and Cancer BioMed*
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428 **Figure 1:** Patient 1 advanced breast cancer (Stage 4)
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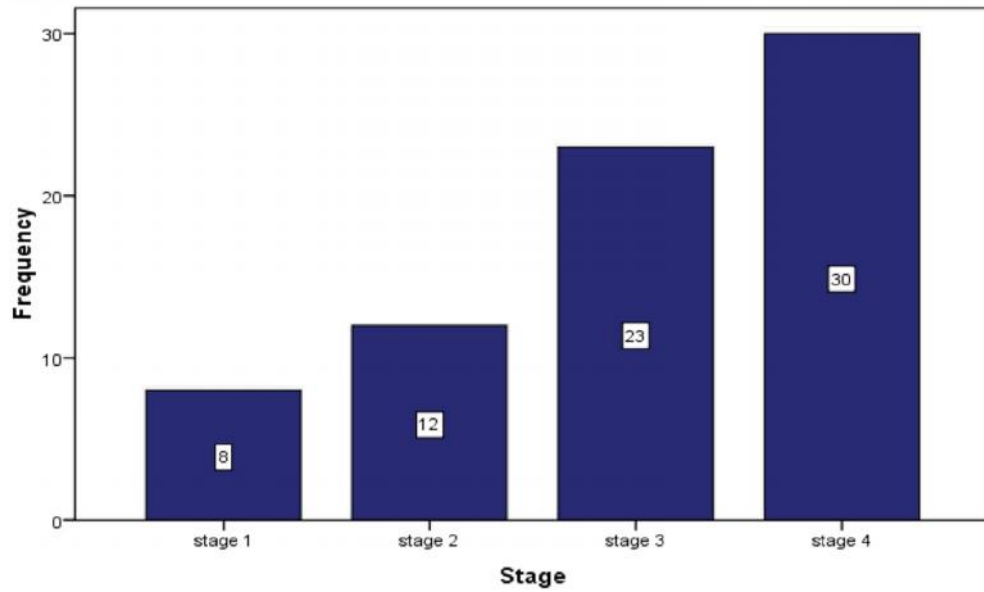
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Figure 2: Patient 2 advanced ulcerated breast cancer (stage 4)



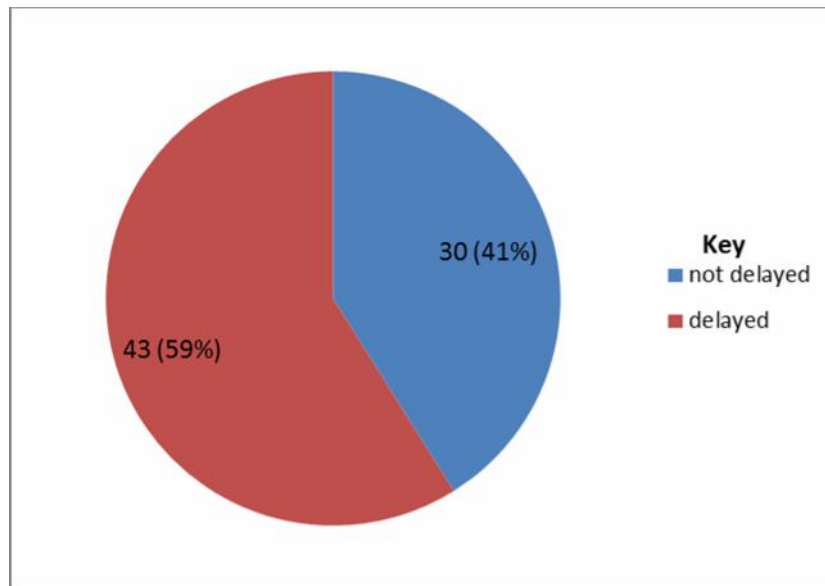
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Figure 3: Patient 3 advanced ulcerated breast cancer (stage 4)



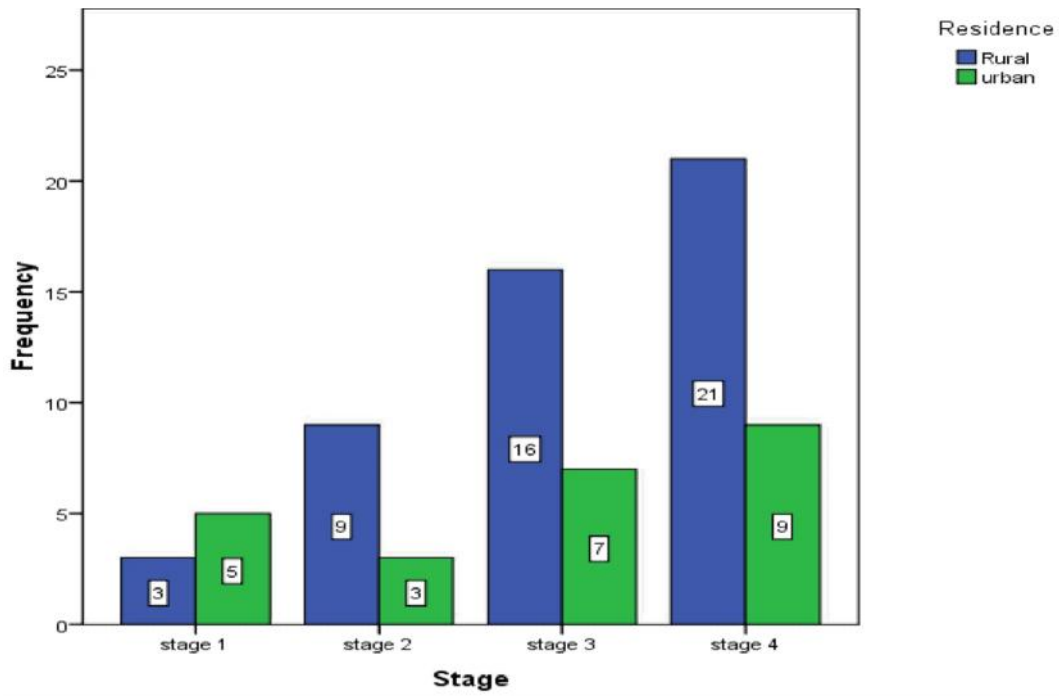
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Figure 4: Stage of the disease and frequency



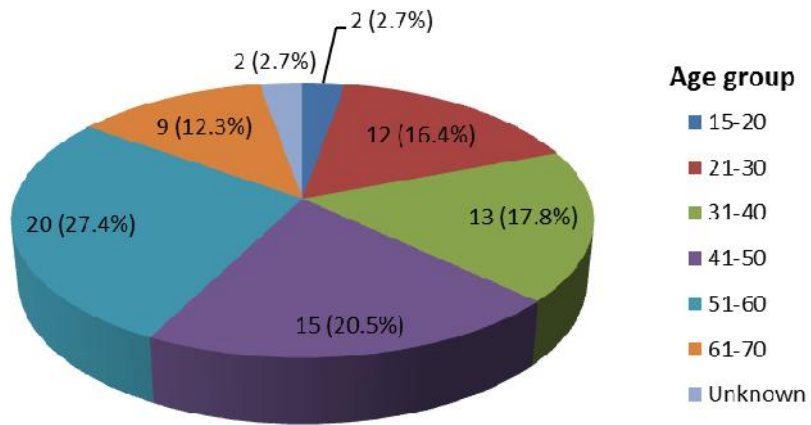
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Figure 5: Prevalence of self-delay



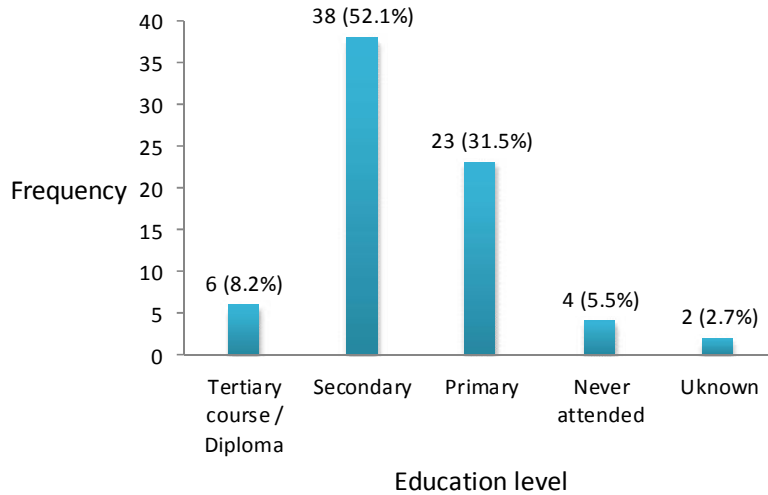
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Figure 6: Clinical Stage vs Domicile

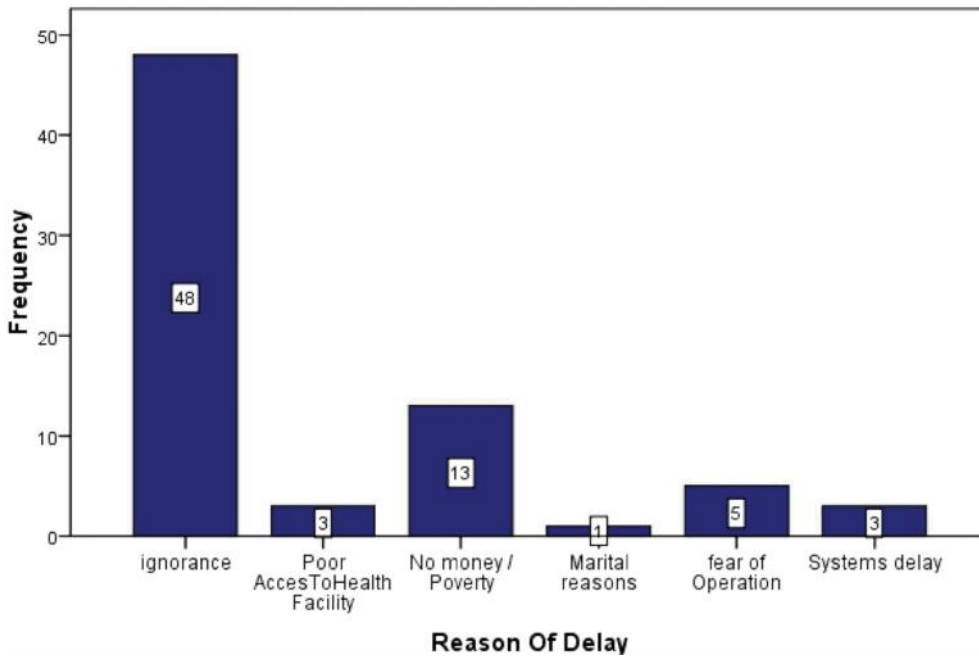


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Figure 7: Breast cancer-age distribution



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462 **Figure 8: Highest level of education**
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465 **Figure 9: Frequency distribution of reasons for delay**
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467
468 **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

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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	

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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)

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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

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($p > 0.05$, 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

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Table 6: Relationship between delay and employment status

		Delay								Total	
		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
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

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($p < 0.05$, 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 / Diploma	Secondary	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

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

Reasons	Delayed presentation score	
	No	Yes
<i>HIV Status</i>	20.240	24.526
<i>Age at First Pregnancy</i>	6.169	7.406
<i>Early Menarche</i>	-1.521	-2.525
<i>Family History</i>	.055	.148
<i>Late Menopause</i>	7.697	4.812
<i>Level of Education</i>	5.269	8.898
(Constant)	-91.994	-115.295

Note: Classification Function Coefficients determined by Fisher's linear discriminant functions

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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

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Table 10: Group means and standard deviations

Delay		Mean	Std. Deviation	N	
				Un-weighted	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	1.33	0.58	3	3

Not delayed (< 3 months)	Self Breast Examination (BE)				
	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
	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
	Total	Duration of Symptoms in Months	2.17	1.60	6
Marital Status		2.50	0.55	6	6
Age Group		5.17	0.75	6	6
Employed		1.67	0.52	6	6
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	