Original Research Article

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 presentation, leading to 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 help in reducing delays and morbidity and mortality. This study addresses these concerns.

Aim: To determine factors contributing to delayed breast cancer presentation at Parirenyatwa Group of Hospitals

Methods: A prospective observational study of patients with the clinical and histological diagnosis of breast cancer attending Surgical Outpatient clinics awaiting surgery, or operated on from January 2010 to December 2013 were included.. Patients were interviewed and specific questions relating to breast cancer risk and delay factors were recorded. Relevant investigations, including Human Immune Deficiency Virus (HIV) testing, were done and recorded. 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 breast cancer presentation ranged from 1 to 52 months. The most common reason for delay (66%) was ignorance and secondly (18%) poverty. Fifty three (72.6%) patients were unemployed ($p<0.05$). Primary school was the highest level of education in 23 patients (31.5%), with 38 (52.1%) having attained

secondary level education. Fifty-seven (78.1%) patients presented with a mass (p<0.05%) with pain occurring in 29 (39.7%) of patients. Fifty four patients (74%) had no knowledge of breast self-examination (BSE) and 37 (51%) of these patients were of rural domicile (p<0.05). Of the 37 rural patients with no knowledge of BSE 35 (94.5%), had primary level education (p<0.005). Fifty one (69.9%) patients consented to HIV testing, 7 (13.7%) were HIV positive. A low level of education, ignorance of breast cancer, poor socio-economic status, rural residence and lack of knowledge of BSE were important predictors of breast cancer delay to presentation. Old age, HIV status, level of education and family history were major reasons associated with breast cancer presentation delay.

Conclusion: 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 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

Breast cancer is the most common malignancy in females worldwide. It is the leading cause of cancer related mortality [1]. Over 1-2 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%. Breast cancer mostly affects women and only a very small percentage of men. [2,3] Factors contributing to delayed breast cancer presentation have been studied elsewhere but not in Zimbabwe, despite the large number of deaths due to breast cancer.

Patients who present late (figures 1) have lower survival rates [4]. 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 in-

terval greater than 12 weeks [5]. Provider delay is when patients are referred late. This could either be due to wrong diagnoses being made or to failures 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. A proportion of 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 by the time they seek medical help, the disease may 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 [6-10], 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 [10-20]. Knowledge of breast cancer symptoms and self-breast examination (BSE) have been associated with less appraisal and behavioral delays [8, 12, 13, 20-30]. Patient delay may be related to poor socioeconomic status, cultural beliefs, and level of education, ignorance and accessibility to healthcare facilities [14, 22, 30-40] among other factors.

The Zimbabwe National Cancer Registry (2012) report showed on average 1,800 women are affected annually by breast cancer. Approximately 1,200 die from this disease annually.[2, 3] In Zimbabwe, breast cancer affects one in every 10 women.[3,41-46] 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 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 in 2006 which is 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)[46] 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, awaiting surgery or operated on from January 2010 to December 2013 were included in the study. Patients were interviewed and specific questions relating to breast cancer risk and delay factors recorded. Relevant investigations including HIV testing were done and recorded. Final histology results were collected analyzed and recorded. Delayed patient presentation

was defined as a prolonged interval between the 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 over 15 years age attending clinics or admitted to Parirenyatwa University Teaching Hospital

Exclusion Criteria:

Male patients with breast cancer

Patients with breast cancer <15 years

Patients who did not have histological confirmation of breast cancer

Statistical analysis

All data 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 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.

Ethics statement

Ethical approval was sought from Parirenyatwa and College of Health Sciences Joint Research (JREC). Written consent to participate in the study and publish pictures was obtained

Conflict of Interest

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

Results

Descriptive analysis

In this study of73 patients, 53 (72.6%) presented with advanced breast cancer, 8 (11%) were stage 1, 12 (16.4%) were stage 2, 23 (31.5%) were stage 3 and 30 (41.1%) were stage 4. Forty-three patients (59%) self-delayed 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]. Of the 73 study patients, 49 (67.1%) were of rural and 24 (32.9%) urban domicile (figure 2). Thirty-seven of the 53 patients with stage 3 and 4 disease were from rural areas and 16 were urban, p=0.05. Time to breast cancer presentation ranged from 1 to 52 months. The most common reason for delay (48 patients, 66%) was ignorance and secondly poverty (13 patients, 18%). Twenty-three (31.5%) of patients attained a primary school education and 38 (52.1%) went to secondary school (figure 4). The presenting symptom in 57 (78.1%) patients was a mass (p<0.05%) and pain occurred in 39.7% of patients (table 2). Knowledge of BSE was associated with level of education (table 3). Fifty-four (74%) patients had no knowledge of BSE and 37 (68.5%) of these patients were of rural domicile, p<0.05 (table 1).Of the 37 rural patients with no knowledge of BSE, 35 (94.6%) had only a primary education (p<0.005). Most patients, 20 (27.4%), were within an age range of 51-60 years and 15 (20.5%), aged between 41-50 years (figure 3). Fifty-one patients (69.9%) consented to HIV testing, of which 7 (13.7%) were positive.

Discriminant analysis

HIV positive status and a low level of education or ignorance (“a lack of knowledge, understanding, or education”) [23] are among the main reasons for breast cancer treatment delay (table 4 and table 5). Figure 4 and figure 5 show lack of education as

the main indicator of delay. Thus ignorance [23] or "a lack of knowledge, understanding, or education" is another major reason of breast cancer presentation delay.

Coefficients with large absolute values correspond to variables with greater discriminating ability as factors associated with patients who had delayed presentation ,namely old age (Coefficient; 1.061), HIV status (Coefficient; 0.89), level of education (Coefficient; 0.679), and family history (Coefficient; 0.221) (table 5)

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 old age, HIV status, and low level of education. In this study 43 (59%) 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 low educational backgrounds. Knowledge of BSE was lacking. It is recommended that 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, 14-22]. Burgess et al 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 small percentage of patients were HIV positive, the majority of these presented with advanced breast cancer. The stigma associated with HIV is a risk factor for delayed presentation [20]. This correlates with Brazilian studies [40, 41, and 42], one study reviewed breast cancer in a cohort of HIV infected women. The median age at diagnosis was 46 years. The median survival after breast cancer diagnosis was 12 months and breast cancer diagnosis was made within 2 to 15 years of HIV-infection diagnosis. All patients were diagnosed late with breast cancer and thus had a 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 [20]. 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 older age, HIV status, and low level of education respectively. Most were patient delays with low socio-economic background and low educational background. Knowledge of BSE 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. The majority of HIV-positive patients presented with advanced breast cancer and HIV stigma was 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. Breast self-examination must be taught to women at all levels. Rural communities need to be encouraged to advance their education levels. 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

References

1. Hortobagyi GN, dela Garza Salazar J, et al. The global breast cancer burden: variations in epidemiology and survival. *Clin Breast Cancer* (2005); **6**:391-401.
2. Benson JR, Jatoi I, Keisch M. Early breast cancer. *Lancet* (2009); **373**:1642-3.
3. Chokunonga E, et al. Zimbabwe Cancer Registry 2012 Annual Report. African Cancer Registry Network. afcrn.org/membership/membership-list/83-zimbabwe-harare. Accessed February 23, 2016.
4. Thomson CS, Forman D. Cancer survival in England and the influence of early diagnosis. *Br J Cancer* (*2009);101*:S102-9
5. Ramirez A.J. , Westcombe A. M., Burgess C. C., Sutton S., Littlejohns P., and Richards M. A., "Factors predicting delayed presentation of symptomatic breast cancer: a systematic review," The Lancet, vol. 353, no. 9159,(1999).pp. 1127–1131.
6. Facione NC. Delay versus help seeking for breast cancer symptoms: a critical review of the literature on patient and provider delay. *Soc Sci Med* (1993);36:1521-34.
7. Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. The influence of delay on survival in patients with breast cancer: a systematic review. *Lancet* (1999);353:1119-1126.
8. Andersen BL, Cacioppo JT. Delay in seeking a cancer diagnosis: delay stages and psychological comparison process. Br J Soc Psychol(1995):34:33-52.
9. Ruiter RA, de Nooijer J, van Breukelen G, Ockhuysen- VermeyCF, de Vries H. Intended coping responses to cancer symptoms in healthy adults: the roles of symptom knowledge, detection behavior, and perceived threat. *Cancer Epidemiol Biomarkers Prev (2008);17:818-26.*
10. Ristvedt SL, Trinkaus KM. Psychological factors related to delay in consultation for cancer symptoms. *Psychooncology* (2005);14:339-50.

11. Burgess CC, Potts HW, Hamed H, et al. Why do older woman delay presentation with breast cancer symptoms? *Psychooncology* (2006);15:962-8.
12. Scott SE, Grunfeld EA, Auyeung V, Mcgurk M. Barriers and triggers to seeking help for potentially malignant oral symptoms: implications of interventions. J *Public Health Dent* (2009);69:34-40
13. De Nooijer J, Lechner L, de Vries H. Social psychological correlates of paying attention to cancer symptoms and seeking medical help. Soc Sci Med (2003);56:915-20
14. Van Osch L, Lechner L, Reubsaet A, de Nooijer J, de Vries H. Passive cancer detection and medical help seeking for cancer symptoms:inadequate behavior and psychological determinants. Eur J Cancer Prev (2007);16:266-74
15. Hunter CP, Redmond CK, Chen VW, et al. Breast Cancer factors associated with stage at diagnosis in black and white woman. Black/ White Cancer Survival Study Group. *J Natl Cancer Inst* (1993);85:1129-37
16. Macleod U, Mitchell ED, Burgess C, Macdonald S and Ramirez AJ; Risk factors for delayed presentation and referral of symptomatic cancer, evidence for common cancers. *British Journal of Cancer* (2011) 101, S92 – S101,pg1
17. Harirchi I, Ghaemmaghami F, Karbakhsh M, et al. Patient delay in women presenting with advanced breast cancer: an Iranian study (2005). *Public Health*, 119, 885-91.
18. Montazeri A, Ebrahimi M, Mehrdad N, et al. Delayed presentation in breast cancer: a study in Iranian women (2003).*BMC Womens Health*, p3, 4.
19. Ramirez AJ, Westcombe AM, Burgess CC, et al. Factors predicting delayed presentation of symptomatic breast cancer: a systematic review (1999).*Lancet*, **353**, 1127-31.
20. Zimbabwe People Living with HIV Stigma Index Report (2014);http://www.stigmaindex.org/sites/default/files/reports/Zimbabwe%20People%20Living%20with%20HIV%20Stigma%20Index%20Report_15-12-14pdf.pdf;accessed 10/28/2016:12:29pm
21. Lancaster JM, Powell CB, Chen LM, et al.(2015): Society of Gynecologic Oncology statement on risk assessment for inherited gynecologic cancer predispositions. Gynecol Oncol 136 (1): 3-7,[PUBMED Abstract]

22. Robson ME, Bradbury AR, Arun B, et al. (2015): American Society of Clinical Oncology Policy Statement Update: Genetic and Genomic Testing for Cancer Susceptibility. J Clin Oncol 33 (31): 3660-7, [PUBMED Abstract]
23. (n.d.). In Merriam-Webster's online dictionary (11th ed.). Retrieved from http://www.merriam-webster.com/dictionary/ignorance; accessed on 1/11/2016, 6:05am.
24. Hortobagyi GN, dela Garza Salazar J, et al. The global breast cancer burden: variations in epidemiology and survival. *Clin Breast Cancer* 2005; **6**:391-401.
25. Benson JR, Jatoi I, Keisch M. Early breast cancer. *Lancet* 2009; **373**:1642-3.
26. Zimbabwe Cancer Registry 2010 statistics
27. Thomson CS, Forman D. Cancer survival in England and the influence of early diagnosis. *Br J Cancer 2009;101*:S102-9
28. Facione NC. Delay versus help seeking for breast cancer symptoms: a critical review of the literature on patient and provider delay. *Soc Sci Med* 1993;36:1521-34.
29. Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. The influence of delay on survival in patients with breast cancer: a systematic review. *Lancet* 1999;353:1119-1126.
30. Andersen BL, Cacioppo JT. Delay in seeking a cancer diagnosis: delay stages and psychological comparison process. Br J Soc Psychol1995:34:33-52.
31. Ruiter RA, de Nooijer J, van Breukelen G, Ockhuysen- VermeyCF, de Vries H. Intended coping responses to cancer symptoms in healthy adults: the roles of symptom knowledge, detection behavior, and perceived threat. *Cancer Epidemiol Biomarkers Prev 2008;17:818-26.*
32. Ristvedt SL, Trinkaus KM. Psychological factors related to delay in consultation for cancer symptoms. *Psychooncology* 2005;14:339-50.
33. Burgess CC, Potts HW, Hamed H, et al. Why do older woman delay presentation with breast cancer symptoms? *Psychooncology* 2006;15:962-8.
34. Scott SE, Grunfeld EA, Auyeung V, Mcgurk M. Barriers and triggers to seeking help for potentially malignant oral symptoms: implications of interventions. J *Public Health Dent* 2009;69:34-40
35. de Nooijer J, Lechner L, de Vries H. Social psychological correlates of paying attention to cancer symptoms and seeking medical help. Soc Sci Med 2003;56:915-20

36. van Osch L, Lechner L, Reubsaet A, de Nooijer J, de Vries H. Passive cancer detection and medical help seeking for cancer symptoms:inadequate behavior and psychological determinants. Eur J Cancer Prev 2007;16:266-74
37. Hunter CP, Redmond CK, Chen VW, et al. Breast Cancer: factors associated with stage at diagnosis in black and white woman. Black/ White Cancer Survival Study Group. *J Natl Cancer Inst* 1993;85:1129-37
38. Pace, L. E., Mpunga, T., Hategekimana, V., Dusengimana, J.-M. V., Habineza, H., Bigirimana, J. B., … Keating, N. L. (2015). Delays in Breast Cancer Presentation and Diagnosis at Two Rural Cancer Referral Centers in Rwanda. *The Oncologist*, *20*(7), 780–788. http://doi.org/10.1634/theoncologist.2014-0493
39. Borges *et al*, (2013). Predicting risk of cancer during HIV infection: the role of inflammatory and coagulation biomarkers. *AIDS* 27(9).
40. De Andrade AC, Luz PM, Veloso VG, *et al,* (2011). Breast cancer in a cohort of human immunodeficiency virus (HIV)-infected women from Rio de Janeiro, Brazil: a case series report and an incidence rate estimate. *Braz J Infect Dis*;15:387-93
41. Shiels MS, Pfeiffer RM, Gail MH, Hall HI, Li J, Chaturvedi AK, *et al*. (2011). Cancer burden in the HIV-infected population in the United States. *J Natl Cancer Inst*, 103:753–62. 10.1093/jnci/djr076
42. Jessica L CastilhoEmail author, Paula M Luz, Bryan E Shepherd, Megan Turner, Sayonara R Ribeiro, Sally S Bebawy, Juliana S Netto, Catherine C McGowan, Valdiléa G Veloso, Eric A Engels, Timothy R Sterling and Beatriz Grinsztejn.(2015). HIV and cancer: a comparative retrospective study of Brazilian and U.S. *clinical cohorts Infectious Agents and Cancer BioMed Central*.doi: 10.1186/1750-9378-10-4.
43. Muguti GI (1993) Experience with breast cancer in Zimbabwe. *J R Coll Surg Edinb* 38(2): 75–78 | PubMed | ChemPort |

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

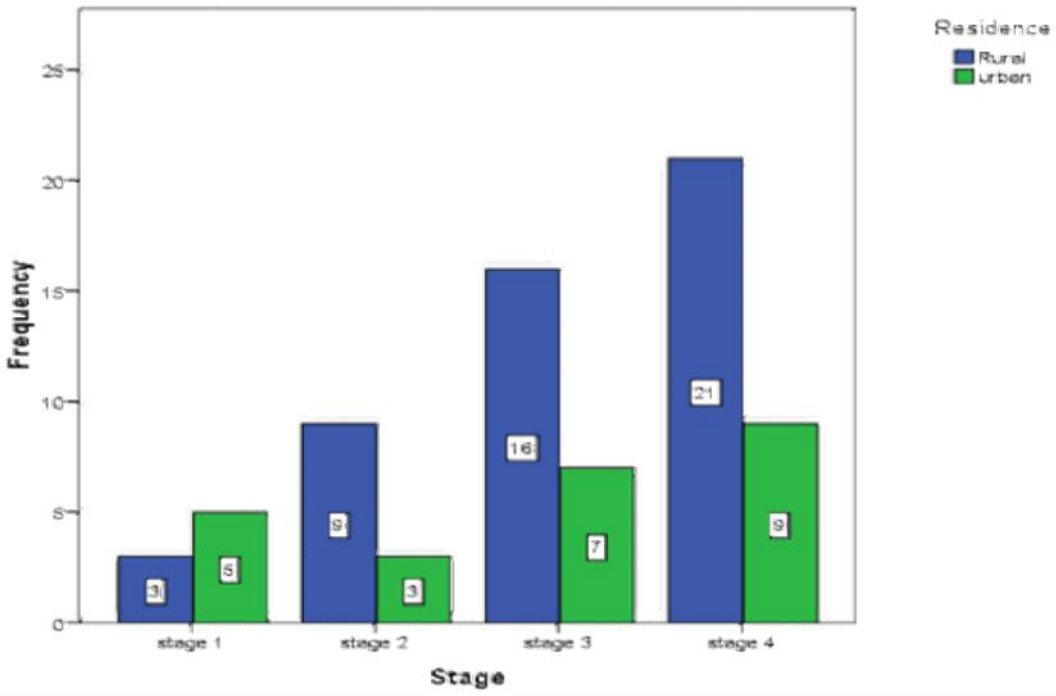

Figure 2: Clinical Stage vs Domicile

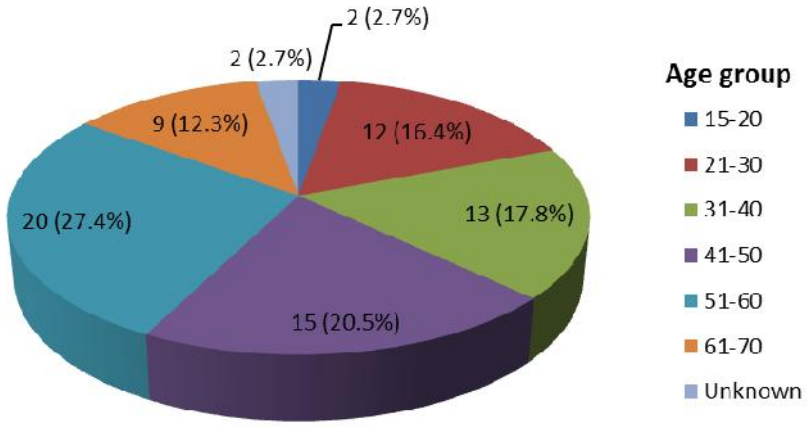

Figure 3: Breast cancer-age distribution

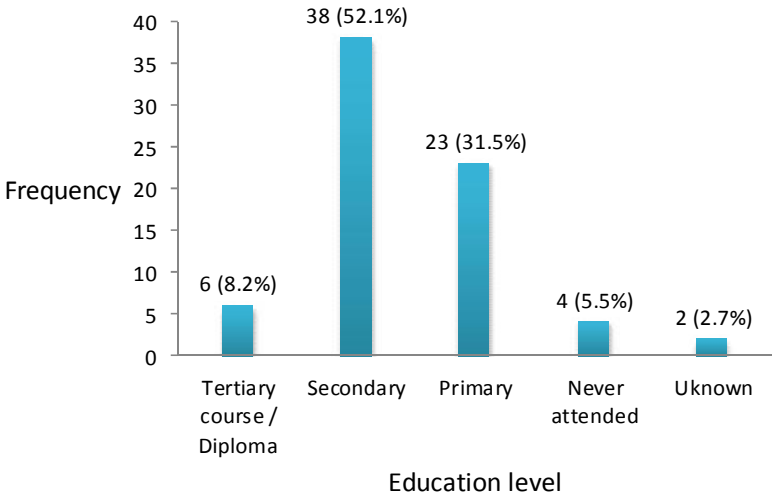

Figure 4: Highest level of education

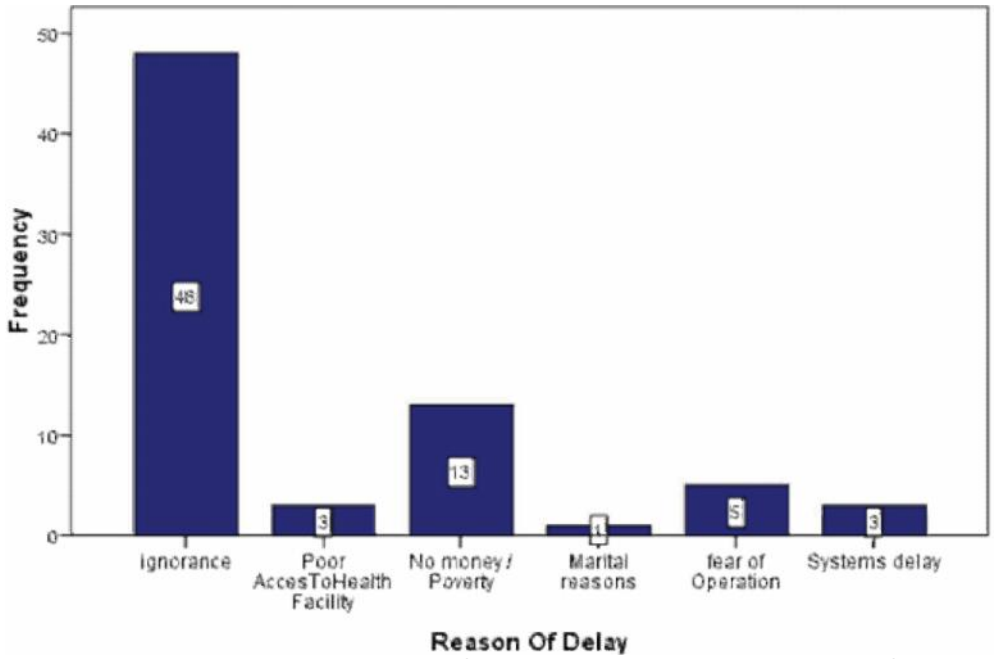

Figure 5: Frequency distribution of patient's perception as reason for delay

Table 1: Knowledge of self- breast examination and Residence

Residence	Knowledge of Breast Self-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)
Note: p < 0.05 ,Statistically significant association			

Table 2: 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 3: Relationship between knowledge of breast self-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*

Table 4: Contributions of specific reasons to delayed breast cancer presentation

Reasons	Delayed presentation score	
	No	Yes
HIV Status	20.240	24.526
Age	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 5: Standardized discriminant Coefficients of patient perceptions as reason

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

464
465
466