A 14-Year Analysis of Breast Cancer Risk Factors and Its Determinants of Mortality in Rural Southwestern Nigeria

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Azeez Oyemomi Ibrahim[1], Adetunji Omonijo[2], Tosin Anthony Agbesanwa[3], Ayodele Kamal Alabi[4], Olayide Toyin Elegbede[1], Kolawole Michael Olusuyi[1], Musah Yusuf[5], Eniola Ayoyemi Afolabi-Obe[6], Olagoke Erinomo[7], Olakunle Fatai Babalola[8], Henry Abiyere[8], Olayinka Tesleem Orewole[9] and Shuaib Kayode Aremu[10]

[1]Department of Family Medicine, Afe Babalola University, Ado Ekiti, Nigeria. [2]Department of Family Medicine, Federal Teaching Hospital Ido-Ekiti, Ido-Ekiti, Nigeria. [3]Department of Family Medicine, Ekiti State University, Ado-Ekiti, Nigeria. [4]Department of Community Medicine, Federal Teaching Hospital Ido-Ekiti, Ido-Ekiti, Nigeria. [5]Department of Medicine, Afe Babalola University, Ado-Ekiti, Nigeria. [6]Department of Family Medicine, Lagos State University Teaching Hospital, Ikeja, Nigeria. [7]Department of Pathology, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria. [8]Department of Surgery, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria. [9]Department of Anaesthesia, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria. [10]Department of Otorhinolaryngology, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.

ABSTRACT

BACKGROUND: Research on breast cancer risk factors and mortality is gaining recognition and attention globally; there is need to add more information on its determinants among patients admitted in hospital. Some studies on risk factors and mortality of breast cancer in Nigeria hospitals conducted in the urban and suburban areas have been documented. Therefore, an addition of a study conducted in the setting of a rural health institution is necessary. This study assessed the risk factors and determinants of mortality among patients admitted for breast cancer in rural Southwestern Nigeria.

METHODS: A retrospective observational study was conducted on 260 patients who were admitted for breast cancer between January 2010 and December 2023 using a data form and a standardized information form. The data were analyzed using SPSS version 22.0. The risk factors and the determinants of mortality of patients with breast cancer were identified using multivariate regression model.

RESULTS: The breast cancer risk factors were old age, family history, tobacco smoking, combined oral contraceptives, and hormonal therapy use. The case fatality rate was 38.1%, and its determinants of mortality were patients who were older (adjusted odds ratio [AOR], 1.956; 95% confidence interval [CI]:1.341-4.333), obese (AOR, 2.635; 95% CI: 1.485-6.778), stage IV (AOR, 1.895; 95% CI: 1.146-8.9742), mastectomy (AOR, 2.512; 95% CI: 1.003-6.569), discontinued adjuvant chemotherapy (AOR, 1.785; 95% CI: 1.092-4.6311), and yet to commence adjuvant chemotherapy (AOR, 2.568; 95% CI: 1.367-5.002).

CONCLUSION: The study revealed that patients with breast cancer were associated with high mortality. Sustained health education to promote early diagnosis, managed co-morbidities, and access to treatment may contribute to reduction in breast cancer mortality in rural Nigeria.

KEYWORDS: Breast cancer, risk factors, determinants, mortality, rural Nigeria

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CORRESPONDING AUTHOR: Olayide Toyin Elegbede, Department of Family Medicine, Afe Babalola University, PMB 5454, Ado Ekiti, Ekiti State, Nigeria. Email: elegbedeot@abuad.edu.ng

Introduction

All over the world, the most commonly diagnosed cancer was breast cancer with 2.26 million cases and 685 000 deaths reported in 2020 where it ranked the fifth leading cause of death.[1] In the United States, the chance of a woman with risk of developing breast cancer is 1 of 8.[2] Although, the incidence of breast cancer is higher in advanced countries, there is reported higher rates of morbidity and mortality in less-advanced countries.[3,4] In Nigeria and other Sub-Saharan Africa (SSA) countries, breast cancer has been recognized as an important cause of death in women.[3,4] The incidence of breast cancer in low-middle-income countries (LMICs) is likely to increase in future as a results of unhealthy lifestyle and ongoing demographic changes such as gender and the aging of the population.[5–7] In Nigeria, data on all new cancers among women revealed that 22.7% were breast cancer.[1]

Previous studies have shown that a woman's chance of being diagnosed with or dying of breast cancer included female genders,[8] postmenopausal age,[9] family history, smoking, alcohol consumption, and combined oral contraceptive (COC) use.[6,7,10] Other factors were co-morbid conditions such as hypertension, diabetes mellitus, obesity, and human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS).[4,5,10] Despite the perception of all these risk factors, most women who were diagnosed of breast cancer do not have identifiable risk factors.[5]

There is a need to improve on the existing cancer registration process in accordance with recommendation of the National Cancer Control Plan of Nigeria (2018-2022).[11] Aside this, research on breast cancer risk factors and mortality is gaining recognition and attention globally. Some studies on risk factors and mortality of breast cancer in Nigeria hospitals conducted in the urban and suburban areas have been documented. There is a need to add more information on its determinants and therefore, an addition of a study conducted in the setting of a rural health institution is necessary. The results would help to design appropriate cause control strategies, improve on cancer control measures, and assess the effectiveness of these strategies.[5,12] Therefore, this study assessed the risk factors and determinants of mortality among patients admitted for breast cancer in rural Southwestern Nigeria. We hypothesized that socio-demographics, advanced stage at diagnosis, co-morbidities, and lack of treatment would be associated with higher breast cancer mortality in this population.

Materials and Methods

Study setting

The study was conducted between January 2010 and December 2023 at the Accident and Emergency Department (AED) of Federal Teaching Hospital Ido-Ekiti (FETHI), Ekiti State in Southwestern Nigeria. The place where the hospital is located is one of the rural communities of the State and head-quarter of the local government area, which is about 15 km from the State capital. It has a total land area of 332 km^2 and as at last population census of 2006, it had a total population of 159,114 with an annual growth rate of 3.2%.[13] Most residents of the community engage in farming and trading activities with a few in the formal sector are either civil servants or retirees.[13] The hospital receives patients from all over the state and its neighboring states and offers different treatment modalities in form of diagnostic, chemotherapy, palliative, and surgical services for patients with breast cancer. The hospital is accredited for training of resident doctors to become specialist in various fields.

Study design

This was retrospective observational review of hospital records of patients with breast cancer admitted at adult AED between 1 January, 2010 and 31 December, 2023.

Study population

This included all patients with breast cancer who were diagnosed, registered, and admitted between 1 January, 2010 and 31 December, 2023.

Sample size

This retrospective study involved all patients with breast cancer who were on admission during the study period and had fulfilled the inclusion and exclusion criteria. This sample size was derived by census approach using patients' medical records and nursing report books to review all patients with breast cancer who were registered and admitted during the study period. A total of 260 patients were reviewed and this represented the sample size.

Inclusion criteria

This included patients with breast cancer who were permanent residents of the rural area and whose diagnoses were confirmed by the report of histology biopsy and were documented in their folder.

Exclusion criteria

This included patients with breast cancer who were foreigners or whose data were incomplete or not available.

Sampling technique

A consecutive sampling technique which allows for inclusion of every eligible patient was used for this study

Procedure for data collection

The researchers designed the instrument for data collection, and these contained variables to be measured based on the previous literature and using global surveillance on cancer incidence.[12] This instrument included a data form and patient information form which was used to obtain de-identified demographic and clinical information from the case records of each patient and admission and discharge from the nursing report books. Information retrieved included the date and year of admission, demographic profiles, place of residence, suspected risk factors, and co-morbid conditions. The methods of treatment which could either be surgically including the type of surgery or/and by adjuvant chemotherapy were extracted and recorded. Histology report for each patient was examined for clinical stage and type of tumor. The patients who died on admission were recorded in the data. The research assistants included 2 casualty doctors, a resident doctor from pathology unit, and a nursing officer who were trained to collect the data. The collected data were cross-checked by the principal investigator. The reporting of this study conforms to the strengthening of the reporting of observational

studies in Epidemiology (STROBE) statement.[14] All patients' details have been de-identified.

Statistical analysis

The data that were collected were checked for completeness and entered into Epi info version 7 and were later exported to SPSS version 22.0 for analysis. Continuous variables were expressed as mean and standard deviation, while categorical variables as frequencies and percentages. The chi-square (χ^2) test and Fischer's exact test were used to determine the association between respondents' socio-demographics, breast cancer risk factors, co-morbid conditions, clinical, and histological findings, treatment options, and the breast cancer mortality. All factors found to have a significant association with breast cancer mortality in the bi-variate analysis (p-value $<$ .05) were entered in a stepwise multivariate logistic regression model to determine the factors that were independently associated with breast cancer mortality, and results were presented as adjusted odds ratios with corresponding 95% confidence intervals (CIs). The multivariate regression analysis used in this study was used to control all confounding variables.

Results

A total of 265 patients with breast cancer were diagnosed from January 2010 to December 2023 in the study center. Among these samples, 260 patients had their data completed and were analyzed in this study. The mean age of the patients was 47.8 ± 11.7 (range: 26-72) years, and the patients age group 40 to 59 was the largest 151/260 (58.1%) compared with other age groups. Of the total patients, 194/260 (74.6%) were married, 246/260 (94.6%) had formal education, and 88/260 (33.8%) were traders (Table 1).

In this study, only 35/260 (13.5%) had family history of breast cancer, 7/260 (2.7%) had smoked tobacco, 24/260 (9.2%) had consumed alcohol, 40/260 (15.4%) attained menarche after 15 years of age, 31/260 (11.9%) attained menopause after 50 years of age. Also, only 63/260 (24.2%) had less than 3 children, 21/176 (11.9%) had taken COCs, and 21/260 (8.1%) had taken hormonal replacement therapy (Table 2).

Furthermore, 40/260 (15.4%) were hypertensive, 230/260 (88.5%) had ductal-type of histology, 113/260 (43.5%) were stage IV, 40/260 (15.4%) had mastectomy, and 135/260 (51.9%) were discontinued on chemotherapy. Overall, 99/260 (38.1%) were confirmed dead (Table 3).

After adjusting for possible cofounders documented for each patient, such as socio-demographic factors, risk factors for breast cancer, co-morbid conditions, clinical, and histological findings, the odds of breast cancer mortality was 1.956 times (95% CI:1.341-4.333) more likely among the patients who were 60 years and above compared with those who were less than 40 years, 2.635 (95% CI: 1.485-6.778) times more likely among the patients who were obese compared with those who were of normal weight, 1.895 times (95% CI: 1.146-8.974) more likely among the patients who were stage IV compared with those who were stage I, 2.512 times (95% CI: 1.003-6.569) more likely among the patients who had mastectomy compared with those who had lumpectomy, 1.785 times (95% CI: 1.092-4.631), more likely among patients who discontinued chemotherapy, and 2.568 times (95% CI: 1.367-5.002) more likely among patients who were yet to commence chemotherapy compared with those who were on treatment (Table 4)

Table 1. Socio-demographic characteristics of studied patients (N = 260).

VARIABLE	FREQUENCY N = 260	PERCENTAGE (%)
Age (in years)		
<40	69	26.5
40-59	151	58.1
⩾60	40	15.4
Mean age ± SD	47.8 ± *11.7*	
Range (Min.-Max.)	26-72	
Marital status		
Single	9	3.5
Married	194	74.6
Separated	24	9.2
Divorced	20	7.7
Widowed	13	5.0
Education		
Informal	14	5.4
Formal	246	94.6
Occupation		
Civil servant	81	31.2
Trader	88	33.8
Artisan	48	18.5
Housewife	43	16.5

Discussion

The mean age of patients with breast cancer in this study was 47.8 ± 11.7 years. This was comparable to the mean age of 48.7 ± 11.8 years in Nigeria[6] and 49.0 years in Ghana.[15] The mean age in our study and these other studies was not surprised, given the fact that breast cancer is most prevalent around these ages. In contrast, a higher mean age of 61 years was reported in a retrospective study conducted in western Ethiopia.[5] The variation in the mean age of our study compared with the later study in Ethiopia may be due to variation in the source populations and the age ranges observed in the 2 studies.

Table 2. Risk factors of breast cancer (N=260).

VARIABLE	FREQUENCY N=260	PERCENTAGE (%)
Family history		
Yes	35	13.5
No	225	86.5
Tobacco smoking		
Yes	7	2.7
No	253	97.3
Alcohol intake		
Yes	24	9.2
No	236	90.8
Age at menarche		
⩾15 years	40	15.4
<15 years	220	84.6
Age at menopause		
>50 years	31	11.9
⩽50 years	229	88.1
Number of children		
<3	63	24.2
⩾3	197	76.8
Age at first child		
⩾30 years	32	12.3
<30 years	228	87.7
Taken combined oral contraceptive (COC)		
Yes	31	11.9
No	229	88.1
Taken hormonal replacement therapy		
Yes	21	8.1
No	239	91.9

Table 3. Clinical findings in the studied patients (N=260).

VARIABLE	FREQUENCY N=260	PERCENTAGE (%)
Co-morbid condition		
None	117	55.0
Yes		
Obesity (BMI > 30 kg/m²)	51	19.6
Diabetes mellitus	18	6.9
HIV/AIDS	8	3.1
Hypertension	40	15.4
Histology report		
Ductal	230	88.5
Lubular	30	11.5
Staging		
Stage I	33	12.7
Stage II	38	14.6
Stage III	76	29.2
Stage IV	113	43.5
Treatment		
Surgical operation		
Lumpectomy	22	8.5
Mastectomy	40	15.4
Adjuvant chemotherapy		
Completed	34	13.1
Discontinued	135	51.9
Scheduled	29	11.1
Treatment outcome		
Dead	99	38.1
Alive	161	61.9

In this study, 13.5% of patients were found to have family history of breast cancer. This was comparable higher than 6.2% reported in another Nigeria study.[6] Several other studies have reported first-degree relatives as significant association between family history and the incidence of breast cancer.[16,17] The inheritable genes such BRCA1 and BRCA2 have been implicated in the cause of breast cancer.[16,17] Despite the implication of these genes, the incidence of breast cancer linked to these susceptibility genes only occurs in less than 5% of the total occurrence of breast cancer.[18]

This study found an association between patients with breast cancer and incidence of smoking in 2.7% of patients. Though the incidence of smoking in this study is low, its value should not be jettisoned, given its implications as potential modifiable risk factor for breast cancer development and its poor prognostic factor for patients with other co-morbid conditions. Our study supports the existing literature that links smoking with increased incidence of hormone-receptor breast cancer.[19] However, a study by Zeinomar et al[20] found no association between smoking and incidence of breast cancer in women.

In this study, 9.2% of patients with breast cancer were recorded to have consumed alcohol. This was consistent with previous study in Southwestern Nigeria which links alcohol

Table 4. Bivariate and multivariate analysis for the determinants of breast cancer mortality (N = 260).

VARIABLE	DEAD N (%)	ALIVE N (%)	COR (95% CI)	P	AOR (95% CI)	P
Age (in years)						
<40 (ref)	41 (59.4)	28 (40.6)	1.000		1.000	
40-59	88 (58.3)	63 (41.7)	0.953 (0.535-1.703)	.068	0.357 (0.045-1.365)	.543
⩾60	32 (80.0)	8 (20.0)	2.732 (1.098-6.800)	.028*	1.956 (1.341-4.333)	.028*
Occupation						
Civil servant (ref)	37 (45.7)	44 (54.3)	1.000		1.000	
Trader	67 (76.1)	21 (23.9)	3.794 (1.967-7.317)	<.001*	1.635 (0.738-3.025)	.478
Artisan	29 (60.4)	19 (39.6)	1.807 (0.879-3.748)	.171	1.477 (0.741-2.511)	.562
Housewife	28 (65.1)	15 (34.9)	2.220 (1.029-4.768)	.039*	1.116 (0.478-3.458)	.941
Family history						
Yes	29 (82.9)	6 (17.1)	3.405 (1.360-8.530)	.006*	1.602 (0372-2.149)	.658
No (ref)	132 (58.7)	93 (41.3)	1.000		1.000	
Hormonal replacement therapy						
Yes (ref)	7 (33.3)\	14 (66.7)	1.000		1.000	
No	154 (64.4)	85 (356)	3.624 (1.408-9.324)	.005*	3.128 (0.241-9.365)	.710
Obesity (BMI > 30 kg/m^2)						
Yes	42 (82.4)	9 (17.6)	3.529(1.634-7.624)	.001*	2.635 (1.485-6.778)	.037*
No (ref)	119 (56.9)	90 (43.1)	1.000		1.000	
Histology report						
Ductal	149 (64.8)	81 (35.2)	2.759 (1.266-6.013)	.009*	2.639 (0.417-7.223)	.510
Lubular (ref)	12 (40.0)	18 (60.0)	1.000		1.000	
Staging						
Stage 1 (ref)	14 (42.4)	19 (57.6)	1.000		1.000	
Stage 2	22 (57.9)	16 (42.1)	1.866 (0.726-4.797)	.211	1.698 (0.4151-6.301)	.450
Stage 3	46 (60.5)	30 (39.5)	2.067 (0.908-4.770)	.093	2.365 (0.741-6.398)	.366
Stage 4	79 (69.9)	34 (30.1)	3.153 (1.419 - 7.010)	.004*	1.895 (1.146-8.974)	.024*
Treatment (surgical operation)						
Lumpectomy (ref)	4 (16.7)	20 (83.3)	1.000		1.000	
Mastectomy	18 (41.9)	25 (58.1)	3.600 (1.049-12.350)	0.035*	2.512 (1.003-6.569)	.048*
Adjuvant chemotherapy						
Completed (ref)	19 (51.4)	18 (48.6)	1.000		1.000	
Discontinued	101 (74.3)	35 (25.7)	2.734 (1.291-5.754)	0.023*	1.785 (1.092-4.631)	.041*
Yet to commence	22 (75.9)	7 (24.1)	2.966 (1.345-6.478)	0.011*	2.568 (1.367-5.002)	.022*

Abbreviations: AOR, adjusted odd ratio; COR, crude odd ratio; ref, reference category.
*Significant at 0.05 level.

consumption to incidence of breast cancer.[21] The risk of breast cancer is said to increase by approximately 10% for each 10 g of daily alcohol consumption.[22] However, despite previous study linking BRCA1 and BRCA2 mutation carriers to breast cancer, such study found no link between alcohol consumption and breast cancer incidence.[23]

Furthermore, 84.6% of women with breast cancer in this study attained menarche at ages considered early, and 11.9% of women with breast cancer attained menopause at ages considered late. Several studies have linked early commencement of menses, late attainment of menopause, and later stage at first pregnancy to increasing incidence of breast cancer.[24,25] These studies also found that for every 2 deliveries, the risk reduced by approximately16%.[24,25]

The International Agency for Research in Cancer (IARC) has found a link between women who currently or recently use COC and incidence of breast cancer.[25] A meta analysis showed that current users of COC have approximately 24% higher breast cancer risk compared with never users.[26] The active ingredient in COC, which is a synthetic sex hormone, may explain the link between women who use COC and incidence of breast cancer.[21] This study revealed that the incidence of breast cancer occurred in 11.9% of women who were users of COC.

Breast cancer incidence was positively associated with mortality rates in rural Southwestern Nigeria, which suggests that more breast cancer cases are associated with more breast cancer deaths. This finding was comparable to a study conducted in rural South Dakota where it was reported that the more the incidence of breast cancer, the more the mortality attributed to breast cancer.[27]

This study revealed that 38.1% of patients with breast cancer died during the study period. The high case fatality rate is comparable to findings in other studies reported among African women.[4,5,7] The delay in seeking diagnosis of, and treatment of breast cancer among African women may explain this observation.[5] Almost 72.7% of patients with breast cancer in this study were diagnosed at least in stage III, which has been reported by several studies as stages of palliative treatment with worse outcome.[5,26,28] Poor access to quality health care, negative interpretation of breast cancer symptoms, and religious and cultural beliefs are factors contributed to the delay in hospital presentation.[5,28]

After adjusting for possible cofounders, older patients aged 60 years and above were determinants of patients with breast cancer mortality. This was in agreement with other African studies which identified increasing age as risk factor, and predictor of breast cancer mortality in women.[5,28] However, comparing age with age, improved health promotion, breast cancer prevention and management, and access to advanced therapeutic and diagnostic methods by patients in developed countries are factors contributing to positive prognosis compared with patients in SSA.[29]

This study found breast cancer stage IV as determinant of breast cancer mortality. This result suggests that cancer stage is an important prognostic factor for slowly response after delay treatment. This was comparable with Shih et al,[30] which revealed that at stage IV, a higher risk existed between treatment delay and breast cancer mortality especially among people of older age groups. Our finding was also in agreement with previous studies in other African countries, which have most patients with breast cancer presented with late stage of the disease.[5,28] These studies have identified management of patients with breast cancer stage III and IV as mainly palliative with poor outcome. The implication of this finding is that awareness campaign to promote early diagnosis of breast cancer at each level of health care delivery point may be needed to reduce breast cancer mortality in rural Nigeria.

Furthermore, obesity in this study is observed to increase the risk of breast cancer mortality and is in agreement with study by Blair et al,[31] which found stage III and IV breast cancer disease more in women who were obese relative to normal weight. The mechanism of obesity in the cause of breast cancer is multifactorials. Obesity has been linked to enhance greater tumor size, higher grade, and substantially increases risk of metastases.[31] Biological mechanism linking increased fat deposit in obese women to poor prognostic outcome include inflammatory markers, steroid hormones, cytokines, and insulin-like growth factors.[31,32] Other study had linked breast cancer mortality in obese women to possibility of delay in diagnosis and treatment.[33]

This study revealed that delayed or noninitiation of adjuvant chemotherapy was associated with breast cancer mortality. This finding was consistent with study by Yu et al,[34] which concludes that longer delay of initiation of adjuvant chemotherapy significantly associated with worse survival and advocate for early initiation of adjuvant chemotherapy for patients with aggressive tumor subtypes. Another study by Peto et al,[35] observed that adjuvant chemotherapy decreases by 30% to 40% the risk of breast cancer mortality compared with patients who do not receive chemotherapy. Adjuvant chemotherapy is one of the most important therapies for breast cancer patients.[36] It decreases the risk of breast cancer mortality mainly through eradication of micro-metastatic tumor deposits in breast cancer patients.[36] However, study by Jara Sánchez et al[37] found no significant association between time of initiation of adjuvant chemotherapy and breast cancer mortality.

Strength of this study

Overall, the strength of this study was that it provides important epidemiological data on breast cancer from a rural Nigeria population which has been understudied. By analysis over a decade of medical records, it identified predominant risk factors as well as modifiable barriers to reducing mortality. It has a clear implication for public health practice and highlight priorities for improving breast cancer outcomes in similar low-resource settings.

Limitations

The data for this study were retrospectively collected from a single center, and in addition with small sample size, and therefore, the finding should not be compared with those from general population, and involving multicenters. Also, our study

population included age ⩾ 60 years with many of them with co-existing co-morbid conditions, known to contribute to reduction of life span in SSA. Thus, the finding should not be generalized to a younger population. There was no recorded postmortem test performed on any of the dead patients to ascertain on the possible cause of death, and this also serves as limitation.

Conclusion

The study revealed that 38.1% of patients with breast cancer died during the study period. Old age and family history were the nonmodifiable risk factors while tobacco smoking, COC, and hormonal therapy use were the modifiable breast cancer risk factors in this study. The independent determinants of breast cancer mortality in this study were older patients, breast cancer stage IV, obesity, and noninitiation of adjuvant chemotherapy. The late stage, lack of treatment and access to screening may contribute difference between this study and other studies in urban settings. The finding calls for sustained awareness campaign for early detection, and improved access to quality health care as priorities to reduce breast cancer mortality in rural settings. Future research in rural settings is encouraged to further understand the specific determinants of breast cancer mortality.

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Author Contributions

AOI—Conceptualization, Investigation, Data curation, Drafted the initial manuscript, Writing review and editing.
AO: Data curation, Methodology, Writing review and editing.
TAA: Formal analysis, Supervision, Writing review and editing.
AKA: Formal analysis, Methodology, Writing review and editing.
OTE: Data curation, Supervision, Writing review and editing.
KMO: Formal analysis, Methodology, Writing review and editing.
EAA: Data curation, Methodology, Writing review and editing.
OE: Formal analysis, Supervision, Writing review and editing.
OFB: Formal analysis, Investigation, Writing review and editing.
HA: Formal analysis, Methodology, Writing review and editing.
OTO: Formal analysis, Investigation, Writing review and editing.

Availability of Data and Materials

All requests for raw and analyzed data materials will be promptly reviewed by the division of Oncology, Federal Teaching hospital, Ido-Ekiti, Nigeria to verify whether the request is subject to any intellectual property or confidential obligations. Patients related data not included in the manuscript may be subject to confidentiality. Any data that can be shared will be released upon a reasonable request from the corresponding author

Ethics Approval and Consent to participate

This retrospective study was approved by the Ethics and Research Committee (ERC)/Institution Review Board (IRB) of Federal Teaching Hospital Ido-Ekiti (FETHI), Ekiti State in Southwestern Nigeria with reference number (ERC/2022/02/25/1134A). The IRB waived the requirement for informed consent

Consent for Publication

Not applicable

ORCID iD

Olayide Toyin Elegbede https://orcid.org/0000-0001-7918-7223

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