Incidence and Laterality of Breast Carcinoma Among Patients Who Attended Aminu Kano Specialist Hospital, Kano State, Nigeria

Ibrahim, H. K[1]., Abdu, I.T.[1*], Gudaji, A.[1], Umar, A.B.[2]

[1]Department of Anatomy,
Faculty of Basic Medical Sciences,
College of Health Science,
Bayero University Kano,
Nigeria.

[2]Department of Histopathology,
Aminu Kano Teaching Hospital,
Kano State,
Nigeria.

Email: gwtel4u@gmail.com

Abstract

Breast cancer is the commonest malignancy in females and a major cause of cancer-related mortality worldwide. Previously, histological subtypes of breast carcinoma were determined in Aminu Kano Teaching Hospital, however, the commonest sides of breast carcinoma infection among the patients attending the facility received less attention. The study was retrospective and aimed to evaluate the mean age, incidence and laterality of breast carcinoma cases among patients who attended Aminu Kano Teaching Hospital (AKTH) from 2016 to 2020. A total of five-hundred and seventy-seven (577) data records on breast carcinoma of the patients comprised of histology reports, age, sex, and side of carcinoma were all extracted. The Patients' ages were categorized and mean age was determined. Data were analyzed using Minitab (17) presented in tables, charts and figures using Microsoft word excel, 2019. The results showed the mean age of breast carcinoma as 45.02±12.26, 48.28±13.06, 45.80±13.70, 48.59±13.64 and 46.66±13.35 in 2016, 2017, 2018, 2019 and 2020 respectively. The incidence of breast carcinoma was also dominant in the age group 40-59 and least in the age group 0-19 years. The laterality in breast carcinoma was 54% (226) on the left, 45% (189) affected on the right, and 1.0% (6) on both sides of the breast respectively. In conclusion, although breast carcinoma incidence showed a similar pattern in the five years studied, menopause was the commonest age of risk of breast carcinoma infections and the infections were more on the left breasts than the right among the patients who attended the facility.

Keywords: Breast carcinoma, incidence, laterality, Nigeria, patients

INTRODUCTION

Breast cancer is the commonest malignancy in females and a major cause of cancer-related deaths worldwide. Over 1.4 million women are diagnosed with breast cancer annually (Siegel

et al., 2012; Ferlay *et al.*, 2010). About 32% of all cancer cases and 18% of all cancer deaths in women are reportedly due to breast cancer (Ahmad, 2003).

The incidence and histological subtypes of breast carcinoma vary from one region of the world to the other, and increasing awareness of breast cancer has stimulated profound interest in breast diseases (Ihekwaba, 1992). There has been a steady increase in the incidence of breast cancer in Nigeria annually (Adebamowo and Ajayi, 2000; Jedy-Agba *et al.*, 2012). Breast cancer was reported as the second most commonest type of cancer in the Kano Cancer Registry (KCR) after cervical cancer (Mohammed *et al.*, 2008), and histological subtypes of breast carcinoma vary with age (Ibrahim, *et al.*, 2015).

Studies have consistently reported that women are more likely to be diagnosed with left breast cancer than right (Senie *et al.*, 1980; Ekbom *et al.*, 1994). The fact that left-sided tumours are not large and do not impact overall survival (Kamby *et al.*, 1991), may influence subsequent management, especially in elderly patients with ischemic heart disease.

The breast is a paired organ that shares many of the risk factors known to contribute to the development of cancer: genetics, environmental exposure, diet, estrogen exposure, etc (Sughrue and Brody, 2014). Previous studies established the patterns of histological subtypes of breast carcinoma in Kano (Mohammed *et al.*, 2008; Ibrahim, *et al.*, 2015). However, the evaluation of laterality in breast carcinoma cases among patients who attended Aminu Kano Teaching Hospital (AKTH) received less attention in the literature. Therefore, we aimed to evaluate the mean age, incidence and laterality of breast carcinoma cases among patients who attended Aminu Kano Teaching Hospital (AKTH) from 2016 to 2020. Studying laterality in breast carcinoma infection is essential in controlling the common risk factors and paving the way to unravelling the genesis of how breast carcinoma develops in general. It may also provide a cheap and quick diagnostic strategy as knowledge of the laterality in breast carcinoma infection provides an easy and non-invasive method for understanding commonest side carcinoma infections and development, especially in resource-limited settings such as Nigeria where cases of breast carcinoma incidence are on the increase while diagnostic facilities were either limited or absent.

METHODOLOGY

The study was retrospectively designed to evaluate all histologically diagnosed breast carcinoma cases in the Histopathology Unit of the Pathology Department, Aminu Kano Teaching Hospital (AKTH) over 5 years, from January 2016 to December 2020. An approval from the hospital ethical committee was obtained (NHREC/28/01/2020/AKTH/3027). A total of five-hundred and seventy-seven (577) data on breast cancer patients comprised of males (1.0%) and females (99.9%) age mean, 46.95±13.22 years, were deducted from the registers. The laboratory request forms and duplicate copies of the histology reports of all cases were retrieved. The patients' age, sex, and side of carcinoma were extracted. The ages of the patients were categorized into five groups each 19 years intervals.

Inclusion and Exclusion criteria: Data of breast carcinoma patients diagnosed and registered in the Histopathology Unit of Pathology Department, Aminu Kano Teaching Hospital (AKTH) by incision biopsies, core needle biopsies, excision biopsies and mastectomies were included. And any other patient's data (cancer or non-cancer) not diagnosed or incompletely diagnosed were all excluded from the study.

Limitations of the Study
Only patients' records with a side of breast carcinoma infection were extracted from the register.

Statistical Analysis
The data obtained were expressed as Mean±SD to determine the mean age of breast carcinoma infection in the patients. The demographic and clinical data were analyzed using *Minitab* (17) in percentage frequencies and presented using tables, charts and figures to determine common histological subtypes, distribution patterns, and laterality of the breast carcinoma using Microsoft word excel, 2019.

Results
Table 1 shows the descriptive statistics of the mean age of breast carcinoma patients who attended the hospital. Generally, the incidences were all recorded at menopause. The mean age pattern recorded as 48.59±13.64 years in 2019 as the highest mean age of breast carcinoma cases and the least mean age 45.02±12.26 years, was recorded in 2016. The mean age decreased slightly by about 6% in 2017. However, the trend declined in 2018. In 2019, the mean age recorded a slight increase of 6%. Interestingly, 15 and 95 years were recorded as the minimum and maximum ages of the patients who attended the hospital both in 2020.

Table 2 presents histological types of breast carcinoma records obtained from the patients that attended AKTH from 2016 to 2020. The frequency shows that invasive ductal carcinoma (IDC) has the highest record 461 (79.90%). This was followed by Metaplastic (squamous) breast carcinoma with 25(4.33%), Mucinous and Invasive Lobular Carcinoma (ILC) breast carcinoma, 16(2.77%) respectively. Medullary breast carcinoma was recorded in 15(2.60%), Apocrine, 12(2.08%), Papillary breast carcinoma, 9(1.59%), and Sebaceous breast carcinoma, 5(0.87%) respectively. Adenoid cystic carcinoma, Pleomorphic invasive lobular, Micropapillary and Secretory breast carcinoma each recorded 3(0.52%) cases respectively during the period. While Clear cell carcinoma and ductal carcinoma in situ (DCIS) recorded cases each of 2(0.35%) respectively, Tubular and Small cell breast carcinoma had the least case of 1(0.17%) respectively in all the breast carcinoma recorded among the patients attended the facility over the period.

Figure 1. shows the incidence patterns of the breast carcinoma patients who attended the hospital for diagnosis from 2016 to 2020. There was a gradual decline in the incidence recorded of the patients who attended the facility from 2016 to 2018. A total number of 135(23.40%), 112(19.93%), and 87(15.08%) were recorded in 2016, 2017 and 2018 respectively. However, the recorded incidence increased up to 87(21.66%) in 2019 and slightly decreased to 115(19.93%) in 2020 respectively. The maximum incidence recorded was 135 patients in 2016 while the minimum was 87 patients in 2018.

Figure 2. shows a sidedness in breast carcinoma cases in patients who attended AKTH from 2016 to 2020. 54% (226) were found to affect the left side breast, while 45% (189) affected the right-side breast. In 1.0% (6) cases, both right and left breasts were affected.

Table 1. Mean Age of Breast Carcinoma Cases By Year Among Patients who Attended AKTH

YEAR	Mean±SD	Min.	Max.
2016	45.02±12.26	20.00	73.00
2017	48.28±13.06	18.00	80.00
2018	45.80±13.70	18.00	90.00
2019	48.59±13.64	22.00	85.00
2020	46.66±13.35	15.00	95.00

Table 2. Histological Subtypes of Breast Carcinoma of Patients who Attended AKTH

Carcinoma	Age					Total (%)
	0-19	20-39	40-59	60-79	80+	
ADC	1	1	-	1	-	03(0.52)
AC		1	6	5		12(2.08)
CCC	-	-	2	-	-	02(0.35)
DCIS	-	-	2	-	-	02(0.35)
IDC	-	130	232	92	7	461(79.90)
ILC	-	6	10	-	-	16(2.77)
MC		6	8	1	-	15(2.60)
MET	-	8	13	2	2	25(4.33)
MPC	-	1	1	1	-	03(0.52)
MUC		2	8	5	1	16(2.77)
IPC	-	3	2	4	-	09(1.56)
PILC	1	1	1	-	-	03(0.52)
SC	1	-	1	3	-	05(0.87)
SEC	-	2	1	-	-	03(0.52)
SCC	-	-	1	-	-	01(0.17)
TC	-	-	1	-	-	01(0.17)
Total	**3**	**161**	**289**	**114**	**10**	**577(100.00)**

ADC= Adenoid Cystic; **AC**= Apocrine Carcinoma; **CCC**= Clear Cell Carcinoma; **DCIS**= Ductal Carcinoma *In situ*; **IDC**=Invasive Ductal Carcinoma; **ILC**=Invasive Lobular Carcinoma; **MC**=Medullary Carcinoma; **MET**= Metaplastic Carcinoma; **MPC**=Micropapillary Carcinoma; **MUC**=Mucinous Carcinoma; **IPC**= Invasive Papillary Carcinoma; **PILC**= Pleomorphic; **SC**= Sebaceous Carcinoma; **SEC**= Secretory Carcinoma; **SCC**= Small Cell Carcinoma; **TC**= Tubular Carcinoma.
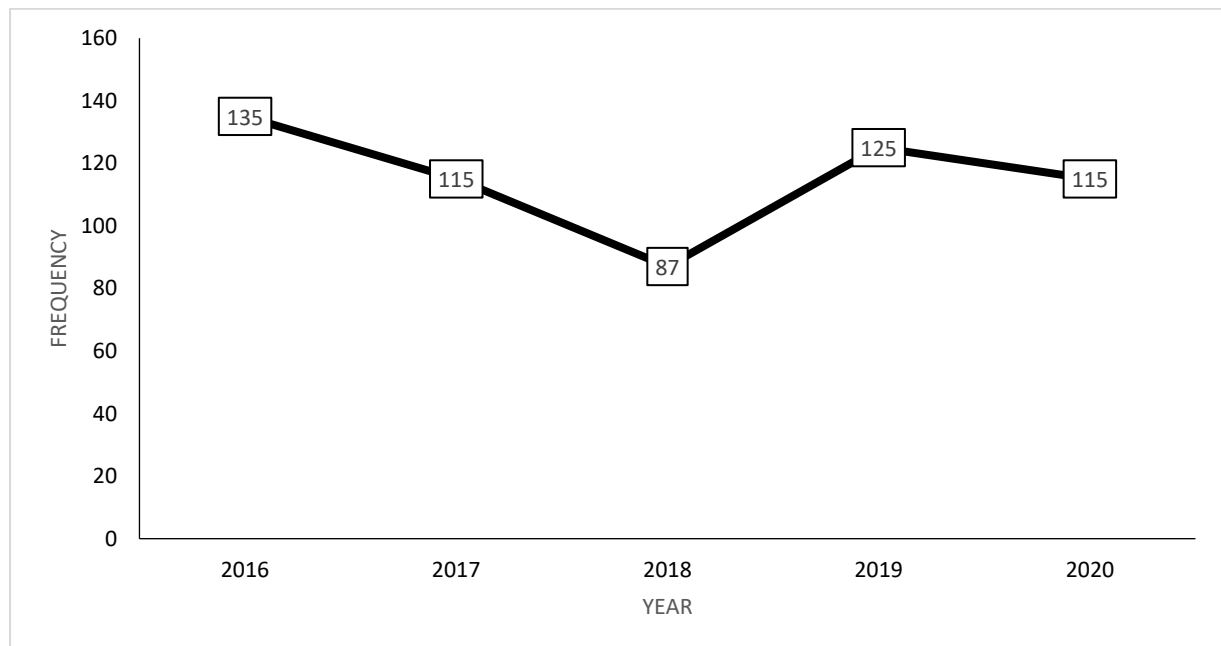

Figure 1. Incidence Patterns of Breast Carcinoma Cases in AKTH from 2016-2020.
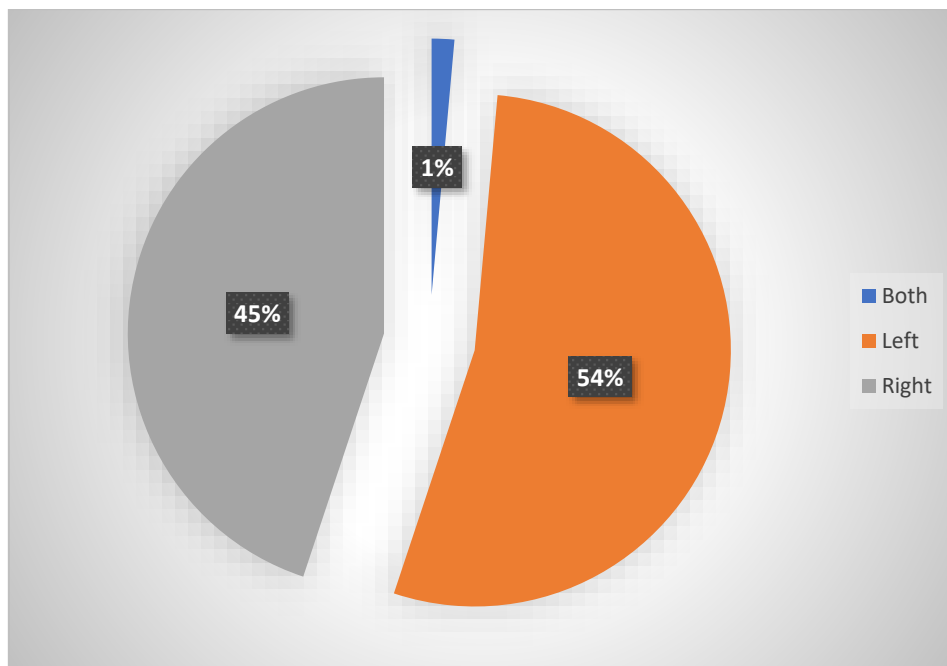
Figure 2. Laterality of Breast Carcinoma in Patients who Attended AKTH from 2016 to 2020.

DISCUSSION

The risk of breast carcinoma doubles each decade until menopause, after which the increase slows. However, breast cancer is more common after menopause (McPherson *et al.*, 2000). The descriptive statistics on the age of breast carcinoma patients had similar patterns across the years. This conforms to other previous findings obtained in the facility (Mohammad *et al.*, 2008). It further proved that menopause was the commonest age of risk of breast carcinoma cases among the patients who attended the facility. This pattern was in tune with the situation in western countries where breast cancers are usually seen among menopausal females (Morris *et al.*, 2007). While it is not certain exactly why this is so, the role of genetic, biological, ever-changing carcinogenic environmental factors might not be ruled out. Although lack of diagnostic facilities cannot be ruled out in resource-limited settings like Nigeria. This calls for public campaign awareness and sensitization on breast carcinoma evaluation status in premenopausal age to reduce the incidence at menopause.

Breast carcinoma among women varies in clinical and histopathologic features, suggesting that these tumours also differ in aetiology. Descriptive studies have shown that the classically recognized revolving point of age-specific breast cancer incidence rates overall around menopause (Clemmesen, 1948). Our age distribution trend showed that the peak incidence of breast carcinoma cases occurs between the 40-59 years age bracket. This indicates that menopause forms the largest breast carcinoma burden. Previous studies have reported similar findings in Nigeria, (Nwafor and Keshinro, 2015; Ezike *et al.*, 2020), Africa (Bewtra, 2010) and developing countries (Ngwogu *et al.*, 2017). Although the incidence of menopausal breast carcinoma burden was worrisome, more alarming was the pre-menopausal incidence recorded in the study. The frequency of cases at less than 20years of age signals unsafety from the infection of the disease among all humans. Accumulating evidence supports etiologic

heterogeneity between pre-and postmenopausal breast cancer. Several lifestyle factors, including childbirth (Schedin, 2006), obesity (White *et al.*, 2015), and cigarette smoking (Johnson *et al.*, 2010), have been reported to have differential associations with breast cancer risk before and after menopause. In the United States, incidence rates of advanced breast cancer have increased among premenopausal women in recent decades, whereas they have consistently decreased among women ages 60 and older during the same period (Johnson *et al.*, 2013). The fact that the postmenopausal record of breast carcinoma was low implied the probability of the death of patients before the age.

Breast neoplasms ordinarily develop unilaterally (von Fellenberg, 1940; Chen, 2013). Dysregulation of developmental stability or fluctuating asymmetry between left and right breasts may lead to cancer creation in one breast (Chen, 2013). The present study witnessed 99% of the patients being diagnosed with unilateral breast cancer with 1% being diagnosed with bilateral breast cancer. The finding was generally similar to the previous findings from Nigeria (Oluyemi, 2015) Africa and the western world with minimal variations (Kollias *et al.*, 2001). Most patients had unilateral primary breast cancer, mainly as a single primary or in association with other primary cancers, either concurrently or sequentially (Amer, 2014). The breast is a paired organ, so hormonal, environmental, and genetic factors are likely to affect the breast over time. Therefore, bilateral breast cancer is not uncommon. Bilateral breast cancer was much more noticeable in patients with hereditary disorders. Women who carry a germline mutation in either the *BRCA-I* or *BRCA-II* genes face a high risk of developing contralateral breast cancer (Amer, 2014). Usually, such patients presented at a younger age, with a small-sized tumour, low-grade histology, lymph node-negative malignancy, at an earlier stage of disease, were more likely to have lobular histology but no angiolymphatic invasion commonly had a strong family history in first-degree relatives and lived long enough to experience bilateral disease (Kollias *et al.*, 2001). The actual risk varies from 29.5% to 40% at 10 years (Woodward *et al.*, 2003). These characteristics suggest a possible genetic predisposition.

Breast cancer (BC) is the most prevalent type of cancer affecting females in both the developed and developing countries (Ferley *et al.*, 2010) and also the primary cause of mortality due to cancer in females around the globe (Lakhani *et al.*, 2012). The breast cancer incidence in Africa was reported to continue increasing and is projected to double by 2050 (Chokunonga *et al.*, 2013). The present study shows a decline in the incidence pattern of breast carcinoma cases between 2016 and 2018. This was however followed by a gradual increase in the record of the number of patients who attended the facility with breast carcinoma in 2019. Despite the pattern of the disease across the years of the present study, generally, the rate of the cases increases when compared with previous findings (Mohammed *et al.*, 2008; Ibrahim *et al.*, 2015) from the same facility. An increase in breast cancer was also reported in Nigeria and Africa respectively (Chokunonga, *et al.*, 2013; Oluyemi, 2015). Although we observed limited entries in the carcinoma records, it is noteworthy that only patients that attended the facility and were confirmed by the histopathologist were used. Many cases would have been missed or died due to limited professional facilities in their area of coverage. The declined rate of the carcinoma cases observed in 2020 however, might not be unconnected to the global COVID-19 pandemic, where many patients were rendered helpless as a result of the inability to access diagnostic centres due to global lockdown policies adopted by many countries to curb the menace and spread of the pandemic. COVID-19 is a novel viral disease caused by a single-stranded RNA virus belonging to the *Corona viridae* family (Lu *et al.*, 2020) which caused global

severe unprecedented mortality and morbidity that resulted in serious public health emergencies.

Left breast cancer was diagnosed more than right in women (Senie *et al*., 1980; Ekbom *et al*., 1994). This does not influence overall survival (Kamby *et al*., 1991), but subsequent management, especially in elderly patients with ischemic heart disease (Amer, 2014). Coincidently, we observed a preponderance of left-sided breast carcinoma in the patients, with the left-side leading by 9% over the right. Previous studies from Nigeria, Africa and the western world reported similar patterns (Amer, 2014). Generally, the laterality of invasive breast cancer is proposed to associate with several factors including pro-angiogenic, and pro-thrombotic conditions, and suggested to consider laterality as a prognostic factor of invasive breast cancer (Barbara *et al*., 2020). The majority of women are right-handed, so it might be easier to detect a palpable lump in the left breast compared with the right (Senie *et al*., 1980). This probably necessitates early and quick detection of left breast carcinoma when compared to left. Several reports have shown that the left breast size is somewhat larger than the right, and therefore has more tissue at risk of cancer (Senie *et al*., 1980; Ekbom *et al*., 1994; Perkins *et al*., 2004). As such more emphasis might be placed on the left than the right breast carcinoma. A study on breast asymmetry in women that used mammography noted that the left breast was larger than the right in 55% of healthy women (Senie *et al*., 1980). Therefore, keeping this in mind, the breast carcinoma diagnosis was probably on the left breast. Breast hypertrophy and the development of breast cancer were also reported to be more common on the left side (Olsson and Ingvar, 1991). Right-handedness was postulated to be more common in women, hence, most mothers would use the left arm to support the baby they feed, hence the left breast is used more often in lactation (Amer, 2014). Several studies have suggested that handedness is inversely related to breast cancer risk (Geschwind and Galaburda, 1985). Other studies have also evaluated the relationship between handedness and breast tumour laterality; their results suggest a correlation between left-handedness and tumours of the left breast, although inconclusively (Klar, 2011), as personal handedness depends on virtually on social, environmental, and developmental factors, normal or reversed brain asymmetry which might accurately define developmental changes concerning subsequent development of cancer (Barbara *et al*., 2020).

CONCLUSION

Although, menopause was the commonest age risk of breast carcinoma infection the incidence pattern of breast carcinoma was similar across the years of studied. A few cases of breast carcinoma infections were recorded on both breasts, but more cases were recorded on the left than the right breast. Therefore, there is a need for public awareness sensitization campaign for premenopausal checks and evaluations of breast carcinoma status to reduce the burden of the menopausal records.

REFERENCES

Adebamowo, C. and Ajayi, O., 2000. Breast cancer in Nigeria. *West African Journal Of Medicine*, 19(3), pp.179–191.

Ahmad, M., 2003. Risk factors for breast cancer among women attending breast clinic in University Malaya Medical Centre Kuala Lumpur. *NCD Malaysia*, 2(4), pp.23-31.

Amer, M.H., 2014. Genetic factors and breast cancer laterality. Cancer Management and Research, 6, pp.191–203.

Barbara, R., Piotr, R., Kornel, B., Elżbieta, Z., Danuta, R. and Eduardo, N., 2020. Divergent Impact of Breast Cancer Laterality on Clinicopathological, Angiogenic, and Hemostatic Profiles: A Potential Role of Tumor Localization in Future Outcomes. *Journal of Clinical Medicine*, 9(6), p.1708.

Bewtra, C., 2010. Fibroadenoma in women in Ghana. *Pan African Medical Journal*, 2(1).

Chen, J., Chan, S., Yeh, D., Fwu, P., Lin, M. and Su, M., 2013. Response of bilateral breasts to the endogenous hormonal fluctuation in a menstrual cycle evaluated using 3D MRI. *Magnetic Resonance Imaging*, 31(4), pp.538-544.

Chokunonga, E., Borok, M., Chirenje, Z., Nyakabau, A. and Parkin, D., 2013. Trends in the incidence of cancer in the black population of Harare, Zimbabwe 1991-2010. *International Journal of Cancer*, 133(3), pp.721-729.

Clemmesen, J., 1948. I. Results from Statistical Research. *The British Journal of Radiology*, 21(252), pp.583-590.

Ekbom, A., Adami, H., Trichopoulos, D., Lambe, M., Hsieh, C. and Pontén, J., 1994. Epidemiologic correlates of breast cancer laterality (Sweden). *Cancer Causes & Control*, 5(6), pp.510-516.

Ezike, K., Raphael, S., Okwudire-Ejeh, I. and Okonkwo, D., 2020. Breast lesions in a district hospital: Demographic and histopathologic characteristics. *Ann Trop Pathol*, 11, pp.113-8.

Ferlay, J., Shin, H., Bray, F., Forman, D., Mathers, C. and Parkin, D., 2010. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *International Journal of Cancer*, 127(12), pp.2893-2917.

Geschwind, N. and Galaburda, A., 1985. Cerebral Lateralization. *Archives of Neurology*, 42(6), pp.521-552.

Ibrahim, I., Iliyasu, Y. and Mohammed, A., 2015. Histopathological Review of Breast Tumors in Kano, Northern Nigeria. *Sub-Saharan African Journal of Medicine*, 2(1), p.47.

Ihekwaba, F., 1992. Breast cancer in Nigerian women. *British Journal of Surgery*, 79(8), pp.771-775.

Jedy-Agba, E., Curado, M., Ogunbiyi, O., Oga, E., Fabowale, T., Igbinoba, F., Osubor, G., Otu, T., Kumai, H., Koechlin, A., Osinubi, P., Dakum, P., Blattner, W. and Adebamowo, C., 2012. Cancer incidence in Nigeria: A report from population-based cancer registries. *Cancer Epidemiology*, 36(5), pp.e271-e278.

Johnson, K., Miller, A., Collishaw, N., Palmer, J., Hammond, S., Salmon, A., Cantor, K., Miller, M., Boyd, N., Millar, J. and Turcotte, F., 2010. Active smoking and secondhand smoke increase breast cancer risk: the report of the Canadian Expert Panel on Tobacco Smoke and Breast Cancer Risk (2009). *Tobacco Control*, 20(1), pp.e2-e2.

Johnson, R., Chien, F. and Bleyer, A., 2013. Incidence of Breast Cancer With Distant Involvement Among Women in the United States, 1976 to 2009. *JAMA*, 309(8), p.800.

Kamby, C., Andersen, J., Ejlertsen, B., Birkler, N., Rytter, L., Zedeler, K. and Rose, C., 1991. Pattern of Spread and Progression in Relation to the Characteristics of the Primary Tumour in Human Breast Cancer. *Acta Oncologica*, 30(3), pp.301-308.

Klar, A., 2011. Breast cancer predisposition and brain hemispheric laterality specification likely share a common genetic cause. *Breast Disease*, 33(1), pp.49-52.

Kollias, J., Ellis, I., Elston, C. and Blamey, R., 2001. Prognostic significance of synchronous and metachronous bilateral breast cancer. *World Journal of Surgery*, 25(9), pp.1117-1124.

Lakhani, S., Ellis, I., Schnitt, S., Tan, P. and Van de Vijver, M., 2019. *WHO classification of tumours. Breast Tumours*. 4th ed. Lyon: International Agency for Research on Cancer.

Lu, H., Stratton, C. and Tang, Y., 2020. Outbreak of pneumonia of unknown aetiology in Wuhan, China: The mystery and the miracle. *Journal of Medical Virology*, 92(4), pp.401-402.

McPherson, K., 2000. ABC of breast diseases: Breast cancer---epidemiology, risk factors, and genetics. *BMJ*, 321(7261), pp.624-628.

Mohammed, A., Edino, S., Ochicha, O., Gwarzo, A. and Samaila, A., 2008. Cancer in Nigeria: A 10-Year Analysis of the Kano Cancer Registry. *Nigerian Journal of Medicine*, 17(3).

Morris, G., Naidu, S., Topham, A., Guiles, F., Xu, Y., McCue, P., Schwartz, G., Park, P., Rosenberg, A., Brill, K. and Mitchell, E., 2007. Differences in breast carcinoma characteristics in newly diagnosed African–American and Caucasian patients. *Cancer*, 110(4), pp.876-884.

Ngwogu, K., Offiah, S., Ngwogu, A., Ndubuka, G. and Ekperi, O., 2017. Prevalence And Histopathological Pattern Of Breast Cancer Among Patients At Abia State University Teaching Hospital, Aba, South Eastern Nigeria. *International Journal Of Basic, Applied And Innovative Research (IJBAIR)*, 6(4), pp.100 - 106.

Nwafor, C. and Keshinro, S., 2015. The pathology of breast biopsies in a sample of Nigerian patients: Review and analysis. *Ann Afr Surg*, 12, pp.89-94.

Olsson, H. and Ingvar, C., 1991. Left-handedness is uncommon in breast cancer patients. *European Journal of Cancer and Clinical Oncology*, 27(12), pp.1694-1695.

Perkins, C., Hotes, J., Kohler, B. and Howe, H., 2004. Association between Breast Cancer Laterality and Tumor Location, United States, 1994–1998. *Cancer Causes & Control*, 15(7), pp.637-645.

Schedin, P., 2006. Pregnancy-associated breast cancer and metastasis. *Nature Reviews Cancer*, 6(4), pp.281-291.

Senie, R., Rosen, P., Lesser, M., Snyder, R., Schottenfeld, D. and Duthie, K., 1980. Epidemiology of breast carcinoma II: Factors related to the predominance of left-sided disease. *Cancer*, 46(7), pp.1705-1713.

Siegel, R., Naishadham, D. and Jemal, A., 2012. Cancer statistics, 2012. *CA: A Cancer Journal for Clinicians*, 62(1), pp.10-29.

Sughrue, T. and Brody, J., 2014. Breast Tumor Laterality in the United States Depends Upon the Country of Birth, but Not Race. PLoS ONE, 9(8), p.e103313.

Von Fellenberg R. Schweizerische Erhebung uber maligne Tumoren 1933–1935 [Switzerland. Survey of malignant tumors] Bull. des Eidgenoss. Gesundheitsamt. 1940. nr 35, Bern. German

White, A., Nichols, H., Bradshaw, P. and Sandler, D., 2015. Overall and central adiposity and breast cancer risk in the sister study. *Cancer*, 121(20), pp.3700-3708.

Woodward, W., Strom, E., McNeese, M., Perkins, G., Outlaw, E., Hortobagyi, G., Buzdar, A. and Buchholz, T., 2003. Cardiovascular death and second non–breast cancer malignancy after postmastectomy radiation and doxorubicin-based chemotherapy. *International Journal of Radiation Oncology*Biology*Physics*, 57(2), pp.327-335.