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Survival Analysis of Cancer Patients in North Eastern Nigeria from 2004 – 2017 – A Kaplan - Meier Method

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Abstract

BACKGROUND: Cancer is a deadly malignant disease and is prevalent in Sub Saharan Africa. The North East part of Nigeria in particular and the country, in general, are struggling to cope with the increasing burden of cancer and other communicable and non-communicable diseases. The situation is worsened by the ongoing insurgency and terrorist activities in the area.

AIM: The aim of this paper is to present the research findings from a cohort study aimed at the analysis of the estimation of the survivorship time of the real data of cancer patients in the North-eastern part of Nigeria and to establish if the insurgency in the region has contributed negatively to the life expectancy of its inhabitants.

MATERIAL AND METHODS: The record of 1,090 patients from medical records departments of the University of Maiduguri Teaching Hospital (UMTH), located in Maiduguri, the capital city of Borno State in northeast Nigeria was obtained. The record showed patients that were diagnosed and died of one type of cancer or the other from 2004 to 2017. All the cancer cases included in the present study were grouped into sex, age, marital status, occupation, date admitted and date of death/discharge. Descriptive statistics and Kaplan-Meier method were used to analyse the data using SPSS version 23 while Microsoft EXCEL and Minitab 16.0 were used for data cleansing and organisation.

RESULTS: Of the 1,090 patients analysed, 920 (84.40%) experienced the event, i.e. death, while 170 (15.60%) patients were censored. The data were analysed based on the ages and sex of the patients. 50.20% of the patients were of ages 21-50 years. The proportions of patients in this age bracket surviving past 7 days are 75%, while those between ages 80 years and above is 12 days. Others are of survival time of 5 days (ages 0-20 years) and 7 days (51-79 years). Using sex, 75% of the patients' survival time is 7 days in the case of male and 6 days for females. It is safe to say that the survival time for cancer patients of the university the Maiduguri is 6 days and the result reflects the Northeastern part of Nigeria. This is because the hospital is one of few tertiary healthcare facilities in that area and consequently, cancer cases are often referred there.

CONCLUSION: Cancer incidence is high, and the probability of survival reduces as the survival time increases. This is a dire situation in need of urgent intervention from the government, groups and individuals to tackle the scourge of cancer, thereby improving on the life expectancy battered by the ongoing Boko Haram insurgency in that region.

Introduction

Sub Saharan Africa is one of the areas that plagued with the prevalence of non-communicable diseases, especially cancers which is on the increase. Cancer of any type is the most common and lethal malignancies in developing countries like Nigeria. Cancer is an unwelcome guest in every home, and it is seen as a death sentence in Nigeria. Northeast Nigeria is one of the least developed areas of the country, lagging dangerously behind in virtually every development index. The region is notoriously staggering under the weights of poverty [1], insurgency and terrorism [2], [3], [4], hunger and low life expectancy [5], polio, maternal and child mortality [6], [7] and so on.

Cancer is not only prevalent in the North East, Nigeria [8], [9], but to the entire country which are battling to cope with other health challenges such as mental health [10], [11], maternal and child health [12], [13] and HIV AIDS [14]. The high case fatality rate of cancer in Nigeria is due to low level of cancer awareness and screening, late discovery, unhealthy lifestyle, superstitious beliefs, limited or poorly funded healthcare facilities, the dearth of experts in oncology and others to mention but a few.

A patient's journey along a disease pathway can be highly complex and can be impacted by recurrences, co-morbidities, and interventions, to

name a few. Cancer as one of the world's best killer disease, for example, has killed many and left only a few to tell the tale. To disentangle the complexities, we need special kinds of survival models. These enable us to investigate diverse aspects of disease aetiology and explore the impact of risk factors at all stages. Crucially, we can then attempt to communicate risk profiles in many ways, understandable to both patient and clinician, through easily interpretable measures (such as the impact on life expectancy, postponable deaths, survival and transition probabilities). The study of survival of cancer patients will be an immense contribution to the fight against the dreaded disease.

Regard to sound statistical practice, in particular, the use of statistical approaches that provide clinically and peer-reviewed relevant information, will help maximise the potential of molecular markers for the care of cancer patients. Kaplan-Meier (K-M) method otherwise known as the product limit method is a statistical technique used to analyse cancer data. It is applied in analyzing the distribution of the patient's survival times following their recruitment into the study. The analysis expresses this in terms of the proportion of patients still alive up to a given time t, following the recruitment or entry into the study.

This paper aims to present the research findings from a cohort study focused at the analysis of the estimation of the survivorship time of the real data of cancer patients in the North-eastern part of Nigeria and to establish if the insurgency in the region has contributed negatively to the life expectancy of its inhabitants. Also, the result that established the observed relationship between survival time and survival probability is presented. Kaplan-Meier method was used in the survival data analysis of the cancer data, and the findings were discussed extensively.

Material and Methods

Data Collection

The record of 1,090 patients from medical records departments of the University of Maiduguri Teaching Hospital (UMTH), located in Maiduguri, the capital city of Borno State in northeast Nigeria was obtained.

The record showed patients that were diagnosed and died of one type of cancer or the other from 2004 to 2017. All the cancer cases included in the present study were grouped into sex, age, marital status, occupation, date admitted and date of death/discharge.

In survival analysis, follow up periods are calculated from when subjects were enrolled in the study (i.e. date admitted).

Research on cancer is often very interesting because of the high fatality rate of the disease is diagnosed later and or untreated. One of the methods used in the survival analysis in oncology and epidemiology studies is the Kaplan-Meier method (K-M) [15], [16], [17], [18], [19], [20], [21], [22], [23], [24]. K-M method is usually used in conjunction with Cox proportional hazard regression, immunohisto-chemistry, lognormal, hazard ratio, Chi-squared test, log-rank test and so on.

A summary of the use of the K-M method in conjunction with other statistical methods is given in Table 1.

Table 1: Kaplan-Meier and other statistical methods used in the survival analysis of different types of cancer

Type of Cancer	Statistical methods	Cases investigated	Author
Breast	KM, Chi-squared test, Cox regression	207	[25]
Breast	KM, Cox regression	300	[26]
Breast	KM, Cox regression	135	[27]
Gastric	KM	179	[28]
Breast	KM	308	[29]
Breast	KM, Cox regression	139	[30]
Leukemia	KM, Cox regression	527	[31]
Ovarian	KM	81	[32]
Rectal	KM, Cox regression	3786	[33]
Liver	KM, Cox regression	30,954	[34]
Thyroid	KM, Cox regression	12,128	[35]
Gastric	KM, Chi-squared test, Cox regression	4596	[36]
Breast	KM, Cox regression	1391	[37]
Breast	KM, Hazard ratio	10 226	[38]
Prostate	KM, Cox regression	579,608	[39]
kin	KM, Cox regression, Log-rank test	83	[40]

Data Preparation

In preparing the data for Kaplan-Meier survival analysis, each subject (patient) of the data component is mainly characterized by 3 variables: 1) their serial time (in days or years); 2) their status at the end of their serial time (event occurrence or censored); and 3) the study group or stage they are in.

For the computation of survival time curves and probabilities, the serial times for the patients are arranged from the shortest to the longest without regards to when they are recruited into the study as long as left censorship is not encountered. By this move, it can be ensured that all subjects within the group or stage begin the analysis at the same point and all are surviving independently until (event or censor) occurs.

Reasons for adopting the K-M method

The methodology is adopted for the following reasons. Firstly, the main target is to estimate a population survival curve from the sample obtained from the teaching hospital. Secondly, if every subject (patient) is followed until death, the curve may be estimated simply by computing the fraction surviving at each time t. Lastly, Kaplan-Meier curves have gravitated characteristics, which perhaps explains

their wide applicability in medical research as they provide a pictorial depiction of all the raw data, the failure times and the censoring times; yet they also provide a mathematical estimate of the given survival model.

It is glad to note that the data presented in this article did not violate the six assumptions of the K-M method. The assumptions are stated as follows: 1) The data is composed of two mutually exclusive and exhaustive states known as an event or censored; 2) The survival time was clearly defined and accurately measured; 3) The data is right censored; 4) The censoring and the event are independent. This is vital since the efficiency of the K-M method depends on the analysis of observed data; 5) No trend was observed in the data; 6) Right censoring is similar in all the groups (sex and age).

Data Processing

Raw data are stored in MS EXCEL format using actual calendar date and time. During analysis, serial time may be automatically calculated, and this is used in curve construction and data analysis. The first step in the preparation of K-M analysis involves the construction of a table using Minitab or Excel spreadsheet or in SPSS containing the three key elements required for input. These are: 1) serial time, 2) status at serial time (1 = Alive, 0 = Death) and 3) age group.

Results

These were performed using SPSS version 23.0. Data were reported by sex, age, marital status, occupation, date of admission and date of death/discharge. A descriptive analysis of the data was carried out, and each character was described by frequencies and percentages. Kaplan-Meier analyses were conducted to mainly estimate overall survival rates of the various types of cancer. The survival time of a patient is referred to the number of months or days (duration) from the date of diagnosis of cancer to the date of the patient died or last contact (censored) or the date of the end of the study for patients who were still alive or date of loss to follow-up (censored). The differences in survival between the stages were compared by the log-rank test. A two-tailed p-value of < 0.05 was considered as statistically significant.

Descriptive Statistics

Data on 1,090 cancer cases were gathered of which 478 (43.9%) were male, while 612 (56.10%) were female, shown in Table 2.

Table 2: The sex distribution of the patients

Sex	Frequency	Per cent	Cumulative Percent
Male	478	43.9	43.9
Female	612	56.1	100.0
Total	1090	100.0	

From Table 3, it can be seen that 50.20% of the patients were between the ages of 21-50 years old, 17.70% were of ages below 20 years old, 29.9% were between ages 51-79 years while 1.9% were 80 years and above.

Table 3: The age distribution of the patients

	Age	Frequency	Percent	Cumulative Percent
Valid	0-20	193	17.7	17.8
	21-50	547	50.2	68.1
	51-79	326	29.9	98.1
	80 & Above	21	1.9	100
	Total	1087	99.7	
Missing		3	0.3	
Total		1090	100	

A group of 227 (20.8%) of the patients are single, 832 (76.3%) are married, 12 (1.1%) are widowed, and 19 (1.7%) are missing values, shown in Table 4.

Table 4: Marital status of the patients

Marital status	Frequency	Per cent
Single	227	20.8
Married	832	76.3
Widow/Widower	12	1.1
Missing	19	1.7
Total	1090	100

Of the 478 females, 40.1% were housewives. 10.8% of the patients were children while 13.9% were civil servants. The details of the other occupation are given in Table 5.

Table 5: the Recorded occupation of the patients

	Occupation	Frequency	Percent	Cumulative Percent
Valid	Applicant	12	1.1	1.1
	Soldier	4	0.4	1.5
	Banker	1	0.1	1.6
	Bricklayer	1	0.1	1.7
	Business Man	71	6.5	8.4
	Butcher	1	0.1	8.5
	Civil Servant	151	13.9	22.7
	Caterer	1	0.1	22.7
	Cattle Rearer	5	0.5	23.2
	Child	118	10.8	34.3
	Clergy	1	0.1	34.4
	Contractor	1	0.1	34.5
	Police Officer	4	0.4	34.9
	Driver	11	1	35.9
	Politician	3	0.3	36.2
	Farmer	97	8.9	45.3
	Retired	19	1.7	47.1
	Fisherman	2	0.2	47.3
	Scholar	5	0.5	47.7
	House Wife	437	40.1	88.8
	Security Man	4	0.4	89.2
	Mechanic	2	0.2	89.4
	Student	85	7.8	97.4
	Tailor	5	0.5	97.8
	Teacher	8	0.7	98.6
	Technician	2	0.2	98.8
	Widow/Widower	13	1.2	100
	Total	1064	97.6	
Missing	System	26	2.4	
Total		1090	100	

The weird occupations seen in Table 5 can be attributed to high illiteracy of the patients and poor record keeping by the staff of the hospital. Finally, it

can be seen from Table 6, that 170 (15.6%) were alive and 920 (84.4%) were dead after admission in the hospital.

Table 6: End status of the patients

Status	Frequency	Per cent	Cumulative Percent
Dead	920	84.4	84.4
Alive	170	15.6	100
Total	1090	100	

Kaplan-Meier Results

The data presented in this subsection are from the K-M analysis. These are given as: case summary for age (Table 7), case summary for sex (Table 8), means and medians for survival time for age (Table 9), means and medians for survival time for sex (Table 10), overall comparison tests for the age (Table 11) and overall comparison tests for the age (Table 12).

Table 7: Case processing summary for age

Age	Total N	N of Events	Censored	
			N	Per cent
0-20	193	150	43	22.30%
21-50	547	473	74	13.50%
51-79	326	274	52	16.00%
80 & Above	21	20	1	4.80%
Overall	1087	917	170	15.60%

Table 7 displays the age of the cancer patients (categorised into age groups from 0-20 years, 21-50 years, 51-79 years and 80 years and above), the total number of patients in each age group, number of patients experienced events, and censored patients. Age 0-20 years has a total number of 193 patients with 150 been number of events and 43 (22.3%) as censored patients, age 21-50 has a total number of 547 patients with 473 patients that have experienced the event and 74 (13.5%) as censored patients, age 51-79 has a total number of 326 patients with 274 patients that have experienced the event and 52 (16.0%) as censored patients and age 80 and above has a total number of 21 patients with 20 total number of events and 1 (4.8%). It was noted that age group 21-50 has the highest number of events followed by 51-79 and age group 80 and above with the lowest number of events.

Table 8: Case processing summary for sex

Sex	Total N	N of Events	Censored	
			N	Per cent
Male	478	401	77	16.10%
Female	612	519	93	15.20%
Overall	1090	920	170	15.60%

Table 8 displays the sex of patients diagnosed with cancer, the total number of patients for each sex group, number of patients experienced events, and censored patients. Four hundred seventy-eight male patients were admitted with 401 been number of events and 77 (16.1%) as censored patients while there were a total of 612 females with 519 patients that have experienced the event and 93 (15.2%) as censored patients Clearly, the male patients have the lowest number of events.

Table 9: Means and medians for survival time for age

AGE	Mean				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
0-20	26.035	3.225	19.715	32.356	14	1.949	10.18	17.82
21-50	30.89	2.414	26.159	35.622	16	1.488	13.084	18.916
51-79	35.808	4.234	27.509	44.107	19	1.182	16.683	21.317
80 & Above	29.651	6.487	16.936	42.366	20	4.577	11.028	28.972
Overall	31.41	1.839	27.807	35.014	17	0.864	15.306	18.694

Table 9 gives a quick quantitative comparison of the typical survival times to effect for each of the age groups. The median survival time is calculated as the smallest amount of survival time for which the survivor function is less than or equal to 0.5.

The overall median survival time (i.e. the time at which the survival probability is 50% or 0.5) is 31 days. In other words, for cancer patients in the North, the chance of living beyond 31 days is 50%. The median survival time for ages 0-20 was 26 days, 30 days for ages 21-50, 35 days for age 51-79 and ages 80 and above was 29 days. These clearly show that the chance of living beyond 26 days, 30, 35 and 29 for ages 0-20, 21-50, 51-70 and above 80 years respectively after being admitted/diagnosed with the disease is 50%.

It can be seen that the higher the estimated mean time, the greater the chances of survival. This goes to show that ages 51-79 has the highest chance of survival while ages 0-20 years has the least chance of survival.

The log-rank test can be applied if the confidence limits do not overlap between the given levels. Clearly, from Table 9, there is no overlap between ages in the confidence intervals; hence differences in effect on time to an event can be inferred using the log-rank test.

Table 10: Means and medians for survival time for sex

Sex	Mean				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
Male	32.947	2.984	27.099	38.795	19	1.236	16.578	21.422
Female	30.184	2.286	25.703	34.665	16	1.33	13.394	18.606
Overall	31.355	1.833	27.762	34.948	17	0.852	15.331	18.669

From Table 10, it can be seen that the estimated mean time until death is 32 days for male, 30 days for females, which shows that females have a slightly increased chance of survival than males.

The median survival time for a male is 19 days while that of females is 16 days. These clearly show that the chance of living beyond 19 and 16 days for males and females, respectively for cancer patients in the Northeastern part of Nigeria is 0.5 after being diagnosed with the disease.

Clearly, from Table 10, there is a lot of overlap in the confidence intervals; hence it is unlikely that there is much difference in the average survival time.

Table 11: Overall Comparison Tests for the age

Test of equality	Chi-Square	Df	Sig.
Log Rank (Mantel-Cox)	3.812	3	0.283
Breslow (Generalized Wilcoxon)	6.845	3	0.077
Tarone-Ware	5.622	3	0.131

Table 11 is the test of equality of survival distributions for the different levels of age. The significance values of the tests (0.283, 0.077, 0.131) are all greater than 0.05. The interpretation of this is the acceptance of the null hypothesis means that there is no significant evidence of a difference in the observed survival times for the categories of age considered.

Table 12: Overall Comparison Tests for the sex

Test of equality	Chi-Square	Df	Sig.
Log Rank (Mantel-Cox)	1.440	1	0.230
Breslow (Generalized Wilcoxon)	3.573	1	0.059
Tarone-Ware	2.814	1	0.093

Table 12 is the test of equality of survival distributions for the different levels of sex. It shows that the significance values of the tests (0.230, 0.059 and 0.093) are all greater than 0.05. The interpretation of this is the acceptance of the null hypothesis implies that there is no significant evidence of a difference in the observed survival times for the categories of age considered.

Although, females have a slightly increased chance of survival even though, as inferred from the log-rank test, sex is not a barrier to death.

Plots of the Survival Functions and survival probability estimation

The survival curves (Figures 1 and 2) give a visual depiction of the life tables, the horizontal axis represents the time to the event, and the vertical axis shows the estimated probability of survival.

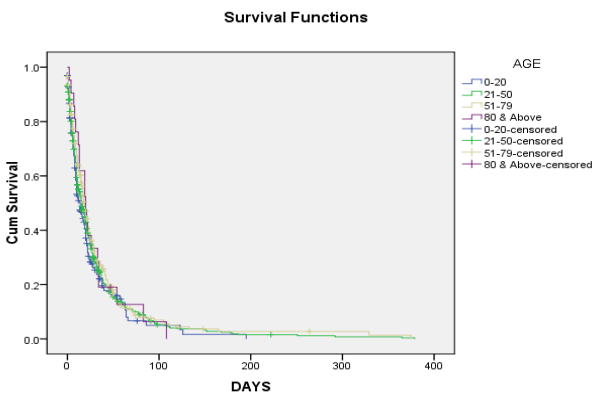

Figure 1: Kaplan-Meier survival plot for the ages

In this plot, drops in the survival curve occur whenever the patients experience the event

Also, the summary of survival probability estimate with the survival time for the age and sex are presented in Table 13 and 14 respectively.

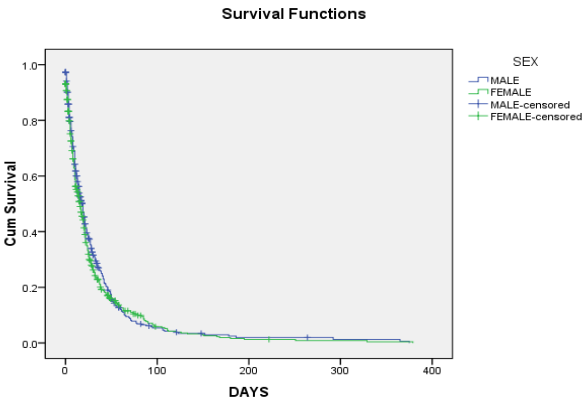

Figure 2: Kaplan-Meier survival plot for the sex

From Table 13, the proportion of subjects or patients surviving past 5 days is 75%, the proportion of subjects or patients surviving past 14 days is 50% and the proportion of subjects or patients surviving past 32 days is 25% for age 0-20 years.

Table 13: Survival probability estimate with the survival time for age

Age	25		50		75	
	Estimate	Std. Error	Estimate	Std. Error	Estimate	Std. Error
0-20	32	4.755	14	1.949	5	0.915
21-50	35	2.56	16	1.488	6	0.561
51-79	40	3.279	19	1.182	7	0.97
80 & Above	34	4.799	20	4.577	12	2.588
Overall	35	1.815	17	0.864	6	0.443

Note; Survival time is given in days (D). This can easily be seen in Figure 1.

The proportion of subjects or patients surviving past 6days is 75% and the proportion of subjects or patients surviving past 16 days (which is the median survival time) is 50% and the proportion of subjects or patients surviving past 35 days is 25% for age 21-50 years.

The proportion of subjects or patients surviving past 7 days is 75%, the proportion of subjects or patients' surviving past 19 days is 50% and the proportion of subjects or patients surviving past 40 days is 25% for age 51-79 years.

The proportion of subjects or patients surviving past 12 days is 75%, the proportion of subjects or patients surviving past 20 days is 50% and the proportion of subjects or patients surviving past 34 days is 25% for ages 80 years and above.

From this analysis, the probability of survival reduces as the survival time increases.

From Table 14, the proportion of subjects or patients surviving past 7 days is 75%, the proportion

of subjects or patients' surviving past 19 days is 50% and the proportion of subjects or patients surviving past 39 days is 25% for Males.

Table 14: Survival probability estimate with the survival time for sex

Sex	25% Estimate		50% Estimate		75% Estimate	
	Estimate (days)	Std. Error	Estimate (days)	Std. Error	Estimate (days)	Std. Error
Male	39	2.69	19	1.236	7	0.829
Female	32	2.048	16	1.33	6	0.52
Overall	35	1.816	17	0.852	6	0.44

Note; Survival time is given in days (D). This can easily be seen in Figure 2.

The proportion of subjects or patients surviving past 6days is 75% and the proportion of subjects or patients surviving past 16 days (which is the median survival time) is 50% and the proportion of subjects surviving past 32 days is 25% for Females.

Also, from this analysis, the probability of survival reduces as the survival time increases.

Discussion

A good glance at the results shows most patients died the same day or few days to date of admission. Hence, it was not a surprise that the analysis shows overall survival time of 6 days for 75% of patients with cancer at the University Teaching Hospital, Maiduguri. This is a far-cry to survival data obtained in another part of the country. The study shows that over 84% of the cancer cases died. We have more of the cases for women than for men. Over 40% of the cases for female were those who reported their occupation as housewives. Over 50% of the cases were age 21-50 years old. Only 1.9% of the cases were of ages 80years and above.

Following the result of the research, it is obvious that we have a major problem with the management of cancer in the region under review and Nigeria in general. The reasons for this might not be a difference of the below points.

The Northeast part of Nigeria is one of the poorest parts of Nigeria. Years of corruption and lack of investment in the health facilities have contributed to a near collapse of the health facilities of the region in particular and Nigeria in general. Poverty, illiteracy and superstition are contributory factors why diseases like cancer are endemic in the area. This is exacerbated by the ongoing Boko Haram insurgency and herdsman attacks. The insurgency has added to the already strain on the few available health facilities in the area and drastically reduction to access to health care. The effect is not limited to cancer, but other illness such as HIV AIDS epidemic, a cholera outbreak and others. It can be noted that the University of Maiduguri teaching is the only major tertiary health facility that covers Borno, Yobe, Gombe and Taraba states, an area and population that is greater than London, United Kingdom.

The precarious political and social factors are drivers to the culture of patients reporting of their cases very late. Most cancers have different stages, one, two, three and four. While stage one and two can achieve a cure, stage three and four are usually advanced where you no longer talk about radical treatment but palliative treatment to see how you can prolong the patient's life and improve the quality of life. The data for this research did not include the stage of cancer upon admission at the hospital, we suggest most cases to be at stage three and four going by the time to the event.

Most patients do not go for screening; they mostly consult roadside chemists, extreme cases among the people approach churches, Muslim clerics and herbalist.

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