Transactions of the Nigerian Association of Mathematical Physics
***Volume 11, (January - June, 2020 Issue*), pp151 – 156**

SURVIVAL ANALYSIS OF PNEUMONIA FATALITY ON INFANTS IN IRRUA SPECIALIST TEACHING HOSPITAL, EDO STATE, NIGERIA

[1]Edosomwan O.S. and [2]Izomo E.J.

Department of General Studies/Statistics, Edo State Polytechnic, Usen, Edo State, Nigeria

Abstract

The research studied the epidemiological aspects and identified risk factors for incidence and case fatality of Pneumonia among children aged 0 -5 years treated as in-patient at Irrua Specialist Teaching Hospital, Irrua Edo Central Senatorial District of Edo State, Nigeria. The statistical analysis procedure was carried out using survival analysis; a statistical technique that measures the number of Patients survived or saved after intervention over a period of time with the Kaplan-Meier estimator and curves of survival probabilities drawn. Statistical difference among the data collected and sex of the in-patients were compared and checked using the Log-rank test. Results obtained from the survival distribution analysis from Irrua Specialist Teaching Hospital, Irrua, reveals that when the number of days (time) was 70.8days the chances of survival was 0.95 but as the days (time) increases to 197.1 the chances of survival declined rapidly to 0.5 with a statistical significant difference of P Value = 0.03< 0.05.Similarly, mortality trend indicates that survival probabilities declined with the passage of time. This is at variance with the projected achievement of the 4th Millennium Development Goals (MDG 4 Target 5), hence adequate measures should be taken in eradicating or reducing this scourge to the barest minimum so as to achieving the United Nations SDG'S Sustainable Development Goal 3 which stipulates good health and well-being for all at all ages by 2030.Keywords: Survival, Pneumonia, Log-Rank, Kaplan-Meier, Mortality.

1. INTRODUCTION

This research examines Pneumonia fatality in infants 0-5years old in Edo Central Senatorial District of Edo State, Nigeria, with Irrua Specialist Hospital Irrua as a case study using Survival analysis.

Nigeria is one of the nation's globally with high mortality in children [1]. Mortality refers to a death that occurs within a population at a given period of time. Infant mortality is the number of infants' death occurring within one year after birth per one thousand live births for the given year. Universally, childbirth event attracts celebration but due to the high risk in childbirth delivery encountered by both mother and child, the tragedy of deaths does occur especially during the first few days [2]. Annually, Nigeria records one quarter of babies born not surviving within their first 28-30 days and before their fifth birthday [3]. This unhealthy trend has become a matter of great concern, calling for concerted approach from all and sundry. Pneumonia against the natural believe, is not caused by exposure to cold weather rather by a common bacteria known as *streptococcus pneumoniae* [4]. Pneumonia is a leading cause of morbidity and mortality in children 0-5 years old responsible for approximately one of every five under-five mortality cases in Nigeria [5].

Survival analysis is commonly used in clinical trials and biomedical sciences. It is a statistical method in which the response variable is time. Survival analysis is generally defined as a set of methods for analyzing data where the outcome variable is the time until the occurrence of an event of interest, the event can be death or an occurrence of a disease [6]. Survival analysis incorporates various statistical methods specific to data on time until an event of interest occurs. The event is often death, giving rise to the phrase "survival analysis" [7].The dependent variable or response is the waiting time until the occurrence of a well-defined event of death [8].The conventional end-point in survival analysis is death. Statistical survival analysis shows the magnitude of the expected increase or decline in mortality from clinical trials [9].. Survival analysis is used to investigate time-to-event outcomes which are common in medical research as they offer more information than simply whether or not an event occurred. Two functions that are dependent on time in survival analysis are the survival function and the hazard function [10]. They are the key concepts in survival analysis for describing the distribution of event times. The survival function gives for every time, the probability of surviving taking into account cases of survivorship, while the hazard function gives the potential that the event of death will occur per time unit given that an individual has survived up to the specified time. For efficiency and more robust application in survival analysis, a non-parametric technique known as the Kaplan-Meier survival method was used in this study. The Kaplan-Meier nonparametric method is widely used in survival analysis than others.

The nonparametric estimator of the survival function known as the Kaplan - Meier method is used to estimate the proportion surviving by any time. It is used to obtain univariate descriptive statistics for survival data [11].The Kaplan - Meier estimator method of nonparametric statistics is also called a nonparametric maximum likelihood estimator used for estimating survival probabilities. The important assumption of the Kaplan-Meier survival function is that the distribution of censoring times is independent of the exact survival times and it accommodates no censoring. A data sample is said to be censored when values of the variable are not observed for some of the items in the sample. Patients may have censored survival time if death or recurrence has not yet occurred and this could happen when they drop out of the study or stop attending clinics for

Correspondence Author: Izomo E.J., Email: Julius_izomo@yahoo.com, Tel: +2348032278713, +2348034474015

follow up. Similarly, certain individuals may drop out from the study or be lost to follow up. Each of these cases is said to be censored while non-censored data are cases where the data entry is complete and the patients completed the treatment. The Kaplan-Meier estimator is assessed by measuring the number of subjects survived or saved after intervention over a period of time. The time starting from a defined point to the occurrence of a given event for example death is called the survival time and the analysis of group data as survival analysis. To test for overall differences between estimated survival of two or more groups of subjects, such as males versus females, or treated versus untreated, survivals or deaths, the log rank test is used. The log rank test is a method used for comparing the Kaplan - Meier estimate for each group of subjects [12].

The level of mortality in any country is an important indicator of the health status of a population and its overall development which tells the quality of life and standard of living [13].An increase in mortality rate shows a decline in the health status of a population and this is largely attributable to availability of health care, while a reduction in mortality signifies a tremendous increase in health care delivery services [14]. This is a major challenge in the Nigerian health care sector hence a number of preventable diseases lead to death most especially in infants. Child mortality is associated with Categories of acquired ailments of infectious diseases of which pneumonia has claimed the lives of many before their fifth birthday [15].This poses a great danger for our children because with global immunization advocacy this infectious disease can be prevented. The survival of our children basically is dependent on adequate health care facilities and the absence of this factor poses a health risk and hazards to infants who are vulnerable to this disease[5].
Children living in rural settings stand greater risk of not surviving than those in urban settings due to shortfalls in health programmes. If not given the needed attention by government policies on health care, it will lead to a drastic increase in morbidity and mortality [16].Unhygienic environments are breeding grounds for germs and bacterial infections which easily contaminate children[4]. In Nigeria most poor people live and give birth in unsafe and unclean environments making their babies more vulnerable to childhood killer diseases contacted from germs and bacterial infections. Poor people give birth to more children than the rich and the natural belief amongst them is that “God Almighty will take care of them” putting them at the probability of survival or death. Pneumonia usually starts when the germs is breathed into the lungs. The bacteria get into the body either through the mouth or other openings in the body and it contaminates the blood and respiratory apparatus. This makes it hard for the lungs to fight the infection. The likelihood of contacting the disease comes after having a cold or flu. The signs and symptoms include fever, chills, cough, shortness of breath and fatigue. These symptoms are followed by coughing out mucus sputum which is rusty, greenish or tingled with blood, sharp chest pain, shaking, teeth chattering, increased respiratory rate, nausea, vomiting, weakness of the body and diarrhoea[4]. Based on these challenges, this research introduces a statistical approach to the incidence of pneumonia through the use of survival analysis to ascertain the mortality rate. The overall aim of this study is to carryout statistical analysis on the incidence of pneumonia on infant mortality in Edo Central Senatorial District of Edo State, Nigeria. The Specific objectives are to determine the incidence rate of pneumonia in infants, its occurrence and impact, whether it is on the increase or decrease over the given time period and to investigate long term survivals of patients admitted to a public hospital with diagnosis of Pneumonia in Edo Central Senatorial District of Edo State, Nigeria.

2. MATERIALS AND METHODS

The methodologies used in this research study are the nonparametric estimator of the survival function known as the Kaplan-Meier and the Log Rank test. The Kaplan-Meier method is a nonparametric estimator also called “Product Limit Estimate” which involves computing of probabilities of occurrence of event at a certain point of time. It is widely used in clinical trials because of its versatility in estimating a population survival curve from a sample. In instances where every patient is followed until death, the curve may be estimated simply by computing the fraction surviving at each time. One unique feature of the Kaplan-Meier method is that it allows censoring and non-censoring. That means it allows estimation of survival over time even when patients drop out or are studied for different length of time. It works for each interval as survival probability is calculated by the number of patients surviving divided by the number of patients at risk, did not survive or dropped out. The Kaplan-Meier and the Log Rank test is introduced in this study because they are more popular in survival analysis due to its simplicity as well as the assumption of free property. It is used to estimate conditional probabilities at each time an event occurs and taking the product limit of the probabilities to estimate the survival rate at each point in time.
To generate results needed in this study R-Statistical software is implemented.
For large samples the Kaplan Meier method is approximately normally distributed with mean s(t) and variance is estimated by the Green wood's estimator formula.
The Kaplan - Meier estimator of the survivorship function or survival probability
$s(t) = \rho(T > t)$ is defined

$$\hat{S}(t) = \prod_{t_i \le t}\left(1 - \frac{d_i}{R_i}\right) \quad (1)$$

where
ŝ(t) = survivorship function.
$\prod_{t_i \le t}$ = product sum of ordered time.
t_i= *ith* ordered follow-up time
d_i = number of deaths at *ith* ordered time
R_j = number of uncensored observation at *ith* ordered time
R_i = number of subjects at risk at *ith* ordered time
Given the Kaplan-Meier survival estimator the Green wood’s variance estimator formula is

$$\hat{V}\left[\hat{S}(t)\right] = \hat{S}(t)^2 \sum_{t_{(i)} \le t} \frac{d_i}{R_i(R_i - d_i)} \quad (2)$$

the purpose here is to derive two approximate 95% confidence intervals for *s(t)* for a fixed *t*, or in general, $(1-\alpha)\times 100\%$

$$\text{Lower} = \hat{S}(t) - 1.96.\hat{S}(t)\sum_{t_i \le t}\sqrt{\frac{d_i}{R_i(R_i - d_i)}} \quad (3)$$

Upper= $\hat{S}(t)+1.96\hat{S}(t)\sum_{t_i\le t}\sqrt{\frac{d_i}{R_i(R_i-d_i)}}$ (4)

Given the Kaplan - Meier survival estimator and Green wood's variance estimator we can use a Z statistic to compare (test) the probability of survival beyond a certain time, for two groups of subjects.

$H_o: S_1(t_o)=S_2(t_o)$ (5)

$H_1: S_1(t_o)\neq S_2(t_o)$ (6)

where:

H_o : there are no differences in survival distributions

H_1 : there are differences in survival distributions

Comparing survival function

$$Z=\frac{\hat{S}_1(t_o)-\hat{S}_2(t_o)}{\sqrt{\hat{V}\left[\hat{S}_1(t_o)\right]+\hat{V}\left[\hat{S}_2(t_o)\right]}} \quad (7)$$

where

Z = Z test statistics

$\hat{S}_1(t_o)$ = survival function of group 1

$\hat{S}_2(t_o)$ = survival function of group 2

$\hat{V}$ = variance of the survival function

Log Rank Test:

It is a confirmatory test used to compare the entire survival function for two groups of subjects. It is one of the most popular tests for comparing two survival distributions. It is more powerful than an analysis based simply on proportions. The Log rank test is a comparing survival function used for each expected observed number of deaths in each group. It is used to compare the total expected ϵ_j death in each group to the total observed death O_j. It is a type of Chi square test used to test overall difference in survival analysis

$$\varepsilon_{ij}=\left(\frac{R_{1j}}{R_{1j}+R_{2j}}\right)(d_{ij}+d_{2j}) \quad (8)$$

where for each *j* defined

ε_{ij} = expected number of deaths

d_{1j}= number of deaths in group 1

d_{2j}= number of deaths in group 2

R_{1j} = is the number at risk in set group 1

R_{2j} = is the number at risk in set group 2

The Log Rank Test Statistic is

$$\chi^2=\sum_{i=1}^{2}\frac{(O_1-E_1)^2}{\hat{v}_1} \quad (9)$$

$$\hat{V}_1=\sum_{j=1}^{k}\frac{R_{1j}R_{2j}(d_{ij}+d_{2j})(R_{ij}+R_{2j})-d_{ij}-d_{2j}}{(R_{ij}+R_{2j})^2(R_{ij}+R_{2j}-1)} \quad (10)$$

$H_o: S_1(t)=S_2(t)$ for all *t* (11)

$H_1: S_1(t)\neq S_2(t)$ for some *t* (12)

where

χ^2 = chi square of observed deaths

$\hat{V}_1$ = variance of the number of deaths and the number at risk

H_o = there are no differences in the survival function of the two groups

H_1 = there are differences in the survival function of the two groups

R-statistical Software

The statistical package used in this research study is the R-statistical software.

R is a free software environment for statistical computing and graphics. The R software contains built in functions for a large number of statistical procedures, linear and generalized linear models, time series analysis, classical parametric and nonparametric test. Its package, "*survival*" is used for survival analysis.

RESULTS AND DISCUSSIONS

Data used in this study are of secondary source and obtained from Irrua Specialist Teaching Hospital, Irrua, Edo State, Nigeria. Data collected covers the period of 2007-2016.The data collected is on reported cases of children treated, survived and did not survive of Pneumonia for 2007-2016.To facilitate easy analysis, R-Statistical software was implemented in the study.

Adopting notation of time normalization, data presented are analyzed based on the estimates of proportion surviving by any time using the Kaplan-Meier methodology as shown in Tables 1. The Log Rank Test was used to compare curves from different groups showing the mortality trend in the hospital under consideration as shown in Figures 1.

Table 1: Time and Incidence Table for Irrua Specialist Teaching HospitalIrrua (ISTH).

Year	Survival	Death	surv-death ratio (ϖ)	status	Sex	Time(days)
2007	292	18	16.222	1	1	112.500
2008	266	15	17.733	1	1	102.914
2009	260	24	10.833	1	1	168.462
2010	255	25	10.200	1	1	178.922
2011	215	33	6.515	0	1	280.116
2012	206	45	4.578	0	1	398.665
2013	239	44	5.432	0	1	335.983
2014	205	31	6.613	0	1	275.976
2015	235	43	5.4651	1	1	282.284
2016	208	26	8.000	0	1	228.125
2007	361	14	25.786	1	2	70.776
2008	281	18	15.611	1	2	116.904
2009	257	25	10.280	1	2	177.529
2010	182	27	6.741	0	2	270.742
2011	250	27	9.259	1	2	197.100
2012	190	24	7.917	0	2	230.526
2013	309	24	12.875	1	2	141.748
2014	234	27	8.667	1	2	210.577
2015	246	24	10.250	1	2	162.222
2016	249	31	8.032	0	2	227.209

Time normalization was used here to transform the Data. Covariate of sex 1 represents males while sex 2 represents females. Time factor in survival analysis have varying values not fixed. Since our time is for all the years, transformation of variables and effects were carried out using penalty term for optimum performance. Time and incidence table for Irrua Specialist Teaching Hospital, Irrua, Edo State, were obtained by transformation technique and was generated using R-Statistical fit *xlab* for patient time (years/days) and *ylab* for survival probabilities. The Kaplan-Meier curve estimate percentiles of the survival distribution with a primary interest being the median surviving time and mean time in years**.** The survival distribution for ISTH showing the confidence interval, standard error, the survival rate, the number at risk at a particular event is displayed in the following Table 2.

TABLE 2: Survival Distribution ForIrrua Specialist Teaching Hospital, Irrua, Edo State.

Time	n.risk	n.event	Survival	std.err	lower.95%.CI	upper.95%.CI
70.8	20	1	0.95	0.0487	0.859	1
102.9	19	1	0.9	0.0671	0.778	1
112.5	18	1	0.85	0.0798	0.707	1
116.9	17	1	0.8	0.0894	0.643	0.996
141.7	16	1	0.75	0.0968	0.582	0.966
162.2	15	1	0.7	0.1025	0.525	0.933
168.5	14	1	0.65	0.1067	0.471	0.897
177.5	13	1	0.6	0.1095	0.42	0.858
178.9	12	1	0.55	0.1112	0.37	0.818
197.1	11	1	0.5	0.1118	0.323	0.775

From Table 2 it is observed that at days (time) 70.8 the survival probability was 0.95 but as the days (time) increases to 197.1, the chances of survival drops to 0.5 indicating that as time progresses the probability of survival decreases drastically as can also be seen in Figures 1 and 2.The Survival probability for this data is presented in Table 3.

TABLE:3 SURVIVAL PROBABILITY

Year	Sex	Reported cases	Number of survivals	Survival probability
2007	1	310	292	0.941935
2008	1	281	266	0.946619
2009	1	284	260	0.915492
2010	1	280	255	0.910714
2011	1	248	215	0.866935
2012	1	251	206	0.820717
2013	1	283	239	0.844522
2014	1	236	205	0.868644
2015	1	278	235	0.845323
2016	1	234	208	0.888888
2007	2	375	361	0.962666
2008	2	299	281	0.939799
2009	2	282	257	0.911347
2010	2	209	182	0.870813
2011	2	277	250	0.902527
2012	2	214	190	0.887850
2013	2	333	309	0.927927
2014	2	261	234	0.896551
2015	2	270	246	0.911111
2016	2	280	249	0.889285
		5,485	4940	0.900638

For each time interval, Survival probability is the proportion of patients that survive beyond a specified time. These estimates of Survival probability are frequently referred to as reliability estimates. It is calculated as the number of patients surviving divided by the number of patients at risk. The Survival probability is 0.900638<1.00.This shows that the probability of survival within the given period of time is low hence the increase in mortality. The Survival time follows an exponential distribution with mean time of 160T (2.91years) and a median value 165.35T (2.26years) with its 95% Confidence Interval (C.I 2.147-2.373). This is shown in Table 4.

Table 4: Survival Time for ISTH.

Mean Time	C.I at 95%	Median Time 50% Percentile	P. Value Sig. Difference
160T (2.91years)	2.147-2.373	165.35T (2.26 years)	P= 0.03 < 0.05

As the length of time increases, survival probability drops as shown in Figures 1 and 2 below. The Kaplan-Meier estimate is in solid line and its 95% confidence intervals are in dotted lines. It was generated using R function plot(fit, *xlab*=”Patient time (years)”, *ylab*=”survival probability”).

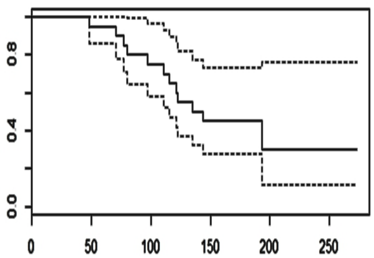

Figure 1:*The Kaplan -Meier Curve of pneumonia patients in* ISTH

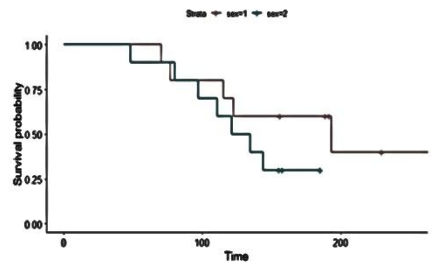

Figure 2 : Survival time of patients with sex as covariate [1 = Male 2 = Female]

From Figure 2 the orange coloured solid line represents the Male sex covariates in group 1 while the green line represents the Female sex covariates in group 2.The trend shows that the proportion of under-five Male Children not surviving as a result of pneumonia is higher than that of the Females in the transformed time. The Kaplan-Meier estimate was used to examine the model fit. The curve checks whether the observed number of events is significantly different from the expected number of events in groups differentiated by risk scores. When reading the curves, the horizontal lines represents the survival duration for the interval while the height of the vertical lines shows the change in cumulative probability and censored observation are indicated by tick marks which helps to reduce the cumulative survival between the intervals. It should be noted that an interval is terminated by an event. To test for statistical significance, the Log Rank statistics test was adopted as presented in Table 5.

TABLE 5: Log Rank Test of Patients in ISTH.

	N	Observed	Expected	$\frac{(0-E)^2}{E}$	$\frac{(0-E)^2}{V}$
Sex = Male	10	5	6.87	0.509	1.28
Sex = Female	10	7	5.13	0.681	1.28

Chisquare = n-1 degree of freedom, p = 0.03

The logrank test is the most commonly used statistical test for comparing the survival distributions of two or more groups (such as different treatment groups in a clinical trial). According to the log rank test of patients in ISTH,there is statistical significant evidence of the survival distributions between the male and female respondents with (*P-value =0 .03).*Since0.03<0.05 the null hypothesis is rejected.

MEAN SURVIVAL RATE

The Mean Survival Rate is the percentage of people in a study or treatment group still alive for a given period of time after diagnosis. It is a statistic that describes how long an average person will survive for a particular amount of time.

$$MSR = \frac{\text{Total number of deaths in a defined time period}}{\text{Total number of persons in the population at the beginning of the time period 2007-2016 in the treatment group}} \times \frac{100}{1}$$

TABLE 6: MEAN SURVIVAL RATE FOR MALE PATIENTS IN ISTH, IRRUA 2007-2016

Year	Sex	Number Of Persons Treated	Number of Deaths	MSR (%)
2007	1	310	18	5.80645
2008	1	281	15	5.33807
2009	1	284	24	8.45070
2010	1	280	25	8.92857
2011	1	248	33	13.30645
2012	1	251	45	17.92828
2013	1	283	44	15.54770
2014	1	236	31	13.13559
2015	1	278	43	15.46762
2016	1	234	26	11.11111
		2,685	304	11.32216

TABLE 7: MEAN SURVIVAL RATE FOR FEMALE PATIENTS IN ISTH, IRRUA 2007-2016

Year	Sex	Number Of Persons Treated	Number of Deaths	MSR (%)
2007	2	375	14	3.73333
2008	2	299	18	6.02006
2009	2	282	25	8.86524
2010	2	209	27	12.91866
2011	2	277	27	9.74729
2012	2	214	24	11.21495
2013	2	333	24	7.20720
2014	2	261	27	10.34482
2015	2	270	24	8.88888
2016	2	280	31	11.07142
		2,800	241	8.60714

TABLE 8: ISTH IRRUA, MSR

SEX	MSR	N (2007-2016)	$\overline{\text{MSR}}$
MALE	11.32216	10	1.132216
FEMALE	8.60714	10	0.860714

In comparism, the mean survival rate at ISTH, Irrua for male is 1.132216> 0.860714within the given time period. This goes to indicate that the mean survival rate (Bar) proportion of Patients surviving is higher in ISTH Irrua male infants than females.

CONCLUSION

The Kaplan-Meier survivorship estimates was used to examine the model fit. The curve checks whether the observed number of events is significantly different from the expected number of events in groups differentiated by risk scores. When reading the curve; horizontal lines represent survival duration for the interval; an interval is terminated by an event, the height of vertical lines shows the change in cumulative probability and censored observations are indicated by tick marks, which help reduce the cumulative survival between intervals. Results obtained from data analyzed for ISTH, Irrua, showed that at 70.8 days (time) the chances of survival was 0.95 but with the length of time at 197.1 the chances of survival decreases to 0.5. The log rank test shown in Table 4states there was statistical significant difference ($P = 0.03 < 0.05$) between male and female respondents negating the null hypothesis. The survival time for the hospital follows an exponential distribution with mean time of (2.19years) for ISTH The median survival time was estimated to be 165.35T (2.26years, with its 95% confidence interval 2.147-2.373 years).

Data analyzed and the results obtained from the hospital reveals a similar trend showing that as the length of time increases the proportion surviving decreases indicating an increase in mortality among under five infants (0-5 years) over time as a result of the effect of Pneumonia. The results obtained from the data analyzed from the hospital using the Kaplan-Meier estimator, the Log Rank Test statistics and implemented by the R-Statistical software shows that hospitalization of Pneumonia patients in our hospital is associated with poor long term survival. To achieving the Sustainable Development Goal 2030 (MDG 3) which stipulates good health and well-being for all at all ages which could not be realized in MDG 4 and 5 measures should be taken to combat the scourge of Pneumonia in Edo State, Nigeria. Sequel to the conclusion drawn in this study the following recommendations are made. There is need for Government and health care providers to eradicate Pneumonia from our society with a view of reducing infant mortality which is still on the increase over the period of time based on the findings of this research work using the Kaplan-Meier estimator and the Log Rank statistics test. There is need for improved health care delivery with the aim of addressing incidence and prevalent rates of reported cases of Pneumonia. There is great need to scale up immunization of children against this childhood killer disease Pneumonia and other preventable diseases based on the data examined in this research study.

REFERENCES

[1] Udofia, I. &Okonofua, F. (2008): Preventing primary post-partum hemorrhage in unskilled births in Africa. *Journal of Africa Reproductive Health* 12: 7-9.

[2] Ogbonaya, R &Aminu, M. (2009): Nigeria North-West Battling malnutrition, Child and maternal mortality. This Day, all Africa.com: retrieved 07/06/2018

[3] Ogunjimi, L.O, Ibe, R. & Ikorok, M.M. (2012): Curbing maternal and child mortality: The Nigerian experience. *Experience International Journal of Nursing and Midwifery* 4:33 39.

[4] Okumale, O. (2017): *Journal on perfect Health Initiative PHI.2:21-28.*

[5] Kuti, B.P. & Oyelami, A.O. (2015): Childhood community acquired pneumonia at the Wesley guild hospital Ilesa, Prevalence, pattern and outcome determinants. *Niger Journal on Health Sciences* 15: 98-104.

[6] Simona.D.(2008):Cornellstatisticalconsulting*http//www.escu./cornell.edu. accessed 07/06/2018*

[7] Kleinbaun, G & Klein, M. (2012): New York Springer. Survival Analysis 3rd Edition. A self-learning text 3:31-37.

[8] Dafni, U. (2011): Landmark analysis. *Journal on cardiovascular outcomes*. 4: 363-371.

[9] Ahmed, F.E, Vos, D.W. & Holbert, D. (2007): Modeling survival in colon Cancer a Methodological Review. Statistical primer basics of survival analysis, 6:15-21

[10] Hosmer, D.W, Lemeshow, S & May S. (2008): Applied Survival. Analysis Regression modelling of time to event data, Wiley 34: 1352 - 1361.

[11] Baulies, S, Belin, L & Mallon P. (2015): Time - Varying effect and Long term survival analysis in breast cancer patients. *Journal of Applied Sciences.* 6: 113-130.

[12] George, B, Seals, S &Aban, I. (2014): Survival analysis and regression models *Journal on Cardiological Studies.* 21: 686 – 694

[13] NDHS(2008):Nigerian Demographic and Health Survey Report, Federal Republic of Nigeria, Abuja.

[14] Adetoro, G.W. &Amoo, E.O. (2014): A statistical analysis of child mortality Evidence from Nigeria Journal of Demography and Social Statistics, 1: 110 - 120.

[15] Katrona, P &Katona A.J. (2008): The Interaction between nutrition and infection. *Clinical infectious Diseases Oxford Journal* 46: 1582-1588

[16] Finlay, E, Ozaltin, J & Canning F. (2011): Association of maternal age with infant mortality, child anthropometric failure, diarrhoea and anaemic for first births, evidence from 55 low and middle income countries.*BM journal* 1: 2-8.