

A SURVIVAL ANALYSIS ON THE INCIDENCE OF PNEUMONIA AND INFANT MORTALITY RATE IN EDO CENTRAL SENATORIAL DISTRICT OF NIGERIA

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Accepted 8th June, 2020

The aim of this work is to study the epidemiological aspects of pneumonia and identify the risk factors for incidence rate of pneumonia among children aged 0-5 years treated as in-patients, at Irrua Specialist Teaching Hospital, Edo State, Nigeria. Adopting survival analysis technique, the number of patients that survived or remained after intervention over a period of time with the Kaplan-Meier estimator was computed and curves of survival probabilities were plotted. Statistical difference among the sex of the in-patients were compared and checked using the Log-rank test. Results obtained from the survival distribution reveal that as the number of days (time) increases, the chances of survival decline rapidly with a p – value of 0.03. The study shows that at 70.8 days, the chance of survival was 0.95 but as the days increased to 197.1 the chances of survival declined rapidly to 0.5. Mortality trend from the result also indicates that survival probabilities declined with the passage of time, and that the mean survival rate of male infants is higher than that of females.

Key words: Pneumonia, survival distribution function, mortality rate, Kaplan-Meier estimator, survival probabilities, log- rank test.

INTRODUCTION

Nigeria is one of the nations of the world with high pneumonia mortality in children (Udofia and Okonofua, 2008). 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 a 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 after childbirth (Ogbonaya and Aminu, 2009). Annually, Nigeria records one quarter of babies born not surviving within their first 28-30 days and before their fifth birthday, Ogunjimi et al. (2012). This unhealthy trend has become a matter of great concern, calling for concerted approach from all and sundry. Pneumonia, against the natural belief, is not caused by exposure to cold weather, but rather by a

common bacterium known as *Streptococcus pneumonia* (Okumale, 2017). Pneumonia is a leading cause of morbidity and mortality in children 0-5 years old; it is responsible for approximately ratio 1:5 mortality cases in Nigeria (Kuti and Oyelami, 2015).

An increase in mortality rate shows a decline in the health status of a population and this is largely attributed to non- availability of health care; while a reduction in mortality signifies a tremendous increase in health care delivery services (Adetoro and Amoo, 2014). 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 (Katrona and Katona, 2008). This poses a great danger for our children, but 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 hazard to infants who are vulnerable to this disease (Kuti and Oyelami, 2015).

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 (Finlay et al. (2011). Okumale (2017) advocates that unclean and unhygienic environments are breeding grounds for germs and bacterial infections which easily contaminate children. 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. Pneumonia usually starts when germs are breathed into the lungs. Bacteria get into the body either through the mouth or other openings in the body and they contaminate 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 diarrhea (Okumale, 2017).

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 specific objectives of this work 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. The Kaplan-Meier together with the log rank test was adopted in this study because of its assumption free property in survival analysis. It is used to estimate conditional probabilities at

each time an event occurs and take the product limit of the probabilities to estimate the survival rate at each point in time.

THE KAPLAN-MEIER METHOD AND THE LOG RANK TEST STATISTIC

Survival analysis is commonly used in clinical trials and biomedical sciences as a statistical tool in which the response variable is time. It is generally defined as a set of methods for analyzing data where the outcome variable is the time taken for the occurrence of a disease or death (Simona, 2008; Kleinbaum and Klein, 2012). The dependent or response variable is the waiting time until the occurrence of a well-defined event of death (Dafni, 2011). Statistical analysis of survival data shows the magnitude of the expected increase or decline in mortality from clinical trials (Ahmed et al., 2007). Two functions that are dependent on time in survival analysis are the survival function and the hazard function (Hosmer et al., 2008). The survival function gives for every time the probability of surviving that takes into account cases of survivorship; while the hazard function gives the potential that the event of death will occur per time unit an individual has survived up to the specified time (Hosmer et al., 2008).

The non-parametric estimator of the survival function known as the Kaplan - Meier method is used to estimate the proportion of surviving by any time. It is used to obtain univariate descriptive statistics for survival data (Baulies et al., 2015). The Kaplan-Meier estimator method of non-parametric statistics is also called a non-parametric 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 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 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 complete the treatment.

The Kaplan-Meier estimator is assessed by measuring the number of subjects that survived after intervention over a period of time. The time starting from a defined point to the occurrence of a given event (death) is called the survival time and the analysis of group of data as survival analysis. The Kaplan-Meier method is a non-parametric estimator 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 or did not survive or dropped out. For large samples the Kaplan Meier method is approximately normally distributed with mean $s(t)$ and variance $\hat{V}(\hat{S}(t))$, the Kaplan - Meier estimator of the survivorship function or survival probability is given by:

$$s(t) = \rho(T > t) \tag{1}$$

is defined as

$$\hat{S}(t) = \prod_{t_i \leq t} \left(1 - \frac{d_i}{R_i}\right) \tag{2}$$

where $\hat{s}(t)$ = survivorship function, $\prod_{t_i \leq t}$ = 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 and the Green wood's variance estimator is denoted by:

$$\hat{V}[\hat{S}(t)] = \hat{S}(t)^2 \sum_{t_i \leq t} \frac{d_i}{R_i(R_i - d_i)} \tag{3}$$

In order to derive two approximate 95% confidence intervals for $s(t)$ for a fixed t , or in general $(1-\alpha)100\%$, the lower and upper limits are denoted as follows:

$$LowerLimit = \hat{S}(t) - 1.96\hat{S}(t) \sum_{t_i \leq t} \sqrt{\frac{d_i}{R_i(R_i - d_i)}} \tag{4}$$

and

$$UpperLimit = \hat{S}(t) + 1.96\hat{S}(t) \sum_{t_i \leq t} \sqrt{\frac{d_i}{R_i(R_i - d_i)}} \tag{5}$$

To compare the probability of survival beyond a certain time for two groups of subjects, the Z statistic is appropriate for the given test hypothesis:

$$H_o : S_1(t_o) = S_2(t_o) \tag{6}$$

$$H_1 : S_1(t_o) \neq S_2(t_o) \tag{7}$$

and

$$Z = \frac{\hat{S}_1(t_o) - \hat{S}_2(t_o)}{\sqrt{\hat{V}[\hat{S}_1(t_o)] + \hat{V}[\hat{S}_2(t_o)]}} \tag{8}$$

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, H_o : there are no differences in survival distributions, H_1 : there are differences in survival distributions.

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 comes to mind. The log rank test is a method used for comparing the Kaplan - Meier estimate for each group of subjects (George et al., 2014).

Log rank test statistic

It is a confirmatory test used to compare the entire survival function for two groups of

subjects. It is more powerful because its analysis is 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 death (ϵ_j) in each group to the total observed death (O_j). It is a type of chi square test used to assess the overall difference in survival analysis as denoted by:

$$\epsilon_{ij} = \left(\frac{R_{1j}}{R_{1j} + R_{2j}} \right) (d_{ij} + d_{2j}) \tag{9}$$

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} = the number at risk in set Group 1, R_{2j} = the number at risk in set group 2. The log rank test statistic is denoted by:

$$\chi^2 = \sum_{i=1}^2 \frac{(O_i - E_i)^2}{\hat{v}_i} \tag{10}$$

such that

$$\hat{v}_1 = \sum_{j=1}^k \frac{R_{1j}R_{2j}(d_{ij} + d_{2j})(R_{ij} + R_{2j}) - d_{ij} - d_{2j}}{(R_{ij} + R_{2j})^2 (R_{ij} + R_{2j} - 1)} \tag{11}$$

and the test hypothesis is given by

$$H_o : S_1(t) = S_2(t) \text{ for all } t \tag{12}$$

$$H_1 : S_1(t) \neq S_2(t) \text{ for some } t \tag{13}$$

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

Mean survival rate (MSR)

To measure the mean survival rate, the percentage of people in a study or treatment group still alive for a given period of time after

diagnosis is taken into consideration. It is a statistic that describes how long an average person will survive for a particular amount of time. It is the total number of deaths (d_{ij}) in a defined time period divided by the total number of persons in the population (R_{ij}) at the beginning of the time period of the experiments or treatment group multiplied by 100%; it is denoted by:

$$MSR = \frac{d_{ij}}{R_{ij}} \times \frac{100}{1} \tag{14}$$

METHODOLOGY

The methodologies used in this study are a non parametric estimator of the survival function known as the Kaplan-Meier survival function and the Log Rank test. The data for this paper are secondary data from Irrua Specialist Teaching Hospital, Irrua, Edo State, Nigeria. The data are on reported cases of children treated, survived and did not survive for 2007-2016 periods. In order to facilitate the computational efficiency, R-Statistical software is used in this paper to implement the method. The R-Statistical software has a package known as “Survival” used for survival analysis.

Data presentation and analysis

Data used in this study are obtained from Irrua Specialist Teaching Hospital (ISTH), Irrua, Edo State Nigeria. The data are on reported cases of children treated, survived and did not survive of pneumonia for 2007-2016 as presented in Appendix Table 1. To facilitate easy analysis, some notations compactable to r-statistical software were implemented as presented in Appendix 2. Adopting notation of time normalization in Appendix 2, data presented are analyzed based on the estimates of proportion surviving at time (t) using the Kaplan-Meier method. The results are shown in Table 1.

RESULTS AND DISCUSSION

From Table 1, covariate of sex 1 represents males while sex 2 represents females. Time factor in survival analysis has varying values. Since time is

Table 1. Time and incidence of pneumonia at ISTH.

| Year | Survival | 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 |

all through the years, transformation of variables and effects was carried out for optimum performance. Time and incidence table was obtained by transformation technique which was generated using r-statistical fit *xlab* for patient time (years/days) and *ylab* for survival probabilities. The Kaplan-Meier curve

was used to estimate percentiles survival distribution of median time and mean time in years; the survival distribution showing the 95% confidence interval, standard error, survival rate, and number at risk at a particular event is displayed in Table 2 and the survival probability is presented in Table 3.

Table 2. Survival distribution of pneumonia cases.

| Time | Risk | Event | Survival | Std. Error | Lower C.I. | Upper C.I. |
|-------|------|-------|----------|------------|------------|------------|
| 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 chances of survival were 0.95; but as the days (time) increases to 197.1, the chances of survival dropped to 0.5. This indicates that as time progresses the chances of survival decrease drastically as can also be seen in

Figures 1 and 2. As the length of time increases, survival probability drops as shown in Figures 1 and 2. The Kaplan-Meier estimate is in solid line and its 95% confidence intervals are in dotted lines as indicated in Figure 1. From Figure 2, line 1 (blue color) represents the male sex covariates

Table 3. Survival probability of pneumonia cases.

| Year | Sex | Reported cases | 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 |

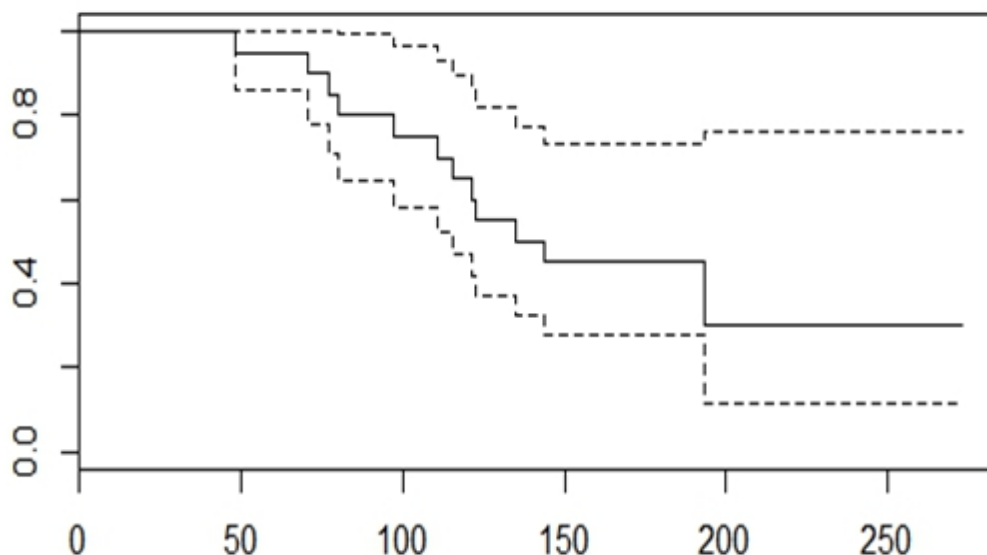


Figure 1. The Kaplan -Meier curve of pneumonia patients.

in Group 1 while line 2 (red color) represents the female sex covariates in Group 2. The trend shows that the proportion of under-five male children surviving under pneumonia is higher than that of the females in the transformed time. From the curves, the horizontal lines represent the survival duration for the interval while the height of the vertical lines shows the change in cumulative probability; censored observation are indicated by tick marks. This

helps to reduce the cumulative survival between the intervals. 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 time follows an exponential distribution with mean time of 160T (2.19 years), median value of

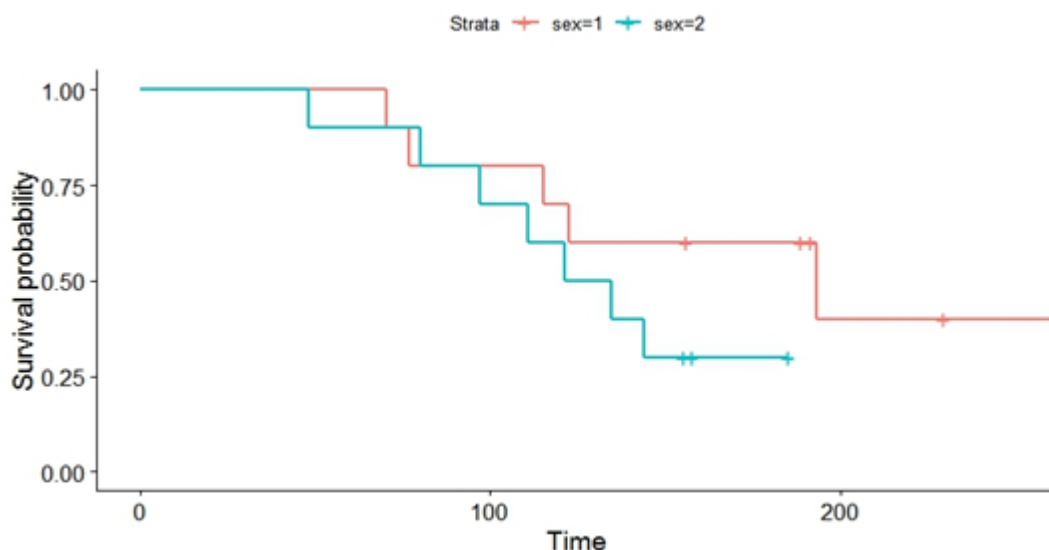


Figure 2. Survival time of pneumonia patients.

165.35T (2.26years) and 95% confidence interval (C.I 2.147-2.373) (Table 4). The log rank test shows that there is statistical

significant evidence of the survival distributions between the male and female respondents (p-value =0 .03 < 0.05) (Table 5).

Table 4. Survival time of patients.

| Mean time | C.I at 95% | Median time 50% | P<value (Sig. Diff.) |
|-------------------|-------------|----------------------|----------------------|
| 160T (2.19 years) | 2.147-2.373 | 165.35T (2.26 years) | P= 0.03 < 0.05 |

Table 5. Log rank test of patients.

| | N | Observed | Expected | (O-E)^2/E | (O-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.

With a p-value $0.03 < 0.05$, there is a statistical significant difference in the survival distributions between the male and female respondents; this negates the null hypothesis. This indicates that the expected mean surviving rate of male children age under-five (6.87) is significantly higher than that of the female children age under-five (5.13) with a p-value of 0.03. However, Table 6 indicates that the mean survival rates of both male and female are 11.32216 and 8.60714 respectively, and the mean survival rate (bar) as presented in Table 7 indicates that male is 1.132216, while female is 0.860714 within the given time period. This goes to indicate that the mean survival rate

(bar) proportion of male patients surviving is higher than that of the females.

Results obtained from the analysis showed that at 70.8 days (time), the chance of survival was 0.95 but with the length of time at 197.1 the chances of survival decreased to 0.5. This trend reveals that as the length of time increases the proportion of surviving decreases, indicating an increase in mortality of infants under five (0-5 years) over time. The Kaplan-Meier estimate is in solid line and its 95% confidence intervals are in dotted lines as indicated in Figure 1. From Figure 2, line 1 (blue color) represents the male sex covariates in group 1 while line 2 (red color) represents the female sex covariates in group 2.

Table 6. Mean survival rate for male and female patients.

| Year | Male | Treated cases | Deaths cases | MSR (%) | Female | Treated cases | Deaths cases | MSR (%) |
|------|------|---------------|--------------|---------|--------|---------------|--------------|---------|
| 2007 | 1 | 310 | 18 | 5.80645 | 2 | 375 | 14 | 3.73333 |
| 2008 | 1 | 281 | 15 | 5.33807 | 2 | 299 | 18 | 6.02006 |
| 2009 | 1 | 284 | 24 | 8.4507 | 2 | 282 | 25 | 8.86524 |
| 2010 | 1 | 280 | 25 | 8.92857 | 2 | 209 | 27 | 12.9187 |
| 2011 | 1 | 248 | 33 | 13.3065 | 2 | 277 | 27 | 9.74729 |
| 2012 | 1 | 251 | 45 | 17.9283 | 2 | 214 | 24 | 11.215 |
| 2013 | 1 | 283 | 44 | 15.5477 | 2 | 333 | 24 | 7.2072 |
| 2014 | 1 | 236 | 31 | 13.1356 | 2 | 261 | 27 | 10.3448 |
| 2015 | 1 | 278 | 43 | 15.4676 | 2 | 270 | 24 | 8.88888 |
| 2016 | 1 | 234 | 26 | 11.1111 | 2 | 280 | 31 | 11.0714 |
| | | 2,685 | 304 | 11.3222 | | 2,800 | 241 | 8.60714 |

Table 7. Mean Survival Rate (Bar).

| Sex | MSR | N (2007-2016) | MSR (Bar) |
|--------|----------|---------------|------------|
| Male | 11.32216 | 10 | 1.132216 |
| Female | 8.60714 | 10 | 0.860714 |

The trend shows that the proportion of under-five male children surviving pneumonia is higher than that of the females in the transformed time. The survival time follows an exponential distribution with mean time of 160T (2.19 years), median value of 165.35T (2.26years) and 95% confidence interval (C.I 2.147-2.373) as shown in Table 4. The log rank test shows that there is statistical significant evidence of the survival distributions between the male and female respondents (p -value = $0.03 < 0.05$) (Table 5). However, Table 6 indicates that the mean survival rate of both male and female children are 11.32216 and 8.60714 respectively, and the mean survival rate (bar) as presented in Table 7 indicates that male is 1.132216, while female is 0.860714 within the given time period. This goes to indicate that the mean survival rate (bar) proportion of male patients is higher than that of the 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. Results obtained from the analysis

showed that at 70.8 days (time), the chance of survival was 0.95 but with the length of time at 197.1 the chances of survival decreased to 0.5. This trend reveals that as the length of time increases the proportion of surviving decreases indicating an increase in mortality of infants under five (0-5 years) over time as a result of the effect of pneumonia. The log rank test shown in Table 4 indicates significant difference ($p = 0.03 < 0.05$) between male and female respondents. The survival time for the hospital follows an exponential distribution with mean time of 2.19years, while the median survival time was estimated to be 165.35T (2.26years, with its 95% confidence interval of 2.147-2.373 years).

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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Appendix Table 1. Data of reported cases of children treated, survived and died of pneumonia in Irrua Specialist Teaching Hospital (ISTH), Irrua.

| Infants age group | Reported cases males | Survival males | Death recorded males | Reported cases females | Survivals females | Death recorded female |
|-------------------|----------------------|----------------|----------------------|------------------------|-------------------|-----------------------|
| 0-28DAYS | 121 | 116 | 5 | 151 | 148 | 3 |
| 29-364 DAYS | 86 | 81 | 6 | 92 | 87 | 5 |
| 1-4 YEARS | 66 | 62 | 4 | 71 | 68 | 3 |
| 4+ 5 YEARS | 37 | 33 | 3 | 61 | 58 | 3 |
| TOTAL 2007 | 310 | 292 | 18 | 375 | 361 | 14 |
| 0-28DAYS | 101 | 98 | 3 | 132 | 125 | 7 |
| 29-364 DAYS | 93 | 88 | 5 | 83 | 79 | 4 |
| 1-4 YEARS | 39 | 37 | 2 | 47 | 46 | 1 |
| 4+ 5 YEARS | 48 | 43 | 5 | 37 | 31 | 6 |
| TOTAL 2008 | 281 | 266 | 15 | 299 | 281 | 18 |
| 0-28DAYS | 127 | 121 | 6 | 115 | 111 | 4 |
| 29-364 DAYS | 87 | 78 | 9 | 94 | 87 | 7 |
| 1-4 YEARS | 31 | 28 | 3 | 42 | 36 | 6 |
| 4+ 5 YEARS | 39 | 33 | 6 | 31 | 23 | 8 |
| TOTAL 2009 | 284 | 260 | 24 | 282 | 257 | 25 |
| 0-28DAYS | 111 | 107 | 4 | 83 | 76 | 7 |
| 29-364 DAYS | 75 | 68 | 7 | 58 | 53 | 5 |
| 1-4 YEARS | 51 | 43 | 8 | 26 | 20 | 6 |
| 4+ 5 YEARS | 43 | 37 | 6 | 42 | 33 | 9 |
| TOTAL 2010 | 280 | 255 | 25 | 209 | 182 | 27 |
| 0-28DAYS | 102 | 93 | 9 | 103 | 94 | 9 |
| 29-364 DAYS | 82 | 71 | 11 | 92 | 85 | 7 |
| 1-4 YEARS | 35 | 27 | 8 | 36 | 30 | 6 |
| 4+ 5 YEARS | 29 | 24 | 5 | 46 | 41 | 5 |
| TOTAL 2011 | 248 | 215 | 33 | 277 | 250 | 27 |
| 0-28DAYS | 99 | 88 | 11 | 93 | 87 | 6 |
| 29-364 DAYS | 68 | 53 | 15 | 33 | 26 | 7 |
| 1-4 YEARS | 48 | 34 | 14 | 47 | 39 | 8 |
| 4+ 5 YEARS | 36 | 31 | 5 | 41 | 38 | 3 |
| TOTAL 2012 | 251 | 206 | 45 | 214 | 190 | 24 |
| 0-28DAYS | 104 | 90 | 14 | 131 | 125 | 6 |
| 29-364 DAYS | 82 | 70 | 12 | 79 | 71 | 8 |
| 1-4 YEARS | 35 | 23 | 12 | 45 | 39 | 6 |
| 4+ 5 YEARS | 62 | 56 | 6 | 78 | 74 | 4 |
| TOTAL 2013 | 283 | 239 | 44 | 333 | 309 | 24 |
| 0-28DAYS | 111 | 102 | 9 | 104 | 97 | 7 |
| 29-364 DAYS | 58 | 49 | 9 | 92 | 84 | 8 |
| 1-4 YEARS | 36 | 29 | 7 | 25 | 17 | 8 |
| 4+ 5 YEARS | 31 | 25 | 6 | 40 | 36 | 4 |
| TOTAL 2014 | 236 | 205 | 31 | 261 | 234 | 27 |
| 0-28DAYS | 118 | 103 | 15 | 110 | 104 | 6 |
| 29-364 DAYS | 69 | 58 | 11 | 82 | 73 | 9 |
| 1-4 YEARS | 29 | 18 | 11 | 31 | 25 | 6 |
| 4+ 5 YEARS | 62 | 56 | 6 | 47 | 44 | 3 |
| TOTAL 2015 | 278 | 235 | 43 | 270 | 246 | 24 |

Appendix Table 1. Continue

| | | | | | | |
|-------------------|------------|------------|-----------|------------|------------|-----------|
| 0-28DAYS | 101 | 93 | 8 | 131 | 123 | 8 |
| 29-364 DAYS | 73 | 67 | 6 | 66 | 55 | 11 |
| 1-4 YEARS | 28 | 21 | 7 | 43 | 36 | 7 |
| 4+ 5 YEARS | 32 | 27 | 5 | 40 | 35 | 5 |
| TOTAL 2016 | 234 | 208 | 26 | 280 | 249 | 31 |

Source: Records Department ISTH (2017).

Appendix 2. Time normalization notations.

$$Surv - death = \varpi = \frac{survival_i}{death_j} \dots\dots\dots(a), \text{ where } i = \text{survival at } i\text{-th term, and } j = \text{death at } j\text{-th term}$$

$$death - surv = \varpi' = \frac{death_j}{survival_i} \dots\dots\dots(b), \text{ where } i = \text{survival at } i\text{-th term, and } j = \text{death at } j\text{-th term}$$

$$Summation \text{ Ratio} = \psi = \frac{\sum_{i=1}^n survival}{\sum_{j=1}^m death}, \quad i = 1 \dots n; \quad j = 1 \dots m \dots\dots\dots(c)$$

$$Summation \text{ Penalty}(\lambda) = \psi - 10\% \psi \Rightarrow \lambda = \psi - 0.1 * \psi \dots\dots\dots(d)$$

$T = 365 * 5 = 1825$, hence,

$$time(t_j) = \varpi' * T \dots\dots\dots(e)$$

$$Status = \begin{cases} 1, & \text{if } \varpi > \lambda \\ 0 & \text{otherwise} \end{cases} \dots\dots\dots(f)$$

$$rescaled \text{ time}(t'_j) = t_j \times \frac{5}{365} \dots\dots\dots (g)$$