

Parametric Survival Modeling of Maternal Obstetric Risk; a Censored Study

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Abstract The world mortality rate has declined 45% since 1990, but still 800 women die every day from pregnancy or childbirth related causes. According to the United Nations Population Fund (UNFPA) this is equivalent to "about one woman every two minutes and for every woman who dies, 20 or 30 encounter complications with serious or long-lasting consequences. Young mothers face higher risks of complications and death during pregnancy than older mothers, especially adolescents aged 15 years or younger. Adolescents have higher risks for postpartum hemorrhage, thus, an increased risk of death during pregnancy or childbirth compared with older women. The study is therefore focused on addressing the issue of good statistical estimators, is born out of the weaknesses of the estimators in use, and the apparent lack of research into the application of other methods. Survival analysis technique was employed, once the survival function has been developed, various tests and the modeling of Maternal Mortality, as well as the determination of the appropriate distributions that best describes maternal mortality was done, using both the parametric and non-parametric methods. These include the identification of prognostic factors through regression analysis and the determination of an appropriate distribution for maternal survival. Results of its application to data from Oyo State, Nigeria showed that while about 90% of pregnant women made it alive to delivery, only 86% of them survived to the end of the postpartum period. There were significant differentials by location, and Maternal Age: The Weibull distribution described maternal survival well.

Keywords Maternal Mortality, Hazard, Survival Analysis, Weibull Distribution, Maternal Survival, Maternal Cox Regression

1. Introduction

Maternal death is defined as "The death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and the site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes [1]. The world mortality rate has declined 45% since 1990, but still 800 women die every day from pregnancy or childbirth related causes. According to the United Nations Population Fund (UNFPA) this is equivalent to "about one woman every two minutes and for every woman who dies, 20 or 30 encounter complications with serious or long-lasting consequences. Most of these deaths are injuries are entirely preventable" [2]. UNFPA estimated that 289000 women died of pregnancy or childbirth related causes in 2013 [3]. These causes range from severe bleeding to

obstructed labour, all of which have highly effective interventions. As women have gained access to family planning and skilled birth attendance with backup emergency obstetric care, the global maternal mortality ratio has fallen from 380 maternal death per 100000 live births in 1990 to 210 deaths per 100000 live births in 2013. This has resulted in many countries having their maternal death rates [4] while there has been a decline in world-wide mortality rates; much more has to be done. High rates still exist, particularly in impoverished communities with over 85% living in Africa [5]. The effect of a mother's death results in vulnerable families and their infants, if they survive, are more likely to die before reaching their second birthday [6]. Factors that increase maternal death can be direct or indirect. Generally, there is a distinction between a direct maternal death that is the result of a complication of the pregnancy, delivery, or management of the two, and an indirect maternal death [7] that is a pregnancy-related death in a patient with a preexisting or newly developed health problem unrelated to pregnancy. Fatalities during but unrelated to a pregnancy are termed accidental, incidental, or non-obstetrical maternal deaths. The most common cause of postpartum bleeding (15%), complications from unsafe abortion (15%), hypertensive disorders of pregnancy (10%), postpartum

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infections (8%), and obstructed labour (6%) [8]. Other causes of maternal death include blood clot (3%) and pre-existing conditions (28%) [9]. Indirect causes are malaria, anemia, [10] HIV/AIDS, and cardiovascular disease, all of which may complicate pregnancy or be aggravated by it. Socio-demographic factors such as age, access to resources and income level are significant indicators of maternal outcome. Young mothers face higher risks of complications and death during pregnancy than older mothers, [11] especially adolescents aged 15 years or younger. [12] Adolescents have higher risks for postpartum hemorrhage, puerperal endometritis, operative vaginal delivery, episiotomy, low birth weight, preterm delivery, and small-for-gestational age infants, all of which can lead to maternal death [12]. Surgical support and family support influences maternal outcomes. Furthermore, social disadvantage and social isolation adversely affects maternal health which can lead to increase in maternal death [13]. Additionally, lack of access to skilled medical care during childbirth, the travel distance to the nearest clinic to receive proper care, number of prior births, barriers to accessing prenatal medical care and poor infrastructure all increases maternal deaths. Unsafe abortion is another major cause of maternal death. According to the World Health Organization, every eight minutes a woman dies from complications arising from unsafe abortions. Complications include hemorrhage, infection, sepsis and genital trauma [14]. Globally, preventable deaths from improperly performed procedure constitute 13% of maternal mortality, and 25% or more in some countries where maternal mortality from other causes is relatively low, making unsafe abortion the leading single cause of maternal mortality worldwide [15-20]. This study is therefore focused on addressing the issue of good statistical estimators, is born out of the weaknesses of the estimators in use, and the apparent lack of research into the application of other methods. As stated in [21], the challenge arising from having some censored data, at most one event occurring per subject and highly skewed observations, make the use of standard statistical techniques inappropriate: hence our proposal of the use of survival analysis technique provides more informative estimates with measurable precision and is a much better way of estimating obstetric risk with broader parametric and non-parametric prospects.

2. Materials and Method

In applying Survival analysis techniques to Maternal Mortality, we make the assumption that the time of maternal deaths are a function of the random process and therefore the time of death is a random variable with a probability distribution and consequently, other related distributions.

2.1. Basic Concepts in Survival

Let T , denote the survival time of a woman from her time of conception. The distribution of T can be characterized by three equivalent functions [22].

Survival Function, $S(t)$

$$S(t) = P(\text{a woman who has conceived surviving longer than time } t \text{ from conception}) \\ = P(T > t)$$

$$S(t) = 1 - P(\text{a woman who has conceived dying before time } t \text{ from conception}) \\ = 1 - F(t)$$

$S(t)$ is a non increasing function of time with properties

$$S(t) = \begin{cases} 1 & \text{for } t = 0 \\ 0 & \text{for } t = \infty \end{cases}$$

2.1.1. Probability Density Function

The probability density function of the survival time is defined as the limit of the probability that a woman dies in the short interval, t to $t + \Delta t$, per unit width, Δt , or simply the probability of dying in a small interval per unit time. It can be expressed as

$$h(t) = \frac{\lim_{\Delta t \rightarrow 0} P \left[\begin{array}{c} \text{a woman who has conceived dying in the} \\ \text{interval } (t, t + \partial t) \text{ given that the woman} \\ \text{has survived to } t \end{array} \right]}{\Delta t} \\ h(t) = \frac{\lim_{\Delta t \rightarrow 0} P[X_t \in (t, t + \partial t)]}{\Delta t}$$

Where X_t denotes a woman who has conceived, dying after she has survived to time t . These functions are related by;

$$h(t) = \frac{f(t)}{S(t)}$$

2.1.2. Estimating the Survival Functions

Survival functions can be estimated using a number of options; the Kaplan-Meier and the Life Table Method. In this study, the Life table method, a non-parametric method to estimate the survival functions was used. This method, which uses time intervals, estimates the survival functions up to the upper limit of each interval, and estimates the hazard and density functions at the midpoint of each interval [23]. For the i_{th} interval, let t_i be the end time and q_i be the conditional probability of dying. Then;

$$\hat{f}(t_{mi}) = \frac{\hat{S}(t_i) - \hat{S}(t_{i-1})}{b_i} = \frac{\hat{S}(t_i)\hat{q}_i}{b_i}$$

$$\hat{S}(t_i) = \prod_{j=1}^{i-1} (1 - \hat{q}_j)$$

$$\hat{h}(t_{mi}) = \frac{d_i}{b_i(n_i - 0.5d_i)} = \frac{2\hat{q}_i}{b_i(1 - \hat{p}_i)}$$

Where,

t_{mi} is the mid-point of the i_{th} interval.

d_i is the number of women dying in the i_{th} interval after their conception.

n_i is the number of women exposed in the i_{th} interval after conception.

$q_i = \frac{d_i}{n_i}$ is the conditional probability of a woman dying in the i_{th} interval after conception

$p_{i=(1-q_i)}$ is the conditional probability of a woman dying in the i th interval after conception.

b_i is the width of the i th interval.

The standard error of the survival function [18] is estimated by:

$$s.e.(\hat{S}(t_i)) \approx \hat{S}(t_i) \sqrt{\sum_{j=1}^{i-1} \frac{\hat{q}_j}{n_j(1-\hat{q}_i)}}$$

while that of the hazard function [19] is estimated by;

$$s.e.(\hat{h}(t_{mi})) \approx \hat{h}(t_{mi}) \sqrt{\frac{1 - \left[\frac{1}{2} \hat{h}(t_{mi}) b_i\right]^2}{n_i \hat{q}_i}}$$

The probability density function [19] is estimated by;

$$s.e.(\hat{f}(t_{mi})) \approx \hat{S}(\hat{t}_i) \hat{q}_i \sqrt{\frac{\sum_{j=1}^{i-1} \frac{\hat{q}_j}{n_j(1-\hat{q}_j)} + \frac{1-\hat{q}_j}{n_j(1-\hat{q}_j)}}{b_i}}$$

2.1.3. Modeling and Other Tests Based on Survival Techniques

Once the survival function has been developed, various tests and the modeling of Maternal Mortality, as well as the determination of the appropriate distributions that best describes maternal mortality can be done, using both the parametric and non-parametric methods [24]. These include the identification of prognostic factors through regression analysis and the determination of an appropriate distribution for maternal survival.

2.1.4. The Log-Rank Test

The Log-rank test, [25] a non-parametric test of difference for survival functions, is the most widely used technique when data is censored. It measures the difference in the survival for the different groups at each of the given times. For a k factor group, this test the hypothesis that;

$$H_0 : S_1(t) = S_2(t) = \dots = S_k(t) \text{ for all } t$$

$$H_1 : \text{not all } S_j(t) \text{ are equal. } j = 1, 2, \dots, k$$

where $S_j(t)$ is the survival function for the j th group

This is tested as a chi-square test which compares the observed numbers of failures to the expected number of failures under the hypothesis. Thus, given that O_j and E_j is the observed and expected number of deaths respectively for the j th group, the test statistic is given by;

$$X^2 = \sum_{j=1}^k \frac{(O_j - E_j)^2}{E_j}$$

Where

$$E_j = \sum_{all\ t} e_{jt}$$

$$e_{jt} = \frac{n_{jt}}{\sum_{all\ j} n_{jt}} * d_t$$

n_{jt} is the number of women still exposed to the risk of dying at time up to t for the j th group.

d_t is the total number of deaths for all groups at time t . Thus,

$$d_j = \sum_{all\ t} d_{jt}$$

has approximately a chi-square distribution with $k - 1$ degrees of freedom. A large chi-square value will lead to a rejection of the null hypothesis in favor of the alternative that the k groups do not have the same survival distribution.

2.1.5. Proportional Hazard Regression

The Cox proportional regression [26-28] was used to determine the effect of some socio economic and demographic factors on maternal survival based on the assumption of proportionality. In this model, the hazard for an individual is assumed to be related to the covariates through the equation;

$$h_i(t) = \lambda_0(t) \exp\{\beta_1 x_{i1} + \dots + \beta_k x_{ik}\}$$

Taking the logarithm of both sides, the model can also be written as

$$\log h_i(t) = \alpha(t) + \beta_1 x_{i1} + \dots + \beta_k x_{ik}$$

Where $\alpha(t) = \log \lambda_0(t)$.

The ratio of the hazard for the two individuals i and j (say rural women and urban women) is then given by;

$$\frac{h_i(t)}{h_j(t)} = \frac{\lambda_0(t) \exp\{\beta_1 x_{i1} + \dots + \beta_k x_{ik}\}}{\lambda_0(t) \exp\{\beta_1 x_{j1} + \dots + \beta_k x_{jk}\}}$$

$$= \exp\{\beta_1(x_{i1} - x_{j1}) + \dots + \beta_k(x_{ik} - x_{jk})\}$$

Where β_1, \dots, β_k measures the relative risk for the i th woman over the j th, with respect to the change in the l th covariate, $l = 1, \dots, k$ respectively.

2.1.6. Determination of an Appropriate Distribution

Graphical and analytical method exists for the determination of an appropriate distribution for survival data. In this study, the hazard plotting technique [29], a graphical plotting technique designed to handle censored data was used. The shape of the hazard plot gives a good indication of the distribution that could best fit it: For instance, a constant hazard would suggest an exponential distribution; while a first increasing and then decreasing hazard would suggest a log normal or log-logistic model, a monotonically distribution could suggest a log-logistic model; The Weibull distribution could have an increasing, decreasing or constant hazard. The monotonically increasing shape of the hazard plot for maternal mortality, suggests that the assumption that maternal survival had a Weibull distribution. The parameters of the assumed Weibull distribution were then estimated using the hazard plotting technique. The adequacy of the fit was also assessed using R-squared value of the linear plot of $\log(t)$ against $H(t)$: $H(t)$ is the cumulative hazard at time t .

3. Results and Discussion

Table 1. Maternal Survival Estimates

Time from conception (month)	Probability of failure	S.E	Survival probability	S.E	Hazard	S.E	Density	S.E
0 to 1	0.00000	0.00000	1.00000	0.00000	0.00000	*	0.00000	*
1 to 2	0.00000	0.00000	1.00000	0.00000	0.00000	*	0.00000	*
2 to 3	0.00125	0.00125	0.98879	0.00125	0.00125	0.00125	0.00125	0.00125
3 to 4	0.01807	0.00501	0.99674	0.00528	0.01941	0.00528	0.01804	0.00528
4 to 5	0.00507	0.00299	0.96547	0.00608	0.00512	0.00298	0.00502	0.00272
5 to 6	0.00527	0.00405	0.96436	0.00782	0.00628	0.00406	0.00802	0.00441
6 to 7	0.01011	0.00512	0.95626	0.00808	0.01024	0.00518	0.01004	0.00521
7 to 8	0.02069	0.00825	0.93438	0.01189	0.02203	0.00841	0.01999	0.00819
8 to 9	0.01227	0.00887	0.90272	0.01418	0.01675	0.00924	0.02164	0.00811
9 to 10	0.09669	0.02799	0.86121	0.02678	0.11281	0.03187	0.09013	0.03575

Table 1 summarizes the survival estimates with their measures of precision. It shows that, in Delta State Nigeria, approximately 90 percent of pregnant women make it through to delivery while 86 percent make it to the end of the postpartum period: This means a maternal mortality of 14 percent. Approximately 10 percent of women, who conceived, lost their lives during the first month after delivery: representing over 50 percent of the total maternal deaths. This makes the first month after delivery the most risky period for a pregnant woman. Thus, a woman, once pregnant, has approximately a 1 in 10 chance of dying before delivery and a 2 in 10 chance of dying by the end of the ten month after conception (up to one month after delivery). Accordingly, if a pregnant Woman delivered safely, she still had approximately a 1 in 10 chance of dying within one month after delivery. A focus therefore on a mother's health immediately after she was delivered and up to one month thereafter, could reduce maternal mortality by up to half.

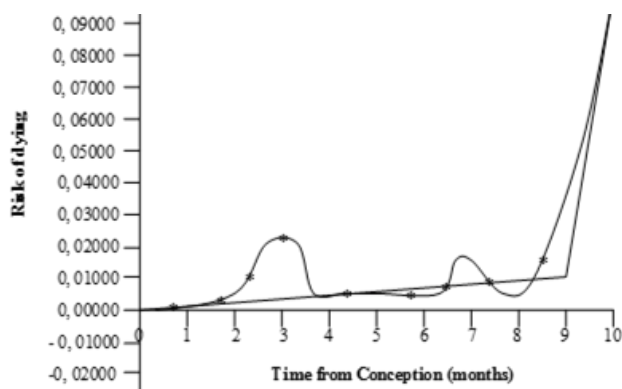


Figure 1. Hazard plot for Maternal Survival against time

From the Hazard plot in figure 1 above, we clearly see that maternal mortality increased at an increasing rate. This plot also suggests a possible two part mortality trend: the period before delivery and the period after delivery, with the latter being more perilous.

Table 2. Log-Rank Test of Differences in Maternal Survival

	Variable	χ^2	d. f	p-value
1	Ever Given Birth	4.71126	1	0.038
2	Mother Ever Schooled	0.11025	1	0.752
3	Marital Status	6.11881	3	0.042
4	Type of Town	19.16420	3	0.000
5	Age of Mother at birth	6.26881	4	0.160
6	Mother's total number of births	110.14811	8	0.000
7	Region	6.17817	9	0.611

The results of the Log-rank tests shown in Table 2, show that, Type of town, ever given birth, marital status and Age of Mother at birth are all associated with maternal mortality.

Table 3. Maternal Cox Regression

Variable	β	S.e	Wald	d. f	p-value	Exp (β)
Town (compared to Rural)	0.347	0.335	1.0733	1	0.001	1.415
Urban	-0.890	0.262	11.539	1	0.204	0.411
Mother Ever Schooled (compared to never)	0.221	0.242	0.834	1	0.420	1.247
Ever given birth (Compare d to never)	-0.833	0.249	11.192	1	0.000	0.435
Age of mother at Pregnancy	-0.051	0.021	5.898	1	0.004	0.950

From Table 3, the results of the Cox regression shows that a mother who has ever given birth has a 67 percent less risk of dying due to pregnancy related issues than a woman who has never given birth. Generally, as a woman grows older, the risk of dying decreases by 4.5 percent for every additional year of age: These results are statistically significant. Area differences were also significant with rural folks having a 67% less risk than urban folks: Thus, the more urban the locality, the higher the risk of maternal deaths. This could be a reflection of interventions in rural communities to make motherhood safer or of the data inadequacies or unreliability.

Table 4. Summary of fitted distribution for Maternal Survival

Variable	Assumed Distribution	Parameter Estimates	R ² Estimates
Maternal Survival	Weibull	$\gamma = 1.84902$ $\lambda = 0.02861$	0.9806

The estimated parameters of the fitted Weibull distribution, and its appropriateness, are displayed on Table 4, the results shows that the Weibull distribution describes Maternal Survival very well.

4. Conclusions and Recommendations

This study has clearly shows that Survival Techniques can be applied to the study of Maternal Survival. Mortality is adequately described by a Weibull model. The Weibull distribution which described maternal survival, had shape and scale parameters $\gamma, \lambda, > 0$, indicating an increasing risk of mortality with time and thus a hazard that increases at an increasing rate. The prognosis factors that influences the hazard, and hence survival, are the determinants of the Weibull distribution that described maternal survival for this data was determined to be $\gamma = 1.84902$ and $\lambda = 0.02861$ respectively.

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