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Clinical Study of Acute Myelogenous Leukaemia Patients Data

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ABSTRACT

Acute leukaemia is a malignancy of the white blood cells that is aggressive and progressing. The illness can be further divided into two subtypes, each of which affects different types of white blood cells. Since, Myeloid cells are a type of white blood cell that protects the body against parasites, reduces the frequency of tissue damage, and fights bacterial infections. Lymphocytes are primarily involved in the defence against viral infections. The aim of this study is to analyze the lifetime of the survival patients with acute myeloid leukemia. Since, clinical data provides important tools for a possible development of surveillance system for the acute myeloid leukemia. In survival analysis, to performing an experiment up to a certain period of time or getting the desired number of failures is time-consuming and costly. Many of the available observations remains censored and only give the survival information of testing units up to a noted time and not about the exact failure times. In this article, the Akshaya distribution is considered as a survival lifetime model. Censoring time is also assumed to follow Akshaya distribution with a different parameter. A survival study will be perform for the Acute Myelogenous Leukaemia patients data.

Keywords: Acute Myelogenous Leukaemia, Akshaya Distribution, Random Censoring, Maximum Likelihood Estimation, Bayesian Analysis.

1. Introduction

The Acute myelogenous leukaemia is a blood and bone marrow cancer in human beings, which affects the spongy region inside bones where blood cells are produced. Sincethe word ”acute” denotes the disease’s rapid progression in acute myelogenous leukemia. Myelogenous leukaemia is defined as a kind of leukaemia that affects a group of white blood cells known as myeloid cells, which develop into various types of mature blood cells such as red blood cells, white blood cells, and platelets. Acute myelogenous leukemia is also known as acute myeloid leukemia, acute myeloblastic leukemia, acute granulocytic leukemia and acute nonlymphocytic leukemia. Acute myelogenous leukaemia develops when the genetic material or Deoxyribonucleic acid (DNA) of a bone marrow cell changes. The DNA of a cell includes the instructions that tell it what to do. Normally, the cell’s DNA directs it to grow at a predetermined rate and die at a specific time. The mutations in acute myelogenous leukaemia tell the bone marrow cell to keep growing and dividing. Acute myelogenous leukemia occurs when a bone marrow cell develops changes in its genetic material or DNA. A cell’s DNA contains the instructions that tell a cell what to do. The Blood cell production becomes uncontrollable as a result of this. The bone marrow generates immature cells that progress into myeloblasts, which are leukemic white blood cells. These dysfunctional cells can accumulate and crowd out healthy cells

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because they are unwilling operate properly. Although it's exactly what causes the DNA alterations that lead to leukaemia, doctors have identified risk factors. The risk factors that may be increased risk of acute myelogenous leukemia include increasing age, sex, previous cancer treatment, exposure to radiation, dangerous chemical exposure, smoking, other blood disorders, genetic disorders. Pathologists used bone marrow biopsy, aspirate, and peripheral smears to determine the diagnosis of acute myelogenous leukemia. Following that, the haematologist who treated the patients for acute myelogenous leukaemia looked at each of them. Patients with breast cancer are at an increased risk of developing a secondary cancer. This could be due to the dose and length of treatment with these drugs. Since, Embury et al. (1977) discussed and observed the efficacy of maintenance chemotherapy for acute myelogenous leukaemia and conducted by at Stanford University. After reaching a stage of remission through treatment by chemotherapy, patients were randomized into two groups. Patients were randomly assigned to one of two groups after achieving remission with chemotherapy. The first group received chemotherapy for maintenance, while the second group did not. The main aim of experiment to examine that the maintenance in chemotherapy to increase the length of the remission. The material presented here was used to conduct a preliminary study in October 1974.

1.1 Statistical Methodology

In clinical trials, the medical researchers undertake survival experiment on humans, animals, and the environment, among other things, with the primary objective of understanding the fundamental principle of observed lifetime. Survival analysis is important when the time between exposure and event is of clinical interest. The majority of medical and epidemiological investigations are undertaken with the goal of determining the occurrence of a specific outcome event. The Clinical studies are primarily concerned with determining the time to event or outcome. The time to an event could differ from the time to a fatal event, such as death, or the time to occur. In such experiments, generally, conducting life-testing examinations cost, time and resources, and it necessitate a significant amount of money and human resources. Different kinds of censoring schemes that have been developed and discussed in the literature for reduce the cost and duration of experimentation. These censoring schemes are also useful for performing experiments with limited resources and time. Few popular censoring schemes are Type-I and Type-II in which the experiment time and maximum number of failures, respectively, are being fixed in advance in a given experiment. However, with both censoring schemes, either additional time is required or the necessary numbers of failure items are not obtained. A randomly censored sample when both the experimental unit and censoring time points are independent of each other outcomes. A patient who moves away from the experimental environment before the event of interest occurs is considered a randomly censored value i.e. A randomly censored value is a participant who leaves the experimental environment before the event of interest occurs. Such patients do not complete the course of treatment in actual situations, especially in clinical trials, and they leave owing to a variety of environmental conditions before even the experiment's end point. The entry and exit times of participants in an investigation are unpredictable in a random censoring environment. As a result, each unit has an independent and identically distributed by censoring time, as well as corresponding failure times at the stipulated time. In this scenario, the observed sample is determined by measuring the minimum from the censoring

time and failure time. For random censoring, various lifetime distributions for the failure time and censoring time have been investigated, including exponential, Normal, Maxwell, Rayleigh, gamma, and Weibull, among others.

In literature, many authors have discussed the random censoring setup by considering different lifetime models. In this regard, Nandi and Dewan (2010) used the expectation maximization (EM) algorithm to estimate the parameters of the Marshall-Olkin bivariate Weibull distribution in the presence of random censoring. Kumar and Garg (2014) discussed the parameter estimation procedure for the parameters of bivariate Weibull distribution under random censoring by using the EM algorithm. The extensive simulations are conducted to indicate that the calculators perform random censorship efficiently. Krishna et al. (2015) presented the maximum likelihood estimates of the parameters of the Maxwell distribution under the random censoring scheme with their confidence intervals and also discussed the Bayesian procedure for calculating the estimate of the related function under the squared error loss function. For the randomly censored data, Kim (2016) considered statistical conclusions about estimating the parameters of a Weibull distribution. The estimates of parameter are derived by ML and approximation ML methods. Kumar (2018) discussed the procedure of parameter estimation and analyzed reliability characteristics under a randomly censored sample when both are followed by the loglogistic distribution. In continuation of this, Kumar and Kumar (2019) analyzed the parameter estimation procedure of the inverse Weibull distribution under a random censoring setup under the classical and Bayesian paradigms. Ajmal et al. (2021) considered the random censorship model using Weibull distribution and compare it with maximum likelihood and Jeffreys methods. They found that closed-form formulations are not practicable for the Bayes estimators, which meant that the approximate Bayes estimates were utilized for this importance sampling technique.

Many well-known distributions are used in life testing experiments. But for particular real data, the search for a more suitable model is always in demand. Common objectives of all scientists are to be analyzing the lifetime data. This information is from their experiments, which could be in areas such as demography, engineering, life science, health management, and so on. The main focus of an analytic technique is on statistics that can be used to plan future events. Modeling of the data can be done in a variety of ways, both basic and complicated. A well-established methodology is to fit the data using a distribution based procedure and then acquire the relevant statistics. The benefit of this technique is that once a good model for the gathered observations in an experiment is found, all of the model's properties can be used immediately. Shanker (2017) introduced the Akshaya distribution, a new one-parameter continuous distribution for lifetime modeling in medical and engineering science. Since, the hazard function of the Akshaya distribution increases or decreases (depending on its parameter), this distribution is adaptable to real-world analysis. Shanker (2017) studied the Akshaya distribution's statistical features and determined the maximum likelihood function for both complete and censored sample situations. They exemplify the fitting and analysis of an actual data set. Ramadan et al. (2021) show the basic properties of the generalized power Akshaya distribution and discussed the classical and Bayesian estimation procedure for the parameter.

Let us define the underlying lifetime Akshaya distribution, if X be a random variable follows Akshaya distribution and the probability density function (pdf) is given as

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$$f(x.\theta) = \frac{\theta^4(1+x)^3 e^{-\theta x}}{\theta^3+3\theta^2+6\theta+6}\ ; \qquad x, \theta > 0 \tag{1}$$

where θ is the scale parameter of Akshaya distribution. The survival function at given time t of Akashaya distribution is given by

$$S(t,\theta) = \frac{e^{(-\theta x)}}{\psi(\theta)}[\theta^3(t^2+1) + 3\theta^2 t^2(\theta+1) + 3(\theta t+1)(\theta^2+2\theta+2)] \tag{2}$$

where, $\psi(\theta) = \theta^3 + 3\theta^2 + 6\theta + 6$.

The hazard function of Akashaya distribution is given by

$$h(t,\theta) = \frac{\theta^4(1-x)^3}{\xi(y,\theta)} \tag{3}$$

where, $\xi(y,\theta) = [\theta^3(t^2+1) + 3\theta^2 t^2(\theta+1) + 3(\theta t+1)(\theta^2+2\theta+2)]$ is the function of x and θ.

In this paper, we studied the Akshaya lifetime model under the random censoring setup and obtained the estimates of the parameters under classical and Bayesian approaches. In Section 2, the failure model is derived under random censoring when the failure time and censoring variable are considered to follow the Akashaya distribution. The expressions of the probability of failure before censoring time and observed time to test are also given in this section. In Section 3, the maximum likelihood (ML) estimates are obtained with the asymptotic confidence intervals (ACIs) for distribution parameter. The Bayesian estimation procedure for parameters under squared error loss function by using the inverted gamma prior is discussed in Section 4. The Bayes estimates are obtained under the squared error loss function by using the Markov chain Monte Carlo (MCMC) method. Finally, Section 5 dedicated to real data analysis to study the applications.

2. Setup of Problem

Suppose the n subjects are put in the experiment with their lifetimes denoted as $X_1, X_2, \dots, X_n$ which are independent and identically distributed *(i.i.d.)* random variables having probability density function (*pdf*) $f_X(x,\theta)$) and cumulative distribution function *(cdf)* $F_X(x,\theta)$, respectively. Also, let $T_1, T_2, \dots, T_n$ denotes the random censoring times with *pdf* and *cdf* are $g_T(t, \beta)$ and $G_T(t, \beta)$, respectively, where β is the scale parameter. Moreover, let us assume that the random variables

$X_i's$ and $T_i's$, i=1, 2 ,…, n be mutually independent. Note that, in the between of $X_i's$ and $T_i's$, only one will actually be observed at any particular time. Let us denote the actual observation time by $Y_i = min.(X_i, T_i); i = 1, 2, \dots, n$. Also, define a new indicator variableD_i, such that

$$D_i = \begin{cases} 1, & \text{if } X_i \le T_i \\ 0, & \text{if } X_i > T_i \end{cases}$$

For a model of random censorship, Koziol and Green (1976) introduced a special model with For a model of random censorship, [6] introduced a special model with

$$1 - G_t = (1 - T_x)^{\alpha}, \text{ for some } \alpha > 0.$$

Hence, $\alpha(\alpha+1)$ is the expected proportion of the censored observations and α is called the censoring parameter. The case α = 0 corresponds to no censoring. Since, Di follows to Bernoulli distribution with parameter p so the probability mass function of Di is given by

$$P[D_i = j] = p^j(1-p)^{1-j} \quad ; \quad j = 0, 1 \tag{4}$$

Since, Xi's and Ti's are independent, so Yi's and Di's will also be independent. We define the joint

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density function of Y and D, which is given by

$$f_{Y,D}(y, d, \theta, \beta) = \{f_X(y, \theta)(1 - G_T(y, \beta))\}^d \{g_T(y, \beta)(1 - F_X(y, \theta))\}^{1-d}. \quad (5)$$

$y, \beta, \theta > 0$, $d = 0, 1$. Since, the X and T are follows to Akashaya distribution with parameter θ and β, respectively. By using the pdf and cdf of Akashaya distribution given in (1) and (2), we have

$$f_{Y,D}(y, d, \theta, \beta) = \frac{\theta^4 \beta^{4(1-d)}(1 - y)^3}{\psi(\theta)\psi(\beta)} e^{-y(\theta+\beta)} \xi(y, \theta)^{1-d} \xi(y, \beta)^d$$

Since, the probability of failure is defined by a unit fails before it is censored. So Akashaya distribution lifetime model, the mathematical expression of probability of failure is given by

$$P[\text{an items fails}, d = 1] = P[X \leq T] = \int_0^\infty \frac{\beta^4 (1 - t)^3 e^{-t(\theta+\beta)} \xi(t, \theta)}{\psi(\theta)\psi(\beta)} dt$$

We can solve probability value by numerically for different values of θ and β. Table 1 shows the probability of failure (p) before the censoring time for different values of θ and β. We observed that the values of p increase with increasing values of β, for a fixed value of θ while a decrease in the values of p with increasing values of θ for a fixed value of β.

$\theta \setminus Q$	**0.5**	**1.0**	**1.5**	**2.0**	**2.5**	**3.0**
0.5	0.5000	0.7102	0.7742	0.8412	0.8901	0.9478
1.0	0.2898	0.5000	0.6147	0.7045	0.7837	0.8867
1.5	0.2258	0.3853	0.5000	0.6137	0.7228	0.8142
2.0	0.1588	0.2955	0.3863	0.5000	0.6248	0.7645
2.5	0.1099	0.2163	0.2772	0.3752	0.5000	0.6412
3.0	0.0522	0.1133	0.1858	0.2355	0.3588	0.5

2.1 Expected Time on Test

In lifetime experiments, the researchers are interested to estimate the total time of the test in the experiments. Since the cost of the experiment depends on the time of test. We derived the mathematical expression of expected time on test (ETT) and obtain for various values of θ, β and n in the random censoring scenario. Let us define the variable $Z = \max.(Y_1, Y_2, \ldots, Y_n)$, then the cdf of Z is given by

$$F_Z(z) = [P(Y_1 \leq z)]^n; \; z > 0.$$

Since $Y_i, i = 1, 2, 3, \ldots, n$ are *iid* random variables, so we have

$$P[Y_i \leq z] = 1 - \frac{e^{-y(\theta+\beta)} \xi(z, \theta) \xi(z, \beta)}{\psi(\theta)\psi(\beta)}$$

Using this expression, we get the *cdf* of Z as follows

$$F_z(z) = [1 - \frac{e^{-y(\theta+\beta)} \xi(z, \theta) \xi(z, \beta)}{\psi(\theta)\psi(\beta)}]^n$$

Now, the desired ETT can be written as

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$$ETT\ [or\ E(z)] = \int_0^{\infty} (1 - [1 - \frac{e^{-y(\theta+\beta)}\xi(z,\theta)\xi(z,\beta)}{\psi(\theta)\psi(\beta)}]^{n})\, dz \quad (6)$$

In addition to ETT, one more quantity, observed time on test (OBTT) is of great in- terest. In case of random censored sample, OBTT can be given by quantity $Z = max(Y_1, Y_2, \ldots, Y_n)$.

In case of uncensored (complete) sample, we derive the OBTT. Let us define $V = \max(X_1, X_2, \ldots, X_n)$, where $X_1, X_2, \ldots, X_n$ is the observed sample values. Now, the distribution function of V is given by

$$F_V(v) = [P(X_1 \leq v)]^n$$

Since Xi's are i.i.d., therefore, the expected value of V is given by

$$E(V) = \int_0^{\infty} [1 - F_V(v)]dv == \int_0^{\infty} [1 - [P(X_1 \leq v)]^n]dv$$

Thus, for our underlying distribution Akashaya distribution,

$$OBTT = \int_0^{\infty} (1 - [\frac{e^{-v\theta}\xi(v,\theta)}{\psi(\theta)}]^{n})\, dv \quad (7)$$

F this, Firstly we generate 5000 randomly censored samples as defined above section. By using (6) and (7), the easily obtained the value of ETT and OBTT under randomly censored data for different values of θ, β and n.

3. Maximum Likelihood Estimation

Let n subjects are put in the experiment under the random censoring scenario. Let X and T be the survival time and censoring time and both follow to Akshaya distribution with parameter θ and β, respectively. Since observed sample data is defined as the minimum of the X's ad T's. Now, we discuss parameter estimation for this model, we define the likelihood function of the observed sample of $Y_1, Y_2, \ldots, Y_n$ given parameter under random censoring. So, the likelihood function of Y is given by

$$L(y, d, \theta, \beta) = \frac{\theta^{4m}\beta^{4(n-m)} \prod_{i=1}^{n}(1-y_i)^3}{\psi(\theta)^n\psi(\beta)^n} e^{-(\theta+\beta)\sum_{i=1}^{n} y_i} \prod_{i=1}^{n}[\xi(y_i,\theta)^{1-d_i}\xi(y_i,\beta)^{d_i}]$$

where, $m = \sum_{i=1}^{n} d_i$. Now, on taking the logarithm of above equation, the log-likelihood function can be written in the following form

$$l(y, d, \theta, \beta) = 4m\ log(\theta) + 4(n-m)\log(\beta) - n\log(\psi(\theta)) - n\log(\psi(\beta)) + 3\sum_{i=1}^{n}\log(1-y_i)$$
$$- (\theta+\beta)\sum_{i=1}^{n} y_i + \sum_{i=1}^{n} d_i \log\ \xi(y_i,\beta) + \sum_{i=1}^{n}(1-d_i)\log\ \xi(y_i,\theta) \quad (8)$$

Taking the partially differentiation of log likelihood function with respect to θ and β and then equating to zero, we get the ML estimator θˆ and βˆ of θ and β, respectively, as follow

$$\frac{4m}{\theta} - \sum_{i=1}^{n} y_i - n\frac{\psi^F(\theta)}{\psi(\theta)} + \sum_{i=1}^{n}(1-d_i)\frac{\xi^F(y_i,\theta)}{\xi(y_i,\theta)} = 0 \quad (9)$$

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$$\frac{4(n-m)}{\beta} - \sum_{i=1}^{n} y_i - n\frac{\psi^F(\beta)}{\psi(\beta)} + \sum_{i=1}^{n} d_i \frac{\xi^F(y_i,\beta)}{\xi(y_i,\beta)} = 0 \qquad (10)$$

Where, $\xi'(y,\theta) = 3\theta^2(y^2+1)(3y+1) + 6\theta(y^2+2y+6) + 6(y+1)$, $\psi'(\theta) = 3\theta^2 + 6\theta + 6$, $\xi'(y,\beta) = \xi(y,\beta) = 3\beta^2(y^2+1)(3y+1) + 6\beta(y^2+2y+6) + 6(y+1)$ and $\psi'(\beta) = 3\beta^2 + 6\beta + 6$. Here, the ML equations of θ and β are not in closed form for obtaining the ML estimate of parameter. We used the numerical iteration method to solve the given equation.

3.1 Interval Estimation

The confidence intervals are measures of uncertainty in the sampling method. It defines the probability that the given population parameter would lie within the upper and lower set of values. Since the distribution of estimate of θ and β are not in closed-form so we can find the observed Fisher information matrix in the form

$$I(\xi) = \begin{bmatrix} -\frac{\partial^2 l(y,d,\theta,\beta)}{\partial\theta^2} & -\frac{\partial^2 l(y,d,\theta,\beta)}{\partial\theta\,\partial\beta} \\ -\frac{\partial^2 l(y,d,\theta,\beta)}{\partial\beta\,\partial\theta} & -\frac{\partial^2 l(y,d,\theta,\beta)}{\partial\beta^2} \end{bmatrix}_{(\theta=\hat{\theta},\beta=\hat{\beta})}$$

where, $\hat{\xi} = (\hat{\theta},\hat{\beta})$ is corresponding ML estimates of $\xi = (\theta, \beta)$. Thus, using the asymptotic normality of estimators, we get the $100(1-\alpha)\%$ confidence limits of $\hat{\theta}$ and $\hat{\beta}$ by $\hat{\theta} \pm z_{\alpha/2}\sqrt{Var(\hat{\theta})}$ and $\hat{\beta} \pm z_{\alpha/2}\sqrt{Var(\hat{\beta})}$, respectively, where $z_{\alpha/2}$ is upper $100\left(\frac{\alpha}{2}\right)^{th}$ percentile of standard normal variate. The required functions in constructing the asymptotic confidence interval (ACI)'s are given as

$$\frac{\partial^2 l(y,d,\theta,\beta)}{\partial\theta^2}\Big|_{\theta=\hat{\theta}} = -\frac{4m}{\theta^2} + \sum_{i=1}^{n}(1-d_i)\frac{\xi(y_i,\theta)\xi''(y_i,\theta) - (\xi'(y_i,\theta))^2}{(\xi(y_i,\theta))^2} - \frac{\psi(\theta)\psi''(\theta) - (\psi'\theta))^2}{(\psi(\theta))^2}$$

$$\frac{\partial^2 l(y,d,\theta,\beta)}{\partial\beta^2}\Big|_{\theta=\hat{\theta}} = -\frac{4(n-m)}{\beta^2} + \sum_{i=1}^{n} d_i \frac{\xi(y_i,\beta)\xi''(y_i,\beta) - (\xi'(y_i,\beta))^2}{(\xi(y_i,\beta))^2} - \frac{\psi(\beta)\psi''(\beta) - (\psi'\beta))^2}{(\psi(\beta))^2}$$

and

$$\frac{\partial^2 l(y,d,\theta,\beta)}{\partial\beta\,\partial\theta}\Big|_{(\theta,\beta)=(\hat{\theta},\hat{\beta})} = \frac{\partial^2 l(y,d,\theta,\beta)}{\partial\theta\,\partial\beta}\Big|_{(\theta,\beta)=(\hat{\theta},\hat{\beta})} = 0$$

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where, $\xi''(y_i, \theta) = 6(y+1)^2\{\theta(y+1)+1\}$, $\xi''(y_i, \beta) = 6(y+1)^2\{\beta(y+1)+1\}$, $\psi''(\theta) = 6(\theta+1)$ and $\psi''(\beta) = 6(\beta+1)$.

Sometimes in this method, the lower bound of ACIs may be negative. In order to overcome this weakness, one method is to replace the lower bound by zero and another method [Lawless (2011)] is to apply logarithmic transformation to obtain the asymptotic normality of $\log(\theta)$ and $\log(\beta)$as

$$\frac{\ln\hat{\theta}-\ln\theta}{\mathrm{Var}(\ln\hat{\theta})} \sim N(0,1) \quad \& \quad \frac{\ln\hat{\beta}-\ln\beta}{\mathrm{Var}(\ln\hat{\beta})} \sim N(0,1)$$

Therefore, using the above property $100(1-\alpha/2)\%$ ACIs of θ and β in this manner is given by

$$[\hat{\theta}\exp(-z_{\frac{\alpha}{2}}\sqrt{\mathrm{Var}(\ln\hat{\theta})}),\ \hat{\theta}\exp(z_{\frac{\alpha}{2}}\sqrt{\mathrm{Var}(\ln\hat{\theta})})]$$

and

$$[\hat{\beta}\exp(-z_{\frac{\alpha}{2}}\sqrt{\mathrm{Var}(\ln\hat{\beta})}),\ \hat{\beta}\exp(z_{\frac{\alpha}{2}}\sqrt{\mathrm{Var}(\ln\hat{\beta})})].$$

4. Bayesian Estimation

The Bayesian inferential approaches give a standardized mechanism for combining prior information obtained from previous imaging techniques. We apply the Bayes theorem in the Bayesian framework to update the likelihood of a linked event based on some past knowledge. As a result, we regard parameter to be a random variable that follows a previous knowledge distribution. Here, it is considered that the prior distribution of θ and β are gamma distribution, denoted by $G(a_1, b_1)$ and $G(a_2, b_2)$, respectively, and given as

$$\pi_1^*(\theta) = \frac{b_1\theta^{a_1-1}}{\Gamma a_1}e^{-b_1\theta} \ ; \qquad \theta, a_1, b_1 > 0$$

and

$$\pi_2^*(\beta) = \frac{b_2\beta^{a_2-1}}{\Gamma a_2}e^{-b_1\beta} \ ; \qquad \beta, a_2, b_2 > 0$$

where a_1, a_2, b_1 and b_2 are the hyper-parameter of prior distribution for θ and β. Since θ and β are independent, so the joint prior density is obtain by multiplying both priors density and written up to proportionality constants as follows

$$\pi^*(\theta, \beta, y, d) \ \propto \ \theta^{a1-1}\beta^{a2-1}e^{-(b_1\theta+b_2\beta)} \qquad (11)$$

For obtaining the posterior distribution, we have to merge the likelihood function in (8) and the joint prior density in (11). The required posterior distribution of (θ, β) for given observation, comes out to be as follows

$$\Pi(\theta, \beta, y, d) \ \propto \frac{\theta^{4m+a_1-1}\,\beta^{4(n-m)+a_2-1}\prod_{i=1}^{n} y_i}{\psi^n(\theta)\psi^n(\beta)}\ exp\left[-\theta\ (b_1 + \sum_{i=1}^{n} y_i) - \beta\,(b_2 + \sum_{i=1}^{n} y_i)\right]$$

$$\prod_{i=1}^{n}[\xi^{1-d_i}(y_i,\theta)\xi^{d_i}(y_i,\beta)] \qquad (12)$$

The Bayes estimate of $k(\vartheta) = k(\theta, \beta)$, say, is the function of θ and β under squared error loss

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function (SELF), can be obtained as follows

$$E\{k(v)\} = \frac{\iint k(v)\Pi(\theta, \beta. y, d\ )d\theta d\beta}{\iint \Pi(\theta, \beta. y, d\ )d\theta d\beta} \tag{13}$$

We observe that the direct solution of the ratio of integral in (13) is not possible. In this regards, we have to utilize the Bayesian approximation technique which is available in literature. Here we used MCMC method for drive the Bayes estimate of parameter. For this purpose, the full condition distributions are given below

$$\Pi(\theta|\ \beta, y, d\ )\ \propto \frac{\theta^{4m+a_1-1}}{\psi^n(\theta))}\ exp\ [-\theta\ (b_1 + \sum_{i=1}^{n} y_i)]\ \prod_{i=1}^{n} [\xi^{1-d_i}(y_i, \theta)] \tag{14}$$

$$\Pi(\ \beta|\ \theta, y, d\ )\ \propto \frac{\beta^{4(n-m)+a_2-1}}{\psi^n(\beta)}\ exp\ [-\beta\ (b_2 + \sum_{i=1}^{n} y_i)]\ \prod_{i=1}^{n} [\xi^{d_i}(y_i, \beta)] \tag{15}$$

We observe that the marginal posterior distributions of θ and β cannot be obtained in the closed form, which is essential in order to obtain the Bayes estimates of parameters.

4.1 MCMC Method

In MCMC method, the Metropolis Hasting (MH) algorithm [Chen et al. (2012)] is utilized to generate the random sample from the full conditional of θ and β defined in (14) and (15). Here, the full conditional posterior densities of θ and β are independent of each other, so we can draw the samples θ and β from their (posterior marginal) density by MH algorithm independently. The necessarily steps to generate samples by the MH algorithm from conditional densities are given as follows:

1. Set h=1 and take the initial value of parameters $\theta^{(0)} = \hat{\theta}$ and $\beta^{(0)} = \hat{\beta}$
2. Generate candidate points θ^* and β^* from proposal density $q_1 \sim N(\hat{\theta}, var(\hat{\theta}))$ and $q_2 \sim N(\beta, var(\beta))$, respectively, we can easily generate the points u_1 and u_2 from a uniform distribution U(0, 1). Based on the initial value of parameter and u_1 and u_2 , we compute an acceptance ratio at the t th stage by the following expression

$$r_1 = \frac{\pi_1(\theta^*, y\ d\ )q_1(\theta^{(t-1)})}{\pi_1(\theta^{(t-1)}, y\ d\ )q_1(\theta^*)} \quad \text{and} \quad r_2 = \frac{\pi_2(\beta^*, y\ d\ )q_2(\beta^{(t-1)})}{\pi_2(\beta^{(t-1)}, y\ d\ )q_2(\beta^*)}$$

3. Let $P_1(\theta^{(t-1)}, \theta^*) = \min(r_1, 1)$, then set $\theta^{(t)} = \theta^*$ if $u_1 \leq P_1(\theta^{(t-1)}, \theta^*)$, otherwise $\theta^{(t)} = \theta^{((t-1))}$. Similarly let $P_2(\beta^{(t-1)}, \beta^*) = \min(r_2, 1)$, then set $\beta^{(t)} = \beta$ if $u_2 \leq P_2(\beta^{(t-1)}, \beta^*)$, otherwise $\beta^{(t)} = \theta^{((t-1))}$.
4. set $t = t + 1$.
5. Repeat steps (2)-(4) N' times to get the sequence $\theta^1, \theta^2, \ldots, \theta^{N^F}$ and $\beta^1, \beta^2, \ldots, \theta^{N^F}$
6. where N' is a large number.

From the sample generated by the MH algorithm, we discard the first few values from the generated chain to remove the dependency of initial value effects. Also, by using cumsum and ACF plots, we can diagnose the stationary in this chain. After that, we get a sample of size N,

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based on which we can draw the required inferences. Additionally, we calculated the Bayesian credible intervals (BCIs) and highest posterior density (HPD) intervals of the parameter[Chen and Shao (1999)].

5.1 Simulation Data

Here we consider a simulated sample for analysis to show that how one can use the results obtained in the previous sections, to solve a real life problem. In this scenario, we consider that both observed time and censoring time follow Akshaya distribution with parameters θ = 2.0 and β = 1.5, respectively. We generated an observed sample under random censoring of size n = 35. The observed sample is 0.05955, 0.06205, 0.13182, 0.18183+, 0.18581, 0.20109, 0.21115, 0.23109, 0.25333, 0.30313+, 0.32741, 0.34921, 0.35559+, 0.44733+, 0.47636, 0.53807, 0.58269, 0.58340, 0.63321, 0.63373, 0.71466, 0.73164, 0.81143, 0.83814+, 0.88371+, 0.92740, 0.98780+, 1.13410+, 1.50894+, 1.56649+, 1.60643+, 1.62566+, 1.78527, 2.25083 and 3.73654, where y+ denoting the observed censored time. On the basis of the observed sample, the estimated values of parameters and other functions have been obtained. We consider the hyper-parameter values $a_1 = a_2 = 2$and $b_1 = b_2 = 3$ for obtained the respected outcomes. The ML and Bayes estimate value of parameters and related functions are presented in Table 2.

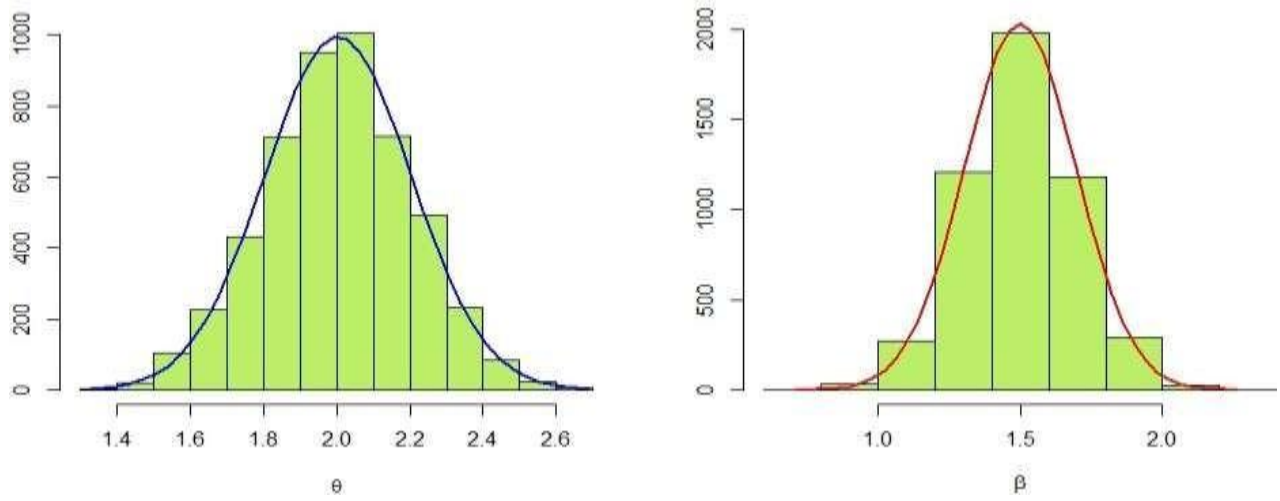

Figure 1: Histogram plot of posterior sample of θ and β.

Table 2: The ML and Bayes Estimates values, *ACI*, *BCI*, *HPD* for θ and β, *ETT* an *OBTT* for Simulated Data set

Estimate Value	θ	β
MLE	1.9742	1.5284
ACI	(1.7428, 2.4938)	(1.3947, 1.6481)
Bayes Estimate	2.0664	1.5370
BCI	(1.7542, 2.4285)	(1.3475, 1.6840)
HPD	(1.8746, 2.1412)	(1.4033, 1.6234)
ETT	2.4582	
OBTT	1.4580	

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5.2 Real Data Study

In this section, we illustrate estimation procedures as discussed in the previous sections with the help of real data. since, the Acute myeloblastic leukaemia is a blood cell malignancy that affects the myeloid line. An excess of immature myleloid cells in the bone marrow hinders the normal synthesis of red blood cells, leading in anaemia and reduced platelet production, or thrombocytompenia. Patients with Acute myeloblastic leukaemia seek medical help because of exhaustion caused by anaemia or bleeding and bruising caused by a lack of platelets. The survival times (in days) of 23 Acute myeloblastic leukaemia patients were reported by Miller (1997). In the Figure 3, KM and QQ plots are given and it can be seen t+ hat the survival time of Acute myeloblastic leukaemia data time data fits Akashaya distribution. The KS test statistics (D) is found to be 0.2084 with p value greater than 0.05, which indicates that the there is no evidence to reject the hypothesis that the data is from Akshaya distribution. The random censored samples are obtained as: 5, 5, 8, 8, 9, 12, 13, 13+, 16+, 18, 23, 23, 27, 28+, 30, 31, 33, 34, 43, 45, 45+, 48, 161+, where y+ denoting the censored time. There are 18 observations which are observed as exact failure time and 5 as randomly censored. Figure 2 present the patient survival time with their cause and boxplot for Acute myeloblastic leukaemia data. We assume the non-informatics prior density for the θ and β in Bayesian procedure. This sample considered as randomly censored data and estimates for the data are given in Table 3. Figure 4 shows the fitting of the distribution and Figure 5 presented the data *cumsum*, *iteration* and marginal posterior density plot of given data.

Figure 2: Survival time and Boxplot for the Acute Myeloblastic Leukaemia patients data.

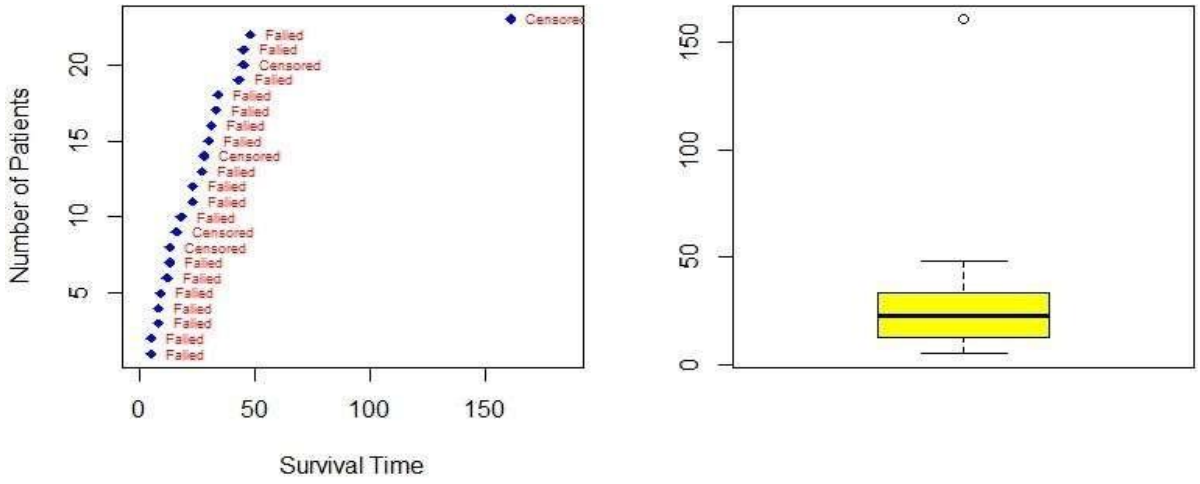

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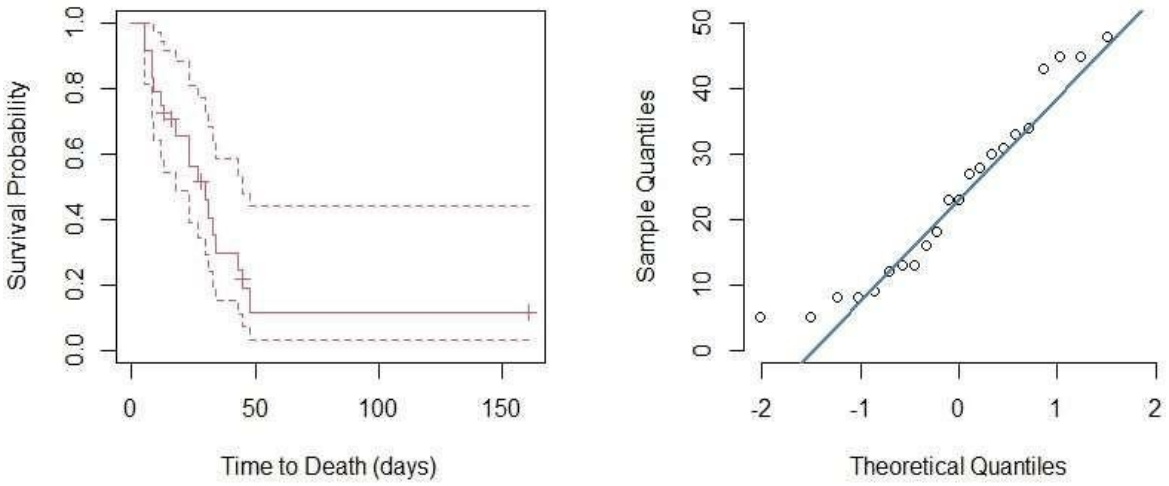
Figure 3: Kaplan–Meier and Q-Q plot for the Acute Myeloblastic Leukaemia patients data.



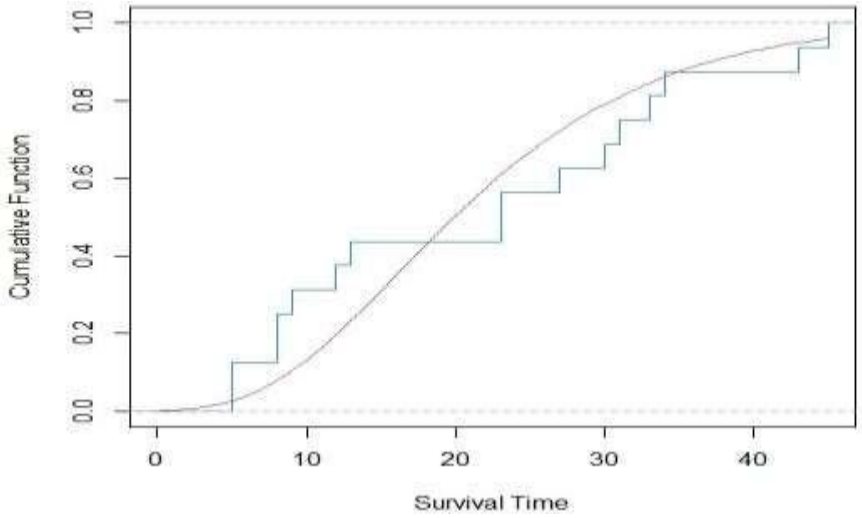


Figure 4: *ecdf* plots of Acute Myeloblastic Leukaemia patients data.

Table 3: The ML and Bayes estimates for AML data set

Estimate Value	θ	β
MLE	0.1754	0.0746
ACI	(0.1684,0.1807)	(0.0622,0.0846)
Bayes Estimate	0.1742	0.0719
BCI	(0.1698,0.1782)	(0.0674,0.0822)
HPD	(0.1712,0.1773)	(0.0692,0.808)
ETT	157	
OBTT	45	

6. Discussion

In this paper, We investigated the Akashaya distribution estimation process process us- ing the

random censoring scenario. For different combination of parameter values, we determined the probability of an item failing before censoring time. We also calculated the actual and expected exam time in both complete and censored environments. Un- der both classical and Bayesian scenario, parameter estimators and associated confidence intervals are determined. The proposed model is supported by simulation and survival data. For AML data, parameter and interval estimates are provided. All of the findings are favorable and support the desired research.

7 Conclusion

A cancer diagnosis offers a chance to become closer to you and assess how you might live a life that you like. Some patients respond better to treatment in their health than others. If an individual is treated for chemotherapy and their cancer will not return after five years. According to World Health organization, the palliative care is proper treatment for those who have a serious disease. Palliative care refers to any treatment that aims to alleviate symptoms, improve quality of life, and provide support to patients and their families. Palliative care is available to everybody, regardless of age, cancer kind, or stage.

Palliative care works best when it is initiated as early as possible in the cancer treatment process. People are frequently treated for leukaemia at the same time as they are treated for adverse effects. Patients who receive both at the same time report having fewer severe symptoms, a higher quality of life, and a higher level of satisfaction with their treatment. Medication, nutritional adjustments, relaxation techniques, emotional support, and other therapies are common palliative treatments. You may also undergo palliative therapies such as chemotherapy or radiation therapy, which are comparable to those used to treat leukaemia. Discuss the aims of each treatment in the treatment plan with your doctor.

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Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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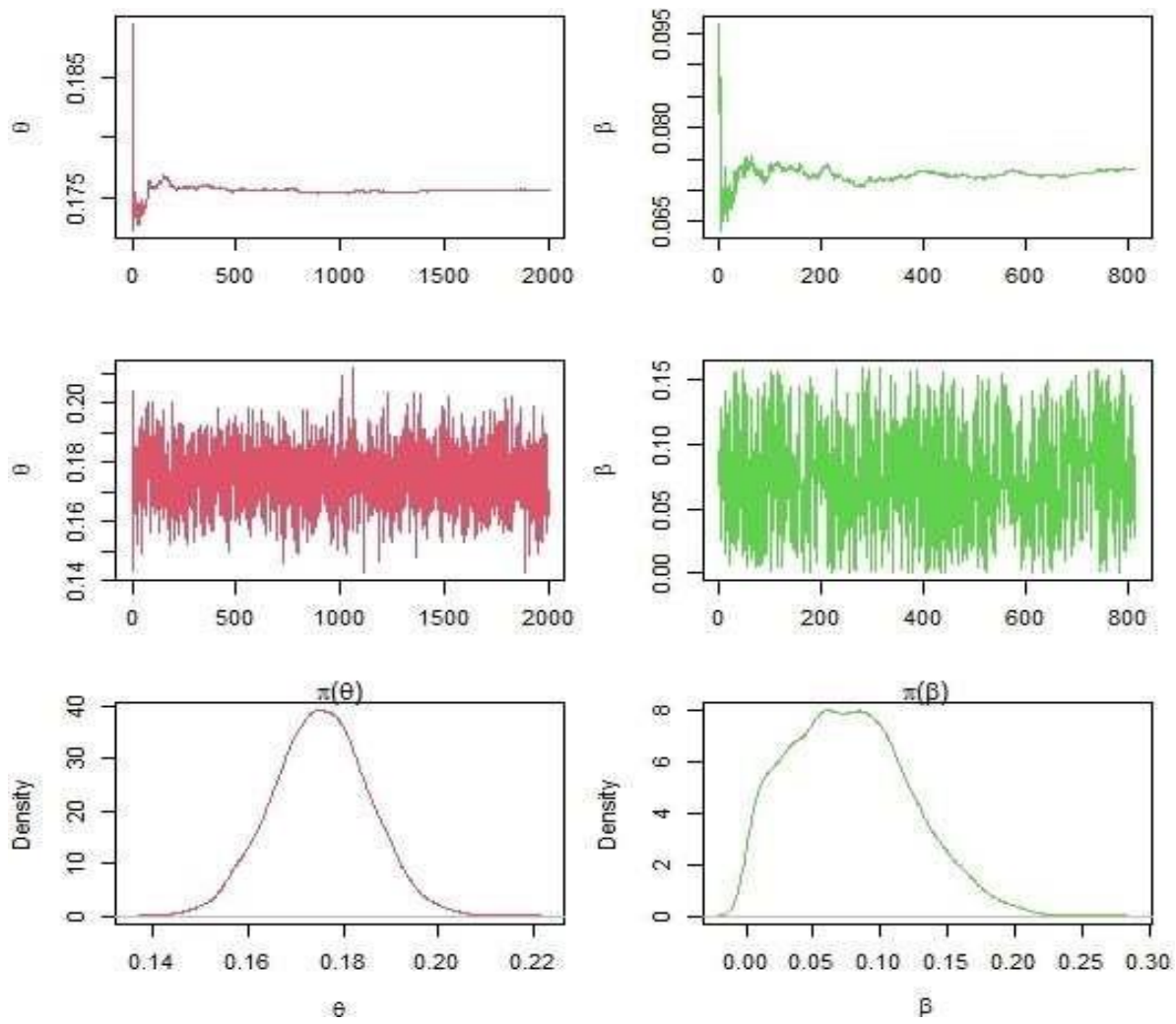

Figure 5: *cumsum*, *Iteration* and *density* plots based on marginal posterior distribution for θ and β based on Acute Myeloblastic Leukaemia patients data.

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