

Analysis of Kidney infection Data Using Correlated Inverse Gaussian Frailty Model

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Abstract

Frailty models are used in the survival analysis to account for the unobserved heterogeneity in individual risks to disease and death. To analyze the bivariate data on related survival times, the shared frailty models were suggested. Shared frailty models are used despite their limitations. To overcome their disadvantages correlated frailty models may be used. In this paper, we introduce the inverse Gaussian correlated frailty models with three different baseline distributions namely, the Pareto, Burr and the linear failure rate distributions. We introduce the Bayesian estimation procedure using Markov Chain Monte Carlo (MCMC) technique to estimate the parameters involved in these models. We apply these models to a real life bivariate survival data set of McGilchrist and Aisbett (1991) related to the kidney infection data and a better model is suggested for the data.

Key words: Bivariate survival; Copula; Correlated inverse Gaussian frailty; Cross-ratton function; Hazard rate.

1. Introduction

The frailty model is a random effect model for time to event data which is an extension of the Cox's proportional hazards model. Shared frailty models are the most commonly used frailty models in literature, where individuals in the same cluster share a common frailty. Frailty models (Vaupel et al. 1979) are used in the survival analysis to account for the unobserved heterogeneity in the individual risks to disease and death. The frailty model is usually modeled as an unobserved random variable acting multiplicatively on the baseline hazard function. Hanagal and Dabade (2013), Hanagal and Bhambure (2015, 2016) and Hanagal and Pandey (2014a, 2014b, 2015a, 2015b, 2016, 2017a) analyzed kidney infection data and Australian twin data using shared gamma and inverse Gaussian frailty models with different baseline distributions for the multiplicative model. Hanagal and Sharma (2013, 2015a, 2015b, 2015c) analyzed acute leukemia data, kidney infection data and diabetic retinopathy data using shared gamma and inverse Gaussian frailty models for the multiplicative model. Hanagal and Bhambure (2014) developed shared inverse Gaussian frailty model based on the reversed hazard rate for Australian twin data. Hanagal et al.(2017) discussed correlated gamma frailty models for bivariate survival data to analyze kidney infection data and Hanagal

and Pandey (2017b) proposed correlated gamma frailty models for bivariate survival data based on reversed hazard rate for Australian twin data. Hanagal (2017) gave extensive literature review on different shared frailty models.

In a univariate frailty model, let a continuous random variable T be a lifetime of an individual and the random variable Z be frailty variable. The conditional hazard function for a given frailty variable, $Z = z$ at time $t > 0$ is,

$$h(t | z) = zh_0(t)e^{\mathbf{X}\beta}, \quad (1)$$

where $h_0(t)$ is a baseline hazard function at time $t > 0$, \mathbf{X} is a row vector of covariates, and β is a column vector of regression coefficients. The conditional survival function for given frailty at time $t > 0$ is,

$$S(t | z) = e^{-\int_0^t h(x|z)dx} = e^{-zH_0(t)e^{\mathbf{X}\beta}}, \quad (2)$$

where $H_0(t)$ is the cumulative baseline hazard function at time $t > 0$. Integrating over the range of frailty variable Z having density $f_Z(z)$, we get the marginal survival function as,

$$\begin{aligned} S(t) &= \int_0^\infty S(t | z)f_Z(z)dz \\ &= \int_0^\infty e^{-zH_0(t)e^{\mathbf{X}\beta}} f_Z(z)dz \\ &= L_Z(H_0(t)e^{\mathbf{X}\beta}), \end{aligned} \quad (3)$$

where $L_Z(\cdot)$ is the Laplace transformation of the distribution of Z . Once we get the survival function at time $t > 0$, of life time random variable for an individual, we can obtain probability structure and make their inferences based on it.

Shared frailty explains correlation's between subjects within clusters. However, it does have some limitations. Firstly, it forces the unobserved factors to be the same within the cluster, which may not always reflect reality. For example, at times it may be inappropriate to assume that all partners in a cluster share all their unobserved risk factors. Secondly, the dependence between survival times within the cluster is based on marginal distributions of survival times. However, when covariates are present in a proportional hazards model with gamma distributed frailty the dependence parameter and the population heterogeneity are confounded (Clayton and Cuzick, 1985). This implies that the joint distribution can be identified from the marginal distributions (Hougaard, 1986). Thirdly, in most cases, a one-dimensional frailty can only induce positive association within the cluster. However, there are some situations in which the survival times for subjects within the same cluster are negatively associated. For example, in the Stanford Heart Transplantation Study, generally the longer an individual must wait for an available heart, the shorter he or she is likely to survive after the transplantation. Therefore, the waiting time and the survival time afterwards may be negatively associated.

To avoid these limitations, correlated frailty models are being developed for the analysis of multivariate failure time data, in which associated random variables are used to characterize the frailty effect for each cluster. Correlated frailty models provide not only variance parameters of the frailties as in shared frailty models, but they also contain additional parameter for modeling

the correlation between frailties in each group. Frequently one is interested in construction of a bivariate extension of some univariate family distributions (e.g., gamma). For example, for the purpose of genetic analysis of frailty one might be interested in estimation of correlation of frailty. It turns out that it is possible to carry out such extension for the class of infinitely-divisible distributions (Iachine 1995a, 1995b). In this case an additional parameter representing the correlation coefficient of the bivariate frailty distribution is introduced.

2. Inverse Gaussian Frailty

The gamma distribution is most commonly used frailty distribution because of its mathematical convenience. Another choice is the inverse Gaussian distribution. The inverse Gaussian makes the population homogeneous with time, whereas for gamma the relative heterogeneity is constant (Hougaard, 1984). Duchateau and Janssen (2008) fit the inverse Gaussian (IG) frailty model with Weibull hazard to the udder quarter infection data. The IG distribution has a unimodal density and is a member of the exponential family. While its shape resembles that of other skewed density functions, such as lognormal and gamma, it provides much flexibility in modeling. Furthermore, there are many striking similarities between the statistics derived from this distribution and those of the normal; see Chhikara and Folks (1986). These properties make it potentially attractive for modeling purposes with survival data. The models derived above are based on the assumption that a common random effect acts multiplicatively on the hazard rate function.

Alternative to the gamma distribution, Hougaard (1984) introduced the inverse Gaussian as a frailty distribution. It provides much flexibility in modeling, when early occurrences of failures are dominant in a life time distribution and its failure rate is expected to be non-monotonic. In such situations, the inverse Gaussian distribution might provide a suitable choice for the lifetime model. Also inverse Gaussian is almost an increasing failure rate distribution when it is slightly skewed and hence is also applicable to describe lifetime distribution which is not dominated by early failures. Secondly, for the inverse Gaussian distribution, the surviving population becomes more homogeneous with respect to time, where as for gamma distribution the relative heterogeneity is constant. The inverse Gaussian distribution has shape resembles the other skewed density functions, such as log-normal and gamma. These properties of inverse Gaussian distribution motivate us to use inverse Gaussian as frailty distribution. The inverse Gaussian distribution has a history dating back to 1915 when Schrodinger and Smoluchowski presented independent derivations of the density of the first passage time distribution of Brownian motion with positive drift. Villman et al., (1990) have studied the histomorphometrical analysis of the influence of soft diet on masticatory muscle development in the muscular dystrophic mouse. The muscle fibre size distributions were fitted by an inverse Gaussian law. Barndorff-Nielsen (1994) considers a finite tree whose edges are endowed with random resistances, and shows that, subject to suitable restrictions on the parameters, if the resistances are either inverse Gaussian or reciprocal inverse Gaussian random variables, then the overall resistance of the tree follows a reciprocal inverse Gaussian law. Gacula and Kubala (1975) have analyzed shelf life of several products using the IG law and found to be a good fit. For more real life applications (see Seshadri, 1999).

Consider a continuous random variable Z follows inverse Gaussian distribution with parameters μ and σ^2 then density function of Z is,

$$f_Z(z) = \begin{cases} \left[\frac{1}{2\pi\sigma^2} \right]^{\frac{1}{2}} z^{-\frac{3}{2}} e^{-\frac{(z-\mu)^2}{2z\sigma^2\mu^2}} & ; z > 0, \mu > 0, \sigma^2 > 0 \\ 0 & ; \text{otherwise,} \end{cases} \quad (4)$$

and the Laplace transform is,

$$L_Z(s) = \exp \left[\frac{1}{\mu\sigma^2} - \left(\frac{1}{\sigma^4\mu^2} + \frac{2s}{\sigma^2} \right)^{\frac{1}{2}} \right]. \quad (5)$$

The mean and variance of frailty variable are $E(Z) = \mu$ and $V(Z) = \mu^3\sigma^2$. For identifiability, we assume Z has expected value equal to one i.e. $\mu = 1$. Under this restriction, the density function and the Laplace transformation of the inverse Gaussian distribution reduces to,

$$f_Z(z) = \begin{cases} \left[\frac{1}{2\pi\sigma^2} \right]^{\frac{1}{2}} z^{-\frac{3}{2}} e^{-\frac{(z-1)^2}{2z\sigma^2}} & ; z > 0, \sigma^2 > 0 \\ 0 & ; \text{otherwise,} \end{cases} \quad (6)$$

and the Laplace transform is,

$$L_Z(s) = \exp \left[\frac{1 - (1 + 2\sigma^2 s)^{\frac{1}{2}}}{\sigma^2} \right], \quad (7)$$

with variance of Z as σ^2 . The frailty variable Z is degenerate at $Z = 1$ when σ^2 tends to zero. Let T_1 and T_2 be failure times of the pair of individuals like kidney, lungs, eyes or any paired organ of an individual or lifetimes of twins. The unconditional bivariate distribution function of lifetimes T_1 and T_2 with inverse Gaussian frailty is,

$$\begin{aligned} L_Z(H_1(t_1) + H_2(t_2)) &= \exp \left[\frac{1 - (1 + 2\theta(H_1(t_1) + H_2(t_2)))^{\frac{1}{2}}}{\theta} \right] \\ &= S(t_1, t_2) \end{aligned} \quad (8)$$

where $H_1(t_1)$ and $H_2(t_2)$ are the cumulative baseline hazard functions of the lifetime T_1 and T_2 respectively. Clayton (1978) define cross-ratio function as,

$$\theta^*(t_1, t_2) = \frac{\frac{\partial^2 S(t_1, t_2)}{\partial t_1 \partial t_2} S(t_1, t_2)}{\frac{\partial S(t_1, t_2)}{\partial t_1} \frac{\partial S(t_1, t_2)}{\partial t_2}}$$

The cross ratio function of inverse Gaussian frailty is,

$$\theta^*(t_1, t_2) = 1 + \frac{1}{\frac{1}{\theta} - \ln(S(t_1, t_2))}$$

The highest value is obtained at the start and equals $1 + \theta$, and goes to one as the survival function goes to zero. It is decreasing function of t_1, t_2 .

The joint bivariate survival functions in (8) can be expressed in terms of survival copula as (see Nelsen (2006) for details)

$$\bar{C}(u, v) = \exp \left\{ \frac{1 - [(1 - \theta \log u)^2 + (1 - \theta \log v)^2 - 1]^{\frac{1}{2}}}{\theta} \right\}$$

where $u = S_{T_1}(\cdot)$ and $v = S_{T_2}(\cdot)$. This is a new copula and not appeared in the earlier literature.

3. Correlated Frailty

The correlated frailty model is the second important concept in the area of multivariate frailty models. It is a natural extension of the shared frailty approach on the one hand, and of the univariate frailty model on the other. In the correlated frailty model, the frailties of individuals in a cluster are correlated but not necessarily shared. It enables the inclusion of additional correlation parameters, which then allows the addressing of questions about associations between event times. Furthermore, associations are no longer forced to be the same for all pairs of individuals in a cluster. This makes the model especially appropriate for situations where the association between event times is of special interest, for example, genetic studies of event times in families. The conditional survival function in the bivariate case (here without observed covariates) looks like

$$S(t_1, t_2 | Z_1, Z_2) = S_1(t_1 | Z_1) S_2(t_2 | Z_2) = e^{-Z_1 H_{01}(t_1)} e^{-Z_2 H_{02}(t_2)}, \quad (9)$$

where Z_1 and Z_2 are two correlated frailties. The distribution of the random vector (Z_1, Z_2) needs to be specified and determines the association structure of the event times in the model. Integrating the above bivariate survival function over Z_1 and Z_2 , we get unconditional bivariate survival function as

$$S(t_1, t_2) = E_{Z_1, Z_2} [e^{-Z_1 H_{01}(t_1)} e^{-Z_2 H_{02}(t_2)}] \quad (10)$$

where (Z_1, Z_2) has some known bivariate frailty distribution.

Consider some bivariate event times – for example, the lifetimes of twins, or age at onset of a disease in spouses, time to blindness in the left and right eye, or time to failure in the left and right kidney of patients. In the (bivariate) correlated frailty model, the frailty of each individual in a pair is defined by a measure of relative risk, that is, exactly as it was defined in the univariate case. For two individuals in a pair, frailties are not necessarily the same, as they are in the shared frailty model. We are assuming that the frailties are acting multiplicatively on the baseline hazard function (proportional hazards model) and that the observations in a pair are conditionally independent, given the frailties. Hence, the hazard of the individual i ($i = 1, 2$) in pair j ($i = j, \dots, n$) has the form

$$h(t | X_{ij}, Z_{ij}) = Z_{ij} h_{0i}(t) e^{\beta' X_{ij}}, \quad (11)$$

where t denotes age or time, X_{ij} is a vector of observed covariates, β is a vector of regression parameters describing the effect of the covariates X_{ij} , $h_{0i}(\cdot)$ are baseline hazard functions, and Z_{ij} are frailties. Bivariate correlated frailty models are characterized by the joint distribution of a two-dimensional vector of frailties (Z_{1j}, Z_{2j}) . If the two frailties are independent, the resulting lifetimes are independent, and no clustering is present in the model. If the two frailties are equal, the shared frailty model is obtained as a special case of the correlated frailty model with correlation one between the frailties (Wienke(2011)).

In order to derive a marginal likelihood function, the assumption of conditional independence of lifespans, given the frailty, is used. Let δ_{ij} be a censoring indicator for individual i ($i = 1, 2$) in pair j ($j = 1, \dots, n$). Indicator δ_{ij} is 1 if the individual has experienced the event of interest, and 0 otherwise. According to (2.2), the conditional survival function of the i th individual in the j th pair is

$$S(t|X_{ij}, Z_{ij}) = e^{-Z_{ij}H_{0i}(t)} e^{\beta' X_{ij}}, \quad (12)$$

with $H_{0i}(t)$ denoting the cumulative baseline hazard function. The contribution of individual i ($i = 1, 2$) in pair j ($j = 1, \dots, n$) to the conditional likelihood is given by

$$\left[Z_{ij} h_{0i}(t) e^{\beta' X_{ij}} \right]^{\delta_{ij}} e^{-Z_{ij} H_{0i}(t_{ij})} e^{\beta' X_{ij}}, \quad (13)$$

where t_{ij} stands for observation time of individual i from pair j . Assuming the conditional independence of lifespans, given the frailty, and integrating out the frailty, we obtain the marginal likelihood function

$$\prod_{j=1}^n \int_{R \times R} \left[u_{1j} h_{01}(t_{1j}) e^{\beta' X_{1j}} \right]^{\delta_{1j}} e^{u_{1j} H_{01}(t_{1j})} e^{\beta' X_{1j}} \left[u_{2j} h_{02}(t_{2j}) e^{\beta' X_{2j}} \right]^{\delta_{2j}} e^{u_{2j} H_{02}(t_{2j})} e^{\beta' X_{2j}} f(z_{1j}, z_{2j}) dz_{1j} dz_{2j} \quad (14)$$

where $f(\cdot, \cdot)$ is the probability density function of the corresponding frailty distribution. All these formulas can be easily extended to the multivariate case, but need a specification of the correlation structure between individuals in a cluster in terms of the multivariate density function, which complicates analysis. For more details see (Hanagal(2011, 2019) and Wienke(2011)).

4. Correlated Inverse Gaussian Frailty Model

Let Z be an infinitely divisible frailty variable with Laplace transformation $L_Z(s)$ and $\rho \in [0, 1]$, then there exist random variables Z_1, Z_2 each with univariate Laplace transform $L_Z(s)$ such that the Laplace transform of Z_1, Z_2 is given by:

$$L(s_1, s_2) = L_Z^\rho(s_1 + s_2) L_Z^{1-\rho}(s_1) L_Z^{1-\rho}(s_2) \quad (15)$$

If Z has a variance the $Corr(Z_1, Z_2) = \rho$.

The respective bivariate survival model is identifiable under mild regularity conditions on Z provided that $\rho > 0$. The case $\rho = 1$ is known as the shared frailty model.

The above equation can be extended to multivariate case ($\rho > 0$) as below.

$$L(s_1, s_2, \dots, s_k) = L_Z^\rho(s_1, s_2, \dots, s_k) L_Z^{1-\rho}(s_1) \dots L_Z^{1-\rho}(s_k).$$

The case $\rho = 1$ leads to shared frailty. If $\rho = 0$, Z_1, \dots, Z_k are mutually independent.

Let Z_i be the inverse Gaussian distributed with mean 1, variance σ^2 , and Laplace transform

$$L(s_i, \sigma^2) = \exp\left[\frac{1 - (1 + 2\sigma^2 s_i)^{\frac{1}{2}}}{\sigma^2}\right] \quad (16)$$

The bivariate Laplace transform for the correlated inverse Gaussian frailty model is given by

$$\begin{aligned} L(s_1, s_2, \sigma^2, \rho) = & \exp\left[\rho \frac{1 - (1 + 2\sigma^2(s_1 + s_2))^{\frac{1}{2}}}{\sigma^2}\right] \exp\left[(1 - \rho) \frac{1 - (1 + 2\sigma^2 s_1)^{\frac{1}{2}}}{\sigma^2}\right] \\ & \exp\left[(1 - \rho) \frac{1 - (1 + 2\sigma^2 s_2)^{\frac{1}{2}}}{\sigma^2}\right] \end{aligned} \quad (17)$$

where $Corr(Z_1, Z_2) = \rho$.

The correlated frailty model with inverse Gaussian frailty distribution is characterized by the bivariate survival function of the form:

$$\begin{aligned} S(t, t_{2j}) = & \exp\left[\rho \frac{1 - (1 + 2\sigma^2 \eta_j (H_1(t_{1j}) + H_2(t_{2j})))^{\frac{1}{2}}}{\sigma^2}\right] \exp\left[(1 - \rho) \frac{1 - (1 + 2\sigma^2 \eta_j H_1(t_{1j}))^{\frac{1}{2}}}{\sigma^2}\right] \\ & \exp\left[(1 - \rho) \frac{1 - (1 + 2\sigma^2 \eta_j H_2(t_{2j}))^{\frac{1}{2}}}{\sigma^2}\right] \end{aligned} \quad (18)$$

where $H_{01}(t_{1j})$ and $H_{02}(t_{2j})$ are the cumulative baseline hazard functions of the life time random variables T_{1j} and T_{2j} respectively.

According to different assumptions on the baseline distributions we get different correlated inverse Gaussian frailty models.

5. Baseline Distributions

5.1 Pareto Distribution

The Pareto distribution is a skewed, heavy-tailed distribution that is sometimes used to model the distribution of incomes. This distribution is not limited to describing wealth or income, but to many situations in which an equilibrium is found in the distribution of the "small" to the "large". In insurance applications, heavy-tailed distributions are essential tools for modeling extreme loss, especially for the more risky types of insurance such as medical malpractice insurance. In financial applications, the study of heavy-tailed distributions provides information about the potential for financial fiasco or financial ruin. The Pareto distribution is great way to open up a discussion on heavy-tailed distribution. A continuous random variable T is said to follow the Pareto distribution with the scale parameter λ and the shape parameter α if its survival function is,

$$S(t) = (\lambda t + 1)^{-\alpha}; t > 0, \lambda > 0, \alpha > 0 \quad (19)$$

and the hazard function and the cumulative hazard function as

$$h(t) = (\alpha\lambda)/(\lambda t + 1); t > 0, \lambda > 0, \alpha > 0 \quad (20)$$

$$H(t) = \alpha \log(\lambda t + 1); t > 0, \lambda > 0, \alpha > 0 \quad (21)$$

Observe that $h(t)$ decreases with t ; $\lambda > 0, \alpha > 0$. Hence this distribution belongs to the decreasing failure rate class. The exponential and Rayleigh are the two most commonly used distributions for analyzing lifetime data. These distributions have several desirable properties and nice physical interpretations. Unfortunately the exponential distribution only has constant failure rate and the Rayleigh distribution has increasing failure rate. The linear failure rate distribution generalizes both these distributions. We consider this is the second baseline distribution.

5.2 Linear Failure Rate Distribution

The linear failure rate distribution of a continuous random variable T with the parameters $\alpha > 0$ and $\lambda > 0$, will be denoted by LFRD (α, λ) has the following survival function

$$S(t) = \exp(-\alpha t - \lambda/2t^2); t > 0, \lambda > 0, \alpha > 0 \quad (22)$$

It is easily observed that the exponential distribution (ED(α)) and the Rayleigh distribution (RD (λ)) can be obtained from LFRD(a,b) by putting $\lambda = 0$ and $\alpha = 0$ respectively. Moreover, the probability density function (PDF) of the LFRD (α, λ) can be decreasing or unimodal but the failure rate function is either constant or increasing only. See for example Bain (1974), Sen and Bhattacharya (1995), Lin et al. (2006), Ghitany and Kotz (2007). The hazard function and the cumulative hazard function of linear failure rate distribution are respectively as stated below:

$$h(t) = \alpha + \lambda t; t > 0, \lambda > 0, \alpha > 0 \quad (23)$$

$$H(t) = \alpha t + \lambda t^2/2; t > 0, \lambda > 0, \alpha > 0 \quad (24)$$

5.3 Burr Distribution (Type XII)

The Burr XII distribution, having logistic and Weibull as special sub-models, is a very popular distribution for modeling life time data and for modeling phenomenon with monotone failure rates. When modeling monotone hazard rates, the Weibull distribution may be an initial choice because of its negatively and positively skewed density shapes. However, it does not provide a reasonable parametric fit for modeling phenomenon with non-monotone failure rates such as the bathtub shaped and the unimodal failure rates that are common in reliability and biological studies. Such bathtub hazard curves have nearly at middle portions and the corresponding densities have a positive anti-mode. Unimodal failure rates can be observed in course of a disease whose mortality reaches a peak after some finite period and then declines gradually. This distribution covers the curve shape characteristics for a large number of distributions. The versatility and flexibility of the Burr-XII distribution turns it quite attractive as a tentative model for data whose underlying distribution is unknown. A continuous random variable T with the parameters $\lambda > 0$ and $\alpha > 0$, will be denoted by Burr(λ, α) has the following survival function

$$S(t) = (1 + t^\lambda)^{-\alpha}; t > 0, \lambda > 0, \alpha > 0 \quad (25)$$

Hazard function and Cumulative hazard function are

$$h(t) = \frac{\alpha \lambda t^{(\lambda-1)}}{1+t^\lambda} \quad (26)$$

$$H(t) = \alpha \log(1+t^\lambda) \quad (27)$$

6. Proposed Models

Substituting cumulative hazard functions for the Pareto, linear failure rate (LFR) and Burr baseline distributions in equation (18), we get the unconditional bivariate survival functions at time $t_{1j} > 0$ and $t_{2j} > 0$ as,

$$S(t, t_{2j}) = \exp \left[\rho \frac{1 - (1 - 2\sigma^2 \eta_j (\alpha_1 \log(\lambda_1 + 1) + \alpha_2 \log(\lambda_2 + 1)))^{\frac{1}{2}}}{\sigma^2} \right] \\ \exp \left[(1 - \rho) \frac{1 - (1 - 2\sigma^2 \eta_j \alpha_1 \log(\lambda_1 + 1))^{\frac{1}{2}}}{\sigma^2} \right] \\ \exp \left[(1 - \rho) \frac{1 - (1 - 2\sigma^2 \eta_j \alpha_2 \log(\lambda_2 + 1))^{\frac{1}{2}}}{\sigma^2} \right] \quad (28)$$

$$S(t, t_{2j}) = \exp \left[\rho \frac{1 - (1 - 2\sigma^2 \eta_j (\alpha_1 t + \lambda_1 t^2/2 + \alpha_2 t + \lambda_2 t^2/2))^{\frac{1}{2}}}{\sigma^2} \right] \\ \exp \left[(1 - \rho) \frac{1 - (1 - 2\sigma^2 \eta_j (\alpha_1 t + \lambda_1 t^2/2))^{\frac{1}{2}}}{\sigma^2} \right] \\ \exp \left[(1 - \rho) \frac{1 - (1 - 2\sigma^2 \eta_j (\alpha_2 t + \lambda_2 t^2/2))^{\frac{1}{2}}}{\sigma^2} \right] \quad (29)$$

$$S(t, t_{2j}) = \exp \left[\rho \frac{1 - (1 - 2\sigma^2 \eta_j (\alpha_1 \log(t^{\lambda_1} + 1) + \alpha_2 \log(t^{\lambda_2} + 1)))^{\frac{1}{2}}}{\sigma^2} \right] \\ \exp \left[(1 - \rho) \frac{1 - (1 - 2\sigma^2 \eta_j \alpha_1 \log(t^{\lambda_1} + 1))^{\frac{1}{2}}}{\sigma^2} \right] \\ \exp \left[(1 - \rho) \frac{1 - (1 - 2\sigma^2 \eta_j \alpha_2 \log(t^{\lambda_2} + 1))^{\frac{1}{2}}}{\sigma^2} \right] \quad (30)$$

Here onwards we call equation (28), (29) and (30) as Model I, Model II, and Model III respectively and they denote correlated inverse Gaussian frailty model with baseline as Pareto, LFR and Burr distributions respectively.

7. Likelihood Specification and Bayesian Estimation of Parameters

Suppose there are n individuals under study, whose first and second observed failure times are represented by (t_{1j}, t_{2j}) . Let c_{1j} and c_{2j} be the observed censoring times for the j^{th} individual ($j = 1, 2, 3, \dots, n$) for first and second recurrence times respectively. We also assume that independence between the censoring time and the life-times of individuals.

The contribution of the bivariate life time random variable of the j^{th} individual in likelihood function is given by,

$$L_j(t_{1j}, t_{2j}) = \begin{cases} f_1(t_{1j}, t_{2j}), & t_{1j} < c_{1j}, t_{2j} < c_{2j}, \\ f_2(t_{1j}, c_{2j}), & t_{1j} < c_{1j}, t_{2j} > c_{2j}, \\ f_3(c_{1j}, t_{2j}), & t_{1j} > c_{1j}, t_{2j} < c_{2j}, \\ f_4(c_{1j}, c_{2j}), & t_{1j} > c_{1j}, t_{2j} > c_{2j}. \end{cases}$$

and the likelihood function is,

$$L(\boldsymbol{\psi}, \boldsymbol{\beta}, \theta) = \prod_{j=1}^{n_1} f_1(t_{1j}, t_{2j}) \prod_{j=1}^{n_2} f_2(t_{1j}, c_{2j}) \prod_{j=1}^{n_3} f_3(c_{1j}, t_{2j}) \prod_{j=1}^{n_4} f_4(c_{1j}, c_{2j}) \quad (31)$$

where θ , $\boldsymbol{\psi}$ and $\boldsymbol{\beta}$ are respectively the frailty parameter $(\sigma_1, \sigma_2, \rho)$, the vector of baseline parameters and the vector of regression coefficients.

The counts n_1, n_2, n_3 and n_4 are the number of individuals for which first and second failure times (t_{1j}, t_{2j}) lie in the ranges $t_{1j} < c_{1j}, t_{2j} < c_{2j}$; $t_{1j} < c_{1j}, t_{2j} > c_{2j}$; $t_{1j} > c_{1j}, t_{2j} < c_{2j}$ and $t_{1j} > c_{1j}, t_{2j} > c_{2j}$ respectively and

$$\begin{aligned} f_1(t_{1j}, t_{2j}) &= \frac{\partial^2 S(t_{1j}, t_{2j})}{\partial t_{1j} \partial t_{2j}} \\ f_2(t_{1j}, c_{2j}) &= \frac{\partial S(t_{1j}, c_{2j})}{\partial t_{1j}} \\ f_3(c_{1j}, t_{2j}) &= \frac{\partial S(c_{1j}, t_{2j})}{\partial t_{2j}} \\ \text{and } f_4(c_{1j}, c_{2j}) &= S(c_{1j}, c_{2j}) \end{aligned} \quad (32)$$

Usually maximum likelihood estimators can be used to estimate the parameters involved in the model. Unfortunately computing the maximum likelihood estimators (MLEs) involves solving a fourteen dimensional optimization problem for Model I and Model III and eleven dimensional optimization problem for Model II and Model IV. As the method of maximum likelihood fails to estimate the parameters due to convergence problem in the iterative procedure, so we use the Bayesian approach. The traditional maximum likelihood approach to estimation is commonly used in survival analysis, but it can encounter difficulties with frailty models. Moreover, standard maximum likelihood based inference methods may not be suitable for small sample sizes or situations in which there is heavy censoring (see Kheiri et al. (2007)). Thus, in our problem a Bayesian approach, which does not suffer from these difficulties, is a natural one, even though it is relatively computationally intensive

To estimate parameters of the model, the Bayesian approach is now popularly used, because computation of the Bayesian analysis become feasible due to advances in computing technology.

To estimate the parameters of the model, the Bayesian approach is now popularly used, because computation of the Bayesian analysis become feasible due to advances in computing technology. Several authors have discussed Bayesian approach for the estimation of parameters of the frailty models. Some of them are, Ibrahim et al.(2001) and references their in, Santos and Achcar (2010). Santos and Achcar (2010) considered parametric models with Weibull and generalized gamma distribution as baseline distributions and gamma, log-normal as frailty distributions. Ibrahim et al. (2001) and references therein considered Weibull model and piecewise exponential model with gamma frailty. They also considered positive stable frailty models.

The joint posterior density function of parameters for given failure times is obtained as,

$$\pi(\alpha_1, \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \theta, \boldsymbol{\beta}) \propto L(\alpha_1, \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \theta, \boldsymbol{\beta}) \\ \times g_1(\alpha_1)g_2(\lambda_1)g_3(\gamma_1)g_4(\alpha_2)g_5(\lambda_2)g_6(\gamma_2)g_7(\theta) \prod_{i=1}^5 p_i(\boldsymbol{\beta}_i)$$

where $g_i(\cdot)$ ($i = 1, 2, \dots, 7$) indicates the prior density function with known hyper parameters of corresponding arguments for baseline parameters and frailty variance; $p_i(\cdot)$ is prior density function for regression coefficient β_i ; $\boldsymbol{\beta}_i$ represents a vector of regression coefficients except β_i , $i = 1, 2, \dots, k$ and likelihood function $L(\cdot)$ is given by equation (31). Here we assume that all the parameters are independently distributed.

To estimate the parameters of the model, we used Metropolis-Hastings algorithm and Gibbs sampler. We monitored the convergence of a Markov chain to a stationary distribution by Geweke test (Geweke 1992)and Gelman-Rubin Statistics (Gelman and Rubin, 1992). Trace plots, coupling from the past plots and sample autocorrelation plots are used to check the behaviour of the chain, to decide burn-in period and autocorrelation lag respectively.

Algorithm consists in successively obtaining a sample from the conditional distribution of each of the parameter given all other parameters of the model. These distributions are known as full conditional distributions. In our case full conditional distributions are not easy to integrate out. So full conditional distributions are obtained by considering that they are proportional to the joint distribution of the parameters of the model.

We have full conditional distribution of the parameter α_1 with frailty as,

$$\pi_1(\alpha_1 \mid \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \theta, \boldsymbol{\beta}) \propto L(\alpha_1, \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \theta, \boldsymbol{\beta}) \cdot g_1(\alpha_1) \quad (33)$$

We have full conditional distribution of the parameter α_1 without frailty as,

$$\pi_1(\alpha_1 \mid \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \boldsymbol{\beta}) \propto L(\alpha_1, \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \boldsymbol{\beta}) \cdot g_1(\alpha_1) \quad (34)$$

Similarly full conditional distributions for other parameters can be obtained.

To estimate parameters of the model, the Bayesian approach is now popularly used, because computation of the Bayesian analysis become feasible due to advances in computing technology.

8. Analysis of Kidney Infection Data

To illustrate the Bayesian estimation procedure we use kidney infection data of McGilchrist and Aisbett (1991). The data related to recurrence times counted from the moment of the catheter insertion until its removal due to infection for 38 kidney patients using portable dialysis equipment. For each patient, the first and the second recurrence times (in days) of infection from the time of insertion of the catheter until it has to be removed owing to infection is recorded. The catheter may have to be removed for reasons other than kidney infection and this is regarded as censoring. So the survival time for a given patient may be the first or the second infection time or the censoring time. After the occurrence or censoring of the first infection sufficient (ten weeks interval) time was allowed for the infection to be cured before the second time the catheter was inserted. So the first and the second recurrence times are taken to be independent apart from the common frailty component. The data consists of five risk variables age, sex and disease type GN, AN and PKD where GN, AN and PKD are short forms of Glomerulo Neptiritis, Acute Neptiritis and Polycyatic Kidney Disease.

Table 1 in appendix shows the first and second recurrence times with recurrence indicator variable (0-censored, 1-recurrence) and covariates age, sex (0-male, 1-female), and three indicator variables GN, AN, and PKD for six patients only. One can get the entire Table from McGilchrist and Aisbett(1991).

Let T_1 and T_2 be the first and the second recurrence time to infection. Five covariates age, sex and presence or absence of disease type GN, AN and PKD are represented by X_1 , X_2 , X_3 , X_4 , and X_5 . First we check goodness of fit of the data for the inverse Gaussian frailty distributions with two baseline distributions and then we apply the Bayesian estimation procedure. To check goodness of fit of kidney data set, we consider Kolmogrove-Smirnov (K-S) test for two baseline distributions. Table 2 gives the p-values of goodness of fit test for Model I and Model III. Thus from p-values of K-S test we can say that there is no statistical evidence to reject the hypothesis that data are from the Model I and Model III in the marginal case and we assume that they also fit for bivariate case.

A widely used prior for frailty parameters $\sigma_1 = \sigma_2$ are the gamma distribution $G(0.0001, 0.0001)$. In addition, we assume that the regression coefficients are normal with mean zero and large variance say 1000. Similar types of prior distributions are used in Ibrahim et al. (2001), Sahu et al. (1997) and Santos and Achcar (2010). So in our study we also use same non informative prior for frailty parameters σ_1, σ_2 and regression coefficients $\beta_i, i = 1, \dots, 5$. Since we do not have any prior information about baseline parameters, $\lambda_1, \alpha_1, \lambda_2$ and α_2 , prior distributions are assumed to be flat. We consider two different non-informative prior distributions for baseline parameters, one is $G(a_1, a_2)$ and another is $U(b_1, b_2)$. All the hyper-parameters a_1, a_2, b_1 and b_2 are known. Here $G(a, b)$ is the gamma distribution with the shape parameter a and the scale parameter b and $U(b_1, b_2)$ represents uniform distribution over the interval (b_1, b_2) . For correlation parameter we use uniform distribution $U(0, 1)$. We use different values of baseline parameters for Model I, Model II and Model III. We assume the value of the hyper-parameters as $a_1 = 1, a_2 = 0.0001, b_1 = 0$ and $b_2 = 100$.

We run two parallel chains for all four models using two sets of prior distributions with the different starting points using the Metropolis-Hastings algorithm and the Gibbs sampler based on

normal transition kernels. We iterate both the chains for 100000 times. As seen in the simulation study here also we got nearly the same estimates of parameters for both the set of prior, so estimates are not dependent on the different prior distributions. The convergence rate of the Gibbs sampler for both the prior sets is almost the same. Also both the chains shows somewhat similar results, so we present here the analysis for only one chain with $G(a_1, a_2)$ as prior for the baseline parameters, for all the four models.

The Gelman-Rubin convergence statistic values are nearly equal to one and the Geweke test statistic values are quite small and the corresponding p-values are large enough to say that the chains attain stationary distribution. The posterior mean and the standard error with 95% credible intervals, the Gelman-Rubin statistics values and the Geweke test values with p-values for Model I to III are presented in Table 3, 4, and 5. The AIC, BIC and DIC values for all three models are given in Table 6. The Bayes factors for all models are given in Table 7.

In order to compare the proposed models we use the Akaike information criteria (AIC), Bayesian information criteria (BIC) and deviance information criteria (DIC). The comparison between three proposed models is done using AIC, BIC and DIC values given in Table 6. The smallest AIC value is Model-II (linear failure distribution with frailty). Same result hold for BIC and DIC value. To take the decision about Model I, Model II, and Model III, we use the Bayes factor. The Bayesian test based on the Bayes factors for Model II against Model I is 40.4254 and Model II against Model III is 48.6518 which are high and strongly support Model II for kidney infection data set. Some patients are expected to be vary prone to infection compared to others with same covariate value. This is not surprising, as seen in the data set there is a male patient with infection time 8 and 16, and there is also male patient with infection time 152 and 562. Table 6 shows that Model II is better then other two models. From Table 6 and 7, we can observe that, Model II is best. We can observe that the regression coefficients for all the three models are different. The credible interval of the regression coefficient β_2 does not contain zero which indicates that the covariate sex is significant for all the models. But in Model I and Model III β_5 is significant. Negative value of β_2 indicates that the female patients have a slightly lower risk for infection. Negative value of β_5 , the regression coefficient corresponding to the covariate X_5 (the disease type PKD) indicates the absence of the disease type PKD in the patients have lover risk of infection in Model I and Model II.

9. Conclusions

In this paper we discuss results for inverse Gaussian correlated frailty models with three different base line distributions. We use the Pareto, LFR and Burr as a baseline distributions. Main aim of our study is to check which distribution with inverse Gaussian correlated frailty fits better. To estimate the parameters in the inverse Gaussian frailty models, we use Bayesian approach.

Different prior gives the same estimates of the parameters. The convergence rate of the Gibbs sampling algorithm does not depend on these choices of the prior distributions in our proposed model for kidney infection data. The estimate of σ from the correlated frailty models show that there is a strong evidence of high degree of heterogeneity in the population of patients. The covariate sex is the only covariate which is significant for all models. Negative value of regression coefficient (β_2) of covariate sex indicates that the female patients have a slightly lower risk of

infection. Negative value of β_5 indicates that the absence of the disease type PKD in the patients have lower risk of infection in Model I and Model II

The comparison between three proposed models is done using AIC, BIC and DIC values. The smallest AIC value is for Model II (linear failure rate distribution with correlated frailty). The same result holds for BIC and DIC values. We observe from Tables 8 and 9 that the Model II is best. Also we can conclude that the correlated inverse Gaussian correlated frailty with the linear failure rate distribution as the baseline distribution is a better fit than other correlated inverse Gaussian correlated frailty models. We compare also with correlated gamma frailty and correlated inverse Gaussian frailty models suggested by Hanagal et al. (2017) and Hanagal and Pandey (2020) and observe that correlated inverse Gaussian frailty with linear failure rate baseline distribution performs better than correlated gamma frailty and correlated inverse Gaussian frailty models proposed by Hanagal et al. (2017) and Hanagal and Pandey (2020) for kidney infection data set. By referring all the above analysis, now we are in a position to say that, we have suggested a new correlated inverse Gaussian frailty model with the linear failure rate distribution as the baseline distribution which is the best in the proposed models for modeling of kidney infection data.

References

- Bain, L. J (1974). Analysis for the linear failure-rate life-testing distribution. *Technometrics*, **16(4)**, 551 – 559.
- Chhikara, R.S. and Folks, J.L. (1986). *The Inverse Gaussian Distribution*. Marcel Dekker, New York.
- Clayton, D. G. and Cuzick, J. (1985). Multivariate generalizations of the proportional hazards model (with discussion). *Journal of Royal Statistical Society, Ser., A*, **148**, 82–117.
- Gacula, M. C. Jr. and Kubala, J. J. (1975). Statistical models for shelf life failures. *Journal of Food Science*, **40**, 404 –409.
- Duchateau and Janssen (2008). *The Frailty Model*. Springer. New York.
- Gelman, A. and Rubin, D. B. (1992). A single series from the Gibbs sampler provides a false sense of security. In *Bayesian Statistics 4* (J. M. Bernardo, J. O. Berger, A. P. Dawid and A. F. M. Smith, eds.). Oxford: Oxford Univ. Press. pp 625-632.
- Geweke, J. (1992). Evaluating the Accuracy of Sampling-Based Approaches to the Calculation of Posterior Moments. In *Bayesian Statistics 4* (eds. J.M. Bernardo, J. Berger, A.P. Dawid and A.F.M. Smith), Oxford: Oxford University Press, pp 169-193.
- Ghitany, M. E. and Kotz, S. (2007). Reliability properties of extended linear failure-rate distributions, *Probability in the Engineering and Information Sciences*, **21**, 441 – 450.
- Hanagal, D. D. (2011). *Modeling Survival Data Using Frailty Models*. Chapman & Hall/CRC. New York.
- Hanagal, D. D. (2017). Frailty Models in Public Health. *Handbook of Statistics*, **37(B)**, 209-247. Elsevier Publishers; Amsterdam.
- Hanagal, D. D. (2019). *Modeling Survival Data Using Frailty Models*. 2nd Edition. Springer; Singapore.

- Hanagal, D. D. and Bhambure, S. M. (2014). Shared inverse Gaussian frailty model based on reversed hazard rate for modeling Australian twin data. *Journal of Indian Society for Probability and Statistics*, **15**, 9–37.
- Hanagal, D. D. and Bhambure, S. M. (2015). Comparison of shared gamma frailty models using Bayesian approach. *Model Assisted Statistics & Applications*, **10**, 25–41.
- Hanagal, D. D. and Bhambure, S. M. (2016). Modeling bivariate survival data using shared inverse Gaussian frailty model. *Communications in Statistics, Theory & Methods*, **45(17)**, 4969–4987.
- Hanagal, D. D. and Dabade, A. D. (2013). Modeling of inverse Gaussian frailty model for bivariate survival data. *Communications in Statistics, Theory & Methods*, **42(20)**, 3744–3769.
- Hanagal, D. D. and Pandey, A. (2014a). Inverse Gaussian shared frailty for modeling kidney infection data. *Advances in Reliability*, **1**, 1–14.
- Hanagal, D. D. and Pandey, A. (2014b). Gamma shared frailty model based on reversed hazard rate for bivariate survival data. *Statistics & Probability Letters*, **88**, 190–196.
- Hanagal, D. D. and Pandey, A. (2015a). Gamma frailty models for bivariate survival data. *Journal of Statistical Computation and Simulation*, **85(15)**, 3172–3189.
- Hanagal, D. D. and Pandey, A. (2015b). Inverse Gaussian shared frailty models with generalized exponential and generalized inverted exponential as baseline distributions. *Journal of Data Science*, **13(2)**, 569–602.
- Hanagal, D. D. and Pandey, A. (2016). Inverse Gaussian shared frailty models based on reversed hazard rate. *Model Assisted Statistics and Applications*, **11**, 137–151.
- Hanagal, D. D. and Pandey, A. (2017b). Correlated Gamma Frailty Models for Bivariate Survival Data Based on Reversed Hazard Rate. *International Journal of Data Science*, **2(4)**, 301–324.
- Hanagal, D. D., Pandey, A. and Ganguly, A. (2017). Correlated gamma frailty models for bivariate survival data. *Communications in Statistics, Simulation and Computation*, **46(5)**, 3627–3644.
- Hanagal, D. D. and Pandey, A. (2020). Correlated inverse Gaussian frailty models for bivariate survival data. *Communications in Statistics, Theory and Methods*, **49(4)**, 845–863.
- Hanagal, D. D. and Sharma, R. (2013). Modeling heterogeneity for bivariate survival data by shared gamma frailty regression model. *Model Assisted Statistics and Applications*, **8**, 85–102.
- Hanagal, D. D. and Sharma, R. (2015a). Bayesian inference in Marshall-Olkin bivariate exponential shared gamma frailty regression model under random censoring. *Communications in Statistics, Theory and Methods*, **44(1)**, 24–47.
- Hanagal, D. D. and Sharma, R. (2015b). Comparison of frailty models for acute leukaemia data under Gompertz baseline distribution. *Communications in Statistics, Theory & Methods*, **44(7)**, 1338–1350.
- Hanagal, D. D. and Sharma, R. (2015c). Analysis of bivariate survival data using shared inverse Gaussian frailty model. *Communications in Statistics, Theory & Methods*, **44(7)**, 1351–1380.
- Hougaard, P. (1984). Life table methods for heterogeneous populations. *Biometrika*, **71(1)**, 75–83.

- Hougaard, P. (1986). Survival models for heterogeneous populations derived from stable distributions. *Biometrika* **73**, 387–396.
- Iachine, I.A. (1995a). *Correlated frailty concept in the analysis of bivariate survival data*. Bachelor project, Department of Mathematics and Computer Science, Odense University, Denmark.
- Iachine, I.A. (1995b). *Parameter estimation in the bivariate correlated frailty model with observed covariates via the EM-algorithm*. Working Paper Series: Population Studies of Aging 16, CHS, Odense University, Denmark.
- Ibrahim, J.G., Ming-Hui C. and Sinha, D. (2001). *Bayesian Survival Analysis*. Springer, Verlag. New York.
- Kheiri, S., Kimber, A. and Meshkani M. R. (2007). Bayesian analysis of an inverse Gaussian correlated frailty model. *Computational Statistics and Data Analysis*, **51**, 5317–5326.
- Lin, C. T., Wu, S. J. S., and Balakrishnan, N. (2006). Monte carlo methods for Bayesian inference on the linear hazard rate distribution, *Communications in Statistics Theory and Methods*, **35**, 575–590.
- McGilchrist, C.A. and Aisbett, C.W. (1991). Regression with frailty in survival analysis. *Biometrics*, **47**, 461–466.
- Sahu, S.K., Dey, D.K. Aslanidou, H. and Sinha, D. (1997). A Weibull regression model with gamma frailties for multivariate survival data. *Life time data analysis*, **3**, 123–137.
- Santos, C. A. and Achcar, J. A. (2010). A Bayesian analysis for multivariate survival data in the presence of covariates. *Journal of Statistical Theory and Applications*, **9**, 233–253.
- Sen, A. and Bhattacharya, G. K. (1995). Inference procedure for the linear failure rate model, *Journal of Statistical Planning and Inference*, **46**, 59 – 76.
- Seshadri, V. (1999). *The Inverse Gaussian Distribution: Statistical Theory and Applications*. Springer Science, New York.
- Vaupel, J. W., Manton, K.G. and Stallaed, E. (1979). The impact of heterogeneity in individual frailty on the dynamics of mortality. *Demography*, **16**, 439–454.
- Wienke, A. (2011). *Frailty Models in Survival Analysis*. Chapman & Hall/CRC. New York.

Appendix : Summary of Tables

Table 1: Kidney infection data

| Pat | Time1 | Ind1 | Time2 | Ind2 | Age | Sex | GN | AN | PKD |
|-----|-------|------|-------|------|------|-----|----|----|-----|
| 1 | 8 | 1 | 16 | 1 | 28 | 0 | 0 | 0 | 0 |
| 2 | 23 | 1 | 13 | 0 | 48 | 1 | 1 | 0 | 0 |
| 3 | 22 | 1 | 28 | 1 | 32 | 0 | 0 | 0 | 0 |
| 4 | 447 | 1 | 318 | 1 | 31.5 | 1 | 0 | 0 | 0 |
| 5 | 30 | 1 | 12 | 1 | 10 | 0 | 0 | 0 | 0 |
| 6 | 24 | 1 | 245 | 1 | 16.5 | 1 | 0 | 0 | 0 |

Table 2: p-values of K-S statistics for goodness of fit test for Kidney infection data set

| Distribution | Recurrence time | |
|--------------|-----------------|--------|
| | first | second |
| Model I | 0.6641 | 0.7349 |
| Model II | 0.7523 | 0.8386 |
| Model III | 0.6256 | 0.7256 |

Table 3: Posterior summary for Kidney infection data set Model I

| Parameter | Estimate | Standard Error | Lower Credible Limit | Upper Credible Limit | Geweke values | p values | Gelman & Rubin values |
|--|----------|----------------|----------------------|----------------------|---------------|----------|-----------------------|
| burn in period = 3150; autocorrelation lag = 300 | | | | | | | |
| α_1 | 7.2734 | 0.32204 | 6.8439 | 7.8768 | 0.005102 | 0.50203 | 1.0014 |
| λ_1 | 0.0879 | 0.0179 | 0.0094 | 0.1076 | -0.001360 | 0.49945 | 1.0089 |
| α_2 | 2.0142 | 0.10723 | 1.6334 | 2.51025 | -0.003313 | 0.49867 | 1.0043 |
| λ_2 | 0.0943 | 0.02331 | 0.0096 | 0.2722 | -0.014091 | 0.49437 | 0.9999 |
| ρ | 0.6594 | 0.05703 | 0.5540 | 0.76740 | -0.018870 | 0.49247 | 1.0009 |
| σ | 0.6009 | 0.04958 | 0.5072 | 0.69349 | -0.004090 | 0.49836 | 1.0008 |
| β_1 | 0.0134 | 0.00802 | 0.0092 | 0.02820 | -0.003226 | 0.49871 | 0.9999 |
| β_2 | -1.0468 | 0.41285 | -1.8688 | -0.81025 | 0.005089 | 0.50203 | 1.0008 |
| β_3 | 0.2210 | 0.22927 | 0.3472 | 0.30237 | 0.006850 | 0.50273 | 1.2086 |
| β_4 | 0.5262 | 0.03882 | 0.3940 | 0.64252 | -0.002433 | 0.49902 | 1.0013 |
| β_5 | -0.7012 | 0.17155 | -0.6208 | -0.81960 | 0.005508 | 0.50219 | 0.9999 |

Table 4: Posterior summary for Kidney infection data set Model II

| Parameter | Estimate | Standard Error | Lower Credible Limit | Upper Credible Limit | Geweke values | p values | Gelman & Rubin values |
|--|----------|----------------|----------------------|----------------------|---------------|----------|-----------------------|
| burn in period = 3500; autocorrelation lag = 300 | | | | | | | |
| α_1 | 0.0318 | 1.59643 | 0.01178 | 0.0563 | 0.00874 | 0.5034 | 1.0010 |
| λ_1 | 0.0316 | 0.01825 | 0.0191 | 0.0495 | -0.00126 | 0.4994 | 1.0089 |
| α_2 | 0.0222 | 0.01799 | 0.0139 | 0.0304 | -0.00242 | 0.4990 | 1.0064 |
| λ_2 | 0.0093 | 0.0019 | 0.0076 | 0.0229 | -0.00082 | 0.4996 | 1.0110 |
| ρ | 0.8053 | 0.09019 | 0.62666 | 0.9720 | 0.00595 | 0.5023 | 1.0005 |
| σ | 0.7014 | 0.30422 | 0.16458 | 1.2912 | -0.00405 | 0.4983 | 1.0026 |
| β_1 | 0.0166 | 0.00960 | -0.00129 | 0.0345 | -0.00481 | 0.4980 | 1.0041 |
| β_2 | -1.9902 | 0.37287 | -2.71766 | -1.2694 | 0.00942 | 0.5037 | 1.0002 |
| β_3 | 0.2212 | 0.21856 | -0.16428 | 0.2657 | -0.01161 | 0.4953 | 1.0015 |
| β_4 | 0.7261 | 0.03457 | -0.08878 | -0.0388 | -0.02241 | 0.4910 | 1.0058 |
| β_5 | -0.9701 | 0.2743 | -2.14538 | -0.7748 | 0.00394 | 0.5015 | 0.9999 |

Table 5: Posterior summary for Kidney infection data set Model III

| Parameter | Estimate | Standard Error | Lower Credible Limit | Upper Credible Limit | Geweke values | p values | Gelman & Rubin values |
|--|----------|----------------|----------------------|----------------------|---------------|----------|-----------------------|
| burn in period = 3500; autocorrelation lag = 300 | | | | | | | |
| α_1 | 2.2412 | 0.19643 | 2.0217 | 2.4363 | 0.00874 | 0.5034 | 1.0010 |
| λ_1 | 0.0071 | 0.0009 | 0.0041 | 0.0098 | -0.00126 | 0.4994 | 1.0089 |
| α_2 | 0.0272 | 0.0199 | 0.0143 | 0.0404 | -0.00242 | 0.4990 | 1.0064 |
| λ_2 | 0.0113 | 0.0009 | 0.0069 | 0.0242 | -0.00082 | 0.4996 | 1.0110 |
| ρ | 0.7045 | 0.08419 | 0.62686 | 0.8720 | 0.00595 | 0.5023 | 1.0005 |
| σ | 0.7324 | 0.2002 | 0.56458 | 0.8912 | -0.00405 | 0.4983 | 1.0026 |
| β_1 | -0.016 | 0.0082 | -0.0712 | 0.0215 | -0.00481 | 0.4980 | 1.0041 |
| β_2 | -1.6413 | 0.1737 | -1.9766 | -1.4694 | 0.00942 | 0.5037 | 1.0002 |
| β_3 | 0.0867 | 0.0185 | -0.16428 | 0.2243 | -0.01161 | 0.4953 | 1.0015 |
| β_4 | 0.2182 | 0.03247 | -0.0987 | 0.3368 | -0.02241 | 0.4910 | 1.0058 |
| β_5 | -0.1284 | 0.0274 | -0.2453 | 0.0848 | 0.00394 | 0.5015 | 0.9999 |

Table 6: Comparison of AIC, BIC and DIC

| Model | AIC | BIC | DIC |
|-----------|----------|----------|----------|
| Model I | 678.3812 | 781.5814 | 660.5836 |
| Model II | 656.4315 | 665.3621 | 641.2143 |
| Model III | 793.2195 | 799.5715 | 774.8951 |

Table 7: Bayes Factor for three models

| Numerator model against denominator model | Bayes factor | Range | Evidence against model in denominator |
|---|--------------|-------|--|
| Model II against Model I | 40.4254 | > 10 | very strong |
| Model I against Model III | 12.3912 | > 10 | very strong |
| Model II against Model III | 48.6518 | > 10 | very strong |