Chapter 2

Shared Gamma Frailty Models

2.1 Shared Gamma Frailty Model

In this chapter we consider the frailty distribution as the gamma distribution because the gamma distribution fits well to the failure data from a computational and analytical point of view. Let a continuous random variable $Z$ follow a gamma distribution. For identifiability, we assume $Z$ has expected value equal to one which introduces restriction on the scale and the shape parameters. Under the restriction, the density function and the Laplace transformation of a gamma distribution reduces to,

$$f_Z(z) = \begin{cases} \frac{1}{\theta} \frac{1}{\Gamma(\frac{1}{\theta})} z^{\frac{1}{\theta} - 1} e^{-\frac{z}{\theta}} & ; z > 0, \theta > 0 \\ 0 & ; \text{otherwise}. \end{cases}$$

(2.1)

and $$L_Z(s) = (1 + \theta s)^{-\frac{1}{\theta}}$$ with variance of $Z$ as $\theta$.

Replacing the Laplace transformation in equation (1.8), we get the unconditional bivariate survival function for the $j^{th}$ individual at the time $t_{1j} > 0$ and $t_{2j} > 0$ as,

$$S(t_{1j}, t_{2j}) = [1 + \theta \eta_j((H_{01}(t_{1j}) + H_{02}(t_{2j})))^{-\frac{1}{\theta}}$$

(2.2)
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.

The bivariate distribution in the presence of covariates, when the frailty variable is degenerate is given by,

\[
S(t_{1j}, t_{2j}) = e^{-\eta_j\{H_{01}(t_{1j}) + H_{02}(t_{2j})\}} \tag{2.3}
\]

According to different assumptions on the baseline distributions we get different shared gamma frailty models.

## 2.2 Baseline Distributions

### 2.2.1 Generalized log-logistic distribution

The log-logistic distribution is very useful in a wide variety of applications, especially in the analysis of survival data (O’Quigley and Struthers 1982; Bennett 1983; Cox and Snell 1989). The log-logistic distribution is very similar in shape to the log-normal distribution, however it has the advantage of having simple algebraic expressions for its survivor and hazard functions and a closed form for its distribution function. It is therefore more convenient than the log-normal distribution in handling censored data. However, due to the symmetry of the log-logistic distribution, it may be inappropriate for modeling censored survival data, especially for the cases where the hazard rate is skewed or heavily tailed. In this chapter we use a generalization of the log-logistic distribution and refer to this as the generalized log-logistic distribution given in Mohammed et al. (1990). The generalized log-logistic distribution reflects the skewness and the structure of the heavy tail and generally shows some improvement over the log-logistic distribution.

Mohammed et al. (1990) show that the distribution function of generalized logistic is given by,
\[ F(x) = \frac{1}{\beta(m, n)} \int_{0}^{\alpha(x)} u^{m-1}(1-u)^{n-1} \, du \]

where \( \beta(m, n) \) is the complete beta function and

\[ F_0(x) = (1 + e^{-x})^{-1}, -\infty < x < \infty \]

is the logistic distribution function. We call \( F(x) \) the generalized logistic distribution with parameters \((m, n)\), and use the notation \( X \sim GLD(m, n) \).

The logarithmic transformation \( X = \gamma \ln(\lambda T) \) applied to \( GLD(m, 1) \) to obtain the generalized log-logistic distribution \( GLLD(m, 1) \). The distribution function of \( T \) is,

\[ F(t) = (1 + (\lambda t)^{-\gamma})^{-m}, t, m > 0, \gamma \geq 1. \]  \hspace{1cm} (2.4)

Similarly logarithmic transformation \( X = \gamma \ln(\lambda T) \) applied to \( GLD(1, n) \) to obtain the generalized log-logistic distribution \( GLLD(1, n) \). The distribution function of \( T \) is,

\[ F(t) = 1 - (1 + (\lambda t)^{\gamma})^{-n}, t, n > 0, \gamma \geq 1. \]  \hspace{1cm} (2.5)

A random variable \( T \) with c.d.f. as given by equation (2.4) and (2.5) are generalized log-logistic distribution with parameters \((m, 1)\) and \((1, n)\) respectively. We call equation (2.4) as generalized log-logistic type I and equation (2.5) as generalized log-logistic type II.

Now rearranging the parameters, the cumulative distribution function of the generalized log-logistic distribution type II is,

\[ F(t) = 1 - (1 + (\lambda t)^{\gamma})^{-a}. \]  \hspace{1cm} (2.6)

The corresponding hazard rate, reversed hazard rate, cumulative hazard rate and cumulative reversed hazard rate are respectively as follows,

\[ h(t) = a \left( \frac{\lambda \gamma t^{\gamma-1}}{1 + \lambda t^\gamma} \right). \]  \hspace{1cm} (2.7)
\[ m(t) = \frac{\alpha \gamma \lambda (\lambda t)^{-1+\gamma} (1 + (\lambda t)^{\gamma})^{-1-\alpha}}{1 - (1 + (\lambda t)^{\gamma})^{-\alpha}}. \] (2.8)

\[ H(t) = \alpha \ln(1 + \lambda t^\gamma) \] (2.9)

\[ M(t) = -\ln(1 - (1 + (\lambda t)^{\gamma})^{-\alpha}) \] (2.10)

When \( \alpha = 1 \), this distribution reduces to log-logistic distribution.

### 2.2.2 Generalized Weibull distribution

In survival analysis, Weibull distribution is the most popular distribution to model life time data. We use the generalized Weibull distribution as a baseline distribution. If a continuous random variable \( T \) follows the generalized Weibull distribution then the distribution function, the cumulative hazard rate function, the cumulative reversed hazard rate function, the hazard rate and the reversed hazard rate are respectively,

\[ F(t) = (1 - e^{-\lambda t^\gamma})^\alpha \quad t > 0, \alpha > 0, \lambda > 0, \gamma > 0 \] (2.11)

\[ H(t) = -\ln(1 - (1 - e^{-\lambda t^\gamma})^\alpha) \] (2.12)

\[ M(t) = -\alpha \ln(1 - e^{-\lambda t^\gamma}) \] (2.13)

\[ h(t) = \frac{\alpha \lambda \gamma t^{\gamma-1} e^{-\lambda t^\gamma} (1 - e^{-\lambda t^\gamma})^{\alpha-1}}{1 - (1 - e^{-\lambda t^\gamma})^\alpha} \] (2.14)

\[ m(t) = \frac{\alpha \lambda \gamma t^{\gamma-1} e^{-\lambda t^\gamma}}{1 - e^{-\lambda t^\gamma}} \] (2.15)

If \( \gamma = 1, \alpha = 1 \), the failure rate is constant (exponential), \( \gamma \neq 1, \alpha = 1 \), the failure rate is monotonic (Weibull), \( \gamma < 1, \alpha < 1 \), the failure rate is decreasing,
\[ \gamma > 1, \alpha > 1, \text{the failure rate is increasing}, \gamma > 1, \alpha < 1, \text{the failure rate is bathtub or increasing and } \gamma < 1, \alpha > 1, \text{the failure rate is unimodal or decreasing.} \]

The generalized Weibull family can be used effectively in the analysis of survival data. The family is versatile, accommodating monotone, unimodal, and bathtub-shaped hazard functions. The scaled TTT transform can be used to identify the shape of the hazard function. The family has closed-form expressions for the distribution functions and the hazard functions, and is closed under proportional hazards modeling. Because of its analytic tractability, the likelihood-based inference in the regular case and an alternative method based on a “modified likelihood” can be easily implemented see Modhalkar et al. (1993, 1995, 1996). Furthermore, it permits testing the goodness of fit of the Weibull distributions as sub models, which is not possible in most of the models with non-monotone hazard functions proposed in the literature.

### 2.3 Proposed Models

Substituting cumulative hazard function for the generalized log-logistic type II and the generalized Weibull baseline distribution in equation (2.2) and equation (2.3), we get the unconditional bivariate survival functions at time \( t_{1j} > 0 \) and \( t_{2j} > 0 \) as,

\[
S(t_{1j}, t_{2j}) = \left[ 1 + \theta \eta_j \{ \alpha_1 ln(1 + \lambda_1 t_{1j}^{\gamma_1}) + \alpha_2 ln(1 + \lambda_2 t_{2j}^{\gamma_2}) \} \right]^{-\frac{1}{\theta}}
\]

(2.16)

\[
S(t_{1j}, t_{2j}) = \exp(-\eta_j \{ \alpha_1 ln(1 + \lambda_1 t_{1j}^{\gamma_1}) + \alpha_2 ln(1 + \lambda_2 t_{2j}^{\gamma_2}) \})
\]

(2.17)

\[
S(t_{1j}, t_{2j}) = \left[ 1 - \theta \eta_j (ln[1 - (1 - e^{-\lambda_1 t_{1j}^{\gamma_1}})^{\alpha_1}] + ln[1 - (1 - e^{-\lambda_2 t_{2j}^{\gamma_2}})^{\alpha_2}]) \right]^{-\frac{1}{\theta}}
\]

(2.18)
\[ S(t_{1j}, t_{2j}) = \exp(\eta_j(\ln[1 - (1 - e^{-\lambda_1 t_{1j}^{\gamma_1}})^{\alpha_1}] + \ln[1 - (1 - e^{-\lambda_2 t_{2j}^{\gamma_2}})^{\alpha_2}])) \]

(2.19)

Here onwards we call equation (2.16), (2.17), (2.18) and (2.19) as Model I, Model II, Model III and Model IV respectively. Model I and Model II are the generalized log-logistic distribution type II with and without frailty; and likewise Model III and Model IV are for the generalized Weibull distribution with and without frailty.

To every bivariate distribution function \( F(t_1, t_2) \) with absolute marginal distribution functions \( F(t_1) \) and \( F(t_2) \), corresponds a unique function,

\[ C : [0, 1] \times [0, 1] \rightarrow [0, 1], \]

is called a copula such that

\[ F(t_1, t_2) = C(F(t_1), F(t_2)) \quad \text{for} \quad (t_1, t_2) \in (0, \infty) \times (0, \infty) \]

(2.20)

For a given copula \( C \), there exists a unique survival copula \( \overline{C} \), such that

\[ \overline{C}(u, v) = u + v - 1 + C(1 - u, 1 - v) \]

(2.21)

and

\[ S_{T_1, T_2}(t_1, t_2) = \overline{C}(S_{T_1}(t_1), S_{T_2}(t_2)) \]

(2.22)

Here \( S_{T_1, T_2}, S_{T_1} \) and \( S_{T_2} \) are the survival functions. Conversely it is possible to construct a bivariate survival function using copula having the desired marginal survivals and a chosen dependence structure, see Nelsen (2006) for details. The joint bivariate survival function (2.16) and (2.18) can be expressed in terms of survival copula as,

\[ \overline{C}(u, v) = \left[u^{-\theta} + v^{-\theta} - 1\right]^{-1/\theta} \]

(2.23)

where \( u = S_{T_1}(\cdot) \) and \( v = S_{T_2}(\cdot) \)
For Model I
\[ S_T(t_i) = [1 + \theta \eta \{\alpha_i \ln(1 + \lambda_i t_i^\gamma_i)\}]^{-\frac{1}{\hat{\eta}}}, i = 1, 2. \]

For Model III
\[ S_T(t_i) = [1 - \theta \eta \ln[1 - (1 - e^{-\lambda_i t_i^\gamma_i})^{\alpha_i}]]^{-\frac{1}{\hat{\eta}}}, i = 1, 2. \]

The above equation (2.23) is often called as Clayton Archimedean copula.

### 2.4 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 \((j = 1, 2, 3, \ldots, n)\) for first and second recurrence times respectively. We also assume that independence between censoring scheme and life times of individuals.

The contribution of 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,

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

(2.24)
where \( \theta \), \( \psi \) and \( \beta \) are respectively the frailty parameter, the vector of baseline parameters and the vector of regression coefficients. For without frailty model likelihood function is,

\[
L(\psi, \beta) = \prod_{j=1}^{n_1} f_1(t_{1j}, t_{2j}) \prod_{j=1}^{n_2} f_2(t_{1j}, c_{2j}) \prod_{j=1}^{n_3} f_3(c_{1j}, t_{2j}) \prod_{j=1}^{n_4} f_4(c_{1j}, c_{2j})
\]

(2.25)

The counts \( n_1, n_2, n_3 \) and \( n_4 \) are the numbers of individuals for which first and the 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

\[
\begin{align*}
   f_1(t_{1j}, t_{2j}) &= \frac{\partial^2 S(t_{1j}, t_{2j})}{\partial t_{1j}\partial t_{2j}} = (1 + \theta)h_{01}(t_{1j})h_{02}(t_{2j})S(t_{1j}, t_{2j})^{\frac{\alpha+2}{\sigma}} \eta_j^2 \\
   f_2(t_{1j}, c_{2j}) &= -\frac{\partial S(t_{1j}, c_{2j})}{\partial t_{1j}} = h_{01}(t_{1j})S(t_{1j}, c_{2j})^{\frac{\alpha+1}{\sigma}} \eta_j \\
   f_3(c_{1j}, t_{2j}) &= -\frac{\partial S(c_{1j}, t_{2j})}{\partial t_{2j}} = h_{02}(t_{2j})S(c_{1j}, t_{2j})^{\frac{\alpha+1}{\sigma}} \eta_j \\
   f_4(c_{1j}, c_{2j}) &= S(c_{1j}, c_{2j})
\end{align*}
\]

Substituting hazard functions \( h_{01}(t_{1j}), h_{02}(t_{2j}) \) and survival function \( S(t_{1j}, t_{2j}) \) for four proposed models into the last relations we get the likelihood function given by equation (2.24) for Model I and Model III and (2.25) for Model II and Model IV.

For Model I

\[
\begin{align*}
   f_1(t_{1j}, t_{2j}) &= (1 + \theta)\alpha_1 \lambda_1 \gamma_1 \alpha_2 \lambda_2 \gamma_2 \frac{t_{1j}^{\gamma_1-1} t_{2j}^{\gamma_2-1}}{1 + t_{1j}^{\gamma_1} + t_{2j}^{\gamma_2}} S(t_{1j}, t_{2j})^{\frac{\alpha+2}{\sigma}} \eta_j^2 \\
   f_2(t_{1j}, c_{2j}) &= \alpha_1 \lambda_1 \gamma_1 \frac{t_{1j}^{\gamma_1-1}}{1 + t_{1j}^{\gamma_1}} S(t_{1j}, c_{2j})^{\frac{\alpha+1}{\sigma}} \eta_j \\
   f_3(c_{1j}, t_{2j}) &= \alpha_2 \lambda_2 \gamma_2 \frac{t_{2j}^{\gamma_2-1}}{1 + t_{2j}^{\gamma_2}} S(c_{1j}, t_{2j})^{\frac{\alpha+1}{\sigma}} \eta_j \\
   f_4(c_{1j}, c_{2j}) &= S(c_{1j}, c_{2j})
\end{align*}
\]

(2.26)

and \( S(t_1, t_2) \) is given by equation (2.16)
For Model II

\[
\begin{align*}
  f_1(t_{1j}, t_{2j}) &= \alpha_1 \lambda_1 \gamma_1 \alpha_2 \lambda_2 \gamma_2 \frac{t_{1j}^{\gamma_1 - 1} e^{-\lambda_1 t_{1j}} (1 - e^{-\lambda_1 t_{1j}}) \gamma_1 - 1}{1 - (1 - e^{-\lambda_1 t_{1j}}) \gamma_1^2} \times \\
  &\quad \times \frac{t_{2j}^{\gamma_2 - 1} e^{-\lambda_2 t_{2j}} (1 - e^{-\lambda_2 t_{2j}}) \gamma_2 - 1}{1 - (1 - e^{-\lambda_2 t_{2j}}) \gamma_2^2} S(t_{1j}, t_{2j}) \eta_j^2 \\
  f_2(t_{1j}, c_{2j}) &= \alpha_1 \lambda_1 \gamma_1 \frac{t_{1j}^{\gamma_1 - 1}}{1 + t_{1j}^{\gamma_1}} S(t_{1j}, c_{2j}) \eta_j \\
  f_3(c_{1j}, t_{2j}) &= \alpha_2 \lambda_2 \gamma_2 \frac{t_{2j}^{\gamma_2 - 1}}{1 + t_{2j}^{\gamma_2}} S(c_{1j}, t_{2j}) \eta_j \\
  f_4(c_{1j}, c_{2j}) &= S(c_{1j}, c_{2j}) \quad (2.27)
\end{align*}
\]

and \(S(t_1, t_2)\) is given by equation (2.17)

For Model III

\[
\begin{align*}
  f_1(t_{1j}, t_{2j}) &= (1 + \theta) \alpha_1 \lambda_1 \gamma_1 \alpha_2 \lambda_2 \gamma_2 \frac{t_{1j}^{\gamma_1 - 1} e^{-\lambda_1 t_{1j}} (1 - e^{-\lambda_1 t_{1j}}) \gamma_1 - 1}{1 - (1 - e^{-\lambda_1 t_{1j}}) \gamma_1^2} \times \\
  &\quad \times \frac{t_{2j}^{\gamma_2 - 1} e^{-\lambda_2 t_{2j}} (1 - e^{-\lambda_2 t_{2j}}) \gamma_2 - 1}{1 - (1 - e^{-\lambda_2 t_{2j}}) \gamma_2^2} S(t_{1j}, t_{2j}) \eta_j^2 \\
  f_2(t_{1j}, c_{2j}) &= \alpha_1 \lambda_1 \gamma_1 \frac{t_{1j}^{\gamma_1 - 1} e^{-\lambda_1 t_{1j}} (1 - e^{-\lambda_1 t_{1j}}) \gamma_1 - 1}{1 - (1 - e^{-\lambda_1 t_{1j}}) \gamma_1^2} S(t_{1j}, c_{2j}) \eta_j \\
  f_3(c_{1j}, t_{2j}) &= \alpha_2 \lambda_2 \gamma_2 \frac{t_{2j}^{\gamma_2 - 1} e^{-\lambda_2 t_{2j}} (1 - e^{-\lambda_2 t_{2j}}) \gamma_2 - 1}{1 - (1 - e^{-\lambda_2 t_{2j}}) \gamma_2^2} S(c_{1j}, t_{2j}) \eta_j \\
  f_4(c_{1j}, c_{2j}) &= S(c_{1j}, c_{2j}) \quad (2.28)
\end{align*}
\]

and \(S(t_1, t_2)\) is given by equation (2.18)

For Model IV

\[
\begin{align*}
  f_1(t_{1j}, t_{2j}) &= \alpha_1 \lambda_1 \gamma_1 \alpha_2 \lambda_2 \gamma_2 \frac{t_{1j}^{\gamma_1 - 1} e^{-\lambda_1 t_{1j}} (1 - e^{-\lambda_1 t_{1j}}) \gamma_1 - 1}{1 - (1 - e^{-\lambda_1 t_{1j}}) \gamma_1^2} \times \\
  &\quad \times \frac{t_{2j}^{\gamma_2 - 1} e^{-\lambda_2 t_{2j}} (1 - e^{-\lambda_2 t_{2j}}) \gamma_2 - 1}{1 - (1 - e^{-\lambda_2 t_{2j}}) \gamma_2^2} S(t_{1j}, t_{2j}) \eta_j^2 \\
  f_2(t_{1j}, c_{2j}) &= \alpha_1 \lambda_1 \gamma_1 \frac{t_{1j}^{\gamma_1 - 1} e^{-\lambda_1 t_{1j}} (1 - e^{-\lambda_1 t_{1j}}) \gamma_1 - 1}{1 - (1 - e^{-\lambda_1 t_{1j}}) \gamma_1^2} S(t_{1j}, c_{2j}) \eta_j \\
  f_3(c_{1j}, t_{2j}) &= \alpha_2 \lambda_2 \gamma_2 \frac{t_{2j}^{\gamma_2 - 1} e^{-\lambda_2 t_{2j}} (1 - e^{-\lambda_2 t_{2j}}) \gamma_2 - 1}{1 - (1 - e^{-\lambda_2 t_{2j}}) \gamma_2^2} S(c_{1j}, t_{2j}) \eta_j \\
  f_4(c_{1j}, c_{2j}) &= S(c_{1j}, c_{2j}) \quad (2.29)
\end{align*}
\]
and $S(t_1, t_2)$ is given by equation (2.19).

Unfortunately computing the maximum likelihood estimators (MLEs) involves solving a twelve dimensional optimization problem for Model I and eleven dimensional optimization problem for Model II. 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. 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 the generalized gamma distribution as the baseline distributions; gamma and the 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 the parameters for given failure times in the proposed frailty models is obtained as,

$$
\pi(\alpha_1, \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \theta, \beta) \propto L(\alpha_1, \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \theta, \beta)
\times g_1(\alpha_1)g_2(\lambda_1)g_3(\gamma_1)g_4(\alpha_2)g_5(\lambda_2)g_6(\gamma_2)g_7(\theta)\prod_{i=1}^{5} p_i(\beta_i)
$$
where $g_i(.) (i = 1, 2, \cdots, 7)$ indicates the prior density function with known hyper parameters of corresponding arguments for baseline parameters and frailty variance; $p_i(.)$ is prior density function for regression coefficient $\beta_i$; $\beta_i$ represents a vector of regression coefficients except $\beta_1$, $i = 1, 2, \ldots, k$ and likelihood function $L(.)$ is given by equation (2.24) or (2.25). Here we assume that all the parameters are independently distributed. In the same way one can write the joint posterior density function of the parameters in the models without frailty.

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 the Geweke test (Geweke, 1992) and the Gelman-Rubin Statistics (Gelman et al. 1992). The trace plots, the coupling from the past plots and the sample autocorrelation plots are used to check the behaviour of the chain, to decide the burn-in period and the 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 $\alpha_1$ with frailty as,

$$
\pi_1(\alpha_1 \mid \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \theta, \beta) \propto L(\alpha_1, \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \theta, \beta) \cdot g_1(\alpha_1)
$$

(2.30)

We have full conditional distribution of the parameter $\alpha_1$ without frailty as,

$$
\pi_1(\alpha_1 \mid \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \beta) \propto L(\alpha_1, \lambda_1, \gamma_1, \alpha_2, \lambda_2, \gamma_2, \beta) \cdot g_1(\alpha_1)
$$

(2.31)
Similarly full conditional distributions for other parameters can be obtained.

### 2.5 Simulation Study

To evaluate the performance of the Bayesian estimation procedure we carried out a simulation study. For the simulation purpose we have considered only one covariate \( X_0 \) which we assume to follow normal distribution. The frailty variable \( Z \) is assumed to have gamma distribution with known variance. Life times \( (T_{1j}, T_{2j}) \) for \( j^{th} \) individual are conditionally independent for given frailty \( Z_j = z_j \). We assume that \( T_{ij} (i = 1, 2; j = 1, 2, \cdots, n) \) follows one of the baseline distributions; the generalized log-logistic distribution type II (Model I) or the generalized Weibull (Model III) distribution. Simulation details of model without frailty are not discussed here.

As the Bayesian methods are time consuming, we generate only 25 pairs of life times. According to the assumption, for given frailty \( (Z) \), life times of individuals are independent. So the conditional survival function for an individual for given frailty, \( Z = z \) and a covariate \( X_0 \) at time \( t > 0 \) is,

\[
S(t \mid z, X_0) = e^{-z\eta}
\]

where \( \eta = e^{X_0\beta_0} \). Equating \( S(t \mid z, X_0) \) to a random number, say \( r (0 < r < 1) \), over \( t > 0 \) we get,

For Model I

\[
t = \left[ r^{-\frac{1}{\eta}} - 1 \right] \frac{1}{\lambda} \quad (2.32)
\]

For Model III

\[
t = \left[ -\frac{ln(1 - (1 - r^{\frac{1}{\eta}}))}{\lambda} \right]^{1/\gamma} \quad (2.33)
\]
Equations (2.32) and (2.33) are generators to generate life times for Model I and Model III respectively. Samples are generated using the following procedure,

1. Generate 25 covariate values for $X_0$ from the binomial distribution with mean 0.5 and variance 0.25.

2. Compute $\eta = e^{X_0 \beta_0}$ with the regression coefficient (known).

3. Generate 25 pairs of lifetimes $(t_{1j}, t_{2j})$ for a given frailty $(Z = z_j)$ using the following generators,

$$t_{ij} = \left[ \frac{1}{r_{ij}^{1/\alpha_1} - 1} \right]^{1/\lambda_i}, \quad i = 1, 2; j = 1, 2, \ldots n$$

$$t_{ij} = \left[ -\frac{\ln(1 - (1 - r_{ij}^{1/\alpha_1})^{1/\alpha_2})}{\lambda_1} \right]^{1/\gamma_i}, \quad i = 1, 2; j = 1, 2, \ldots n$$

for Model I and Model III, $r_{ij}$ is the random variables having $U(0, 1)$ distribution and $\alpha_1$, $\gamma_1$, $\lambda_1$ are the parameters of baseline distribution for the first survival time and $\alpha_2$, $\gamma_2$, $\lambda_2$ are that of the second survival time.

4. Generate the censoring times $(c_{1j}$ and $c_{2j})$ from the exponential distribution with the failure rates 0.3 and 0.1 for Model I and III respectively.

5. Observe the $i^{th}$ survival time $t_{ij}^* = \min(t_{ij}, c_{ij})$ and the censoring indicator $\delta_{ij}$ for the $j^{th}$ individual $(i = 1, 2$ and $j = 1, 2, \ldots, 25)$ where,

$$\delta_{ij} = \begin{cases} 1, & t_{ij} < c_{ij} \\ 0, & t_{ij} > c_{ij} \end{cases}$$

Thus we have data consisting of 25 pairs of survival times $(t_{1j}^*, t_{2j}^*)$ and the censoring indicators $\delta_{ij}$. 

A widely used prior for frailty parameter $\theta$ is 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 non informative prior for frailty parameter $\theta$ and regression coefficients $\beta_0$. Since we do not have any prior information about baseline parameters, $\lambda_1, \gamma_1, \alpha_1, \lambda_2, \gamma_2$ and $\alpha_2$, 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 $\phi, c^2, a_1, a_2, b_1$ 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 $(b_1, b_2)$.

Table 2.1: Baseline Distribution Generalized Log-Logistic Distribution Type II Model I with Gamma frailty (Simulation for Model I ).

<table>
<thead>
<tr>
<th>Parameter (True value)</th>
<th>Estimate</th>
<th>Standard error</th>
<th>Lower Credible Limit</th>
<th>Upper Credible Limit</th>
<th>Geweke p values</th>
<th>p values</th>
<th>Gelman &amp; Rubin values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_1$ (2.0)</td>
<td>2.0003</td>
<td>0.1541</td>
<td>1.7111</td>
<td>2.2951</td>
<td>-0.01199</td>
<td>0.50076</td>
<td>0.9999</td>
</tr>
<tr>
<td>$\alpha_2$ (2.2)</td>
<td>2.1973</td>
<td>0.2223</td>
<td>1.8211</td>
<td>2.6710</td>
<td>-0.01465</td>
<td>0.49416</td>
<td>0.9999</td>
</tr>
<tr>
<td>$\lambda_1$ (1.5)</td>
<td>1.5157</td>
<td>0.2706</td>
<td>1.0286</td>
<td>1.9689</td>
<td>-0.00302</td>
<td>0.49879</td>
<td>1.0014</td>
</tr>
<tr>
<td>$\lambda_2$ (2.5)</td>
<td>2.4927</td>
<td>0.1643</td>
<td>2.2203</td>
<td>2.7806</td>
<td>-0.00101</td>
<td>0.49959</td>
<td>1.0016</td>
</tr>
<tr>
<td>$\gamma_1$ (2.5)</td>
<td>2.3258</td>
<td>0.2369</td>
<td>2.0124</td>
<td>2.8446</td>
<td>-0.01263</td>
<td>0.49496</td>
<td>1.0834</td>
</tr>
<tr>
<td>$\gamma_2$ (2.9)</td>
<td>2.9354</td>
<td>0.1617</td>
<td>2.6161</td>
<td>3.1816</td>
<td>-0.00256</td>
<td>0.49898</td>
<td>1.0027</td>
</tr>
<tr>
<td>$\theta$ (1.6)</td>
<td>1.5674</td>
<td>0.1616</td>
<td>1.3107</td>
<td>1.8651</td>
<td>-0.00209</td>
<td>0.49916</td>
<td>1.0629</td>
</tr>
<tr>
<td>$\beta_0$ (0.5)</td>
<td>0.5039</td>
<td>0.1090</td>
<td>0.3181</td>
<td>0.6908</td>
<td>0.00989</td>
<td>0.50395</td>
<td>0.9999</td>
</tr>
</tbody>
</table>

We use different value of baseline parameters for Model I and Model III, details are given in Table 2.1 and 2.2. 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 Model I and Model III using two sets of prior distributions with the different starting points using Metropolis-Hastings
Table 2.2: Baseline Distribution Generalized Weibull Distribution Model III with Gamma frailty (Simulation for Model III).

<table>
<thead>
<tr>
<th>Parameter (value)</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>Lower Credible Limit</th>
<th>Upper Credible Limit</th>
<th>Geweke values</th>
<th>p values</th>
<th>Gelman &amp; Rubin values</th>
</tr>
</thead>
<tbody>
<tr>
<td>burn in period = 1500; autocorrelation lag = 120</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\alpha_1$ (2.50)</td>
<td>2.4751</td>
<td>0.1285</td>
<td>2.2141</td>
<td>2.7419</td>
<td>-0.00710</td>
<td>0.49717</td>
<td>1.0003</td>
</tr>
<tr>
<td>$\alpha_2$ (2.60)</td>
<td>2.6075</td>
<td>0.2187</td>
<td>2.2266</td>
<td>2.9737</td>
<td>-0.00808</td>
<td>0.49678</td>
<td>1.0188</td>
</tr>
<tr>
<td>$\lambda_1$ (1.80)</td>
<td>1.9058</td>
<td>0.1434</td>
<td>1.5657</td>
<td>2.0932</td>
<td>-0.00999</td>
<td>0.49602</td>
<td>1.0021</td>
</tr>
<tr>
<td>$\lambda_2$ (0.75)</td>
<td>0.6388</td>
<td>0.0942</td>
<td>0.5082</td>
<td>0.8666</td>
<td>-0.01484</td>
<td>0.49408</td>
<td>1.0187</td>
</tr>
<tr>
<td>$\gamma_1$ (6.50)</td>
<td>6.5139</td>
<td>0.2718</td>
<td>6.0439</td>
<td>6.9779</td>
<td>-0.00171</td>
<td>0.49932</td>
<td>1.0049</td>
</tr>
<tr>
<td>$\gamma_2$ (7.00)</td>
<td>6.9767</td>
<td>0.2506</td>
<td>6.5318</td>
<td>7.4479</td>
<td>-0.00200</td>
<td>0.49920</td>
<td>0.9998</td>
</tr>
<tr>
<td>$\theta$ (0.40)</td>
<td>0.3844</td>
<td>0.0982</td>
<td>0.2151</td>
<td>0.5785</td>
<td>-0.00930</td>
<td>0.49629</td>
<td>1.0023</td>
</tr>
<tr>
<td>$\beta_0$ (0.50)</td>
<td>0.5146</td>
<td>0.0975</td>
<td>0.3186</td>
<td>0.6875</td>
<td>-0.00661</td>
<td>0.49976</td>
<td>1.0352</td>
</tr>
</tbody>
</table>

algorithm and Gibbs sampler based on normal transition kernels. We iterate both the chains for 100000 times. There is no effect of prior distribution on posterior summaries because the estimates of parameters are nearly the same and the convergence rate of Gibbs sampler for both the prior sets is almost the same. Also for both the chains the results were somewhat similar. For Model I and Model III the trace plots, the coupling from the past plots, the running mean plots and the sample autocorrelation plots for the simulation study are not provided due to lack of space. Table 2.1 presents the estimates and the credible intervals of the parameters for the Model I based on the simulation study. Table 2.2 gives the Gelman-Rubin convergence statistic and the Geweke test for all the parameters of the Model I based on the simulation study. The Gelman-Rubin convergence statistic values are nearly equal to one and also the Geweke test values are quite small and the corresponding p-values are large enough to say that the chain attains stationary distribution. Simulated values of the parameters have the autocorrelation of lag $k$. So that every $k^{th}$ iteration is selected as a sample from the posterior distribution.
2.6 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 presence or absence of disease type GN, AN and PKD where GN, AN and PKD are short forms of Glomerulo Neptiritis, Acute Neptiritis and Polycyatic Kidney Disease.

Let $T_1$ and $T_2$ represent 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 gamma 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 (2.3) 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.
Table 2.3: p-values of K-S Statistics for goodness of fit test for Kidney Infection data set.

<table>
<thead>
<tr>
<th>Distribution</th>
<th>recurrence time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>first</td>
</tr>
<tr>
<td>Model I</td>
<td>0.44755</td>
</tr>
<tr>
<td>Model III</td>
<td>0.33158</td>
</tr>
</tbody>
</table>

Figure 2.1: Survival function plots for (K-M survival and parametric survival).
Figure (2.1) shows the parametric plot with semi-parametric plot for all the parametric models with frailty and both lines are close to each other.

As in case of simulation, here also we assume same set of prior distributions. 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 trace plots for all the parameters shows zigzag pattern which indicates that parameters move and mix more freely. Thus, it seems that the Markov chain has reached the stationary state. Burn in period is decided by using coupling from the past plot. However, a sequence of draws after burn-in period may have the autocorrelation. Because of the autocorrelation, consecutive draws may not be random, but values at widely separated time points are approximately independent. So, a pseudo random sample from the posterior distribution can be found by taking values from a single run of the Markov chain at widely spaced time points (autocorrelation lag) after burn-in period. The autocorrelation of the parameters become almost negligible after the certain lag. ACF plot after thinning show that observations are independent. We can also use running mean plots to check how well our chains are mixing. A running mean plot is a plot of the iterations against the mean of the draws up to each iteration. In fact running mean plots display a time series of the running mean for each parameter in each chain. These plots should be converging
to a value. Running mean plot for each parameter is converging to the posterior mean of the parameter, thus, represents a good mixing of chain. Thus, our diagnostic plots suggest that the MCMC chains are mixing very well. Due to lack of space we are not able to present the trace plots, the coupling from the past plots, the autocorrelation plots after thinning and the running mean plots for the parameters of all the models.

Table 2.4: Posterior summary for Kidney infarction data set Model I

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>Lower credible Limit</th>
<th>Upper credible Limit</th>
<th>Geweke values</th>
<th>p values</th>
<th>Gelman &amp; Rubin values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_1$</td>
<td>2.3528</td>
<td>0.1563</td>
<td>2.0276</td>
<td>2.7047</td>
<td>0.01339</td>
<td>0.5053</td>
<td>1.0004</td>
</tr>
<tr>
<td>$\lambda_1$</td>
<td>0.0040</td>
<td>0.0019</td>
<td>0.0011</td>
<td>0.0081</td>
<td>0.01348</td>
<td>0.5053</td>
<td>1.0007</td>
</tr>
<tr>
<td>$\gamma_1$</td>
<td>1.3506</td>
<td>0.1719</td>
<td>1.0365</td>
<td>1.7077</td>
<td>-0.00827</td>
<td>0.4967</td>
<td>1.0013</td>
</tr>
<tr>
<td>$\alpha_2$</td>
<td>4.0593</td>
<td>0.5330</td>
<td>3.1651</td>
<td>5.0485</td>
<td>-0.00039</td>
<td>0.4998</td>
<td>1.0049</td>
</tr>
<tr>
<td>$\lambda_2$</td>
<td>0.0017</td>
<td>0.0008</td>
<td>0.0004</td>
<td>0.0036</td>
<td>0.00699</td>
<td>0.5027</td>
<td>1.0027</td>
</tr>
<tr>
<td>$\gamma_2$</td>
<td>1.2729</td>
<td>0.1194</td>
<td>1.0466</td>
<td>1.4893</td>
<td>-0.00597</td>
<td>0.4976</td>
<td>1.0002</td>
</tr>
<tr>
<td>$\theta$</td>
<td>0.4285</td>
<td>0.0594</td>
<td>0.3156</td>
<td>0.5358</td>
<td>0.00292</td>
<td>0.5011</td>
<td>1.0008</td>
</tr>
<tr>
<td>$\beta_1$</td>
<td>0.0184</td>
<td>0.0095</td>
<td>0.0003</td>
<td>0.0384</td>
<td>0.00269</td>
<td>0.5010</td>
<td>1.0010</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>-1.5653</td>
<td>0.4018</td>
<td>-2.3632</td>
<td>-0.7823</td>
<td>-0.00104</td>
<td>0.4995</td>
<td>1.0000</td>
</tr>
<tr>
<td>$\beta_3$</td>
<td>-0.1593</td>
<td>0.2535</td>
<td>-0.6602</td>
<td>0.3361</td>
<td>-0.01254</td>
<td>0.4949</td>
<td>1.0000</td>
</tr>
<tr>
<td>$\beta_4$</td>
<td>-0.0963</td>
<td>0.0462</td>
<td>-0.1883</td>
<td>-0.0072</td>
<td>0.01460</td>
<td>0.5058</td>
<td>1.0053</td>
</tr>
<tr>
<td>$\beta_5$</td>
<td>-1.2407</td>
<td>0.7797</td>
<td>-2.8605</td>
<td>0.2158</td>
<td>-0.00137</td>
<td>0.4994</td>
<td>0.9999</td>
</tr>
</tbody>
</table>

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 IV are presented in Table (2.4), (2.5), (2.6) and (2.7). The AIC, BIC and DIC values for all four models are given in Table (2.8). The Bayes factors for all models are given in Table (2.9).

The comparison between four proposed models is done using AIC, BIC
Table 2.5: Posterior summary for Kidney infarction data set Model II

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>Lower Credible Limit</th>
<th>Upper Credible Limit</th>
<th>Geweke values</th>
<th>p values</th>
<th>Gelman &amp; Rubin values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_1$</td>
<td>1.56069</td>
<td>0.1592</td>
<td>1.23811</td>
<td>1.86376</td>
<td>0.00244</td>
<td>0.5009</td>
<td>0.9999</td>
</tr>
<tr>
<td>$\lambda_1$</td>
<td>0.00917</td>
<td>0.0044</td>
<td>0.00189</td>
<td>0.01828</td>
<td>0.00588</td>
<td>0.5023</td>
<td>1.0066</td>
</tr>
<tr>
<td>$\gamma_1$</td>
<td>1.28285</td>
<td>0.1834</td>
<td>0.96501</td>
<td>1.67353</td>
<td>-0.00184</td>
<td>0.4992</td>
<td>1.0033</td>
</tr>
<tr>
<td>$\alpha_2$</td>
<td>1.28559</td>
<td>0.1448</td>
<td>1.01867</td>
<td>1.53773</td>
<td>-0.00051</td>
<td>0.4997</td>
<td>1.0020</td>
</tr>
<tr>
<td>$\lambda_2$</td>
<td>0.00425</td>
<td>0.0019</td>
<td>0.00101</td>
<td>0.00828</td>
<td>0.00707</td>
<td>0.5028</td>
<td>1.0004</td>
</tr>
<tr>
<td>$\gamma_2$</td>
<td>1.44945</td>
<td>0.1601</td>
<td>1.17399</td>
<td>1.77120</td>
<td>-0.00422</td>
<td>0.4983</td>
<td>1.0016</td>
</tr>
<tr>
<td>$\beta_1$</td>
<td>-0.00081</td>
<td>0.0014</td>
<td>-0.00362</td>
<td>0.00018</td>
<td>0.00250</td>
<td>0.5009</td>
<td>0.9999</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>-0.87672</td>
<td>0.2923</td>
<td>-1.43051</td>
<td>-0.26436</td>
<td>0.00601</td>
<td>0.5002</td>
<td>1.0000</td>
</tr>
<tr>
<td>$\beta_3$</td>
<td>0.17853</td>
<td>0.2649</td>
<td>-0.40278</td>
<td>0.72707</td>
<td>0.00696</td>
<td>0.5027</td>
<td>1.0000</td>
</tr>
<tr>
<td>$\beta_4$</td>
<td>-0.00889</td>
<td>0.0144</td>
<td>-0.03688</td>
<td>0.01721</td>
<td>-0.01237</td>
<td>0.4950</td>
<td>1.0000</td>
</tr>
<tr>
<td>$\beta_5$</td>
<td>0.02356</td>
<td>0.0142</td>
<td>-0.00127</td>
<td>0.05098</td>
<td>0.01150</td>
<td>0.5045</td>
<td>0.9999</td>
</tr>
</tbody>
</table>

Table 2.6: Posterior summary for Kidney infarction data set Model III

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>Lower Credible Limit</th>
<th>Upper Credible Limit</th>
<th>Geweke values</th>
<th>p values</th>
<th>Gelman &amp; Rubin values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_1$</td>
<td>2.5416</td>
<td>0.3068</td>
<td>1.96442</td>
<td>3.17423</td>
<td>0.00674</td>
<td>0.4973</td>
<td>1.0000</td>
</tr>
<tr>
<td>$\lambda_1$</td>
<td>0.1603</td>
<td>0.0308</td>
<td>0.10757</td>
<td>0.22039</td>
<td>-0.00944</td>
<td>0.4962</td>
<td>1.0005</td>
</tr>
<tr>
<td>$\gamma_1$</td>
<td>0.7672</td>
<td>0.0475</td>
<td>0.67774</td>
<td>0.85804</td>
<td>-0.00051</td>
<td>0.4977</td>
<td>1.0000</td>
</tr>
<tr>
<td>$\alpha_2$</td>
<td>5.0844</td>
<td>0.4871</td>
<td>4.12195</td>
<td>5.94377</td>
<td>0.00080</td>
<td>0.5003</td>
<td>1.0000</td>
</tr>
<tr>
<td>$\lambda_2$</td>
<td>0.2101</td>
<td>0.0484</td>
<td>0.12505</td>
<td>0.33359</td>
<td>0.00326</td>
<td>0.5013</td>
<td>1.0019</td>
</tr>
<tr>
<td>$\gamma_2$</td>
<td>0.7087</td>
<td>0.0380</td>
<td>0.63741</td>
<td>0.78077</td>
<td>0.00398</td>
<td>0.5016</td>
<td>0.9999</td>
</tr>
<tr>
<td>$\theta$</td>
<td>0.3890</td>
<td>0.1487</td>
<td>0.11149</td>
<td>0.70859</td>
<td>-0.00577</td>
<td>0.4977</td>
<td>1.0000</td>
</tr>
<tr>
<td>$\beta_1$</td>
<td>0.0019</td>
<td>0.0041</td>
<td>-0.00668</td>
<td>0.00983</td>
<td>-0.01601</td>
<td>0.4936</td>
<td>1.0001</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>-1.7487</td>
<td>0.4005</td>
<td>-2.53640</td>
<td>-0.93005</td>
<td>0.00918</td>
<td>0.4936</td>
<td>1.0015</td>
</tr>
<tr>
<td>$\beta_3$</td>
<td>0.0916</td>
<td>0.1353</td>
<td>-0.19238</td>
<td>0.34828</td>
<td>-0.00389</td>
<td>0.4984</td>
<td>1.0001</td>
</tr>
<tr>
<td>$\beta_4$</td>
<td>-0.0175</td>
<td>0.0139</td>
<td>-0.04558</td>
<td>0.00966</td>
<td>0.00150</td>
<td>0.5006</td>
<td>1.0050</td>
</tr>
<tr>
<td>$\beta_5$</td>
<td>0.0270</td>
<td>0.0286</td>
<td>-0.02627</td>
<td>0.08325</td>
<td>-0.01255</td>
<td>0.4949</td>
<td>1.0037</td>
</tr>
</tbody>
</table>

and DIC values given in Table (2.8). The smallest AIC value is Model-III (generalized Weibull distribution with frailty). Same result hold for BIC and DIC value. To take the decision about Model I, Model II, Model III and Model
Table 2.7: Posterior summary for Kidney infarction data set Model IV

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>Lower Credible Limit</th>
<th>Upper Credible Limit</th>
<th>Geweke p</th>
<th>Gelman &amp; Rubin values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_1$</td>
<td>2.4849</td>
<td>0.30943</td>
<td>1.8992</td>
<td>3.0831</td>
<td>-0.00829</td>
<td>0.4967</td>
</tr>
<tr>
<td>$\lambda_1$</td>
<td>0.2031</td>
<td>0.06863</td>
<td>0.0905</td>
<td>0.3589</td>
<td>-0.00614</td>
<td>0.4975</td>
</tr>
<tr>
<td>$\gamma_1$</td>
<td>0.6049</td>
<td>0.07812</td>
<td>0.4601</td>
<td>0.7620</td>
<td>0.01195</td>
<td>0.5047</td>
</tr>
<tr>
<td>$\alpha_2$</td>
<td>5.0401</td>
<td>0.50556</td>
<td>4.0999</td>
<td>5.9492</td>
<td>0.00073</td>
<td>0.5003</td>
</tr>
<tr>
<td>$\lambda_2$</td>
<td>0.3222</td>
<td>0.08144</td>
<td>0.1758</td>
<td>0.4942</td>
<td>-0.00887</td>
<td>0.4965</td>
</tr>
<tr>
<td>$\gamma_2$</td>
<td>0.5129</td>
<td>0.06162</td>
<td>0.3882</td>
<td>0.6333</td>
<td>0.01124</td>
<td>0.5045</td>
</tr>
<tr>
<td>$\beta_1$</td>
<td>0.0007</td>
<td>0.00279</td>
<td>-0.0044</td>
<td>0.0063</td>
<td>-0.00968</td>
<td>0.4961</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>-1.0716</td>
<td>0.31695</td>
<td>-1.6756</td>
<td>-0.4608</td>
<td>-0.01568</td>
<td>0.4937</td>
</tr>
<tr>
<td>$\beta_3$</td>
<td>-0.0159</td>
<td>0.02781</td>
<td>-0.0677</td>
<td>0.0375</td>
<td>0.00845</td>
<td>0.5034</td>
</tr>
<tr>
<td>$\beta_4$</td>
<td>-0.0041</td>
<td>0.00660</td>
<td>-0.0167</td>
<td>0.0078</td>
<td>-0.00533</td>
<td>0.4978</td>
</tr>
<tr>
<td>$\beta_5$</td>
<td>0.0012</td>
<td>0.00185</td>
<td>-0.0021</td>
<td>0.0046</td>
<td>0.00589</td>
<td>0.5024</td>
</tr>
</tbody>
</table>

Table 2.8: Comparison of AIC, BIC, DIC

<table>
<thead>
<tr>
<th>Model</th>
<th>AIC</th>
<th>BIC</th>
<th>DIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLLD</td>
<td>With Frailty</td>
<td>M I</td>
<td>689.3239</td>
</tr>
<tr>
<td></td>
<td>Without Frailty</td>
<td>M II</td>
<td>696.9474</td>
</tr>
<tr>
<td>GWD</td>
<td>With Frailty</td>
<td>M III</td>
<td>685.439</td>
</tr>
<tr>
<td></td>
<td>Without Frailty</td>
<td>M IV</td>
<td>690.2814</td>
</tr>
</tbody>
</table>

IV, we use the Bayes factor. The Bayesian test based on the Bayes factors for Model I against Model II is 3.73 and Model III against Model IV is 11.72 which are high and strongly support Model I and Model III for kidney infection data set compared to their corresponding models without frailty ($\theta = 0$) and frailty is significant in Model I and Model III.
Table 2.9: Bayes factor values and decision for models fitted to kidney infection data set.

<table>
<thead>
<tr>
<th>Numerator model against denominator model</th>
<th>$2\log(B_{jk})$</th>
<th>Range</th>
<th>Evidence against model in denominator</th>
</tr>
</thead>
<tbody>
<tr>
<td>$M_I$ against $M_{II}$</td>
<td>3.73</td>
<td>2 to 6</td>
<td>positive</td>
</tr>
<tr>
<td>$M_{III}$ against $M_I$</td>
<td>8.17</td>
<td>2 to 10</td>
<td>strong</td>
</tr>
<tr>
<td>$M_I$ against $M_{IV}$</td>
<td>3.54</td>
<td>2 to 6</td>
<td>positive</td>
</tr>
<tr>
<td>$M_{III}$ against $M_{II}$</td>
<td>11.90</td>
<td>&gt; 10</td>
<td>very strong</td>
</tr>
<tr>
<td>$M_{IV}$ against $M_{II}$</td>
<td>0.18</td>
<td>&lt; 2</td>
<td>no difference</td>
</tr>
<tr>
<td>$M_{III}$ against $M_{IV}$</td>
<td>11.72</td>
<td>&gt; 10</td>
<td>very strong</td>
</tr>
</tbody>
</table>

$B_{jk} = 2 \times \ln\left(\frac{M_k}{M_j}\right)$

Some patients are expected to be very prone to infection compared to others with the 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 a male patient with infection time 152 and 562. Table (2.9) shows that frailty models are better than without frailty models and Model III is better than Model I. From Table (2.8) and (2.9), we can observe that, Model III is the best.

Table 2.10: Predictive interval for four models fitted to kidney infection data.

<table>
<thead>
<tr>
<th>Model</th>
<th>99%</th>
<th>95%</th>
<th>90%</th>
<th>75%</th>
<th>50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model I</td>
<td>76</td>
<td>75</td>
<td>69</td>
<td>66</td>
<td>49</td>
</tr>
<tr>
<td>Model II</td>
<td>76</td>
<td>74</td>
<td>69</td>
<td>60</td>
<td>44</td>
</tr>
<tr>
<td>Model III</td>
<td>76</td>
<td>72</td>
<td>71</td>
<td>64</td>
<td>55</td>
</tr>
<tr>
<td>Model IV</td>
<td>75</td>
<td>71</td>
<td>68</td>
<td>60</td>
<td>42</td>
</tr>
</tbody>
</table>

Table (2.10) contains the predictive interval for four models fitted to kidney infection data and it shows that all four models fit well for kidney infection data. To check the adequacy of the Model I, Model II, Model III and Model IV firstly we have constructed 99%, 95%, 90%, 75% and 50% equal tailed predictive intervals of the generated random sample from the predictive distribution.
and counted the total number of intervals in which the $r^{th}$ observation falls in their respective intervals.

Details are given in Table (2.10). Table (2.10) shows that all four models are adequate for the kidney infection data. We can observe that the regression coefficients for all the four models are different. The only credible interval of the regression coefficient $\beta_2$ does not contain zero which indicates that the covariate sex is significant for all the models. But in Model I, $\beta_1, \beta_2$ and $\beta_4$ are significant. Negative value of $\beta_2$ indicates that the female patients have a slightly lower risk for infection. All other covariates other than sex are insignificant except in Model I. For Model I disease type age and AN is also significant.

2.7 Conclusion

In this chapter we discuss results for gamma shared frailty models with two different base line distributions. We use the generalized log-logistic distribution type II and the generalized Weibull as a baseline distributions. Main aim of our study is to check which distribution (with gamma frailty or without frailty) fits better. Models I and III are with gamma frailty and Models II and IV are without frailty. We perform simulation study and also to analyze kidney infection data by using R. The method of maximum likelihood fails to estimate the parameters due to convergence problem in the iterative procedure likelihood equations do not converge and method of maximum likelihood fails to estimate the parameters so we use Bayesian approach. The entire estimation procedure using Bayesian approach took large amount of computational time but the time was more or less the same for all the four models. In terms of convergence rate, we had faster convergence of Model I as compared to Model II, Model III and Model IV.
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 $\theta$ (Model I, $\theta = 0.0019$, Model III, $\theta = 0.3890$) from the frailty models show that there is a strong evidence of high degree of heterogeneity in the population of patients. The Bayes factor is used to test the frailty parameter $\theta = 0$ and it is observed that frailty is present and models with frailty fit better than without frailty models. The covariate sex is the only covariate which is significant for all models. Negative value of regression coefficient ($\beta_2$) of covariate sex indicates that the female patients have a slightly lower risk of infection.

The comparison between four proposed models is done using AIC, BIC and DIC values. The smallest AIC value is Model III (generalized Weibull distribution with frailty). The same result holds for BIC and DIC value. But these difference are not much significant. To take the decision about Model I, Model II, Model III and Model IV, we use the Bayes factor. We observe that, the Model III is the best. We also observe that the gamma frailty models (Models I and Model III) are better than without frailty models. Also we can conclude that the shared gamma frailty with the generalized Weibull distribution as the baseline distribution is a better fit than shared frailty model with the generalized log-logistic distribution type II. By referring all the above analysis, now we are in a position to say that, we have suggested a new shared gamma frailty model with the generalized Weibull distribution as the baseline distribution which is the best in the proposed models for modeling of kidney infection data.