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Survival Analysis of a Stochastic Model on Acute Kidney Injury Progression

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Abstract

The aim of the present paper is to analyze a stochastic model on patient's acute kidney injury progression and to investigate important parameters involved in the model that can be controlled to enhance survivability of the patient. Stochastic modeling and analysis of acute kidney injury patient is carried out using the concepts of Markov process and regenerative point technique. The expressions for mean sojourn time, mean survival time and survivability of the patient are obtained and then conclusions are drawn on the basis of numerical computations and graphical study. Sensitivity and relative sensitivity analyses are also carried out to judge the impact of different parameters on mean survival time and survivability of the patient. The study carries out sensitivity analysis of acute kidney injury patients through stochastic modeling and analysis approach to judge the important parameters that can help to enhance survivability of the patients.

Keywords: *Human kidneys, acute kidney injury progression, mean survival time, survivability, Markov process and regenerative point technique.*

1. Introduction

Biomedical science helps us to understand disease, its cause of occurrence and how we can control, cure and prevent the disease. In human body, kidney is vital organ of urinary system and kidney failure is a one of the most worldwide health problem. There are different types of kidney diseases that may lead to failure of the kidneys and most common disease is chronic kidney disease (CKD). In the progressive CKD, acute kidney injury (AKI) is a fundamental risk factor. Acute kidney injury (AKI) simply means a sudden deterioration in renal function

of kidney that makes difficulty in maintaining fluid, electrolyte and acid-base balance. Acute kidney failure occurs when kidneys suddenly become unable to filter waste products from blood. The diagnosis of AKI and its staging is based on acute changes in serum creatinine (SCr) and/or a reduction in urine output (UO). Gameiro et al. (2020) classified the staging of acute kidney injury according to KDIGO (Kidney Disease Improving Global Outcomes) as under:

Table 1 Stages of Acute Kidney Injury (AKI)

Stage	SCr	UO
1	Increase in SCr ≥ 0.3 mg/dl (≥26.5 μmol/L) or Increase in SCr ≥ 150% to 200% (1.5 to 1.9X)	<0.5ml/kg/h(>6 h)
2	Increase in SCr > 200 to 300% (>2 to 2.9X)	<0.5ml/kg/h(>12 h)
3	Increase in SCr > 300% (≥3X) or Increase in SCr to ≥ 4.0 mg/dl (≥353.6 μmol/L) or initiation of renal replacement therapy	<0.3ml/kg/h(24 h) or anuria 12 h

In recent years, several researchers have focused studies on problems and diseases related to renal function of the human kidneys using different approaches/techniques, e.g. Teo et al. (2019) described a prospective study of clinical characteristics and outcomes of acute kidney injury in a tertiary care Centre. Bao et al. (2021) studied a prediction score model and carried out survival analysis of AKI following orthotopic liver transplantation in adults. Mo et al. (2021) analyzed the risk factors those affects mortality in AKI and developed a prediction model for survival in diabetic patients having AKI. Wang et al. (2022) explained the predictive value of the Oxford acute severity of illness core for clinical outcomes in patients with AKI. Brothers et al. (2022) conducted survival and recovery modeling of AKI in critically ill adults. Haredasht et al. (2023) presented systematic review on validated risk prediction models for outcomes of AKI. Islam et al. (2023) predicted chronic kidney disease on the bases of machine learning algorithms. Nakamura et al. (2024) focused on the prognostic impact and predictors of persistent renal dysfunction in AKI after emergency percutaneous coronary intervention for acute myocardial infarction. Lai et al. (2024) developed a predictive model for AKI in sepsis patients based on recursive partition analysis.

Stochastic modeling is a simple and concise approach to understand the disease progression and for their in depth investigation in comparison to other techniques. Moreover, through the analysis, one can easily predict the disease progression in its different stages. This investigation helps us to take appropriate measures that may slow down the progression of the disease and hence can improve survivability of the patients. Application of stochastic modeling in biomedical science and their uses in controlling disease-related morbidity and mortality have been attempted by some researchers including Lintu et al. (2022). While going through the literature, it has been noticed that for enhancing the survivability of the patients, investigation of AKI progression through sensitivity analysis of a stochastic model has not been reported. To fill up this gap, an attempt has been made.

In the present paper, modeling and analysis of acute kidney injury patients is carried out using the concepts of Markov process and regenerative point technique. The motive of the study is to investigate important parameters of the model that have impact on the human kidneys with acute kidney injury progression at its different stages to enhance survivability of the patients, therefore, the expressions for mean sojourn times, mean survival time and survivability of the patients are obtained. The conclusions are drawn on the basis of numerical computations and graphical study. Sensitivity and relative sensitivity analyses are carried out to judge the impact of different parameters on mean survival time and survivability of the patients. The novelty of the study is sensitivity analysis of acute kidney injury patients through stochastic modeling and analysis approach to judge the important parameters that can help to enhance survivability of the patients.

The model description, notations and state transition diagram are given in the section 2. Various transition probabilities, mean sojourn times and mean survival time are also derived in this section. Section 3 is devoted to numerical computations, graphical and sensitivity analyses. Various conclusions drawn are presented in section 4.

2. Methodology

In this paper, a stochastic model has been developed for a patient having possibility of acute kidney injury (AKI) progression using Markov and regenerative point techniques. Stochastic modeling approach is a simple and concise way in comparison to other techniques to understand the disease progression and for their investigation. Moreover, through this analysis, one can easily predict the disease progression in its different stages. Sensitivity analysis determines how different values of an independent variable affect a particular dependent variable under a given set of assumptions. As there is significant difference among

the parameters considered in the model, the concept of sensitivity analysis has been applied for investigating comparative impacts of the parameters on mean survival time and survivability of the patients having AKI progression.

2.1. Model Description and Assumptions

The model takes in to consideration that the kidneys in urinary system of the human body are initially normal. With due course of time/complications arises in the body, deterioration in any one of the kidneys may starts and patient approaches to AKI Stage1. During that time, the patient goes to an appropriate hospital from where the patient may recover from the problem by any sort of treatments. In case, patient in AKI Stage 1 is not recovered, then the patient at AKI Stage 1 moves to a kidney damaged stage, i.e. AKI Stage 2. If not recovered too at that stage, the complete failure of a kidney of the patient takes place that corresponds to stage 3 of AKI. In the meantime, another kidney may get degraded that lead to major degradation of urinary system. Further, on complete failure of both the kidneys, transplantation of a kidney to the patient is done for which suitable donor is available at the hospital. It is considered that in the hospital, the treatment/surgery for kidney recovery/ transplantation is done with all medical perfections and accuracy by the doctors. A kidney after treatment/recovery at any AKI stage is assumed to work as good as in the just previous AKI stage. Further, other organs of the body are assumed to have no effect on the patient's AKI progression. Other assumptions of the model are as under:

- The patient reaches the hospital in negligible time wherein single doctor/facility for treatments/surgery is available.
- A transplanted kidney works as good as normal one.
- The times to damage, failure, recovery and transplantation of a kidney have exponential distributions whereas other time distributions are general.
- All random variables are mutually independent.

2.2. Notations and State Transition Diagram

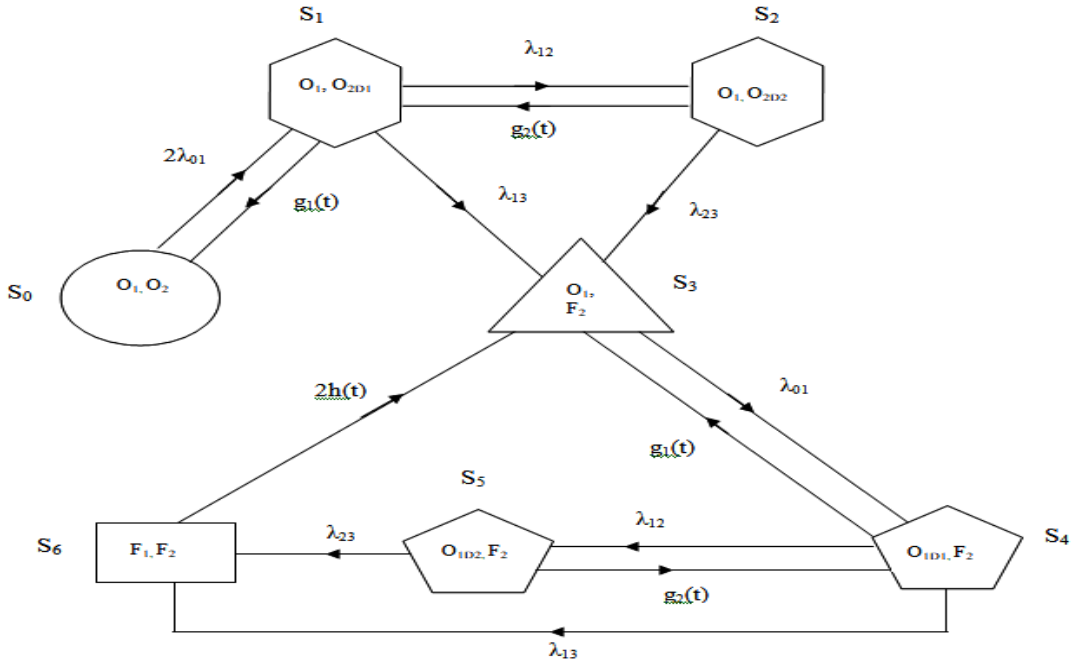
Various notations and states of the model are considered as under:

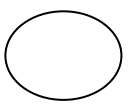
λ_{01}	Damage rate of kidney from normal to AKI Stage 1.
λ_{12}	Damage rate of kidney from AKI Stage 1 to Stage 2.
λ_{13}	Failure rate of kidney from AKI Stage 1 to stage 3.
λ_{23}	Failure rate of kidney from AKI Stage 2 to Stage3.

$g_1(t)/G_1(t)$	p.d.f./ c.d.f. of time of kidney recovery at AKI Stage 1.
$g_2(t)/G_2(t)$	p.d.f./ c.d.f. of time of kidney recovery at AKI Stage 2.
$h(t)/H(t)$	p.d.f./ c.d.f. of time of kidney transplantation.
S_0	Normal/healthy state.
S_1, S_2	Minor degraded state.
S_3	Degraded state.
S_4, S_5	Major degraded state.
S_6	Failed state.

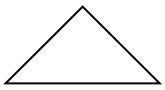
For the model, various states of transition are shown in the state transition diagram given below:

Figure 1 State Transition Diagram

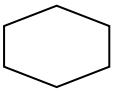




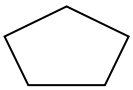
Normal State



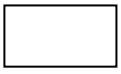
Degraded State



Minor Degraded State



Major Degraded State



Failed State

2.3. Transition Probabilities

The transition probabilities are obtained as follow:

$dQ_{01}(t) = 2\lambda_{01}e^{-(2\lambda_{01})t}dt$; $dQ_{10}(t) = g_1(t)e^{-(\lambda_{12}+\lambda_{13})t}dt$;

$dQ_{12}(t) = \lambda_{12}e^{-(\lambda_{12}+\lambda_{13})t}\overline{G_1(t)}dt$; $dQ_{13}(t) = \lambda_{13}e^{-(\lambda_{12}+\lambda_{13})t}\overline{G_1(t)}dt$;

$dQ_{21}(t) = g_2(t)e^{-(\lambda_{23})t}dt$; $dQ_{23}(t) = \lambda_{23}e^{-(\lambda_{23})t}\overline{G_2(t)}dt$;

$dQ_{34}(t) = \lambda_{01}e^{-(\lambda_{01})t}dt$; $dQ_{43}(t) = g_1(t)e^{-(\lambda_{12}+\lambda_{13})t}dt$;

$dQ_{45}(t) = \lambda_{12}e^{-(\lambda_{12}+\lambda_{13})t}\overline{G_1(t)}dt$; $dQ_{46}(t) = \lambda_{13}e^{-(\lambda_{12}+\lambda_{13})t}\overline{G_1(t)}dt$;

$dQ_{54}(t) = g_2(t)e^{-(\lambda_{23})t}dt$; $dQ_{56}(t) = \lambda_{23}e^{-(\lambda_{23})t}\overline{G_2(t)}dt$;

$dQ_{63}(t) = 2h(t)dt.$

The non-zero elements p_{ij} are given by

$p_{01} = 1$; $p_{10} = g_1^*(\lambda_{12}+\lambda_{13})$;

$p_{12} = \frac{\lambda_{12}\left[1-g_1^*(\lambda_{12}+\lambda_{13})\right]}{\lambda_{12}+\lambda_{13}}$; $p_{13} = \frac{\lambda_{13}\left[1-g_1^*(\lambda_{12}+\lambda_{13})\right]}{\lambda_{12}+\lambda_{13}}$;

$p_{21} = g_2^*(\lambda_{23})$; $p_{23} = 1-g_2^*(\lambda_{23})$;

$p_{34} = 1$; $p_{43} = g_1^*(\lambda_{12}+\lambda_{13})$;

$p_{45} = \frac{\lambda_{12}\left[1-g_1^*(\lambda_{12}+\lambda_{13})\right]}{\lambda_{12}+\lambda_{13}}$; $p_{46} = \frac{\lambda_{13}\left[1-g_1^*(\lambda_{12}+\lambda_{13})\right]}{\lambda_{12}+\lambda_{13}}$;

$p_{54} = g_2^*(\lambda_{23})$; $p_{56} = 1-g_2^*(\lambda_{23})$;

$p_{63} = 2h^*(0).$

From these transition probabilities we observed that

$p_{01} = 1$; $p_{10}+p_{12}+p_{13} = 1$; $p_{21}+p_{23} = 1$;

$p_{34} = 1$; $p_{43}+p_{45}+p_{46} = 1$; $p_{54}+p_{56} = 1$; $p_{63} = 1.$

2.4. Mean Sojourn Time

Expected time taken by the patient in state i before transiting to any other state is called mean

sojourn time. It is given as under by μ_i.

$$\mu_i = \int_0^\infty \Pr(T_i > t)dt,$$

where T_i is the sojourn time in state i. These are obtained as under:

$\mu_0 = \frac{1}{2\lambda_{01}}$; $\mu_1 = \frac{1-g_1^*(\lambda_{12}+\lambda_{13})}{\lambda_{12}+\lambda_{13}}$; $\mu_2 = \frac{1-g_2^*(\lambda_{23})}{\lambda_{23}}$;

$\mu_3 = \frac{1}{\lambda_{01}}$; $\mu_4 = \frac{1-g_1^*(\lambda_{12}+\lambda_{13})}{\lambda_{12}+\lambda_{13}}$; $\mu_5 = \frac{1-g_2^*(\lambda_{23})}{\lambda_{23}}$;

$\mu_6 = \int_0^\infty 2\overline{H(t)dt}.$

The unconditional mean time is mathematically stated as;

$$m_{ij} = \int_0^\infty \mathrm{tq}_{ij}(\mathrm{t})\,\mathrm{dt} = -\mathrm{q}_{ij}^*(0).$$

Thus,

$m_{01} = \frac{1}{2\lambda_{01}}$; $m_{10} = -g_1^{*'}(\lambda_{12}+\lambda_{13})$;

$m_{12} = \frac{\lambda_{12}}{(\lambda_{12}+\lambda_{13})^2} + \frac{\lambda_{12}g_1^{*'}(\lambda_{12}+\lambda_{13})}{(\lambda_{12}+\lambda_{13})} - \frac{g_1^*(\lambda_{12}+\lambda_{13})}{(\lambda_{12}+\lambda_{13})^2}$;

$m_{13} = \frac{\lambda_{13}}{(\lambda_{12}+\lambda_{13})^2} + \frac{\lambda_{13}g_1^{*'}(\lambda_{12}+\lambda_{13})}{(\lambda_{12}+\lambda_{13})} - \frac{g_1^*(\lambda_{12}+\lambda_{13})}{(\lambda_{12}+\lambda_{13})^2}$;

$m_{21} = -g_2^{*'}(\lambda_{23})$; $m_{23} = \frac{1}{\lambda_{23}} + g_2^{*'}(\lambda_{23}) - \frac{g_2^*(\lambda_{23})}{\lambda_{23}}$;

$m_{34} = \frac{1}{\lambda_{01}}$; $m_{43} = -g_1^{*'}(\lambda_{12}+\lambda_{13})$;

$m_{45} = \frac{\lambda_{12}}{(\lambda_{12}+\lambda_{13})^2} + \frac{\lambda_{12}g_1^{*'}(\lambda_{12}+\lambda_{13})}{(\lambda_{12}+\lambda_{13})} - \frac{g_1^*(\lambda_{12}+\lambda_{13})}{(\lambda_{12}+\lambda_{13})^2}$; $m_{54} = -g_2^{*'}(\lambda_{23})$;

$m_{56} = \frac{1}{\lambda_{23}} + g_2^{*'}(\lambda_{23}) - \frac{g_2^*(\lambda_{23})}{\lambda_{23}}$; $m_{63} = -2h^{*'}(0).$

It is clear that

$m_{01} = \mu_0$; $m_{10} + m_{12} + m_{13} = \mu_1$; $m_{21} + m_{23} = \mu_2$;

$m_{34} = \mu_3$; $m_{43} + m_{45} + m_{46} = \mu_4$; $m_{54} + m_{56} = \mu_5$.

2.5. Mean Survival Time

Let $\phi_i(t)$ denotes the cumulative distribution function of first passage time S_i to failure state. The following recursive relations are obtained for $\phi_i(t)$:

$\Phi_0(t) = Q_{01}(t) \& \Phi_1(t)$;

$\Phi_1(t) = Q_{10}(t) \& \Phi_0(t) + Q_{12}(t) \& \Phi_2(t) + Q_{13}(t) \& \Phi_3(t)$;

$\Phi_2(t) = Q_{21}(t) \& \Phi_1(t) + Q_{23}(t) \& \Phi_3(t)$;

$\Phi_3(t) = Q_{34}(t) \& \Phi_4(t)$;

$\Phi_4(t) = Q_{43}(t) \& \Phi_3(t) + Q_{45}(t) \& \Phi_5(t) + Q_{46}(t)$;

$\Phi_5(t) = Q_{54}(t) \& \Phi_4(t) + Q_{56}(t)$;

By L.S.T of these equations and computing for $\Phi_0^{**}(s)$, we obtain

$$\Phi_0^{**}(s) = \frac{N_0(s)}{D_0(s)},$$

where

$$N_0(s) = Q_{01}^{**}(s)Q_{13}^{**}(s)Q_{34}^{**}(s)Q_{46}^{**}(s) + Q_{01}^{**}(s)Q_{12}^{**}(s)Q_{23}^{**}(s)Q_{34}^{**}(s)Q_{46}^{**}(s)$$
$$+ Q_{01}^{**}(s)Q_{13}^{**}(s)Q_{34}^{**}(s)Q_{45}^{**}(s)Q_{56}^{**}(s) + Q_{01}^{**}(s)Q_{12}^{**}(s)Q_{23}^{**}(s)Q_{34}^{**}(s)Q_{45}^{**}(s)Q_{56}^{**}(s),$$

and

$$D_0(s) = 1 - Q_{01}^{**}(s)Q_{10}^{**}(s) - Q_{12}^{**}(s)Q_{21}^{**}(s) - Q_{34}^{**}(s)Q_{43}^{**}(s) + Q_{01}^{**}(s)Q_{10}^{**}(s)Q_{34}^{**}(s)Q_{43}^{**}(s)$$
$$+ Q_{12}^{**}(s)Q_{21}^{**}(s)Q_{34}^{**}(s)Q_{43}^{**}(s) - Q_{45}^{**}(s)Q_{54}^{**}(s) + Q_{01}^{**}(s)Q_{10}^{**}(s)Q_{45}^{**}(s)Q_{54}^{**}(s)$$
$$+ Q_{12}^{**}(s)Q_{21}^{**}(s)Q_{45}^{**}(s)Q_{54}^{**}(s).$$

When the system starts from the state (0) the expression for mean survival time is given by

$$T_0 = \lim_{s \to 0} \frac{1 - \Phi_0^{**}(s)}{s}.$$

By L'Hospital's rule and solving for $\Phi_0^{**}(s)$, we get

$$T_0 = \frac{N_0}{D_0},$$

where

$$N_0 = \mu_0(1 - p_{12}p_{21})(p_{46} + p_{45}p_{56}) + \mu_1(p_{46} + p_{45}p_{56}) + \mu_2 p_{12}(p_{46} + p_{45}p_{56}) +$$
$$\mu_3(p_{13} + p_{12}p_{23})(1 - p_{45}p_{54}) + \mu_4(p_{13} + p_{12}p_{23}) + \mu_5 p_{45}(p_{13} + p_{12}p_{23}),$$

and

$$D_0 = 1 - p_{10} - p_{12}p_{21} - p_{43} + p_{10}p_{43} + p_{12}p_{21}p_{43} - p_{45}p_{54} + p_{10}p_{45}p_{54} + p_{12}p_{21}p_{45}p_{54}.$$

2.6. Survivability

Using the definition of survivability and applying the concept of regenerative process, we derived the recursive relations for $S_i(t)$ as given below:

$S_0(t) = M_0(t) + q_{01}(t) \copyright S_1(t)$;

$S_1(t) = M_1(t) + q_{10}(t) \copyright S_0(t) + q_{12}(t) \copyright S_2(t) + q_{13}(t) \copyright S_3(t)$;

$S_2(t) = M_2(t) + q_{21}(t) \copyright S_1(t) + q_{23}(t) \copyright S_3(t)$;

$S_3(t) = M_3(t) + q_{34}(t) \copyright S_4(t)$;

$S_4(t) = M_4(t) + q_{43}(t) \copyright S_3(t) + q_{45}(t) \copyright S_5(t) + q_{46}(t) \copyright S_6(t)$;

$S_5(t) = M_5(t) + q_{54}(t) \copyright S_4(t) + q_{56}(t) \copyright S_6(t)$;

$S_6(t) = q_{63}(t) \copyright S_{13}(t)$.

Here

$M_0(t) = e^{-2\lambda_{01}t}$; $M_1(t) = e^{-(\lambda_{12}+\lambda_{13})t}\overline{G_1(t)}$; $M_2(t) = e^{-\lambda_{23}t}\overline{G_2(t)}$;

$M_3(t) = e^{-\lambda_{01}t}$; $M_4(t) = e^{-(\lambda_{12}+\lambda_{13})t}\overline{G_1(t)}$; $M_5(t) = e^{-\lambda_{23}t}\overline{G_2(t)}$.

By using LT of these equations and then computing for $S_0^*(s)$,

$$S_0^*(s) = \frac{N_1(s)}{D_1(s)},$$

where

$$\begin{aligned}
N_1(s) &= M_0^*(s) + M_1^*(s)q_{01}^*(s) + M_2^*(s)q_{01}^*(s)q_{12}^*(s) + M_3^*(s)q_{01}^*(s)q_{13}^*(s) - M_0^*q_{12}^*(s)q_{21}^*(s) \\
&+ M_3^*(s)q_{01}^*(s)q_{12}^*(s)q_{23}^*(s) + M_4^*(s)q_{01}^*(s)q_{13}^*(s)q_{34}^*(s) + M_4^*(s)q_{01}^*(s)q_{12}^*(s)q_{23}^*(s)q_{34}^*(s) \\
&- M_0^*(s)q_{34}^*(s)q_{43}^*(s) - M_1^*(s)q_{01}^*(s)q_{34}^*(s)q_{43}^*(s) - M_2^*(s)q_{01}^*(s)q_{12}^*(s)q_{34}^*(s)q_{43}^*(s) \\
&+ M_0^*(s)q_{12}^*(s)q_{21}^*(s)q_{34}^*(s)q_{43}^*(s) + M_5^*(s)q_{01}^*(s)q_{13}^*(s)q_{34}^*(s)q_{45}^*(s) \\
&+ M_5^*(s)q_{01}^*(s)q_{12}^*(s)q_{23}^*(s)q_{34}^*(s)q_{45}^*(s) - M_0^*(s)q_{45}^*(s)q_{54}^*(s) - M_1^*(s)q_{01}^*(s)q_{45}^*(s)q_{54}^*(s) \\
&- M_2^*(s)q_{01}^*(s)q_{12}^*(s)q_{45}^*(s)q_{54}^*(s) - M_3^*(s)q_{01}^*(s)q_{13}^*(s)q_{45}^*(s)q_{54}^*(s) \\
&+ M_0^*(s)q_{12}^*(s)q_{21}^*(s)q_{45}^*(s)q_{54}^*(s) - M_3^*(s)q_{01}^*(s)q_{12}^*(s)q_{23}^*(s)q_{45}^*(s)q_{54}^*(s) \\
&- M_0^*(s)q_{34}^*(s)q_{46}^*(s)q_{63}^*(s) - M_1^*(s)q_{01}^*(s)q_{34}^*(s)q_{46}^*(s)q_{63}^*(s) \\
&- M_2^*(s)q_{01}^*(s)q_{12}^*(s)q_{34}^*(s)q_{46}^*(s)q_{63}^*(s) + M_0^*(s)q_{12}^*(s)q_{21}^*(s)q_{34}^*(s)q_{46}^*(s)q_{63}^*(s) \\
&- M_0^*(s)q_{34}^*(s)q_{45}^*(s)q_{56}^*(s)q_{63}^*(s) - M_1^*(s)q_{01}^*(s)q_{34}^*(s)q_{45}^*(s)q_{56}^*(s) \\
&- M_2^*(s)q_{01}^*(s)q_{12}^*(s)q_{34}^*(s)q_{45}^*(s)q_{56}^*(s)q_{63}^*(s) + M_0^*(s)q_{12}^*(s)q_{21}^*(s)q_{34}^*(s)q_{45}^*(s)q_{56}^*(s)q_{63}^*(s).
\end{aligned}$$

$$D_1(s) = 1 - q_{01}^*(s)q_{10}^*(s) - q_{12}^*(s)q_{21}^*(s) - q_{34}^*(s)q_{43}^*(s) + q_{01}^*(s)q_{10}^*(s)q_{34}^*(s)q_{43}^*(s)$$
$$+ q_{12}^*(s)q_{21}^*(s)q_{34}^*(s)q_{43}^*(s) - q_{45}^*(s)q_{54}^*(s) + q_{01}^*(s)q_{10}^*(s)q_{45}^*(s)q_{54}^*(s) + q_{12}^*(s)q_{21}^*(s)q_{45}^*(s)q_{54}^*(s)$$
$$- q_{34}^*(s)q_{46}^*(s)q_{63}^*(s) + q_{01}^*(s)q_{10}^*(s)q_{34}^*(s)q_{46}^*(s)q_{63}^*(s) + q_{12}^*(s)q_{21}^*(s)q_{34}^*(s)q_{46}^*(s)q_{63}^*(s)$$
$$- q_{34}^*(s)q_{45}^*(s)q_{56}^*(s)q_{63}^*(s) + q_{01}^*(s)q_{10}^*(s)q_{34}^*(s)q_{45}^*(s)q_{56}^*(s)q_{63}^*(s)$$
$$+ q_{12}^*(s)q_{21}^*(s)q_{34}^*(s)q_{45}^*(s)q_{56}^*(s)q_{63}^*(s).$$

In steady state, expected survivability is derived as

$$S_0 = \lim_{s\to 0} sS_0^*(s) = \frac{N_1}{D_1},$$

where

$$N_1 = \mu_3(p_{13} + p_{12}p_{23})(1 - p_{45}p_{54}) + \mu_4(p_{13} + p_{12}p_{23}) + \mu_5 p_{45}(p_{13} + p_{12}p_{23}).$$

and

$$D_1 = \mu_3(p_{46} + p_{43} + p_{45}p_{56})(1 - p_{10} - p_{12}p_{21}) + (\mu_4 + \mu_5 p_{45})(1 - p_{10} - p_{12}p_{21})$$
$$+ \mu_6(1 - p_{10} - p_{12}p_{21})(p_{46} + p_{45}p_{56}).$$

3. Results and Discussion

3.1. Numerical Computation and Graphical Interpretations

The expressions derived for mean sojourn times, mean survival time and survivability are analytic and computationally tedious involving several parameters. Therefore, following particular case is considered for computations and analysis purpose:

$$g_1(t) = \beta_1 e^{-\beta_1 t}\ ;\ g_2(t) = \beta_2 e^{-\beta_2 t}\ ;\ h(t) = \gamma e^{-\gamma t}\ .$$

Here β_1, β_2 and γ are taken constants.

Numerical computations have been done for the above particular case and various graphs have been plotted for mean survival time and survivability giving different values to the parameters λ_{01}, λ_{12}, λ_{13}, λ_{23}, β_1, β_2, γ keeping in view the values as given in Brothers et al. (2022). The following interpretations and conclusions have been drawn from the plotted graphs:

Fig.2 and fig. 3 describe the essence of mean survival time (T_0) and survivability (S_0) respectively with respect to failure rate (λ_{23}) and kidney damage rate (λ_{12}) and for varying values of recovery rate (β_2) and transplantation rate (γ). From the graphs, it can be noticed that patterns of mean survival time (T_0) and survivability (S_0) respectively show downward trends as failure rate (λ_{23}) and kidney damage rate (λ_{12}) rises. Further these patterns have

upward trends for higher values of kidney recovery rate (β_2) and transplantation rate (γ).

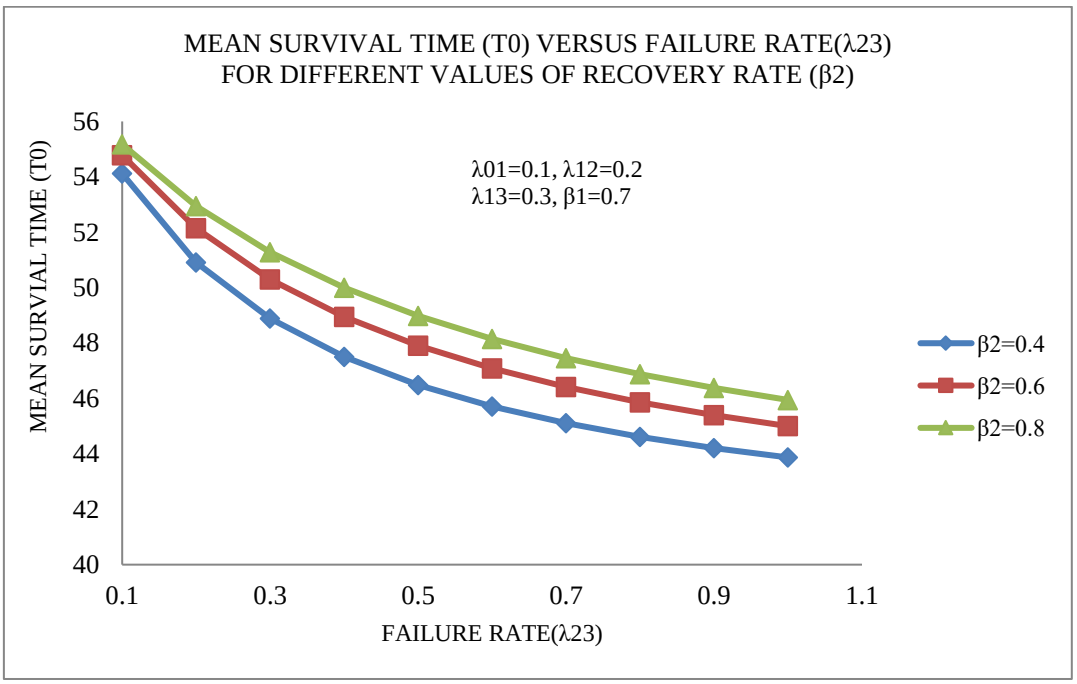


Figure 2 Mean survival time (T_0) versus kidney failure rate (λ_{23}) for varying values of recovery rate (β_2)

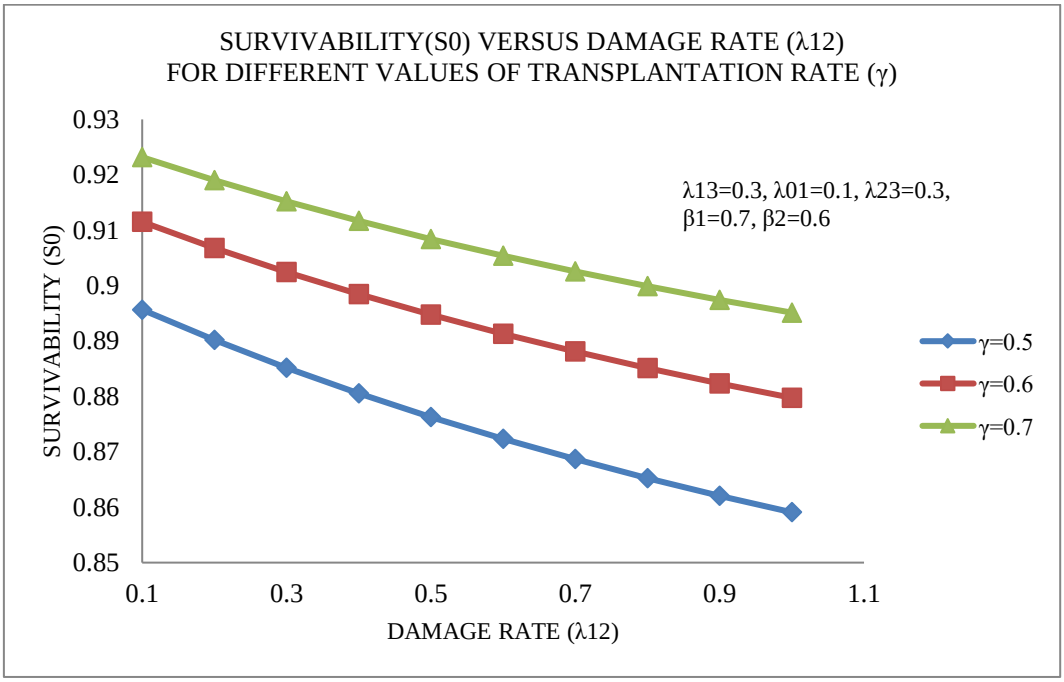


Figure 3 Survivability (S_0) versus kidney damage rate (λ_{12}) for varying values of

transplantation rate (γ)

The fig. 4 and fig. 5 presented the essence of mean survival time (T_0) and survivability (S_0) respectively in terms of recovery rate (β_1) and recovery rate (β_2) for different values of kidney failure rate (λ_{13}) and failure rate (λ_{23}). From these graphs, it can be noticed that the values of mean survival time (T_0) and survivability (S_0) of the patient, respectively rise with the recovery rates (β_1) and (β_2). Further, their values go down with increase in the values of kidney failure rates (λ_{13}) and (λ_{23}).

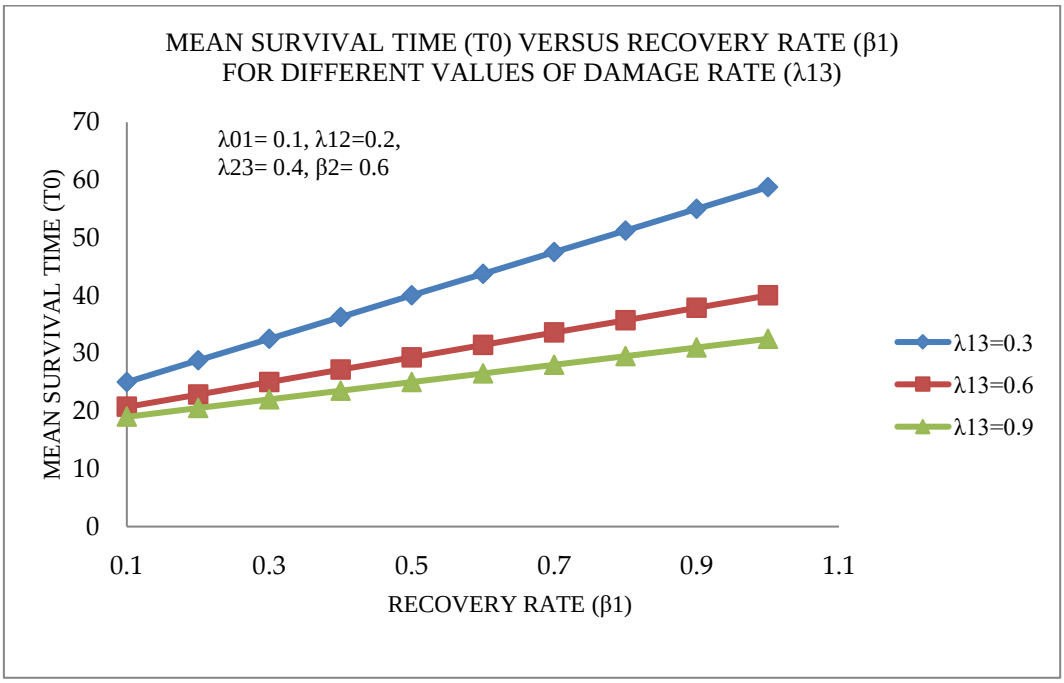


Figure 4 Mean survival time (T_0) versus recovery rate (β_1) for varying values of failure rate (λ_{13})

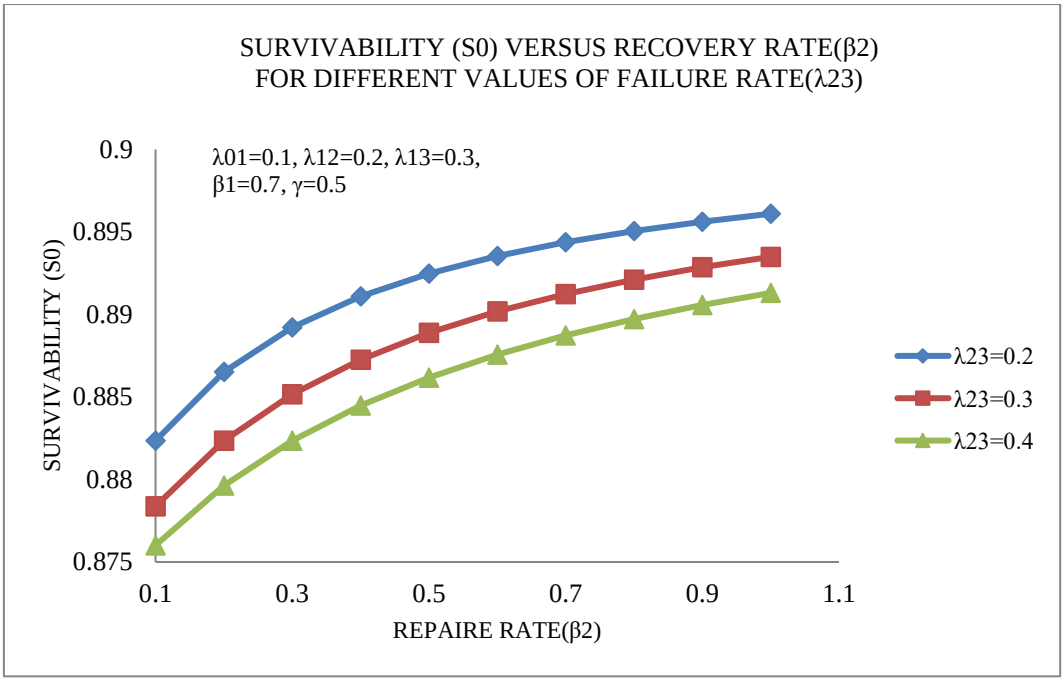


Figure 5 Survivability (S_0) versus recovery rate (β_2) for varying values of failure rate (λ_{23})

It can also be observed from the above graphs that for the lower values of kidney failure rate from AKI Stage 2 to Stage 3, the survivability of the patient is more. For instance, in case of failure rate $\lambda_{23} = 0.2$ and the kidney recovery rate at AKI Stage 2, $\beta_2 = 0.1$, the survivability of the patient is more than 88% whereas for failure rate $\lambda_{23} = 0.4$ with same recovery rate survivability is less than 88%. Further it is observed that the mean survival time and survivability of the patient increase with the rise in the kidney recovery/transplantation rates through medicine/surgery. For instance, for kidney transplantation rate $\gamma = 0.5$ and damage rate at AKI Stage 1, $\lambda_{12} = 0.1$, survivability of the patient is less than 90% whereas for the transplantation rate $\gamma = 0.7$ and at the same damage rate, survivability is more than 90%. This shows that with increase in the kidney transplantation rate, survivability of the patient increases.

3.2. Sensitivity and Relative Sensitivity Analysis

As there is significant difference among the values of parameters considered in the model, we can use the concept of sensitivity analysis for investigating their comparative impacts on mean survival time (T_0) and survivability (S_0) of the patients. The sensitivity and relative sensitivity function for mean survival time (T_0) and survivability (S_0) are given below:

$$\pi_k = \frac{\partial(T_0)}{\partial k}, \qquad \delta_k = \pi_k(\frac{k}{T_0})$$

and

$$\pi_k = \frac{\partial(S_0)}{\partial k}, \qquad \delta_k = \pi_k(\frac{k}{S_0}),$$

where

$k = \lambda_{01}, \lambda_{12}, \lambda_{13}, \lambda_{23}, \beta_1, \beta_2, \gamma.$

Table 2: Sensitivity and relative sensitivity analysis of mean survival time (T_0) with respect to damage rate λ_{01} for $\lambda_{12} = 0.2, \lambda_{13} = 0.3, \lambda_{23} = 0.5, \beta_1 = 0.7, \beta_2 = 0.6$

λ_{01}	$\pi_{\lambda_{01}} = \frac{\partial(T_0)}{\partial \lambda_{01}}$	$\delta_{\lambda_{01}} = \pi_{\lambda_{01}}(\frac{\lambda_{01}}{T_0})$
0.1	-418.6047	-0.8738
0.3	-46.5116	-0.6977
0.5	-16.7442	-0.5806
0.7	-8.5430	-0.4972
0.9	-5.1680	-0.4348
1.1	-3.4595	-0.3863

Table 3: Sensitivity and relative sensitivity analysis of mean survival time (T_0) with respect to damage rate λ_{12} for $\lambda_{01} = 0.1, \lambda_{13} = 0.3, \lambda_{23} = 0.5, \beta_1 = 0.7, \beta_2 = 0.6$

λ_{12}	$\pi_{\lambda_{12}} = \frac{\partial(T_0)}{\partial \lambda_{12}}$	$\delta_{\lambda_{12}} = \pi_{\lambda_{12}}(\frac{\lambda_{12}}{T_0})$
0.1	-43.0402	-0.0832
0.2	-33.6128	-0.1403
0.3	-26.9748	-0.1802
0.4	-22.1253	-0.2085
0.5	-18.4750	-0.2285
0.6	-15.6589	-0.2426

Table 4: Sensitivity and relative sensitivity analysis of Survivability (S_0) with respect to damage rate λ_{01} for $\lambda_{12} = 0.2, \lambda_{13} = 0.3, \lambda_{23} = 0.5, \beta_1 = 0.7, \beta_2 = 0.6, \gamma = 0.5$.

λ_{01}	$\pi_{\lambda_{01}} = \frac{\partial(S_0)}{\partial\lambda_{01}}$	$\delta_{\lambda_{01}} = \pi_{\lambda_{01}}(\frac{\lambda_{01}}{S_0})$
0.1	-0.2737	-0.0283
0.3	-0.1746	-0.0566
0.5	-0.1210	-0.0675
0.7	-0.0888	-0.0710
0.9	-0.0679	-0.0711

Table 5: Sensitivity and relative sensitivity analysis of Survivability (S_0) with failure rate λ_{13} for $\lambda_{01} = 0.1,\ \lambda_{12} = 0.2,\ \lambda_{23} = 0.5,\ \beta_1 = 0.7,\ \beta_2 = 0.6,\ \gamma = 0.5$.

λ_{13}	$\pi_{\lambda_{13}} = \frac{\partial S_0}{\partial\lambda_{13}}$	$\delta_{\lambda_{13}} = \pi_{\lambda_{13}}(\frac{\lambda_{13}}{S_0})$
0.1	-0.0774	-0.0079
0.2	-0.0632	-0.0130
0.3	-0.0525	-0.0163
0.4	-0.0444	-0.0184
0.5	-0.0380	-0.0198
0.6	-0.0329	-0.0206

Table 6: Sensitivity and relative sensitivity analysis of survivability (S_0) with recovery rate β_1 for $\lambda_{01} = 0.1,\ \lambda_{12} = 0.2,\ \lambda_{13} = 0.3,\ \lambda_{23} = 0.5,\ \beta_2 = 0.6$, $\gamma = 0.5$.

β_1	$\pi_{\beta_1} = \frac{\partial S_0}{\partial\beta_1}$	$\delta_{\beta_1} = \pi_{\beta_1}(\frac{\beta_1}{S_0})$
0.1	0.0930	0.0099
0.2	0.0698	0.0147
0.3	0.0543	0.0171
0.4	0.0435	0.0181
0.5	0.0356	0.0185

The sensitivity and relative sensitivity analyses of mean survival time (T_0) and survivability (S_0) of the patient w.r.t. the kidney damage/kidney failure/recovery rates $\lambda_{01}, \lambda_{12}, \lambda_{13}, \beta_1$ have been presented in table 2 to table 6. From these tables, it can be observed that the values

of sensitivity of mean survival time (T_0) w.r.t. the kidney damage/failure rates are negative in sign. For example, in case of sensitivity of mean survival time (T_0) w.r.t. the damage rates $(\lambda_{01}, \lambda_{12})$ shows that increase in the kidney damage rates decrease the value of mean survival time. On the other hand, the sensitivity values of survivability w.r.t. the kidney recovery/transplantation rates are observed positive. For example, in case of sensitivity of survivability w.r.t. the recovery rate at AKI Stage 1, increase in kidney recovery rate leads to increase in survivability of the patient. Further, it can be observed from the analyses that mean survival time and survivability of the patient are more sensitive towards the values of kidney damage rates from normal to AKI Stage 1 as well as from AKI Stage 1 to Stage 2.

4. Conclusion

The stochastic model and analysis presented in the paper is a simple and concise approach for understanding and investigating the patients with acute kidney injury at its different stage of progression or their related issues. This study is quite helpful to make prediction about patient's mean survival time and survivability and accordingly to take appropriate measure to treat/cure the patients. Further graphical and sensitivity analyses of the proposed model highlights the impacts of different rates of kidney damage, failure and recovery at different stages of acute kidney injury progression and kidney transplantation rate on mean survival time and survivability of the patients. The important factors/rates that can help to enhance survivability of acute kidney injury patients can be easily selected.

From the investigations through the graphical study and sensitivity analyses, it is concluded that the mean survival time and survivability of the patient decrease with the rise in the rates of kidney damage/ failure at various stages of the acute kidney injury progression. Further it can be concluded that mean survival time and survivability of the patient are more sensitive towards the kidney damage rates at initial two stages of acute kidney injury progression. More attentions need to be given to the patient at these stages of acute kidney injury.

It is also concluded from the analyses that for lower values of kidney failure rate at second stage of acute kidney injury progression, the survivability of the patient is more. Further, the mean survival time and survivability of the patient increase with the rise in the rates of kidney recovery/transplantation through medicine/surgery. Investigations also conclude that failure rate of kidney from second stage to third stage of acute kidney injury

progression and kidney transplantation rate play crucial roles as far as mean survival time and survivability of the patient is concerned. Thus, survivability of the patient may be enhanced controlling these rates taking appropriate measures.

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