International Journal of Current Research and Modern Education (IJCRME)
ISSN (Online): 2455 - 5428
(www.rdmodernresearch.com) Volume I, Issue I, 2016

A NEW STOCHASTIC MODEL TO ESTIMATE THE SERUM CORTISOL LEVELS USING WEIBULL DISTRIBUTION

A. Dinesh Kumar* & M. Vasuki**
* Assistant Professor, Department of Mathematics, Dhanalakshmi Srinivasan Engineering College, Perambalur, Tamilnadu
** Assistant Professor, Department of Mathematics, Srinivasan College of Arts and Science, Perambalur, Tamilnadu

Abstract:

Hypercortisolism is common in stroke patients. The aim of this study was to investigate possible disturbances at different sites within the hypothalamic-pituitary-adrenal axis. We also studied possible serum cortisol levels with the help of Laplace Transforms. In this paper we derive the distribution of the total downtime of a repairable system during a given time interval. We allow dependence of the failure time and the repair time. The results are presented in the form of Laplace Transforms which can be inverted numerically. We also discuss asymptotic properties of the total downtime.

Key Words: Cortisol, Down Time, Point Process & Weibull Distribution.

1. Introduction:

Many patients with acute stroke show a pronounced hypercortisolism [2] & [7-9]. Increased plasma and urinary cortisol levels are associated with greater mortality and a poorer functional outcome after stroke [2], [7] & [9]. This association has also been demonstrated in other types of brain injury. Theoretically, dysregulation at several sites within the hypothalamic-pituitary-adrenocortical axis may contribute. This includes an increased production rate of cortisol, a change in metabolism and/or clearance rate of cortisol, an increased sensitivity to stimulation of the adrenal glands, and a decreased "shut-off" mechanism of the cortisol axis. In patients with chronic degenerative cerebral disease such as Alzheimer's disease a correlation between cognitive disturbances and hypercortisolism has been demonstrated. It has been hypothesized that hypercortisolism per se may contribute to cognitive disturbances [14]. The acute confusional state commonly occurs in elderly hospitalized patients [5] and may be particularly frequent among stroke patients [4]. It is therefore of interest to study in more detail the different sites within the cortisol axis where possible abnormalities can lead to hypercortisolism early after stroke. Furthermore, we wanted to examine whether there was an association between cortisol levels and acute confusional state and/or motor impairment in these patients.

Consider a repairable system which is at any time either in operation or under repair (down) after failure. The effectiveness of the system can be measured by the total uptime or downtime that is the total amount of time the system is up or down during a given time interval. An expression for the cumulative distribution functions of the total downtime up to a given time t has been derived by using different methods. In this paper we use a different method for computation of the distribution of the total downtime defined in [14]. We also consider a more general situation where we allow dependence of the failure time and the repair time. Here, it is assumed that the failure time and the repair time are independent. Our derivation is based on a representation of the total downtime a functional of a Poisson Point Process.This paper is organized as follows. In Section 2, we define the total downtime and derive its distribution in a fixed time interval. In Section 3, we study the Covariance structure and asymptotic Properties of the total downtime and in Section 4, we give an example.

2. Distribution of Total Downtime:

We consider a repairable system which is at any time either in operation after failure, denoted as 1 and 0 respectively. Suppose the system starts to open at t=0. Let X_i and Y_i,i≥ 1, denote the time spent in the states 1 and 0 respectively during the ith visit to that state. The random variables X_i and Y_i are known as the failure time and the repair time respectively. We assume that the sequence (X_i, Y_i) of random vectors is independent and identically distributed with strictly positive components. However our set-up is more general than that in [3], [6], [10], [11] & [13] as we allow X_i and Y_i to be dependent.

Let $S_n = \sum_{i=1}^{n}(Xi + Yi)$for n ≥1 and $S_0 \equiv 0$, and let N (t) = sup (n≥0: S_n≤t). Then the total down time D (t) can expressed as

$$D(t) = \begin{cases} \left\{\sum_{i=1}^{N(t)} Yi\right\} & if\ S_{N(t)} \le t \le S_{N(t)} + X_{N(t)+1} \\ t - \sum_{i=1}^{N(t)+1} Xi & if\ S_{N(t)} + X_{N(t)} + 1 \le S_{N(t)+1} \end{cases}$$

Denote the state of the system at time t by Z(t). We assume that Z(t) is right continuous. Then the total downtime D(t) can also be expressed as

$$D(t) = \int_0^t 1_{[0]} z((s))ds \qquad (1)$$

Throughout this paper we will use the following notation for CDFs:

$$F(x) = P(X_1 \le x),$$
$$G(y) = P(Y_1 \le y),$$
$$H(x,y) = P(X_1 \le x, Y_1 \le y),$$

K (ω) = $P(X_1 + Y_1 \le \omega)$, The Laplace-Stieltjes transforms of CDF F and a joint CDF H will be denoted by F* and H* respectively, For α,β >0,

$$F^*(\alpha) = \int_0^\infty e^{-\alpha x}\, dF(x) \quad \text{and}$$
$$H^*(\alpha,\beta) = \int_0^\infty \int_0^\infty e^{-(\alpha x+\beta y)}\, dH(x,y).$$

Let. (T_n, $n \ge 1$) be the sequence of partial sums of the variables $U_{i.}$ Then the map

$$\phi : \omega \mapsto \sum_{n-1}^{\infty} \delta(T_n(\omega), X_n(\omega), Y_n(\omega)),$$

Where $\delta(x,y,z)$ is the Dirac Measure in (x,y,z) defines a poisson point process on E= ($\delta(0,\infty)$X$[0,\infty)$x $[0,\infty)$ with Intensity measure v(dt dx dy)= dt d H(x,y);. Note that , for almost all $\omega \in \Omega, \phi(\omega)$ is a simple point measure on E such that there is at most one point from the support of $\phi(\omega)$on each set (t)x$[0,\infty)$x $[0,\infty)$. Let M_P(E) be the set of all point measures on E. We will denote by P_υ the distribution of ϕ over M_p (E) For t∈ $[0,\infty)$, define on M_p(E) the functional.

$$A_X(t)(\mu) := \int_E x 1_{[0,t)}(s)\mu(dsdxdy)$$
$$A_y(t)(\mu) := \int_E y 1_{[0,t)}(s)\mu(dsdxdy) \text{ and}$$
$$A(t)(\mu) \coloneqq A_x(t)(\mu) + A_y(t)(\mu).$$

so, for example , A (t) (μ) is the sum of the x - and the y - coordinates of the points in the set of supp $\mu \cap [o,t] \times [0,\infty) \times [0,\infty)$ where supp μ = $\{(s,x,y) : \mu\{(s,x,y)\} > 0\}$. in the sequel we will write A_x (t,μ) for $A_x(t)$ (μ) and similarly for $A_y(t)$ (μ) and A(t) (μ).

Define also for $t \ge 0$.

$$B(t)(\mu) : = \int 1_{[0,x)}(t - A(s,\mu))A_y(s,\mu) + 1_{[x,x+y]}(t - A(s,\mu))(t - A_x(s+\mu))\mu(dsdxdy)$$

Where $A_x(s+\mu)=\int_E x1_{(0,s)}(r)\mu(dsdxdy)$. In 0 the next lemma we explain the meaning of $B(t)$.

Lemma 1:

With probability 1, $D(t) = B(t)(\phi)$.

Proof:

Let $\omega\epsilon\Omega$such that $\Phi(\omega)$is a simple point measure on E with at most one point of supp μ on each set(t) × $[0,\infty)\times[0,\infty)$. As noted before, the set of these points has Probability1.Then,

$$B(t)(\varphi(\omega))=\{\sum_{i=1}^{\infty}1_{[0,x_i(\omega))}(t-A(T_i(\omega),\varphi(\omega))A_y(T_i(\omega),\varphi(\omega))+$$
$$1_{[X_i(\omega),X_i(\omega)+Y_i(\omega))}(t-A(T_i(\omega),\varphi(\omega))(t-A_xT_i(\omega)+\varphi(\omega))\}$$

Note that$1_{[X_0,X_{i(\omega)+}Y_{i(\omega)})}(t-A(T_i(\omega),\varphi(\omega))=1$

Implies that i =$N(t,\omega)$ + 1. Similary If

$$1_{[X_{i(\omega)},X_{i(\omega)+}Y_{i(\omega)})}(t-A(T_i(\omega),\varphi(\omega))=1$$

Then $i = N(t,\omega) + 1$.]

Since the intervals $\{[S_{i-1,}S_{i-1}+X_i),(S_{i-1}+X_i,S_{i-1}+X_i+Y_i):i\geq 1]\}$

Partition$[0,\infty)$, for any $t>0$ one and only one of the indicators in the sum will be nonzero. So , if$1_{[0,X_{i(\omega)})}(t-A(T_i(\omega),\varphi(\omega))=1$

Then i = $N(t,\omega)+1$ and

$$\mathrm{B}(t)(\varphi(\omega)) = A_y\left(T_{N(i,\omega)+1(\omega)},\varphi(\omega)\right) = \begin{cases}0 & if\ N(t,\omega)=0\\ \sum_{j=1}^{N(t,\omega)} Y_j(\omega) & if\ N(t,\omega)\geq 1,\end{cases}$$

and if$1_{[X_{i(\omega)},X_{i(\omega)+}Y_{i(\omega)})}(t-A(T_i(\omega),\varphi(\omega))=1$

then B(t)($\varphi(\omega)$= $\left(t-A_x\left(T_N(t,\omega)+1(\omega),\varphi(\omega)\right)\right)$ = t - $\sum_{j-1}^{N(t,\omega)+1} X_j(\omega)$

The following theorem gives the distribution of the total downtime D(t) in the form of a double Laplace transform.

Theorem 1:

For $\alpha,\beta>0$

$$\int_0^{\infty} E\,(e^{-\alpha D(t)})e^{-\beta t}dt=\frac{\alpha\left[1-F^*(\beta)\right]+\beta\left(1-H^*(\beta,\alpha+\beta)\right)}{\beta(\alpha+\beta)\left(1-H^*(\beta,\alpha+\beta)\right)} \qquad (2)$$

Proof:

By Lemma 1 and using Fubini'S theorem, we obtain that

$$\int_0^{\infty} E(e^{-\alpha D(t)})e^{-\beta t}dt=\int_0^{\infty} dt\int P_v(d\mu)\exp\{-\alpha\int\mu(dsdxdy)\ [\ 1_{[0,x)}(t-A(s,\mu)A_y(s,\mu)]$$
$$+1_{[x,x+y)}\left(t-A(s,\mu)\right)\left(t-A_x(s+\mu)\right)]]\}e^{-\beta t}$$
$$= I_1 + I_2$$

Where,

$$I_1=\int_{M\,p(E)}P_v(s,\mu)\int_E\mu(dsdxdy)\int_0^{\infty}dt1_{(0,x)}\left(t-A(s,\mu)\right)e^{-\alpha Ay(s,\mu)}e^{-\beta t}$$
$$I_2=\int_{M\,p(E)}P_v(s,\mu)\int_E\mu(dsdxdy)\int_0^{\infty}dt1_{(x,x+y)}\left(t-A(s,\mu)\right)e^{-\alpha Ax(s+\mu)}e^{-\beta t}$$

Using the palm formula and Laplace functional of Poisson Point Processes and we obtain that

$$I_1 = \frac{1-F*(\beta)}{\beta\,[1-H*(\beta,\alpha+\beta)]} \text{ and } I_2 = \frac{F*(\beta)-H*(\beta,\alpha+\beta)}{\alpha+\beta\,[1-H*(\beta,\alpha+\beta)]}$$

Corollary 1:

Taking derivatives with respect to α in (2) and setting α=0, we get

$$\int_0^\infty E\left[D(T)\right]^2 e^{-\beta t}dt = \frac{F*(\beta)-H*(\beta,\beta)}{\beta^2\left[1-H*(\beta,\beta)\right]} \tag{3}$$

And $E\left[D(t)\right]^2 e^{-\beta t}dt = \frac{2}{\beta^3}\left[\frac{F*(\beta)-H*(\beta,\beta)}{1-H*(\beta,\beta)} - \frac{\beta\left[1-F*(\beta)\right]E\left(Y_1 e^{-\beta(x_1+y_1)}\right)}{\left[1-H*(\beta,\beta)\right]^2}\right]$ (4)

Remark 1:

When (X_i)and (Y_j) are independent, (2) simplifies to

$$\int_0^\infty E\left(e^{-\alpha D(t)}\right)e^{-\beta t}dt = \frac{\alpha\left[1-F*(\beta)\right]+\beta\left[1-F*(\beta)G*(\alpha+\beta)\right]}{\beta(\alpha+\beta)\left[1-F*(\beta)G*(\alpha+\beta)\right]} \tag{5}$$

For the independent case [3], [6] & [13] derived the following formula for the distribution function of the total downtime,

$$P(D(t)\le x)=\begin{cases}\sum_{n=0}^{\infty} Gn(x)[F_{n+1}(t-x) & \text{for} \quad t>x\end{cases} \tag{6}$$

Where F_n and G_n are the CDF s of $\sum_{i=1}^n$ Xiand $\sum_{i=1}^n$ Yirespectively. Taking double Laplace transorms on both sides of (6) we obtain (5).

Remark 2:

We can also derive the Laplace transforms of E[D(t)] without using point process. From the definition of D (t) it follows that

$$E\left[D(t)\right] = t - \int_0^t A_{11(s)}ds. \tag{7}$$

Where $A_{11}(t)$= P(Z(t)=1) is the availability of the system. Taking Laplace transforms on both sides of (7) gives

$$\int_0^\infty E\left[D(t)\right]e^{-\beta t}dt = \frac{1}{\beta^2} - \frac{1}{\beta}A_{11}(\beta),$$

Where $\tilde{A}_{11}(\beta) = \int_0^\infty A_{11}(t)e^{-\beta t}dt$ But A_{11} (t) satisfies the following integral equation

$$\tilde{A}_{11}(t) = \bar{F}(t) + \int_0^\infty \bar{F}(t-u)dm(u) \tag{8}$$

Where $\overline{F}(t) = 1 - F(t)$ and $m(t) = E\left[N(t)\right]$. Taking Laplace transforms on both sides of we obtain that

$$\tilde{A}_{11}(\beta) = \frac{1}{\beta}[1-F^*(\beta)][1+m^*(\beta)], \tag{9}$$

Where m* is the Laplace- Stieljes transform of m(t). Moreover, it is well known that

$$m^*(\beta) = \frac{K^*(\beta)}{1-K^*(\beta)} \tag{10}$$

Combining (9) and (10) we obtain that

$$\bar{A}_{11}(\beta) = \frac{1-F^*(\beta)}{\beta\left[1-K^*(\beta)\right]} \tag{11}$$

And

$$\int_0^\infty E\left[D(t)\right]e^{-\beta t}dt = \frac{F^*(\beta)-K^*(\beta)}{\beta^2\left[1-K^*(\beta)\right]}$$

Which is in agreement with (3) since $K^*(\beta)=H^*(\beta,\beta)$.

3. Covariance and Asymptotic Properties of D(t)

We start by considering structure of D(t). let U((t)) = (t) – D((t)) be the total uptime of the system. Obviously, covD((t_1)), D ((t_2)) = cov(U ((t_1)), U ((t_2)]. So we might as well study cov(U(t_1)), U ((t_2)]

The double Laplace transform of E (U ((t_1)), U ($(t_2)$is given in the following proposition, which is a generalization of a result in [11].

Proposition:

For $\alpha,\beta > 0$, $\int_0^\infty E\left[U(t_1)\right]U(t_2)e^{-\alpha t_1-\beta t_2}dt_1dt_2 = \frac{1}{\alpha\beta}\left[\widehat{\varphi}(\alpha,\beta)+\widehat{\varphi}(\beta,\alpha)\right]$,

Where $\widehat{\varphi}(\alpha,\beta) = \frac{\alpha\left[1-F^*(\beta)\right]-\beta\left[F^*(\beta)-F^*(\alpha+\beta)\right]}{\alpha\beta(\alpha+\beta)\left[1-K^*(\alpha+\beta)\right]}$

$$+\frac{\left[1-F^*(\beta)-\beta\right]\left[H^*(\beta,\beta)-H^*(\alpha+\beta,\beta)\right]}{\alpha\beta\left[1-H^*(\beta)\right]\left[1-K^*(\alpha+\beta)\right]} \quad (12)$$

Proof:

First it can easily be verified that, for $0 \le t_1 \le t_2 < \infty$,

$$E[U(t_1)U(t_2)] = 2\int_{x=0}^{t_1}\int_{y=x}^{t_1}\varphi(x,y),dy,dx + \int_{x=0}^{t_1}\int_{y=t1}^{t_2}\varphi(x,y),dy,dx,$$

Where

$$\varphi(x,y) = P(z(x)=1,z(y)=1)$$

$$\int_{t1=0}^{\infty}\int_{t2=t1}^{\infty} E(U(t_1)U(t_2))e^{-\alpha t_1-\beta t_2}dt_2dt_1 = \frac{\tilde{\varphi}(\alpha,\beta)}{\alpha\beta}+\frac{[\alpha-\beta]\tilde{\varphi}(0,\alpha+\beta)}{\alpha\beta(\alpha+\beta)} \quad (13)$$

$$\hat{\varphi}(\alpha,\beta) = \int_0^\infty\int_0^\infty \varphi(x,y)e^{-\alpha x-\beta y}\,dxdy.$$

Now we want to prove that $\hat{\varphi}(\alpha,\beta)$ satisfies (12), for $0 \le x \le y < \infty$,

$$\varphi(x,y) = P(Z(x)=1,Z(y)=1,Y<X_1)$$
$$+P(Z(x)=1,Z(y)=1,x<X_1<y)$$
$$+P(Z(x)=1,Z(y)=1,X_1<x) \quad (14)$$

Obviously, P(Z(x)= 1, Z(y)=1,y<X_1)=1-F(y). For the second term, note that the event

$$\{Z(X)=1,Z(Y)=1,x<X_1<Y\}$$

Is equivalent to the event

$$\{x<X_1 and, for\ some\ n\ge 1, S_n<y<S_n+X_{n+1}\}$$

Where $S_n = \sum_{i=1}^n (X_i+Y_i)$.Let $R_n=\sum_{i=2}^n (X_i+Y_i)$for $n \ge 2$. Then (X_1,Y_1),R_n and X_{n+1} are independent. Using this fact we can prove that

$$P(z(x)=1,Z(y)=1,x<x_1\le x) = \int_{x_1\in[x,y]}\int_{\omega\in[x,y]} A_{11}(y-\omega)dH(x_1,\omega-x_1),$$

Where A_{11} $((t))$ denotes the availability of the system at time t starting 1 at time0. Finally, the last term in (14) can be obtained by conditioning on X_1+Y_1 which gives

$$P(z(x)=1, Z(y)=1, X_1 \le x) = \int_0^x \phi(x-\omega, y-\omega)dK(\omega).$$

Taking the double Laplace transform on both sides of (14) and using (11), (12) follows. Finally, for $0 \le t_2 \le t_1$ we simply interchange α and β in (13). So that the proposition follows. Now we want to address asymptotic properties of the total downtime D(t).

To this end, we use a method of [11] which is based on a comparison with the asymptotic properties of a delayed renewal process related to the process that we are studying. we will use the following notation:

$$\mu_X = E(X_1),\ \ \mu_y = E(Y_1)$$

$$\sigma_x^2 = var\ (X_1),\quad \sigma_Y^2 = var\ (Y_1),\ \ \sigma_{xy} = cov(X_1 Y_1)$$

Theorem 2:

$$\text{If } \mu_X + \mu_Y < \infty, Then \qquad \lim_{t\to\infty}\frac{E[D(t)]}{t} = \frac{\mu Y}{\mu_X+\mu_Y} \tag{15}$$

if σ_X^2 and σ_Y^2 are finite and $X_1 + Y_1$ is a non lattice random variable , then

$$\lim_{t\to\infty}\left(\mathrm{E}[D(\mathrm{t})] - \frac{\mu_Y t}{\mu_X+\mu_Y}\right) = \frac{\mu_Y\sigma_X^2 - \mu_x\sigma_Y^2 \_2\mu_X\sigma_{xy}}{2(\mu_X+\mu_Y)^2} - \frac{\mu_x\mu_Y}{2(\mu_X+\mu_Y)} \tag{16}$$

$$\text{And}\quad \lim_{t\to\infty}\frac{\mathrm{var}\,[\mathrm{D(t)}]}{\mathrm{t}} = \frac{{\mu_X}^2{\sigma_Y}^2 + -{\mu_Y}^2{\sigma_x}^2 - 2\mu_X\mu_Y\sigma_{xy}}{(\mu_X+\mu_Y)^3}$$

Proof:

Let $\tilde{N}(t)$be the delayed renewal process determined by the random variables (V_n), n=0, 1, 2,......, where V_o has the distribution

$$\mathrm{P}(V_o \le x) = (1/\mu x)\int_0^x([1-F(y)]dy for\ x \ge 0)\ and\ P(V_0 \le x) = 0 \text{ otherwise and}$$

$$V_n = X_n + Y_n,\ n = 1,2,3\ldots \tag{17}$$

Then using (3) and Laplace-Stieltjies-transform arguments, we can prove that

$$\mathrm{E}[D(t)] + \mu_X E[\tilde{N}(t)] = t. \tag{18}$$

$Since\ \frac{\lim_{t\to\infty} E[N(t)]}{t} = 1/(\mu_X + \mu_Y)$, the first part of the theorem follows.

To prove (16) from (18) we obtain that

$$\lim_{t\to\infty}\left(\mathrm{E}[D(t)] - \frac{\mu_Y t}{\mu_X+\mu_Y}\right) = -\mu_X\lim_{t\to\infty}\left(\mathrm{E}[\tilde{N}(t)] - \frac{t}{\mu_X+\mu_Y}\right)$$

Now, if is an X_1+Y_1no lattice random variable, then using [13] and by noting that

$$\mathrm{E}(V_0) = (\sigma_X^2 + \mu_x^2)/2\mu_X,\ \text{(16) follows.}$$

To prove asymptotic variance of$D(t)$, we construct another delayed renewal process as follows. Let $\tilde{N}(t)$ be the delayed renewal process determined by the random variables (V_n) n=0,1,2..., where V_o has Laplace transform

$$E\left(e^{-\beta V_0}\right) = \frac{[1-F^*(\beta)]\int_0^\infty\int_0^\infty ye^{-\beta(x+Y)}dH(x,y)}{\beta\mu_X\mu_Y}$$

and (V_n) for is defined as in (17). Then using Corollary 1 and of [13], we can prove that as

$$\mathrm{E}[D(t)]^2 = \frac{{\mu^2}_Y t^2}{(\mu_X+{\mu_Y}^2)}$$

$$= \left[\frac{\mu_X\mu_Y^3 + (\mu_X^2 - 2\sigma_X^2)\mu_Y^2 + (\sigma_Y^2 + 4\sigma_{XY})\mu_X\mu_Y - \mu^2 X\sigma_Y^2}{(\mu_X+\mu_Y)^3}\right]t + 0(t),$$

and hence, by taking (16) into consideration, the last part of the theorem follows.

Remark 3:

The first result (15) of Theorem 2 can also be proved using a Tauberian theorem. From (3),μ_X *and* μ_Y if are finite, we obtain that

$$\int_0^\infty e^{-\beta t}\, dE[D(t)] \sim \frac{\mu_Y}{\beta(\mu_X+\mu_Y)} \text{as} \beta \to 0.$$

Obviously is E[D(t)] non decreasing. So we can use a Tauberian theorem,
Asymptotic distribution of the total downtime is given in the following theorem, which is a generalization of the results in [13] and [10].

Theorem 3:

If $\sigma_{X and}^2\, \sigma_{Y,}^2$ are finite then

$$\frac{D(t)-\mu_Y t/(\mu_X+\mu_Y)}{\sqrt{\left(\frac{\left(\mu_X^2\sigma_Y^2+\mu_Y^2\sigma_X^2-2\mu_{XY}\sigma_{XY}\right)}{(\mu_X+\mu_Y)^3 t}\right)}} \xrightarrow{D} n(0,1) as t \to \infty.$$

Proof:

First note that $\sum_{i=1}^{N(t)} Y_i \le D(t) \le \sum_{i=1}^{N(t)+1} Y_i$

Using the central limit theorem for random sums, we obtain that

$$\left[\frac{\mu_X^2\sigma_Y^2+\mu_Y^2\sigma_X^2-2\mu_X\mu_Y\sigma_{XY}}{(\mu_X+\mu_Y)^3 t}\right]^{-1/2} \left(\sum_{i=1}^{N(t)} Y_i - \frac{\mu_Y t}{\mu_X+\mu_Y}\right) \xrightarrow{D} N(0,1),$$

The proof is complete if we can show that

$$\frac{Y_{N(t)+1}}{\sqrt{t}} \xrightarrow{P} 0 \ as\ t \to \infty.$$

But by the fact that $N(t)/t \xrightarrow{P} 1/(\mu_X+\mu_Y)\ (>0)$ and the assumption that $\sigma_{Y<\infty,}^2$we obtainthat$Y_{N(t)}/\sqrt{N(t)} \xrightarrow{P} 0$ (for an argument), and hence the required statement follows. The effect of dependence of the failure and repair times on the distribution of the total downtime. Suppose that the failure time and the repair time have a joint bivariate distribution given by

$$P(X_1 > x, Y_1 > Y) = e^{-\left(\lambda x+\mu y+v\max(x,y)\,\lambda x\right)}, \quad x,y \ge 0, \mu, v > 0.$$

we compare the graphs of the normal approximations of D (10) where ((X_i) and (Y_j) are independent and both(X_i) and $(Y_j)$are exponentially distributed with parameters $\lambda+\upsilon$ and $(\mu+v)$respectively with the normal approximation of D(10) for various correlation coefficients P_{XY}.In this example we can also calculate explicitly the mean of the total downtime D(t). Using (3), we obtain that

$$\int_0^\infty \mathrm{E}\,[\mathrm{D(t)}]\mathrm{e}^{-\beta t}\mathrm{dt} = \frac{(2\lambda+v)\beta+(\lambda+v)(\lambda+\mu+v)}{\beta^2\left[2\beta^2+3(\lambda+3\mu+4v)\beta+(\lambda+\mu)(\lambda+\mu+3v)+2v^2\right]}$$

This transform can be inverted analytically.

4. Example:

Sixteen patients (11 men, five women; mean ± SD age, 71 ±11 years) with an acute brain infarction were selected for this study from our stroke unit. The median delay from onset until admission was 11 hours (range, 1-100 hours). Based on clinical judgement and on the results of computed tomographic (CT) scans, performed in all patients, 14 patients had a supratentorial brain infarction and two patients had a cerebellar infarction. In the supratentorial brain infarction group, eight patients had a probable nonembolic brain infarction, five patients had an embolic brain infarction, and one patient had a lacunar infarction. Six of the patients in this group had right-sided and eight had left-sided brain lesions. These patients all had an extremity paresis afflicting the contralateral arm or leg at admission. Three patients with left-sided brain lesions also had a slight-to-moderate dysphasia at admission. Both patients with cerebellar infarctions had vertigo, one of them having a right-sided arm paresis as well. None of the patients had a pronounced decrease in consciousness, i.e., more than drowsiness, high fever (>38.5°C), renal failure (plasma creatinine level >200 /xmol/1), known extensive weight loss or malnutrition, hypothyroidism/ hyperthyroidism, pituitary insufficiency, uncontrolled diabetes mellitus, obvious abstinence reactions from alcohol or other central nervous stimulants, or epilepsy. None was treated with medications known to interfere with the test results such as glucocorticoids, estrogens, anticonvulsants, high-dose benzodiazepines, or ephedrine. Two of the patients had non-insulin dependent diabetes mellitus.

As control subjects, nine healthy elderly people were selected from an ongoing study of hormone changes in the elderly (six men, three women; mean ± SD age, 71 ± 9 years). All were thoroughly investigated by a resident in geriatric medicine. CT scan of the brain was normal in all individuals, and none were taking drugs. The patients were examined between the third and seventh day after admission. They were investigated in a standardized manner, with repeated clinical assessments. The extent of extremity paresis was quantified using a four point scale [8]. Acute confusional state was diagnosed using criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R) [4]. A diagnosis of a major depressive episode was based on criteria from DSM-III-R [3]. All tests and interviews with patients, relatives, and staff regarding the diagnoses of acute confusional state and major depression were made by one of the authors.

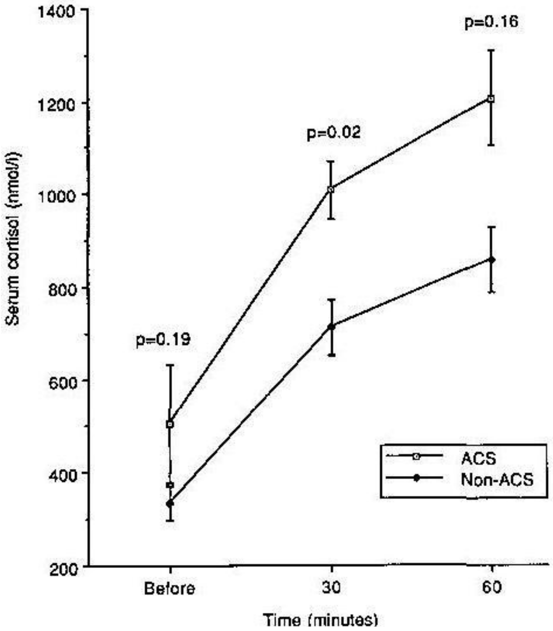

Figure (1): Line graph of Serum Cortisol Before and After the Administration of Adrenocorticotropic Hormone to Stroke Patients

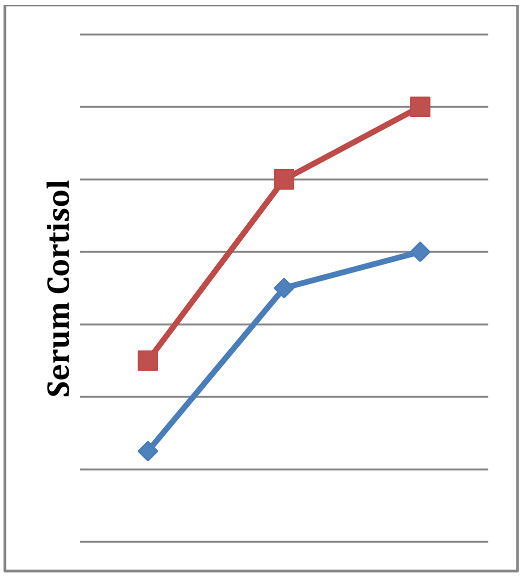

Figure (2): Line graph of Serum Cortisol Before and After the Administration of Adrenocorticotropic Hormone to Stroke Patients (Using Normal Distribution)

A short adrenocorticotropic hormone (ACTH) stimulation test was performed in the fasting state between 8 and 9 AM. In this test 0.25 mg ACTH (1-24 ACTH; Synacthen, CIBA-Geigy) was administered slowly intravenously as a bolus dose. Blood was collected for cortisol analyses before the injection and 30 and 60 minutes after the injection. This was followed by an overnight dexamethasone suppression test in which 1mg dexamethasone was given orally at 11 PM. Blood was drawn on the following day at 8 AM for serum cortisol analysis. Serum cortisol was analyzed with a radioimmunoassay kit with an inter assay coefficient variation <8% for the analysis. The area under the curve for the cortisol response to ACTH was calculated by the trapezium rule [1]. The centered cumulative cortisol response to ACTH was calculated using the following formula: area under the curve [1]. Differences in cortisol levels between groups were analyzed with the Mann-Whitney U test. Spearman correlation coefficients were used for the calculation of correlations.

4. Conclusion:

There are abnormalities in the cortisol axis both at the central level and at the adrenal level early after stroke. Hypercortisolism is closely associated with cognitive disturbances and extensive motor impairment. The serum cortisol levels with the help of Laplace Transform which are fitted with distribution of total down time and the corresponding is obtained {Figure (2)}. There is no significance difference between medical and mathematical reports. The medical reports are beautifully fitted with the mathematical model. Hence the mathematical report {Figure (2)} is coincide with the medical report {Figure (1)}.

5. References:

1. Altman D G, "Practical Statistics for Medical Research", Conference Paper, Chapman and Hall, London, Page Number 431-433, 1991.
2. Feibel J H, Hardy P M, Campbell R G, Goldstein M N & Joynt R J, "Prognostic value of the stress response following stroke", JAMA, Volume 238, Page Number 1374-1376, 1977.
3. Funnaki K & Yoshimoto K, "Distribution of total uptime during a given time interval", IEEE trans. Reliab, 43, 489-492, 1994.
4. Gustafson Y, Olsson T, Eriksson S, Asplund K & Bucht G, "Acute confusional states (delirium) in stroke patients", Cerebrovasc Disorder, Volume 1, Page Number 257-264, 1991.
5. Levkoff S E, Evans D A, Liptzin B, Cleary P D, Lipsitz L A, Wetle T T, Reilly C H, Pilgrim D M & Schor J, "Delirium: The occurrence and persistence of symptoms among elderly hospitalized patients", Architecture International Medicine, Volume 152, Page Number 334-340, 1992.
6. Muth E J, "A Method for predicting system, Downtime", IEEE Trans. Reliah. 17, 97-102, 1968.
7. Oka M, "Effect of cerebral vascular accident on the level of 17-hydroxycorticosteroids in plasma", Ada Med Scand, Volume 156, Page Number 221-226, 1956.
8. Olsson T, Astrom M, Eriksson S & Forssell A, "Hypercortisolism revealed by the dexamethasone suppression test in patients with acute ischemic stroke", Stroke, Volume 20, Page Number 1685-1690, 1989.
9. Olsson T, "Urinary free cortisol excretion shortly after ischaemic stroke", Journal of International Medicine, Volume 228, Page Number 177-181, 1990.
10. Renyi A, "On the asymptotic distribution of the sum of a random number of independent random variables", ACTA Math, Acad. Sci. Hungar, 8, 193-199, 1957.
11. Srinivasan S K, Subramanian R & Ramesh K S, "Mixing of two renewal processes and its applications to reliability theory", IEEE trans. Reliab, 20, 51-55, 1971.
12. Suyono & J.A.M Vander, "Weide method for computing total downtime distributions in repairable systems", J. Appl. Prob, 40, 643-653, 2003.

13. Takacs L, “On certain sojourn time problems in the theory of stochastic processes”, ACTA Math. Acad Sci. Hungar, 8, 169-191, 1957.
14. Wolkowitz O M, Reus V I, Weingartner H, Thompson K, Breier A, Doran A, Rubinow D & Pickar D, “Cognitive effects of corticosteroids”, American Journal of Psychiatry, Volume 147, Page Number 1297-1303, 1990.