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Mathematical model for abnormalities of HPA axis due to stress associated with analytic univalent functions

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Abstract

The main interest of this study is to find the activity of Hypothalamic Pituitary Adrenal axis - HPA due to stress by measuring cortisol level. HPA axis is a major part of the system that controls reaction to stress and the main objective is to observe the response of the system over time due to stress by modeling degradation hazard function $d(x,t) = g(x)q(t), q(t)$ and $g(x)$ are non-negative functions of time and degradation measure and finding probability distribution to obtain results regarding Mean and Shape of Mean Residual Life for the above distribution- MRL. Obtaining Mean Residual Life is an important and interesting measure which gives the expected remaining life with the present age t also comparing the effects of stress by applying Stochastic Dominance. Here we develop two functions $f_1(z)$ and $f_2(z)$ by using the class of functions of the form $f(z) = z + \sum_{n=2}^{\infty} a_n z^n$ which are analytic in the open unit disc $\mathscr{U} = \{z : z \in \mathrm{C}$ and $|z| < 1\}$ whose coefficients a_n are considered as Probability density function of degradation measure distribution, for which the subordination property holds. The prominent Psychologist Selye's findings about human stress effects are adopted and the concept of Selye's theory is applied and we give a real application of stress induced cortisol response for women with High Waist to Hip Ratio (central fat) and with Low Waist to Hip Ratio (peripheral fat). The concluded results coincide with the medical findings.

Keywords

Hypothalamic Pituitary Adrenal (HPA), Waist to Hip Ratio (WHR), Cortisol, Degradation Hazard Function, Stochastic Dominance, Mean Residual Life-MRL, Analytic functions, Univalent functions and Subordination.

AMS Subject Classification

30C45, 30C50, 30C80, 60E, 62E.

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Contents

1. Introduction

Degradation is the reduction in life span of system and reliability. System gets performance degradation as by age or deteriorates due to other factors. It is clear that the degradation measure is a stochastic process [6] . Elsayed [5] classifies the accelerated failure data models as statistics based models.

In the area of reliability modeling, Weibull distribution is widely used to test life and also to find very low probabilities of failure $[1, 12, 16]$. Some familiar relationship between Probability density function- $f(t)$, Cumulative Distribution

Function- $F(t)$, Failure rate function $h(t)$ and Reliability (or) Survival function $R(t)$ is $h(t) = \frac{f(t)}{1-F(t)} = \frac{f(t)}{R(t)}$ Obtaining reliability and Mean Residual Life using degradation data gives prediction of the remaining life of system and is defined as

$$\mu(t) = \int_t^\infty R(x)dx/R(t)$$

For a specific time t, the degradation measure is a random variable that its distribution is time dependent [6] and it can be modeled in several approaches. In our model, the assumptions are improved in this direction, and we utilize the approach of Reliability Estimate using degradation data [3] and special cases are derived for our model.

The degradation hazard function is defined as $\mathrm{r(x;t)} = \frac{\mathrm{f(x;t)}}{\overline{\mathrm{F}}\mathrm{(x;t)}}$ and it considers both degradation measure level and time.

Also the degradation hazard function denoted by $d(x,t)$ is expressed as the product of two functions

$$d(x,t) = g(x)q(t),$$

where $q(t)$ and $g(x)$ are non-negative functions of time and degradation measure. Using properties of cumulative distribution function, rewriting

$$\overline{\mathrm{F}}(\mathrm{x;t}) = \mathrm{P(X > x;t)} = \exp\left(-\int_0^{\mathrm{x}} \mathrm{r(s;t)ds}\right)$$

$$\overline{\mathrm{F}}(\mathrm{x;t}) = \exp\left(-\mathrm{q(t)}\int_0^{\mathrm{x}} \mathrm{g(s)ds}\right).$$

$\overline{\mathrm{F}}(0;\mathrm{t}) = 1$ and $\overline{\mathrm{F}}(\infty;\mathrm{t}) = 0$ gives the constraint $\int_0^\infty \mathrm{g(s)ds} = \infty$.

Constraints on $q(t) : \lim_{t\to 0} q(t) = 0$ and $\lim_{t\to\infty} q(t) = \infty$, since $\lim_{t\to 0}(\bar{F}(x,t)) = 1$ and $\lim_{t\to\infty}(\bar{F}(x,t)) = 0$.

1.1 Comparison of Random Variables and Analytic Functions

Stochastic Orders allows comparison of Random quantities [15]. Stochastic dominance is frequently used in the literature for comparing Random Variables. The most common application of Stochastic dominance is the first degree, which is based on the comparison of the Cumulative Distribution Functions.

We give a beautiful application of this distribution by using the class of functions of the form $f(z) = z + \sum_{n=2}^\infty a_n z^n$ which are analytic in the open unit disc $\mathscr{U} = \{z : z \in \mathrm{C}$ and $|z| < 1\}$ whose coefficient a_n are considered as Probability density function of degradation measure distribution.

Let $\mathscr{A}$ be the class of functions f of the form $f(z) = z + \sum_{t=2}^\infty a_t z^t$ which are analytic in the open unit disc $\mathscr{U} = \{z : z \in \mathrm{C}$ and $|z| < 1\}$ and $\mathscr{S}$ represents the class of all functions in $\mathscr{A}$ | which are univalent in $\mathscr{U}$ [**2**].

Definition 1.1. *[13] Let X and Y be two random variables, and let F_x and F_Y denote their respective cumulative distribution functions. X stochastically dominates Y by the first degree if $F_x(t) \leq F_Y(t)$, for every $t \in R$ It is usually denoted by $X \succeq_{FSD} Y$. For every non decreasing function $u : R \to R$, if and only if F_1 first order stochastically dominates (FOSD) F_2, $u(F_1) = \int u(x)dF_1(x) \geq \int u(x)dF_2(x) = u(F_2)$.*

This implies that F_1 FOSD F_2 then Mean of $F_1 >$ Mean of F_2.

Definition 1.2. *[10] $f(z)$ and $g(z)$ be in the class $\mathscr{A}$. Then $f(z)$ is subordinate to $g(z)$ (written as $f \prec g$) if there exists a function $w(z)$ with $w(0) = 0$ and $|w(z)| < 1$ and analytic in $\mathscr{U}$, such that $f(z) = g(w(z))$. If further $g(z)$ is univalent, then $f \prec g$ if $f(0) = g(0)$ and $f(\mathscr{U}) \subset g(\mathscr{U})$.*

Here we focus on First order stochastic dominance for comparing the Random Variables X_1 and X_2 and using the concept of subordination for the considered analytic functions $f_1(z)$ and $f_2(z)$ by assuming $X_1 \sim F_1$ and $X_2 \sim F_2$ with density $f_1(x,t)$ and $f_2(x,t)$.

Before going for the main result, we make use of the following Lemma:

Lemma 1.3. *[11] Let $f(z) = \sum_{k=0}^\infty a_k z^k$ be analytic in u and $g(z) = \sum_{k=0}^\infty b_k z^k$ be analytic and convex in u. If $f(z) \prec g(z)$, then $|a_k| \leq |b_1|$, for $k = 1, 2, \ldots\ldots$*

1.2 Basic Notations

X_1 : Random variable representing degradation measure for women with LWHR.

X_2 : Random variable representing degradation measure for women with HWHR.

$f_1(x,t)$ and $f_2(x,t)$: Probability density function of X_1 and X_2 at time t.

$d_1(x,t)$ and $d_2(x,t)$: degradation hazard function of f_1 and f_2.

$f_1(z)$ and $f_2(z)$: Analytic functions in the open unit disc $\mathscr{U}$ which satisfies subordination property.

$\mu(t)$: Mean Residual Life function.

2. Development of Mathematical Model

Several studies [14] highlights the complex action of the Hypothalamic Pituitary Adrenal axis – HPA. It is a major part of the human system that controls reaction to stress and the response of the hormones. Here we consider the cortisol response to stress among lean women with a High WHR and Low WHR. Lean women with a High WHR may be at higher risk of disease greater exposure to Cortisol and possible metabolic aberrations related with central fat [4] .

2.1 Assumptions of the Model

1. Women are exposed with number of stresses.

2. Stress effect is the source for increase in Cortisol levels and may contribute to central fat and risk for disease [17].

3. Here we assume the typical measure as Life span.

2.2 Classification

Women - classified in to two categories

- Greater Central fat – High Waist to Hip Ratio - HWHR.
- Greater peripheral fat –Low Waist to Hip Ratio - LWHR.

2.3 Model Formulation

Here we develop degradation hazard function for X_1 and X_2 $d_1(x,t) = g(x)q(t) = \frac{x^{-\gamma}t^{\beta}}{\alpha}$ and $d_2(x,t) = g(x)q(t) = \frac{\gamma x^{\gamma-1}}{\beta\exp(-\alpha t)}$ $\alpha,\beta > 0; 0 < \gamma < 1$ constraints of $g(x)$ and $q(t)$ are satisfied.

By using property of Cumulative Distribution Function we obtain the corresponding probability density function as $f_1(x,t) = \frac{t^{\beta}}{\alpha}x^{-\gamma}\exp\left\{-\frac{t^{\beta}}{\alpha}\left(\frac{x^{1-\gamma}}{1-\gamma}\right)\right\}, x > 0, t > 0, 0 < \gamma < 1$ $f_2(x,t) = \frac{\gamma x^{\gamma-1}}{\beta\exp(-\alpha t)}\exp\left\{\frac{-x^{\gamma}}{\beta\exp(-\alpha t)}\right\}, x > 0, t > 0 \quad 0 < \gamma < 1$.

Special case: If we assume $\gamma = 0$ we obtain $d_1(x,t) = \frac{t^{\beta}}{\alpha}$.

If we assume $\gamma = 1$ we obtain $d_2(x,t) = \frac{1}{\beta\exp(-\alpha t)}$ which reduces to traditional failure rate $\frac{f}{F}$ [12] involving $'t'$ only.

The expected value of X_1 and X_2

$$
\begin{aligned}
\mathrm{E}(X_1) &= \int x f_1(x,t)dx \\
&= \int_0^{\infty} x\frac{t^{\beta}}{\alpha}x^{-\gamma}\exp\left\{-\frac{t^{\beta}}{\alpha}\left(\frac{x^{1-\gamma}}{1-\gamma}\right)\right\}dx \\
&= \frac{\alpha}{t^{\beta}} \\
\mathrm{E}(X_2) &= \int x f_2(x,t)dx \\
&= \int_0^{\infty} x\frac{\gamma x^{\gamma-1}}{\beta\exp(-\alpha t)}\exp\left\{\frac{-x^{\gamma}}{\beta\exp(-\alpha t)}\right\}dx \\
&= \beta e^{-\alpha t}.
\end{aligned}
$$

On substituting α,β and for all $'t' > 0$, we get $\mathrm{E}(X_1) > \mathrm{E}(X_2)$ FOSD holds good. Thus F_1 FOSD F_2 and is shown in Figure 1 and found in the next section 2.4.

2.4 Application

Now we focus our attention on women with central fat –High waist to hip ratio HWHR and women with peripheral fat - Low waist to hip ratio LWHR.

By using degradation hazard function we work with two analytic functions whose coefficients are considered as Probability density function of two life time distributions.

Now consider the class of functions of the form

$$f_1(z) = z + \sum_{t=2}^{\infty} a_t z^t$$

and

$$f_2(z) = z + \sum_{t=2}^{\infty} b_t z^t$$

which are analytic in the open unit disc $\mathscr{U}$ whose coefficients $a_t = f_1(x,t)$ and $b_t = f_2(x,t)$ are considered as Probability density function of two life time distribution.

On substituting α,β,γ,x and vary $'t'$ we have obtained the coefficient for power series and is given in the following table.

t	a_t	b_t
1	$a_1 = .6$	$b_1 = .1$
2	$a_2 = .3$	$b_2 \sim 0$
3	$a_3 = .03 = \frac{a_2}{10}$	$b_3 = 0$

Table 1. Coefficient of Power series

$$
\begin{aligned}
f_1(z) &= z + \sum_{t=2}^{\infty} a_t z^t, |z| < 1 \\
&= z + a_2 z^2 + a_3 z^3 (neglecting\, higher\, order) \\
&= z + a_2 z^2 + \frac{a_2}{10} z^3 \\
&= z + \frac{a_2}{10}\left\{z^3 + 10z^2\right\} \\
f_1(z) &= z + .03\left\{z^3 + 10z^2\right\} \, and \\
f_2(z) &= z + \sum_{t=2}^{\infty} b_t z^t \\
&= z + b_2 z^2 + b_3 z^3 (neglecting\, higher\, order) \\
&= z.
\end{aligned}
$$

Here we focus our attention on Subordination Principle Let $f_1(z) = z + .03\left\{z^3 + 10z^2\right\}$ and $f_2(z) = z$ be analytic in $\mathscr{U}$ There exist $w(z) = \sin z$, analytic in $\mathscr{U}$ with $w(0) = 0$ and $|w(z)| < 1$ $(z \in \mathscr{U})$, such that $f_2(z) = f_1(w(z))(z \in \mathscr{U})$. Further $f_2(z)$ is univalent in $\mathscr{U}$, then $f_2(z) \prec f_1(z)(z\varepsilon\mathscr{U}) \Leftrightarrow f_2(0) = f_1(0)$ and $f_2(\mathscr{U}) \subset f_1(\mathscr{U})$ Hence we say that f_2 is subordinate to f_1 and write $f_2(z) \prec f_1(z)$ Thus the definition and the lemma holds good for the considered functions $f_1(z)$ and $f_2(z)$ On considering the Random Variables X_1 and X_2 we have $\mathrm{E}(X_1) > \mathrm{E}(X_2)\, F_1$ FOSD F_2.

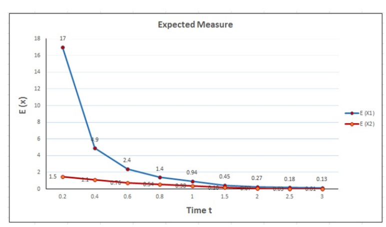

Figure 1

2.5 Shape of Mean Residual Life

Shape of the Weibull hazard rate function is easy to find, since the hazard rate function $h_w(t)$ is decreasing when $\beta < 1$, constant when $\beta = 1$ and increasing when $\beta > 1$ where $h_w(t) = \frac{\beta}{\theta^{\beta}}t^{\beta-1}$.

The shape of MRL is difficult to write explicitly but interest to analyze. Here we apply the results obtained by Pinelis

[7,8,9] concentrating the similarity of the shapes of ratios of the functions $u(t)/v(t)$ and $u'(t)/v'(t)$.

Theorem 2.1. *[7] Let u(t) and v(t) be differentiable functions on (a,b) where $-\infty \leq a < b \leq \infty$. Assume that $v(t)$ and its derivative $v'(t)$ are non-zero on the interval (a,b) and $v'(t)$ does not change its sign on (a,b). Furthermore assume that $u(b-) = 0 = v(b-)$.*

The following statements hold:

(i) If $\mathrm{u}'(\mathrm{t})/\mathrm{v}'(\mathrm{t})$ is increasing on (a,b) then $\mathrm{u}(\mathrm{t})/\mathrm{v}(\mathrm{t})$ is also increasing on (a,b).

(ii) If $\mathrm{u}'(\mathrm{t})/\mathrm{v}'(\mathrm{t})$ is decreasing on (a,b) then $\mathrm{u}(\mathrm{t})/\mathrm{v}(\mathrm{t})$ is also decreasing on (a,b).

3. Results

Here we will describe how we find the shape of Mean Residual Life for both cases of our study using the above results and in consideration to the conditions of the above theorem. The monotonicity of the ratio of $\frac{u(t)}{v(t)}$ holds same as the ratio of $\frac{u'(t)}{v'(t)}$.

Now $\mu(t) = \frac{u(t)}{v(t)} = \frac{\int_t^\infty R(x)dx}{R(t)} = \frac{\int_t^\infty s(x)dx}{s(t)}, \mu'(t) = \frac{u'(t)}{v'(t)} = \frac{-R(t)}{R'(t)} = \frac{-S(t)}{S'(t)}$.

Case 1: Women with Peripheral body fat - LWHR

$$S(x,t) = \bar{F}_1(x,t) = \exp\left(-q(t)\int_0^x g(s)ds\right); q(t) = \frac{t^\beta}{\alpha}, g(s) = s^{-\gamma}$$

$$\mu'(x,t) = \frac{u'(x,t)}{v'(x,t)} = \frac{-S(x,t)}{S'(x,t)} = \frac{\exp\left\{\frac{-t^\beta}{\alpha}\left(\frac{x^{1-\gamma}}{1-\gamma}\right)\right\}}{\frac{t^\beta}{\alpha}x^{-\gamma}\exp\left\{\frac{-t^\beta}{\alpha}\left(\frac{x^{1-\gamma}}{1-\gamma}\right)\right\}}$$

$$= \frac{1}{\frac{t^\beta}{\alpha}x^{-\gamma}}$$

$$= \frac{1}{d_1(x,t)}.$$

The degradation hazard function $d_1(x,t)$ increases as time increases and hence $\frac{1}{d_1(x,t)}$ decreases. $\mu'(x,t)$ decreases and hence $\mu(x,t)$ - the shape of Mean Residual Life function decreases.

Note: Values of $d_1(x,t)$ and $d_2(x,t)$ for a fixed x and varying t is shown in the following table for both the cases of our study. **Case 2:** Women with Central body fat - HWHR

t	$d_1(x,t)$	$d_2(x,t)$
.2	.08	.40
.4	.27	.56
.6	.55	0.80
.8	.93	1.1
1	1.4	1.6

Table 2

$$S(x,t) = \overline{F_2}(x,t) = \exp\left(-q(t)\int_0^x g(s)ds\right);$$

$$q(t) = \frac{1}{\beta\exp(-\alpha t)}, g(s) = \gamma s^{\gamma-1}$$

$$\mu'(x,t) = \frac{u'(x,t)}{v'(x,t)} = \frac{-S(x,t)}{S'(x,t)} = \frac{\exp\left(\frac{-x^\gamma}{\beta\exp(-\alpha t)}\right)}{\frac{\gamma x^{\gamma-1}}{\beta\exp(-\alpha t)}\exp\left(\frac{-x^\gamma}{\beta\exp(-\alpha t)}\right)}$$

$$= \frac{\beta\exp(-\alpha t)}{\gamma x^{\gamma-1}}$$

$$= \frac{1}{d_2(x,t)}.$$

The degradation hazard function $d_2(x,t)$ increases as time increases and hence $\frac{1}{d_2(x,t)}$ decreases. $\mu'(x,t)$ decreases and hence $\mu(x,t)$ - the shape of Mean Residual Life function decreases.

The following figure gives the shape of Mean Residual Life function.

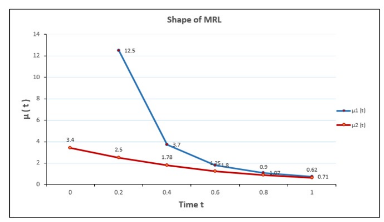

Figure 2. Shape of MRL

4. Conclusion

The result shows that the stress induced cortisol affects at a greater level for Women with High Waist to Hip Ratio than with Low Waist to Hip Ratio.

It is clear from the results obtained that Degradation Hazard function and Mean Residual Life function are inversely related to each other, as time increases degradation hazard also increases during stress and the graph shows that the corresponding Mean Residual Life decreases also the expected life span of Women with LWHR is greater than Women with HWHR. On taking the Probability density function as coefficients for the class of functions used above, the considered analytic functions satisfy the Subordination principle and on comparing the Expected values we conclude that First order Stochastic dominance holds good.

Since the results are consistent it is concluded that women with high WHR respond to greater cortisol reactivity than women with low WHR.

Related life data fitted with our model and the results coincide with the medical findings.

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