IOSR Journal of Engineering (IOSRJEN) **www.iosrjen.org**
ISSN (e): 2250-3021, ISSN (p): 2278-8719
Vol. 04, Issue 04 (April. 2014), ||V4|| PP 28-33

A Bivariate Generalized Exponential Model for the Effect of Endocrine Responses in Human with Postprandial Distress Syndrome

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Abstract: - Suppose a system has two components. Each component is subject to individual independent stress say U_1 and U_2 respectively. The system has an overall stress U_3 which has been transmitted to both the components equally, independent of their individual stresses. Therefore, the observed stress at the two components are $X_1 = max\{U_1, U_3\}$ and $X_2 = max\{U_2, U_3\}$ respectively. If it is assumed that each component has been maintained independently and also there is an overall maintenance. Due to component maintenance, suppose the lifetime of the individual is increased by U_i amount and because of the overall maintenance, the lifetime of each component is increased by U_3 amount. The study in the Application part is fully characterized the neuroendocrine pathways involved in the gastric response to mental stress in patients with PDS. The increased severity of dyspeptic symptoms induced by acute mental stress in patients with PDS is associated with an enhanced sympathetic output and higher serum levels of stress hormones , **ACTH** , and **cortisol.** ***If*** $(X_1, X_2) \sim BVGE(\alpha_1, \alpha_2, \alpha_3)$, then the joint PDF of (X_1, X_2) for $x_1 > 0, x_2 > 0,$ is obtained for the above two variables.

Keywords*: HPA axis, LF/HF ratio, mental stress, postprandial distress syndrome, CRH, ACTH, cortisol. 2010 AMS Classification: 62HXX, 60EXX.*

I. MATHEMATICAL MODEL:

Bivariate generalized exponential distribution:

The univariate GE distribution has the following cumulative distribution function(CDF) and probability density function(PDF) respectively for $x > 0$;

$F_{GE}(x; \alpha, \lambda) = \left(1 - e^{-\lambda x}\right)^{\alpha}$, $f_{GE}(x; \alpha, \lambda) = \alpha\lambda e^{-\lambda x}\left(1 - e^{-\lambda x}\right)^{\alpha-1}$ (1.1)

Here $\alpha > 0$ *and* $\lambda > 0$ are the shape and scale parameters respectively. It is clear that for $\alpha = 1$, it coincides with the exponential distribution [1]. From now on a GE distribution with the shape parameter α and the scale parameter λ will be denoted by $GE(\alpha, \lambda)$. For brevity when $\lambda = 1$, we will denote it by $GE(\alpha)$ and for $\alpha = 1$, it will be denoted by $Exp(\lambda)$ [5]. From now on unless otherwise mentioned, it is assumed that $\alpha_1 > 0, \alpha_2 > 0, \alpha_3 > 0, \lambda > 0$. Suppose $U_1 \sim GE(\alpha_1, \lambda)$, $U_1 \sim GE(\alpha_2, \lambda)$ and $U_3 \sim$ GE(α_3, λ) and they are mutually independent. Here ' ~ ' means follows or has the distribution . Now define $X_1 = max\{U_1, U_3\}$ and $X_2 = max\{U_2, U_3\}$. Then we say that the bivariate vector (X_1, X_2) has a bivariate generalized exponential distribution with the shape parameters α_1, α_2 and α_3 and scale parameter λ [6]. We will denote it by $BVGE(\alpha_1, \alpha_2, \alpha_3, \lambda)$. Now for the rest of the discussions for brevity, we assume that $\lambda = 1$, although the results are true for general λ also. The BVGE distribution with $\lambda = 1$ will be denoted by $BVGE(\alpha_1, \alpha_2, \alpha_3)$. Before providing the joint CDF or PDF, we first mention how it may occur in practice [7,9].

1.1 STRESS MODEL:

Suppose a system has two components. Each component is subject to individual independent stress say U_1 and U_2 respectively. The system has an overall stress U_3 which has been transmitted to both the components equally, independent of their individual stresses. Therefore, the observed stress at the two components are

$X_1 = max\{U_1, U_3\}$ and $X_2 = max\{U_2, U_3\}$ respectively.

1.2 MAINTENANCE MODEL:

Suppose a system has two components and it is assumed that each component has been maintained independently and also there is an overall maintenance. Due to component maintenance,

suppose the lifetime of the individual is increased by U_i amount and because of the overall maintenance, the lifetime of each component is increased by U_3 amount. Therefore, the increased lifetimes of the two components are $X_1 = max\{U_1, U_3\}$ and $X_2 = max\{U_2, U_3\}$ respectively.
The following results will provide the joint CDF, joint PDF and conditional PDF.

Theorem1.1:
If $(X_1, X_2) \sim BVGE(\alpha_1, \alpha_2, \alpha_3)$, then the joint CDF of (X_1, X_2) for $x_1 > 0, x_2 > 0$, is $F_{X_{1,X_2}}(x_1, x_2) = (1 - e^{-x_1})^{\alpha_1}(1 - e^{x_2})^{\alpha_2}(1 - e^{-Z})^{\alpha_3}$, (1.2)
where $z = min\{x_1, x_2\}$.

Corollary 1.1:
The joint CDF of the $BVGE(\alpha_1, \alpha_2, \alpha_3)$, can also be written as

$$\begin{aligned} F_{X_1,X_2}(x_1, x_2) &= F_{GE}(x_1; \alpha_1)F_{GE}(x_2, \alpha_2)F_{GE}(z; \alpha_3) \\ &= F_{GE}(x_1; \alpha_1 + \alpha_3)F_{GE}(x_2, \alpha_2) \quad \text{if} \quad x_1 < x_2 \\ &= F_{GE}(x_1; \alpha_1)F_{GE}(x_2, \alpha_2 + \alpha_3) \quad \text{if} \quad x_2 < x_1 \\ &= F_{GE}(x; \alpha_1 + \alpha_2 + \alpha_3) \quad \text{if} \quad x_1 = x_2 = x. \end{aligned}$$

Theorem 1.2:
If $(X_1, X_2) \sim BVGE(\alpha_1, \alpha_2, \alpha_3)$, then the joint PDF of (X_1, X_2) for $x_1 > 0, x_2 > 0$, is

$$f_{X_1,X_2}(x_1, x_2) = \begin{cases} f_1(x_1, x_2) & if \quad 0 < x_1 < x_2 < \infty \\ f_2(x_1, x_2) & if \quad 0 < x_2 < x_1 < \infty \\ f_0(x) & if \quad 0 < x_1 = x_2 < \infty, \end{cases}$$

Where

$$\begin{aligned} f_1(x_1, x_2) &= f_{GE}(x_1; \alpha_1 + \alpha_3)f_{GE}(x_2; \alpha_2) \\ &= (\alpha_1 + \alpha_3)\alpha_2(1 - e^{-x_1})^{\alpha_1+\alpha_3-1}(1 - e^{-x_2})^{\alpha_2-1}e^{-x_1-x_2} \\ f_2(x_1, x_2) &= f_{GE}(x_1; \alpha_1)f_{GE}(x_2; \alpha_2 + \alpha_3) \\ &= (\alpha_2 + \alpha_3)\alpha_1(1 - e^{-x_1})^{\alpha_1-1}(1 - e^{-x_2})^{\alpha_2+\alpha_3-1}e^{x_1-x_2} \\ f_0(x) &= \frac{\alpha_3}{\alpha_1 + \alpha_2 + \alpha_3} f_{GE}(x; \alpha_1 + \alpha_2 + \alpha_3) \\ &= \alpha_3(1 - e^{-x})^{\alpha_1+\alpha_2+\alpha_3-1}e^{-x}. \end{aligned}$$

Proof :
The expressions for $f_1(.,.)$ and $f_2(.,.)$ can be obtained simply by taking $\frac{\partial^2 F_{X_1,X_2}(x_1,x_2)}{\partial x_1 \partial x_2}$ for $x_1 < x_2$ and $x_2 < x_1$ respectively But $f_0(.)$ cannot be obtained in the same way. Using the facts that

$$\int_0^\infty \int_0^{x_2} f_1(x_1, x_2)dx_1dx_2 + \int_0^\infty \int_0^{x_1} f_2(x_1, x_2)dx_2dx_1 + \int_0^\infty f_0(x)dx = 1, \quad (1.3)$$

$$\int_0^\infty \int_0^{x_2} f_1(x_1, x_2)dx_1dx_2 = \alpha_2 \int_0^\infty (1 - e^{-x})^{\alpha_1+\alpha_2+\alpha_3-1} e^{-x}dx \quad (1.4)$$

$$\int_0^\infty \int_0^{x_1} f_2(x_1, x_2)\, dx_2dx_1 = \alpha_1 \int_0^\infty (1 - e^{-x})^{\alpha_1+\alpha_2+\alpha_3-1} e^{-x}dx \quad (1.5)$$

note that $\int_0^\infty f_0(x)dx = \alpha_3 \int_0^\infty (1 - e^{-x})^{\alpha_1+\alpha_2+\alpha_3-1} e^{-x}dx = \frac{\alpha_3}{\alpha_1+\alpha_2+\alpha_3}$. (1.6)

Therefore, the result follows.

II. APPLICATION

Mental stress may alter gastric sensory motor function. The aim of the study is to assess postprandial autonomic nervous system activity and stress hormones in response to acute mental stress in dyspeptic patients.

Functional dyspepsia (FD) is a highly prevalent gastro-intestinal disorder characterized by symptoms originating from the gastroduodenal region, in the absence of underlying organic diseases that would readily explain the symptoms. Based on the distinction between meal-induced and meal-unrelated symptoms, FD is subdivided into two diagnostic categories (i) Postprandial distress syndrome (PDS) , characterized by postprandial fullness and early satiation , and (ii) epigastric pain syndrome (EPS) characterized by epigastric pain and burning.[2]

Studies concerning the relationship between stressful life events and FD have yielded conflicting results. Some studies have shown that subjects with FD experienced more stressful life events than healthy controls whereas other studies have failed to find any significant differences.[4]

The aim of this study is to thoroughly investigate every step of this intricate link by evaluating the serum concentrations of stress hormones , the autonomous activity of the nervous system (ANS) , and the gastric sensorimotor function, in response to an experimentally induced

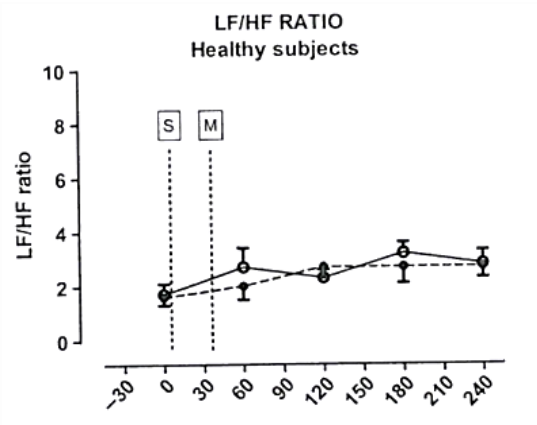
acute mental stress in patients with PDS [8]. The study is designed to test our hypothesis that in this subset of patients , the modulation of gastric function under stressful conditions is related to HPA axis and ANS activity.

We have corrected individuals LF/HF ratio values for the anxiety scores in each subject and performed a comparison between basal and stress conditions , without finding any statistical significance. In patients , a significantly higher ACTH level was found in stress condition , whereas in healthy subjects no modifications was recorded. Patients showed a significantly higher level in stress condition , whereas in healthy subjects cortisol levels in both conditions were similar.

The lack of significant differences between LF/HF ratio values corrected for anxiety score between basal and stress conditions in patients confirms that the higher level of underlying anxiety in patients represents an important factor to determine the enhanced neuroendocrine response to stress.

The study here is to fully characterize the neuroendocrine pathways involved in the gastric response to mental stress in patients with PDS. The increased severity of dyspeptic symptoms induced by acute mental stress in patients with PDS is associated with an enhanced sympathetic output and higher serum levels of stress hormones , **ACTH** , and **cortisol.**

In conclusion , our findings contribute to shed light on complex link between the central nervous system and the gastrointestinal tract , and specifically to help to clarify the mechanisms that underlie functional gut modifications induced by mental stress in FD.



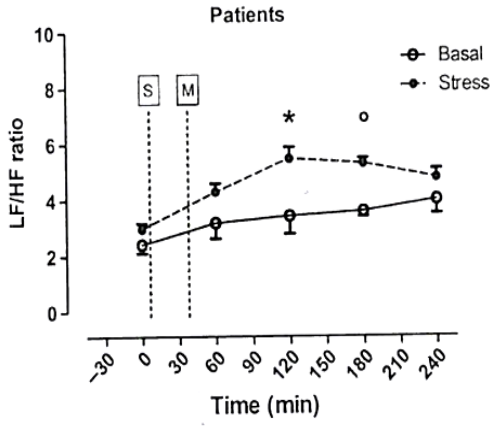
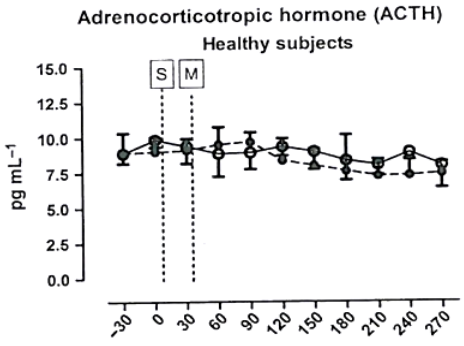


Fig2.1 ***Fig2.2***

Low/high frequency component (LF/HF) ratio in patients and controls during basal and stress sessions of this study. In patients, mental stress induces a prolonged increase of LF/HF ratio in the postprandial period, interpreted as an increase in sympathetic output.In controls, no differences were found between basal and stress condition. Each plotted value on the graph expresses the LF/HF ratio of the previous 60 min. S,stress; M meal.*P<0.01 and ◦ P<0.05 vs basal.



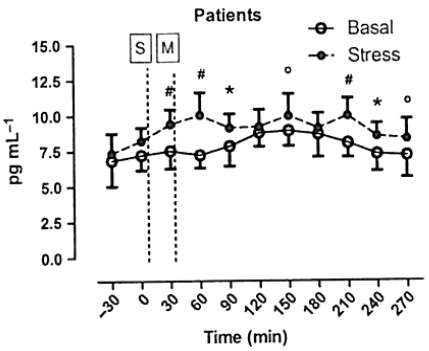
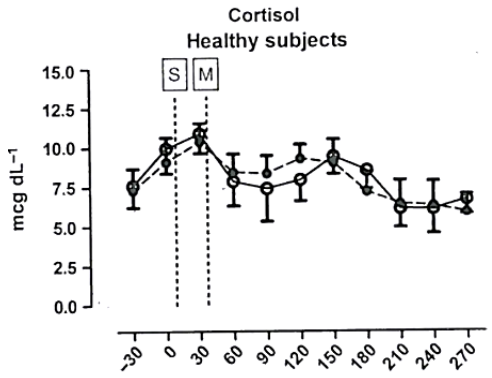


Fig 2.3 *Fig 2.4*

*Adrenocorticotropic hormone (ACTH) serum levels in healthy subjects and patients. In patients, a significantly higher ACTH level was found in stress condition, whereas in healthy subjects no modifications were recorded. S, stress; M, meal.# P<0.001, *P<0.01, and ◦ P<0.05 vs basal.*



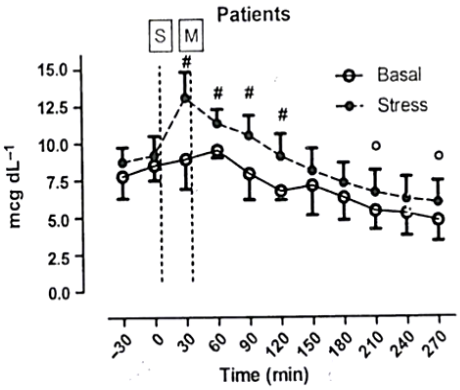


Fig2.5 ***Fig2.6***

Cortisol serum levels in healthy subjects and patients. Patients showed a significantly higher level in stress condition , whereas in healthy subjects cortisol level in both conditions were similar. S, stress; M, meal. #P<0.001 and o P<0.05 basal.

III. MATHEMATICAL RESULTS

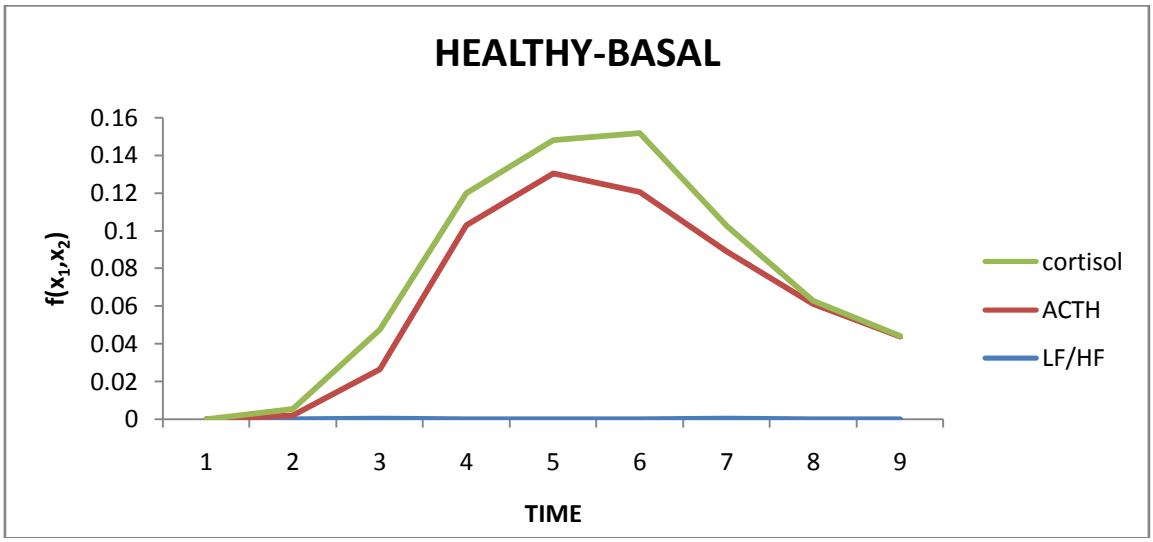


Fig3.1

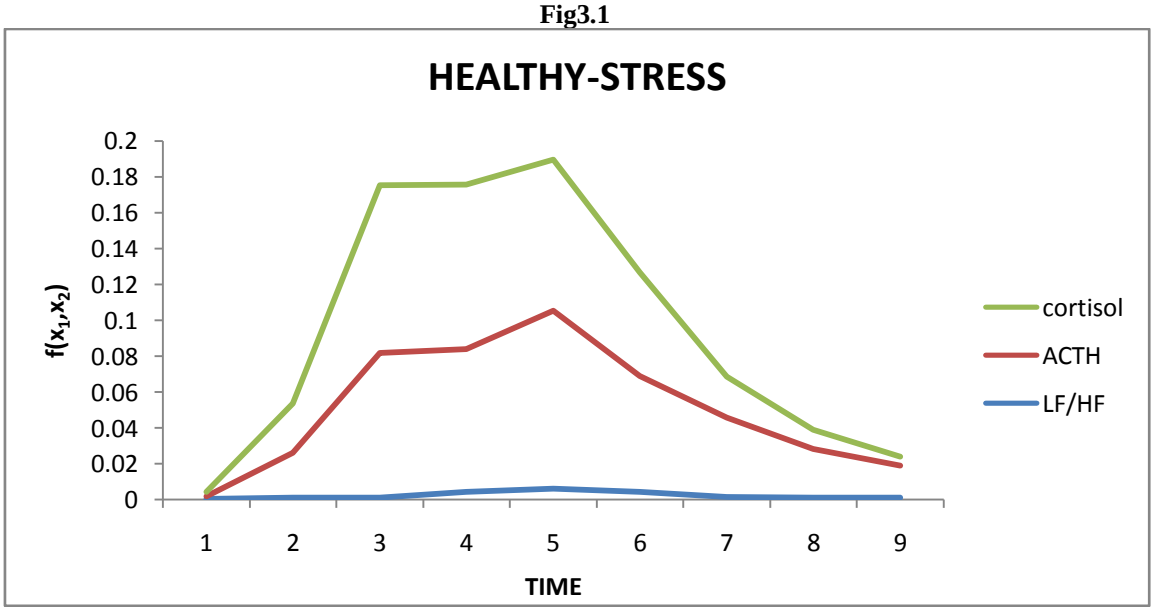


Fig3.2

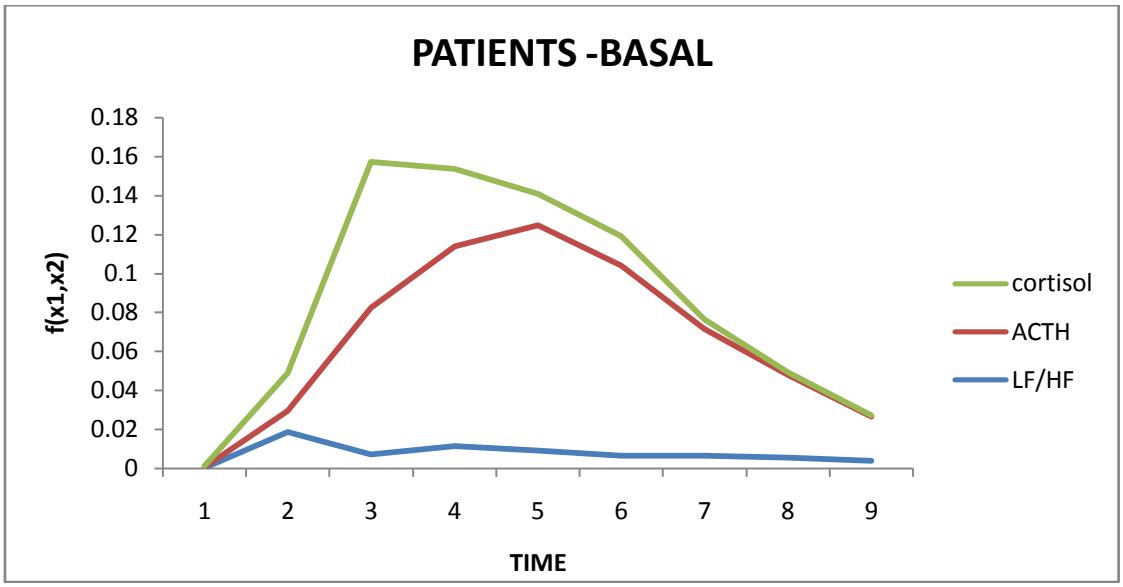


Fig3.3

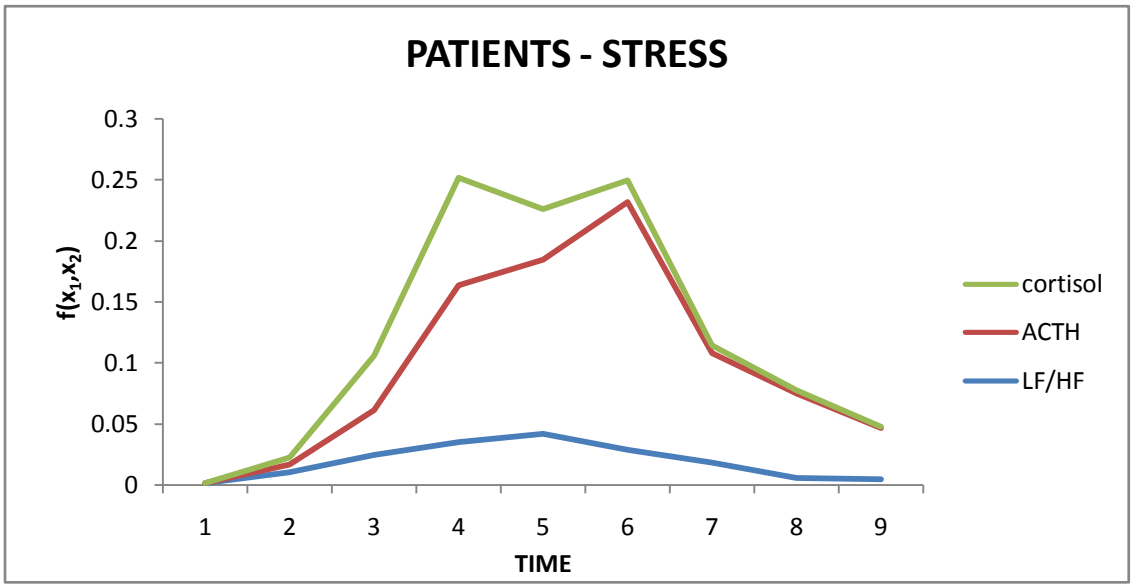


Fig3.4

IV. CONCLUSION

Suppose a system has two components. Each component is subject to individual independent stress say U_1 and U_2 respectively. The system has an overall stress U_3 which has been transmitted to both the components equally, independent of their individual stresses. Therefore, the observed stress at the two components are $X_1 = max\{U_1, U_3\}$ and $X_2 = max\{U_2, U_3\}$ respectively. If it is assumed that each component has been maintained independently and also there is an overall maintenance. Due to component maintenance, suppose the lifetime of the individual is increased by U_i amount and because of the overall maintenance, the lifetime of each component is increased by U_3 amount. The study in the Application part is fully characterized the neuroendocrine pathways involved in the gastric response to mental stress in patients with PDS. The increased severity of dyspeptic symptoms induced by acute mental stress in patients with PDS is associated with an enhanced sympathetic output and higher serum levels of stress hormones , **ACTH** , and **cortisol.** ***If*** $(X_1, X_2) \sim BVGE(\alpha_1, \alpha_2, \alpha_3)$, then the joint PDF of (X_1, X_2) for $x_1 > 0, x_2 > 0$, is obtained for the above two variables which are well explained in the ***figures 3.1, 3.2, 3.3, 3.4*** of the Mathematical Results. There is no change in the level of cortisol and ACTH between the groups of healthy subjects and patients in basal level. But, there is a vast change in the cortisol and ACTH level between the groups of healthy stress and the patients stress. There is no major change in LF/HF for all the four cases.

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