International Journal of Engineering, Science and Mathematics
Vol. 7Issue 2, February 2018,
ISSN: 2320-0294 Impact Factor: 6.765
Journal Homepage: http://www.ijesm.co.in, Email: ijesmj@gmail.com
Double-Blind Peer Reviewed Refereed Open Access International Journal - Included in the International Serial Directories Indexed & Listed at: Ulrich's Periodicals Directory ©, U.S.A., Open J-Gage as well as in Cabell's Directories of Publishing Opportunities, U.S.A

A MATHEMATICAL MODEL USING FOR THE IMPACT OF CORTICOTROPHIN RELEASING HORMONE ON GASTROINTESTINAL MOTILITY AND ACTH HORMONE IN NORMAL CONTROLS AND PATIENTS WITH IRRITABLE BOWEL SYNDROME.

K.Sathishkumar
[*]Asst.Prof. of Mathematics,Anjalai Ammal-Mahalingam Engineering College, Kovilvenni – 614 403.
Thiruvarur Dist.,Tamilnadu, India.

T.Geetha
[**]Asst.Prof. of Mathematics, Kunthavai Naacchiyar Govt. Arts College for women, (Autonomous),
Thanjavur-613 007.Tamilnadu, India

ABSTRACT:

It is possible to build up different software reliability models such as exponentiated Gumbel model, Dhillon model, exponentiated logistic model, Gumbel model and exponentiated log-logistic model. Here we have used exponential Gumbel model and Dhillion model for a psycho neuroendocrinological model. Which are described in section-3 and the corresponding results are obtained in section-5. Finally we have concluded in section-6.

Keywords: ACTH, Software Reliability models, probability density function, cumulative distribution function

1. INTRODUCTION

New classes of reliability models have been proposed based on modifications of the existing model. Several exponentiated models have been studied quite extensively, since the work of **[7]** on exponentiated Weibull model due to the existence of simple elegant closed form solutions to many life testing problems. It can easily be justified under the assumption of constant failure rate but in the real world, the failure rates are not always constant. Hence, indiscriminate use of exponentiated lifetime model seems to be inappropriate and unrealistic. A classical generalization of the exponentiated family is known as Weibull family. Weibull model **[5]** is one of the most commonly used lifetime distributions in reliability and lifetime data analysis. It is flexible in modeling failure time data, as the corresponding hazard rate function can be increasing, constant or decreasing. But in many applications in reliability and survival analysis, the hazard rate function can be of bathtub shape. The hazard rate function plays a central rule to the work of reliability engineers, **[4]** and **[1]** and references therein. Models with a bathtub hazard rate function are needed in reliability analysis and decision making when the life time of the system is to be modeled.

International Journal of Engineering, Science and Mathematics
Vol. 7Issue 2, February 2018,
ISSN: 2320-0294 Impact Factor: 6.765
Journal Homepage: http://www.ijesm.co.in, Email: ijesmj@gmail.com
Double-Blind Peer Reviewed Refereed Open Access International Journal - Included in the International Serial Directories Indexed & Listed at: Ulrich's Periodicals Directory ©, U.S.A., Open J-Gage as well as in Cabell's Directories of Publishing Opportunities, U.S.A

2. MATHEMATICAL MODELS

2.1 .EXPONENTIATED GUMBEL MODEL

The Exponentiated Gumbel model has been proposed as a generalization of the classical Gumbel model **[3]**. Since the Gumbel model yields narrower confidence intervals than the some other extreme value models but has also the risk of under estimating the return level. Hence the choice of model is not insignificant.

Recently a generalization of the Gumbel model also called as Exponentiated Gumbel model was introduced by **[8].** The cumulative distribution function of Exponentiated Gumbel model with two parameters is given by

$$F(X) = \exp\{-\alpha\, exp\ [-(x \div \sigma)]\} : -\infty < x < \infty, \alpha > 0, \rho > 0$$

Where

$\alpha > 0$ *is the shape and* $, \rho > 0$ *is the scale parameter.*

The probability density function is given by

$$f(x) = \frac{\alpha}{\sigma} \exp\left\{-\left[\frac{x}{\sigma}\right]\right\} exp\left(-\alpha \exp\left\{-\left[\frac{x}{\sigma}\right]\right\}\right) : -\infty < x < \infty, \alpha > 0, \rho > 0$$

The two parameter Exponentiated Gumbel model will be denoted by EG (α, ρ)

2.2 DHILLON MODEL

A new reliability model with two parameters which is flexible like the weibull model and with the capacity to also describe a U-shaped hazard function is described in **[2].** This model is revisited by **[7]** and shown that it has an inverted U- shaped similar to the log-logistic hazard function, but with a different curvature, especially after the peak. For $\alpha > 0, \beta > 0$ the two parameter and Dhillon model has the distribution function is given by

$$f(x) = 1 - exp\left\{-[\log(\alpha x + 1)]^{\beta+1}\right\}; x \geq 0, \alpha > 0, \beta > 0$$

Where

$\alpha > 0$ *is the shape and* $, \beta > 0$ *is the scale parameter.*

The probability density function is given by

$$f(x) = \frac{\alpha(\beta+1)}{\sigma x + 1} [\log(\alpha x + 1)]^{\beta} exp\left\{-[\log(\alpha x + 1)]^{\beta+1}\right\}; x \geq 0, \alpha > 0, \beta > 0$$

The two parameter Dhillon model will be denoted by DL (α, β)

International Journal of Engineering, Science and Mathematics
Vol. 7Issue 2, February 2018,
ISSN: 2320-0294 Impact Factor: 6.765
Journal Homepage: http://www.ijesm.co.in, Email: ijesmj@gmail.com
Double-Blind Peer Reviewed Refereed Open Access International Journal - Included in the International Serial Directories Indexed & Listed at: Ulrich's Periodicals Directory ©, U.S.A., Open J-Gage as well as in Cabell's Directories of Publishing Opportunities, U.S.A

3. APPLICATIONS

Basal levels of plasma ACTH were almost identical in both groups (controls: 20.4 (2.5) pg/ml versus IBS patients: 23.3 (2.7) pg/ml). CRH induced a significant increase in plasma ACTH in both groups ($p<0.001$) and produced significantly higher plasma ACTH in IBS patients than in controls ($p<0.01$), especially at 60 minutes after administration (controls: 93.1 (9.2) pg/ml versus IBS patients: 174.5 (35.1) pg/ml, $p<0.05$;

Serum cortisol showed a significant increase after CRH and responses were identical in both groups (from baseline to peak value at 60 minutes, controls: 13.6 (1.2) mg/dl to 28.9 (1.3) mg/dl; IBS patients: 13.6 (1.6) mg/dl to 30.2 (1.8) mg/dl; $p<0.001$).

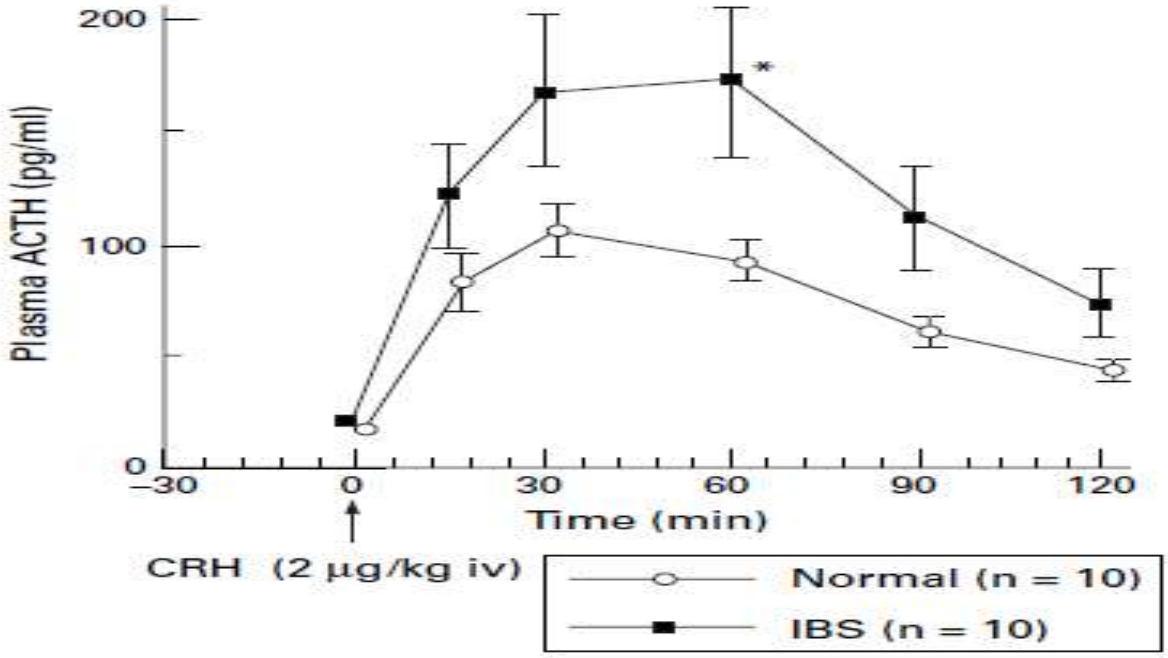


Figure 3.1 (a) Effects of CRH on plasma ACTH *P < 0.05 versus controls by Scheff F test and Mann-Whitney U test

4. DISCUSSION

This is the first paper confirming that exogenous CRH can produce considerable changes in physic contractions in human colon and small intestine. CRH is a peptide containing 41amino acids **[11],** distributed in the whole brain with dense localization in the par ventricular nucleus of the hypothalamus **[9]** and now considered to be a major mediator of the stress response Stress releases CRH from the Para ventricular nucleus and CRH stimulates pituitary ACTH secretion. Our paper provides strong support for the hypothesis

International Journal of Engineering, Science and Mathematics
Vol. 7Issue 2, February 2018,
ISSN: 2320-0294 Impact Factor: 6.765
Journal Homepage: http://www.ijesm.co.in, Email: ijesmj@gmail.com
Double-Blind Peer Reviewed Refereed Open Access International Journal - Included in the International Serial Directories Indexed & Listed at: Ulrich's Periodicals Directory ©, U.S.A., Open J-Gage as well as in Cabell's Directories of Publishing Opportunities, U.S.A

of a role of CRH in alterations of human gastrointestinal motility.

The precise site of action of intravenous CRH on human gastrointestinal motility is unknown. Because intravenous administration of ACTH or β endorphin does not mimic CRH effects on gut motility increased plasma ACTH is not likely be involved in intestinal responses to CRH. There are three forms of CRH receptors: CRH_1, CRH_2 α, and $CRH_{2\beta}$**.[6].** The mRNA for CRH_1 and CRH_2 α is predominantly expressed in the brain, whereas the mRNA for $CRH_{2\beta}$ is expressed in both the brain and the periphery**.** There are functional CRH receptors in the smooth muscle of the colon but the precise subtype of the receptors is unknown. As there is a specific unidirectional brain to blood transport system for CRH, nonspecific penetration of intravenous CRH into the brain is unlikely to occur. A more plausible possibility is that intravenous CRH affects gut motility through brain CRH receptors at circum ventricular organs that are relatively unprotected by the blood-brain barrier.

This hypothesis is supported by the report that CRH given intracerebroventricularly and intravenously was essentially equipotent in modulating intestinal motility. In vitro effects of CRH on contractions of colonic smooth muscle cells are not excitatory but inhibitory. In contrast, in vivo effects of intracerebroventricular CRH on colonic motility is always excitatory. Therefore, altered gastrointestinal motility in our results is probably not mediated by peripheral receptors, but by central CRH receptors in the circum ventricular organs. Administration of a specific antagonist would determine the precise sites and effects of intravenous CRH on gut motility.

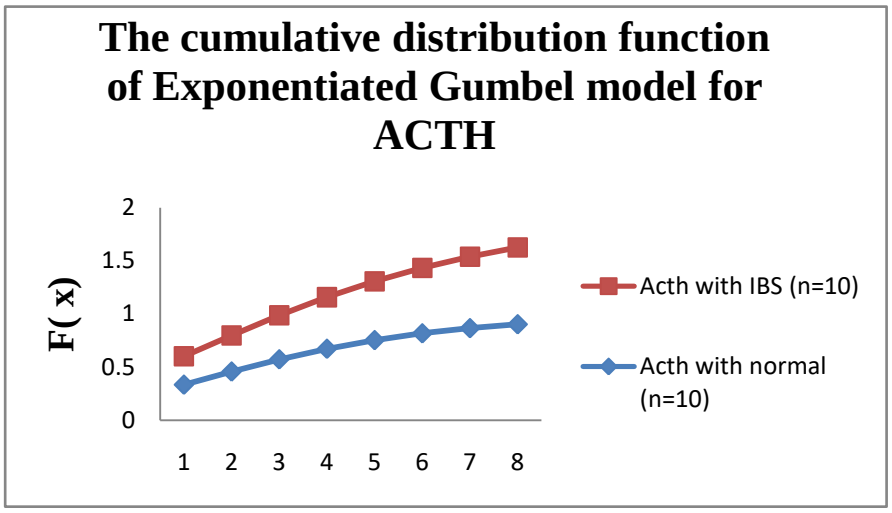
We found an increased ACTH response to CRH in IBS patients. Psychosocial stress induces onset and/or exaggeration of gastrointestinal symptoms in the majority of IBS patients **[10].** A blunted growth hormone response to desipramine in IBS patients, which suggests impaired α_2 adrenergic function, was also reported. Therefore, exogenous CRH induced ACTH hyper secretion in IBS patients may be due to α_2 blockade in the brain. It is also possible that decreased levels of CRH binding protein, which inhibits the ACTH releasing properties of CRH, may play a role in ACTH hyper secretion in IBS patients. This possibility should be explored in the future.

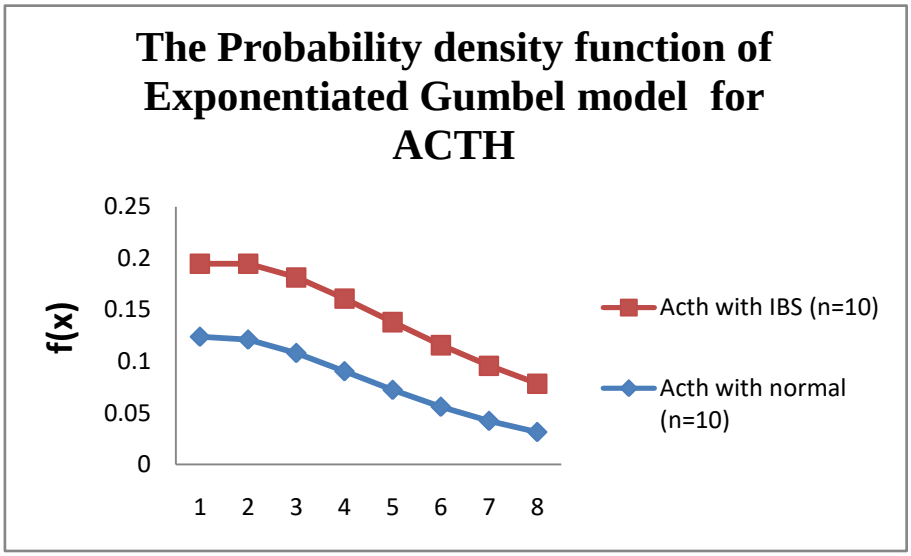
Patients with depression have CRH hyper secretion in the brain, especially the par ventricular nucleus. Neuronal circuits relay visceral information to these nuclei. Distension of the distal colon increases the firing rate of the locus ceruleans. As the majority of IBS patients have a decreased visceral threshold to colonic distension, increased visceral information to the locus ceruleans may cause more activation of CRH neurons in the par ventricular nucleus. Exogenous CRH decreases the visceral threshold to rectal distension in humans **[6]** and this mechanism probably relates to CRH induced abdominal symptoms in IBS patients as well as motility change. Furthermore, intravenous administration of CRH decreases slow wave sleep in humans and the proportion of rapid eye movement (REM) sleep is notably increased in IBS patients. We previously reported the stress

International Journal of Engineering, Science and Mathematics
Vol. 7Issue 2, February 2018,
ISSN: 2320-0294 Impact Factor: 6.765
Journal Homepage: http://www.ijesm.co.in, Email: ijesmj@gmail.com
Double-Blind Peer Reviewed Refereed Open Access International Journal - Included in the International Serial Directories Indexed & Listed at: Ulrich's Periodicals Directory ©, U.S.A., Open J-Gage as well as in Cabell's Directories of Publishing Opportunities, U.S.A

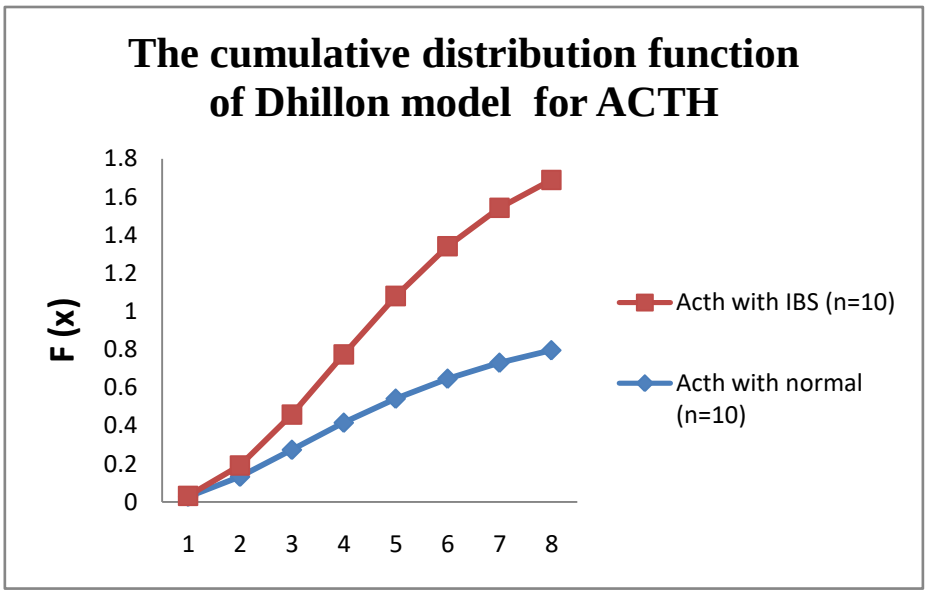
induced increase in electroencephalographic beta power in IBS patients. These findings support our hypothesis that CRH is increased in the brain of IBS patients.

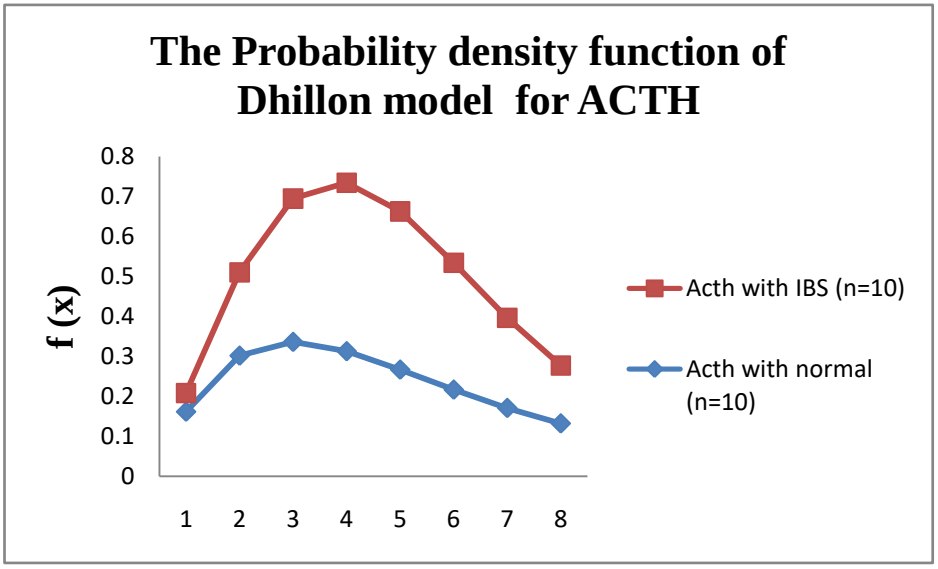
5. MATHEMATICAL RESULTS





International Journal of Engineering, Science and Mathematics
Vol. 7Issue 2, February 2018,
ISSN: 2320-0294 Impact Factor: 6.765
Journal Homepage: http://www.ijesm.co.in, Email: ijesmj@gmail.com
Double-Blind Peer Reviewed Refereed Open Access International Journal - Included in the International Serial Directories Indexed & Listed at: Ulrich's Periodicals Directory ©, U.S.A., Open J-Gage as well as in Cabell's Directories of Publishing Opportunities, U.S.A





International Journal of Engineering, Science and Mathematics
Vol. 7Issue 2, February 2018,
ISSN: 2320-0294 Impact Factor: 6.765
Journal Homepage: http://www.ijesm.co.in, Email: ijesmj@gmail.com
Double-Blind Peer Reviewed Refereed Open Access International Journal - Included in the International Serial Directories Indexed & Listed at: Ulrich's Periodicals Directory ©, U.S.A., Open J-Gage as well as in Cabell's Directories of Publishing Opportunities, U.S.A

6. CONCLUSION

By using Gumbel's exponential distribution and Dhillon's model the Probability density function and Cumulative distributive function have been obtained. Figures in section 5 shows that, when the time is increased the conditional probabilities for secretion of ACTH with IBS and ACTH with normal are decreased and the corresponding Probablitiy density function are also increased. So we conclude that ACTH with IBS significantly enhanced ACTH with normal secretion and ACTH secretion with time which coincides with the medical part.

REFERENCES

[1] Bebbington, M., Lai, C.D. and Zitikis, R. (2007). A flexible Weibull extension, Reliab. Eng. Syst. Safety, 92, 719-726.

[2] Dhillon, B.S. (1981). Life Distributions, IEEE Transactions on Reliability, vol. 30, no. 5.

[3] Gumbel, E.J.(1954). Statistical theory of extreme values and some practical applications. Applied Mathematics Series, 33. U.S. Department of Commerce, National Bureau of Standards.

[4] Lai, C.D. and Xie, M. (2006). Stochastic Ageing and Dependence for Reliability, Springer.

[5] Lakshmi.S and Manickam.A(June 2016) ' A Mathematical Reliability Growth model using for Acute HPA Axis Responses ,Heart Rate and Mood Changes to Psychosocial Stress in Human at Different Times of Day ISBN: 978-81932712-4-7

[6] Lembo T, Plourde V, Shui Z, et al.(1996) Effects of the corticotropin-releasing factor (CRF) on rectal afferent nerves in humans. Neurogastroenterol Motil; 8:9 ± 18.

[7] Mudholkar, G.S. and Srivastava, D.K. (1993). Exponentiated Weibull family for analyzing bathtub failure-rate data, IEEE Transactions on Reliability, 42(2), 299–302.

[8] Nadarajah S. (2006). The Exponentiated Gumbel distribution with climate

application, Environmetrics 17:13-23.

[9] Petrusz P, Merchenthaler I. (1992). The corticotropin-releasing factor system In: NemeroV CB, ed. Neuroendocrinology. Boca Raton, Florida: CRC Press, 129 ± 83.

[10] Young EA, Akil H.(1985) Corticotropin releasing factor stimulation of adrenocorticotropin and endorphin release: effects of acute and chronic stress. Endocrinology 1; 117: 23 ± 30.