IOSR Journal of Mathematics (IOSR-JM)
e-ISSN: 2278-5728, p-ISSN: 2319-765X. Volume 12, Issue 1 Ver. IV (Jan. - Feb. 2016), PP 50-54
www.iosrjournals.org

A Mathematical model for stimulation of the hypothalamic Pituitary ACTH releasing hormone in patients with psoriasis

T.Geetha[1], K.Sathishkumar [2], A. Manickam[3]

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

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

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

Abstract: *In this paper, the two parameter Weibull probability distributions are embedded in a larger family obtained by introducing an additional parameter. We generalize the two parameter Weibull distributions using the quadratic rank transmutation map by Shaw et al [15] to develop a transmuted Weibull distribution. We provide a comprehensive description of the mathematical properties of the subject distribution along with its reliability behavior. The usefulness of the transmuted Weibull distribution for modeling reliability is illustrated using real data. Psychocutaneous diseases constitute a large proportion of psychosomatic dis-orders, with psoriasis being one of the most typical cases. Though alteration of Hypothalamic- Pituitary-Adrenal (HPA) axis function has been suggested as underlying several psychiatric disorders and psychosomatic diseases, there is little evidence of reduced response of the HPA axis in psoriasis after psychosocially induced stress. The aim of the study was to investigate if there is any alteration of the neuroendocrine profile of psoriatic patients. Finally we conclude that the corresponding Mathematical results have been obtained and analysed with the medical solutions. Contrary to previous studies no particular neuroendocrine profile of HPA axis responsiveness was identified in psoriatic patients.*

Key words*: ACTH, Cortisol, Hypothalamus-Pituitary-Adrenal axis, Psoriasis, Stress*
Mathematical subject classification: 62 H_{xx} ; 62NO5; 90B25

I. Introduction

The quality of the procedures used in a statistical analysis depends heavily on the assumed probability model or distributions. Because of this, considerable effort has been expended in the development of large classes of standard probability distributions along with revelent statistical methodologies. However there still remain many important problems where the real data does not follow any of the classical or standard probability models. The Weibull distribution is a very popular distribution named after Waladdi Weibull, a Swedish physicist. He applied this distribution in 1939 to analyze the breaking strength of materials. Since then, it has been widely used for analyzing lifetime data in reliability engineering. It is a versatile distribution that can take on the characteristics of other type of distributions, based on the value of the shape parameter. The Weibull distribution is a widely used as statistical model for studying fatigue and endurance life in engineering devices and materials.

A random variable X is said to have transmuted distribution if its cumulative distribution function (cdf) is given by

$$F(x) = (1+\lambda)G(x) - \lambda\, G(x)^2 |\lambda| \leq 1 \qquad ------(1.1)$$

Where $G(x)$ is the cdf of base distribution Observe that at $\lambda = 0$ we have the distribution of the base random variable. Aryal et al. [7] studied that the transmuted Gumbel distribution and it has been observed that transmuted Gumbel distribution can be used to model climate data. In the present study we will provide mathematical formulation of the transmuted Weibull distribution and some of its properties. We will also provide possible area of applications.

II. Transmuted Weibull Distribution:

A random variable X is said to have a Weibull distribution with parameter $\eta > 0$ *and* $\sigma > 0$ if its probability density function (pdf) is given by

$$g(x) = \frac{\eta}{\sigma}\left[\frac{x}{\sigma}\right]^{\eta-1} \exp\left(-\left(\frac{x}{\sigma}\right)^{\eta}\right) \; x > 0 \qquad ------(2.1)$$

The cdf of X is given by

$$G(x) = 1 - \exp\left(-\left(\frac{x}{\sigma}\right)^{\eta}\right) \qquad ------(2.2)$$

Now using (1.1) and (2.2) we have the cdf of a transmuted weibull distribution

$$F(x) = \left[1 - \exp\left(-\left(\frac{x}{\sigma}\right)^{\eta}\right)\right]\left[1 + \exp\left(-\left(\frac{x}{\sigma}\right)^{\eta}\right)\right] \quad ------(2.3)$$

Hence, the pdf of transmuted Weibull distribution with parameters η , σ *and* λ is

$$f(x) = \frac{\eta}{\sigma}\left[\frac{x}{\sigma}\right]^{\eta-1} \exp\left(-\left(\frac{x}{\sigma}\right)^{\eta}\right)\left[1 - \lambda + 2\lambda \exp\left(-\left(\frac{x}{\sigma}\right)^{\eta}\right)\right] ------(2.4)$$

2.1 Moments and Quantiles:

In this section we shall present the moments and Quantiles for the transmuted Weibull distribution. The k^{th}order moments of a transmuted Weibull random variable X in terms of gamma function $\Gamma(.)$, *is* given by

$$E(X^K) = \sigma^k \Gamma\left(1 + \frac{k}{\eta}\right)\left\{1 - \lambda + \lambda\, 2^{\frac{-k}{\eta}}\right\}$$

Moreover if $\frac{k}{\eta} = r$ is a positive integer then

$$E(X^K) = \sigma^k \, \mathrm{r}\,!\{1 - \lambda + \lambda\, 2^{-r}\}$$

Therefore the expected value $E(X)$ and variance $\mathrm{Var}(X)$ of a tranmutted Weibull random variable X are, respectively, given by

$$E(X) = \sigma\, \Gamma\left(1 + \frac{1}{\eta}\right)\left\{1 - \lambda + \lambda\, 2^{\frac{-1}{\eta}}\right\}$$

$$Var(X) = \sigma^2\left\{\Gamma\left(1 + \frac{2}{\eta}\right)\left\{1 - \lambda + \lambda\, 2^{\frac{-1}{\eta}}\right\} - \Gamma^2\left(1 + \frac{1}{\eta}\right)\left(1 - \lambda + \lambda\, 2^{\frac{-1}{\eta}}\right)^2\right\}$$

III. Applications

Psoriasis constitutes one of the most illustrative examples of the close relation between exacerbations of cutaneous lesions and the psychopathologic burden of the patient's .Furthermore many studies have focused on the relation between stressful life events and exacerbations of the psoriatic disease. According to one of them psoriatic patients whose cutaneous condition is closely connected to their exposure to stressful life events were reported to be up to 80 %.The Hypothalamic-Pituitary-Adrenal (HPA) axis comprises one of the two main regulators of the stress system, with the Locus Ceruleous –Sympatho-Adreno-Medullary (SAM) axis being the other Alterations of its function have been suggested as implicated in a number of sheer psychiatric disorders and psychosomatic diseases as well. In particular, in major depressive disorder (MDD), a hyporeactivity of the HPA axis after stimulation has been proposed as evidenced by blunted ACTH response in the CRT test. In another psychiatric disorder, Post Traumatic Stress Disorder (PTSD), the application of the CRH test exhibited blunted plasma ACTH response, suggesting a possible down regulations of the pituitary's CRH receptors that could indicate either a chronic hypothalamic CRH hyper secretions and / or an increase of circulating glucocorticoids negative feedback action. Rupprecht et al [14] investigated the HPA axis function of patients with atopic dermatitis with applications of the CRH test.

IV. Results

CRH test

After CRH infusion, the mean ±SEM ACTH plasma values in pg/ml for psoriatics were 21.71±4.20, 39.37± 6.47,40.24 ± 7.84 *and* 32.00 ± 6.32and for the controls were 16.10 ± 2.20 ,37.28 ± 5.42 ,35.26 ± 4.94 *and* 27.43 ± 3.53 , measured at 0, 15, 30 and 60 min, respectively. The t test between the mean values at 0 (p: 0.233), 15(p: 0.805), 30(p: 0.590) and 60(p: 0.526) min did not show significant differences (Fig 3.1).

Moreover, the total secretion of ACTH during the CRH test was estimated in both groups as Area under the Curve (AUC) according to the trapezoid rule. The mean± sem total secretion of ACTH as AUC for psoriatic was 2.062 ± 0.379 pg×1000×min/ml and 1.804 ± 0.241 for the controls without significant difference, t:-0.580, df: 45, p: 0.565 (Fig3.1).

The same procedure was followed for serum cortisol values during the CRH test.Specifically,the mean ± sem cortisol values for psoriatics, in µg/dl, at 0, 15, 30 and 60 min were 18.03± 1.98,18.59 ± 1.56, 20.51 ± 1.72 and 18.59 ± 1.33, respectively, while the corresponding cortisol values for healthy volunteers were 16.94 ±1.22, 18.83 ±1.45, 19.8 ±1.73 and 20.06 ± 1.34 µg/dl. The test between the mean values at 0(p: 0.639), 15(p: 0.914), 30(p: 0.775) and60 (p: 0.442) min did not show significant difference between the two groups (Fig 3.2).

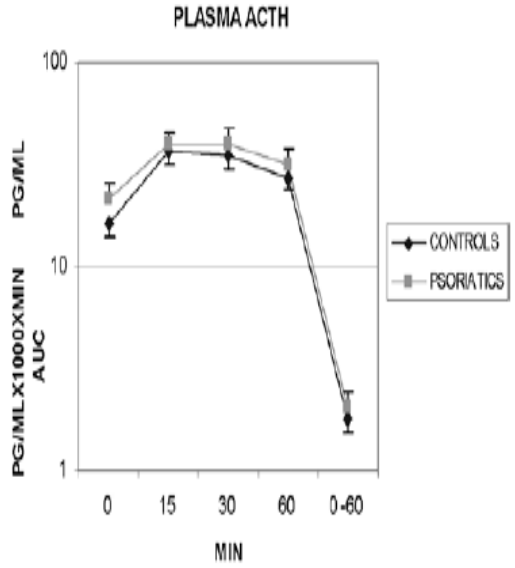

Fig 3.1. Algorithmic graph of mean ± sem ACTH plasma values, in pg/ml, in the control and psoriatic groups, during the CRH test, at 0 min and at 15, 30 and 60 min and secretion of plasma ACTH during 60 min, as AUC, in pg×1000×min/ml. ACTH (pg/ml): To convert to SI units multiply by 0.22.

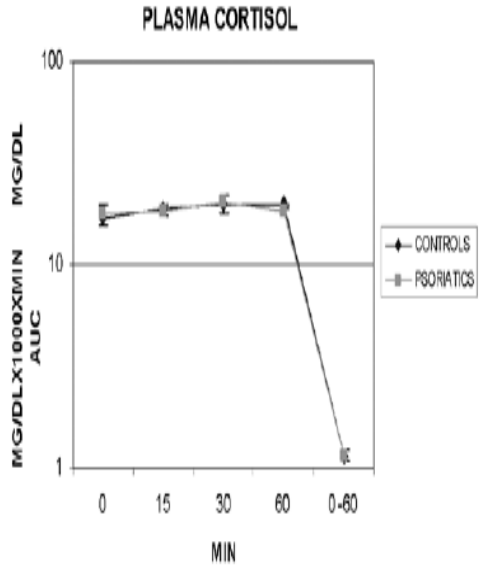

Fig 3.2. Algorithmic graph of mean±sem plasma cortisol values, in µg/dl, in the control and psoriatic groups, during the CRH test, at 0 min and at 15, 30 and 60 min, and secretion of plasma cortisol during 60 min, as AUC, in µg×1000×min/dl.Cortisol (µg/dl): To convert to SI units multiply by 27.6.

Mean plasma ACTH and cortisol levels in both groups increased during the 60- min CRH test without significant difference. The total secretion of plasma ACTH and serum cortisol estimated as Area under the Curve did not show significant difference between the groups either.

V. Discussion

It is widely known that tissues from the nervous and cutaneous systems share common embryological origin and that there is a close relation among derma-toligical disorders mental status and psychopathology. Psoriasis is one of the most typical examples of psychocutaneous disorders as the chronicity of the disease and its course with exacerbations and remissions relate to the stressful life events and their impact on the psychological state. In this research article, the application of the CRH test constitutes a major advantage in relation to the exposure to psychosocial type of stressor, as it evokes less subjective results about the systemic

HPA axis function. The increases of the plasma ACTH and cortisol values during the CRH test did not show significant differences between the groups under study. These findings contradict the hypothesis for a particular neuroendocrine profile of the hypo- reactivity type in psoriasis, while they support the findings of the recent study by Buske- Kirschbaum et al [4] which showed no alteration of the HPA axis function either centrally with the evaluation of the ACTH level after
Stressor exposure or peripherally with the Dexamethasone Suppression Test (DST) application.

Furthermore, the results (hormonal values) from the CRH test did not demonstrate significant correlation with the patients' demographic data such as age and gender, nor with medical variables of the disease, such as the extent of the cutaneous lesions, total duration of the disease and duration of the present episode. The findings of the present study support the suggestion that, in a TH_1 dominant inflammatory condition, the HPA axis could be normal. The application of the CRH test in psoriatic patients for the investigation of the systemic HPA axis responsiveness did not show considerable differences compared with the control group. The divergence of the results between the present study, where a specific neuroendocrine test was applied, and the previous ones, where a psychosocial type of stressor was used, could indicate the diversity of the neuroendocrine response depending on the kind of stressful stimulation in psoriasis. Moreover, the results suggest that the HPA axis might not be the only neuroendocrine system to regulate the initiation and maintenance of the psoriatic condition. The endogenous complexity found to reside in the neuroendocrine mechanisms of psoriasis lays the groundwork for further studies.

VI. Mathematical Results

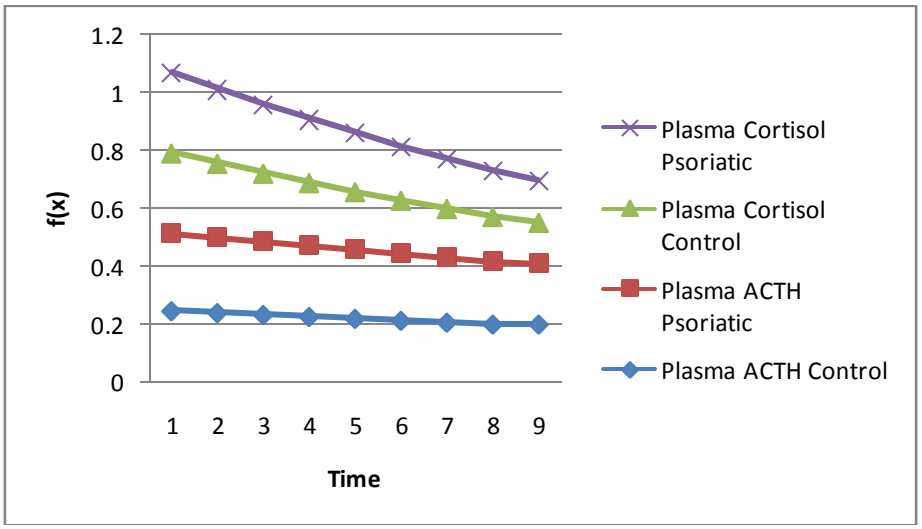

Fig 5.1 (a) Probability density function for ACTH and cortisol (control) corresponding to the fig 5.1 (a)

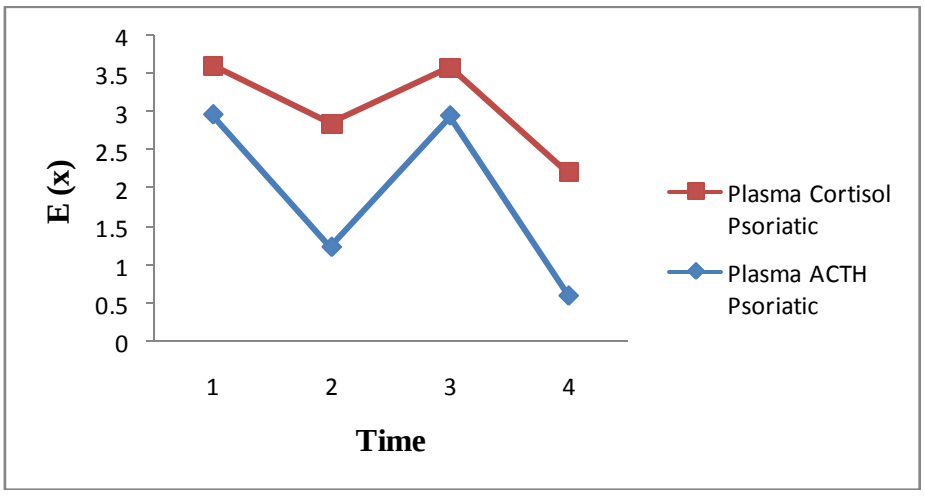

Fig 5.2 (b) Probability for Mean value in plasma (Cortisol & ACTH psoriatic) corresponding to the fig 5.2 (b)

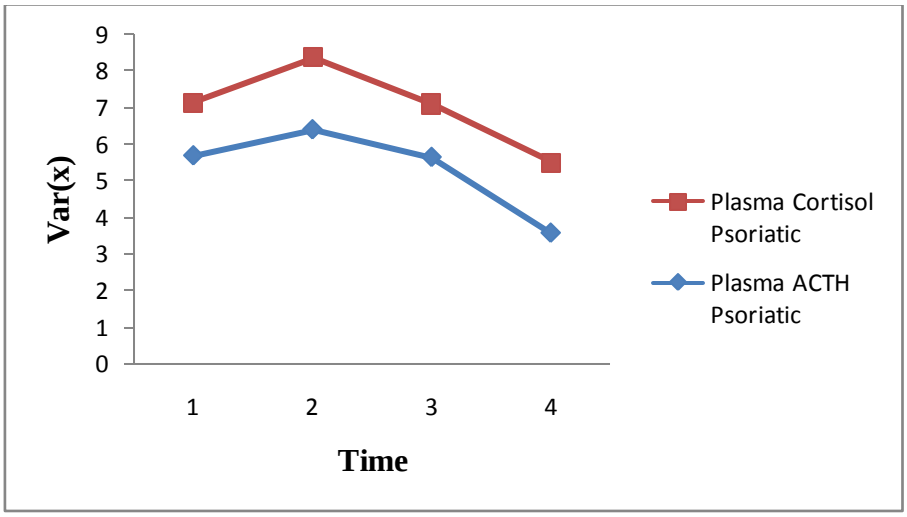

Fig 5.3 (c) Probability for Variance in plasma (cortisol & ACTH psoriatic) corresponding to the fig 5.2 (c)

VII. Conclusions

In this paper we have introduced a new generalization of the weibull distribution called transmuted weibull distribution. The subject distribution is generated by using the quadratic rank transmutation map taking the two parameter weibull distribution as the base distribution. Some mathematical properties along with estimation issues are addressed. The hazard function and reliability behavior of the transmuted weibull distribution shows that the subject distribution can be used to model reliability data. We have studied two data sets published in the literature to show the usefulness of the transmuted weibull distribution and to make comparison with exponential weibull distribution. We expect that this paper will serve as a reference and help to advance future research in this area. Contrary to previous studies no particular neuroendocrine profile of HPA axis responsiveness was identified in psoriatic patients. In the case of ACTH & Cortisol secretion rate the PDF curve for control is higher than the PDF curve for psoriatic and both are monotonic. Finally we conclude that the corresponding Mathematical results have been obtained and analysed with the medical solutions.

References

[1]. Arnetz BB, Fjellner B, Eneroth P, Kallner A, (1991) Endocrine and dermatological concomitants of mental stress. Acta Derm Venereol Suppl (Stockh) 156: 9-12.
[2]. AmsterdamJD, MaislinG, WinocurA, etal,(1987)Pituitary and adrenocortical responses to the ovine corticotropin releasing hormone in depressed patients and healthy volunteers. Arch Gen Psychiatry 44: 775-781.
[3]. Baldaro B, Brocani G, Bossi G, et al, (1989) Psoriasi. Incidenza di eventi stressanti nei sei mesi precedenti la comparsa della malattia. Med Psicosom 34: 47-51.
[4]. Buske-Kirschbaum A, EbrechtM, KernS, Hellhammer DH, (2006) Endocrine stress responses in TH1-mediated chronic inflammatory skin disease (psoriasis vulgaris) do they parallel stress – induced endocrine changes in TH_2 mediatedinflammatorydermatoses(atopicdermatitis)? Psychoneuroendocrinology 31: 439-446
[5]. Chrousos GP, Gold PW, (1992) The concepts of stress and stress system disorders: overview of physical and behavioral homeostasis. JAMA 267: 1244-1252.
[6]. Fava GA, Perini GI, Veller Fornasa C, (1980) Life events and psychological distress in dermatologic disorders: Psoriasis, chronic urticaria and fungal infections. Br J Med Psychol 53: 277-282.
[7]. Gokarna R. Aryal and chris P. Tsokos. (2009). On the transmuted extreme value distribution with application. Nonlinear Analysis: Theory , Methods and Applications, 71 :1401 -1407.
[8]. Govinda Mudholkar ,Deo Srivastava, and George Kollia (1996) A generalization of the weibull distribution with application to the analysis of survival data. Journal of the American statistical Association, 91(436):1575-1583.
[9]. GuptaM,GuptaA,(1996) Psychodermatology:anupdate. J Am Acad Dermatol 34: 1030-1046
[10]. Harvima RJ, Viinamaki H, Harvima IT, et al, (1996) Association of psychic stress with clinical severity and symptoms of psoriatic patients. Acta Derm Venereol 76: 467-471.
[11]. Ithaka .R and Gentleman .R (1996) A language for data analysis and graphics. Journal of Computational and Graphical Statistics, 5:299-314.
[12]. Kono M, Nagata H, Umemura S, et al, (2001) In situ ex- pression of corticotrophin releasing hormone (CRH) andproopiomelanocortin(POMC)genesinhumanskin. FASEB J 15: 2297 - 2299.
[13]. Manal M. Nassar and Fathy H.Eissa.(2003) On the Exponential Weibull Distribution. Communications in Statistics – Theory and Methods, 32 (7):1317-1336
[14]. Rupprecht M, Hornstein PO, Schluter D, et al, (1995) Cortisol, Corticotropin and β-Endorphin Responses to Corticotropin-Releasing Hormone in Patients with Atopic Eczema. Psychoneuroendocrinology 20: 543-551.
[15]. Shaw. W and I. Buckley. (2007) The alchemy of probability distributions: beyond Gram – Charlier expansions and a skew – Kurtotic –normal distributions from a rank transmutation map.