International Journal of Applied and Advanced Scientific Research (IJAASR)
Impact Factor: 5.655, ISSN (Online): 2456 - 3080
(www.dvpublication.com) Volume 5, Issue 2, 2020

STOCHASTIC MODEL TO ESTIMATE THE AH ON CORTISOL PRODUCTION USING WEIBULL DISTRIBUTION

M. Vasuki* & A. Dinesh Kumar**

* Assistant Professor, Department of Mathematics, Srinivasan College of Arts and Science, Perambalur, Tamilnadu

** Associate Professor, Department of Mathematics, Dhanalakshmi Srinivasan Engineering College, Perambalur, Tamilnadu

Cite This Article: M. Vasuki & A. Dinesh Kumar, "Stochastic Model to Estimate the AH on Cortisol Production Using Weibull Distribution", International Journal of Applied and Advanced Scientific Research, Volume 5, Issue 2, Page Number 43-46, 2020.

Abstract:

The adrenal glands are the primary source of minerocorticoids, glucocorticoids, and the so-called adrenal androgens. Under physiological conditions, cortisol and adrenal androgen synthesis are controlled primarily by ACTH. Although it has been established that ACTH can stimulate steroidogenesis, the effects of ACTH on overall gene expression in human adrenal cells have not been established. In this paper, we estimate the Adrenocorticotropic Hormone on cortisol production using Weibull Distribution with the help of Gompertz Makeham function.

Key Words: Adrenocorticotropic Hormone, Cortisol, Weibull Distribution & Gompertz Makeham Function.

1. Introduction:

ACTH is a 39 amino acid polypeptide predominantly synthesized in and secreted from the anterior lobe of the pituitary gland. The synthesis and secretion of ACTH are tightly controlled by the hypothalamic pituitary adrenal axis. Under stress conditions, the paraventricular nucleus of the hypothalamus secretes vasopressin and CRH. These two peptides regulate the anterior lobe of the pituitary gland and stimulate the secretion of ACTH. ACTH subsequently induces adrenal cortex expansion and corticosteroid production (mainly cortisol in humans). Once synthesized, cortisol in turn acts on the hypothalamus and pituitary
(To suppress CRH and ACTH production) causing a negative feedback cycle. In the adrenal glands, ACTH acts by binding to specific cell surface ACTH receptors (Melanocortin 2 Receptor MC2R). MC2R is a seven membrane spanning G-protein coupled receptor that is primarily expressed in adrenocortical cells. Upon ligand binding, the receptor undergoes conformational changes that stimulate adenylyl cyclase, leading to an increase in intracellular cAMP and subsequent activation of protein kinase A (PKA).

Although previous studies have identified some ACTH responsive genes that are involved with the steroidogenic and growth related effects of ACTH [2-3], [6], [8-9], [11] & [18], there is a lack of knowledge regarding the global actions of ACTH on gene expression. Given the critical role of ACTH in adrenal development, steroidogenesis, and disease, it is appropriate to further define the detailed effects of ACTH on human adrenal cell gene expression. In this paper the problem is investigated by the hazard function of [19]. Among the useful functions applicable to real life data and the logit of beta distribution are the Beta Pareto [1]; Beta Laplace [7]; Beta Weibull[5]; Beta Normal [4]; Beta Gumbel [10]. Also we estimate the Adrenocorticotropic Hormone on cortisol production using Weibull Distribution with the help of Gompertz Makeham function.

2. Bio Mathematical Model:

The Gompertz Makeham function is a distribution that gives very good approximations to empirical distributions of life length not only for human populations but also for different biological arts. There will be investigations of some properties of the Gompertz Makeham distribution.

The Gompertz Makeham distribution has the survival function:

$$\overline{F}_{\psi}(m) = \exp\left[-am - b\frac{e^{cm}-1}{c}\right] \qquad (1)$$

Where m is life time always non-negative ($m \geq 0$) and a, b and c are known non negative parameters and $a + bc > 0$ and hence

$$\overline{F}_{\psi}(m) > 0 \text{ for } m > 0 \text{ and } \overline{F}_{\psi}(0) = 1 \qquad (2)$$

How different values of this three parameters influence to the model will be researched. In general the hazard function of the Gompertz Makeham distribution often can be used to express the behavior of the distribution.

The cumulative hazard function of a distribution can be defined by the relation

$$H_{\psi}(m) := \ln\left(\frac{1}{\overline{F}_{\psi}(m)}\right), \quad \psi = (a,b,c) \qquad (3)$$

And the intensity hazard function is the derivative of the cumulative hazard function

$$h_{\psi}(m) := \frac{dH_{\psi}(m)}{dm} \tag{4}$$

The Gompertz Makeham distribution has the cumulative hazard function

$$H_{\psi}(m) = am + b\frac{e^{cm}-1}{c} \tag{5}$$

And the intensity hazard function is

$$h_{\psi}(m) = a + be^{cm}. \tag{6}$$

Formulas (5) and (6) can easily be derived from its survival function (1) and the definitions of the hazard function (3) and (4). Note that $H_{\psi}(m) > 0$ is $m > 0$ due to (2).

Another property that can be derived is the probability density function of the Gompertz Makeham function

$$f_{\psi}(m) = \frac{dF_{\psi}(m)}{dm} = \frac{d(1-e^{-H(m)})}{dm} = h_{\psi}(m)\ e^{-H(m)} = (a+be^{cm})\exp\left[-\left(am + b\frac{e^{cm}-1}{c}\right)\right]. \tag{7}$$

It will be of interest if there exists any points of extremum not at the boundary of the probability density function of the Gompertz Makeham distribution. This knowledge is necessary for the possibility to conclude if the probability density function of the Gompertz Makeham distribution is unimodal or not. The probability density function is unimodal if the derivative is 0 for at most one value of the derivative. The derivative of the probability density function (7) of the Gompertz Makeham distribution is

$$\frac{df_{\psi}(m)}{dm} = \frac{d(h_{\psi}(m)e^{-H(m)})}{dm} = (h^1{}_{\psi}(m) - h^2{}_{\psi}(m)) = \left((cbe^{cm}) - (a+be^{cm})^2\right)e^{-H(m)} \tag{8}$$

Because as stated in expression (6) the intensity hazard function of the Gompertz Makeham distribution is $h_{\psi}(m) = a + be^{cm}$ and therefore the derivative of it is $h^1{}_{\psi}(m) = cbe^{cm}$.

Right hand side of equation (8) is 0 only when the statements $(cbe^{cm}) = (a+be^{cm})^2$ is true, because $0 < H(m) < \infty$ and $e^{-H(m)} > 0$. There exists one or two points of extremum only when $(cbe^{cm}) = (a+be^{cm})^2$ and the values of the life length that gives this equality are positive.

Set $x = be^{cm}$, then (8) can be written as

$$cx = (a+x)^2 = a^2 + 2ax + x^2 \text{ or } x^2 = (c-2a)x - a^2.$$

The value x can be solved by a second grade equation so the roots are

$$x_1 = \frac{c}{2}\left(1 - \sqrt{1-\frac{4a}{c}}\right) - a \text{ and } x_2 = \frac{c}{2}\left(1 + \sqrt{1-\frac{4a}{c}}\right) - a$$

and in time scale

$$m_1 = \frac{1}{c}\ln\left(\frac{1}{b}\left(\frac{c}{2}\left(1 - \sqrt{1-\frac{4a}{c}}\right) - a\right)\right), \tag{9}$$

$$m_2 = \frac{1}{c}\ln\left(\frac{1}{b}\left(\frac{c}{2}\left(1 + \sqrt{1-\frac{4a}{c}}\right) - a\right)\right). \tag{10}$$

As earlier defined $a, b \text{ and } c \geq 0$. We have $m_1 \leq m_2$, otherwise the solution is a natural logarithm of a negative value, which is a complex value and for that case $m_1 \text{ and } m_2$ will have complex time. This fact makes sure that the points of extremum occur at non-negative time if they exist. If m_1 is positive there are two possibilities. Either there exist both a local minimum and a local maximum of the probability density function or there exist an inflection point and there doesn't exist any other point of extremum separated from the boundary of the function, occurs if $m_1 = m_2$. If m_1 is not positive and m_2 is positive then there exist only a local maximum of the density probability function. If m_2 is not positive there are no points of extremum for the

probability density function of the Gompertz-Makeham distribution. The function is unimodal if there are no local maximum not at the boundary of the function.

3. Example:

Figure (1) Time dependent effects of ACTH on cortisol production in human adult adrenal (AA) cells. Primary human AA cells were prepared as described under Materials and methods, and plated at the density of 2,00,000 cells per well in 24 well dishes. Cells were treated with or without ACTH (10nM) for the indicated times, and cortisol was quantified in the medium using EIA. Cortisol data were normalized to protein per well and expressed as the fold change over basal condition (untreated cells) for each time point. Results represent the mean ±S.E.M. of data from at least three independent experiments. Three wells were analyzed for individual treatment in each experiment. Statistics were calculated using one way Anova followed by Dunnett's test, comparing with baseline. **P<0.01 [12-17] & [20].

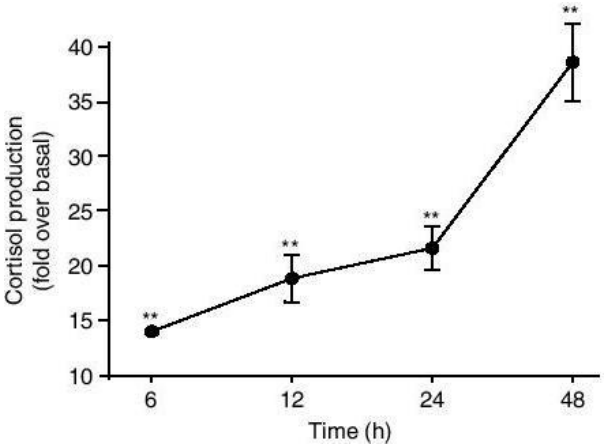

Figure (1): Effects of ACTH on cortisol production in human adult adrenal (AA) cells

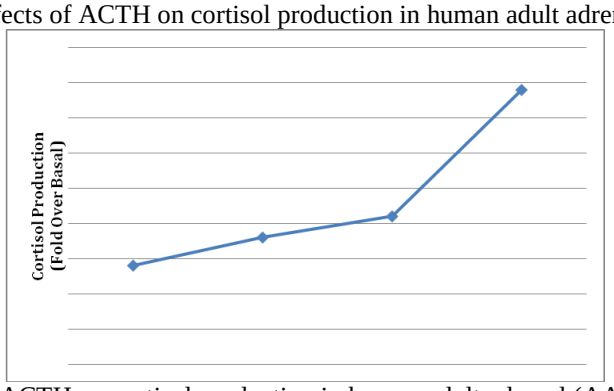

Figure (2): Effects of ACTH on cortisol production in human adult adrenal (AA) cells using Weibull Distribution

4. Conclusion:

By applying a bio mathematical approach, we defined and estimate the genomic effects of ACTH in human adult and FA primary cultures. The newly defined adrenal ACTH responsive genes can provide clues to the mechanism of ACTH regulated steroidogenesis and cell growth, and may lead to further understanding of the global functions of ACTH in the adrenal gland. Gompertz Makeham function with Weibull distribution gives the same as the medical report. 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. Akinsete A, Famooye F & Lee C, "The Beta Pareto Distribution", Statistics, Volume 42, Page Number 547-563, 2008.
2. Banerjee S, Dhar G, Haque I, Kambhampati S, Mehta S, Sengupta K, Tawfik O, Phillips T A & Banerjee S K, "CCN5/WISP-2 expression in breast adenocarcinoma is associated with less frequent progression of the disease and suppresses the invasive phenotypes of tumor cells", Cancer Research, Volume 68, Page Number 7606–7612, 2008.
3. Cecim M, Alvarez Sanz M, Van de Kar L, Milton S & Bartke A, "Increased plasma corticosterone levels in bovine growth hormone (bGH) transgenic mice: effects of ACTH, GH and IGF-I on in vitro adrenal corticosterone production", Transgenic Research, Volume 5, Page Number 187–192, 1996.
4. Eugene N C & Famoye F, "Beta Normal Distribution and Its Applications", Communication in Statistics Theory and Methods, Volume 31, Page Number 497-512, 2002.

5. Famoye F, Lee C & Olugbenga O, "The Beta Weibull Distribution", Journal of Statistical Theory and Applications, Volume 4 (2), Page Number 121-138, 2005.
6. Gaillard I, Keramidas M, Liakos P, Vilgrain I, Feige J J & Vittet D, "ACTH-regulated expression of vascular endothelial growth factor in the adult bovine adrenal cortex: a possible role in the maintenance of the microvasculature", Journal of Cellular Physiology, Volume 185, Page Number 226–234, 2000.
7. Kozubowski T & Nadarajah S, "The Beta Laplace Distribution", Journal of Computational Analysis and Applications, Volume 10 (3), Page Number 305-318. 2008.
8. Le Roy C, Li J Y, Stocco D M, Langlois D & Saez J M, "Regulation by adrenocorticotropin (ACTH), angiotensin II, transforming growth factor-b, and insulin-like growth factor I of bovine adrenal cell steroidogenic capacity and expression of ACTH receptor, steroidogenic acute regulatory protein, cytochrome P450c17, and 3b-hydroxysteroid dehydrogenase", Endocrinology, Volume 141, Page Number 1599–1607, 2000.
9. Markowska A, Rebuffat P, Rocco S, Gottardo G, Mazzocchi G & Nussdorfer G G, "Evidence that an extrahypothalamic pituitary corticotrophin releasing hormone (CRH) adrenocorticotropin (ACTH) system controls adrenal growth and secretion in rats", Cell and Tissue Research, Volume 272, Page Number 439–445, 1993.
10. Nadarajah S & Kotz S, "The Beta Gumbel Distribution", Mathematical Problems in Engineering, Volume 1, Page Number 323-332, 2004.
11. Neri G, Andreis P G & Nussdorfer G G, "Comparison of ACTH and corticotrophin releasing hormone effects on rat adrenal steroidogenesis in vitro", Research in Experimental Medicine, Volume 191, Page Number 291–295, 1991.
12. Senthil Kumar P, Balasubramanian K & Dinesh Kumar A, "A New Mathematical Model to Estimate the Effects of Lipid Induced Insulin Resistance on UPR mRNA Using Normal Distribution", International Journal for Research in Applied Science & Engineering Technology (IJRASET), Volume 3, Issue 9, Page Number 124-130, 2015.
13. Senthil Kumar P, Balasubramanian K & Dinesh Kumar A, "A New Stochastic Model to Find the Insulin Secretion from Human Islets Using Exponential Distribution", IJRDO Journal of Mathematics, Volume 1, Issue 3, Page Number 72-79, 2015.
14. Senthil Kumar P, Balasubramanian K & Dinesh Kumar A, "Stochastic Model to Estimate the Changes in Plasma Insulin and FFAs During OLTT and OGTT Using Normal Distribution", Bulletin of Mathematics and Statistics Research, Volume 3, Issue 3, Page Number 10-16, 2015.
15. Senthil Kumar P, Balasubramanian K & Dinesh Kumar A, "Stochastic Model to Estimate the Insulin Secretion Using Normal Distribution", Arya Bhatta Journal of Mathematics and Informatics (ABJMI), Volume 7, Issue 2, Page Number 277-282, 2015
16. Senthil Kumar P, Abirami R & Dinesh Kumar A, "Fuzzy Model for the Effect of rhIL6 Infusion on Growth Hormone", International Conference on Advances in Applied Probability, Graph Theory and Fuzzy Mathematics (ICAPGF), Proceedings Page Number 246-252, 2014.
17. Senthil Kumar P, Dinesh Kumar A & Vasuki M, "Stochastic Model to Find the Effect of Gallbladder Contraction Result Using Uniform Distribution", Arya Bhatta Journal of Mathematics and Informatics (ABJMI), Volume 6, Issue 2, Page Number 323-328, 2014.
18. Simmonds P J, Phillips I D, Poore K R, Coghill I D, Young I R & Canny B J, "The role of the pituitary gland and ACTH in the regulation of mRNAs encoding proteins essential for adrenal steroidogenesis in the late-gestation ovine fetus", Journal of Endocrinology, Volume 168, Page Number 475–485, 2001.
19. The Gompertz Makeham Distribution by Fredrik Norström Master's thesis in Mathematical Statistics, Umeå University, 1997
20. Yewei Xing, Richard Parker C, Michael Edwards & William E Rainey, "ACTH is a potent regulator of gene expression in human adrenal cells", Journal of Molecular Endocrinology, Volume 45, Page Number 59–68, 2010.