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A Mathematical model for suppression of growth hormone - dependent isoforms of cytochrome P450 in female rats by the somatostain analog octreotide.

V. Appalanaidu[*], A.Manickam[**]

[*] *Assistant Prof of Mathematics, GMR Institute of Technology, GMR Nagar, Rajam – 532 127. Srikakulam District., Andhra Pradesh, India.*

[**]*Senior Assistant Prof of Mathematics, GMR Institute of Technology, GMR Nagar, Rajam – 532 127. Srikakulam District., Andhra Pradesh, India.*

Corresponding Author: V. Appalanaidu

Abstract: *In this study, we introduce a three-parameter Weibull-G exponential distribution (WGED) model to analyze the circulating growth hormone profiles of female rats. The reported data of Octreotide infused female Sprague Dawley rats every 12 h for 6 days at levels considerably greater than typical human therapeutic doses has been taken. It is observed that the suppression of plasma growth hormone profiles of Octreotide-11 dose infused female rats is higher than Octreotide-1 dose and control.*

Keywords: *Exponential distribution, Generalized Exponential, GH, Octreotide.*

Mathematical subject classification: *$60G_{xx}$, $62H_{xx}$, $62P_{xx}$.*

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I. Introduction

The exponential distribution (ED) (Gupta and Kundu, 2001), has a wide range of applications including life testing experiments, reliability analysis, applied statistics and clinical studies. This distribution is a special case of the two parameter Weibull distribution with the shape parameter equal to 1. The origin and other aspects of this distribution can be found in (Gupta and Kundu, 2003). A random variable X is said to have the exponential distribution (ED) with parameters $\lambda > 0$ if it's probability density function (pdf) is given by

$$g(x) = \lambda e^{-\lambda x},\ x > 0. \tag{1.1}$$

While the cumulative distribution function (cdf) is given by

$$G(x) = 1 - e^{-\lambda x}, x > 0. \tag{1.2}$$

The survival function is given by the equation

$$S(x) = 1 - G(x) = e^{-\lambda x}, x > 0. \tag{1.3}$$

And the hazard function is

$$h(x) = \lambda \tag{1.4}$$

Weibull distribution introduced by (Weibull, 1951) is a popular distribution for modeling phenomenon with monotonic failure rates. But this distribution does not provide a good fit to data sets with bathtub shaped or upside-down bathtub shaped (unimodal) failure rates, often encountered in reliability, engineering and biological studies. Hence a number of new distributions modeling the data in a better way have been constructed in literature as ramifications of Weibull distribution.

Octreotide is a potent somatostain analog most commonly used to reduce blood levels of growth hormone and insulin-like growth factor-1 (IGF-1), also known as somatomedin C, in acromegaly patients (Yang and Keating, 2010). Whereas a single dose of the drug to humans (Marbach et al., 1985) or rats (Turner and Tannenbaum, 1995) can profoundly reduce plasma growth hormone concentrations for many hours, the herapeutic goal, however, is to achieve normalization of growth hormone and IGF-I levels in patients (Yang and Keating, 2010). The therapeutic intent of octreotide administration is to simply reduce elevated plasma concentrations of growth hormone to near normal without altering the characteristic profile. Banerjee et al., have been studied the expression levels of key CYP isoforms as well as IGF-1 and growth hormone receptor as indicators or markers of alterations, possibly subtle, but physiologically significant, in the feminine growth hormone profile resulting from octreotide infusion. In the present paper, we have taken the reported data (Banerjee et al., 2013) and analyzed using Weibull-G exponential distribution.

II. Mathematical Model And Assumptions

The three parameters Weibull-G exponential distribution (WGED) has been studied in this section. The cumulative distribution function (cdf) of the Weibull-G exponential distribution (WGED) is given by

$$F(x;a,b,\lambda)=1-e^{-a[e^{\lambda x}-1]^b},a,b,\lambda>0, \tag{2.1}$$

The pdf corresponding to Eq. (2.1) is given by

$$f(x;a,b,\lambda)=ab\lambda e^{\lambda x}[e^{\lambda x}-1]^{b-1}e^{-a[e^{\lambda x}-1]^b},\lambda>0, \tag{2.2}$$

Where $a,b>0$ and $\lambda>0$ are two additional shape parameters.

We denote by $X\sim WGED(a,b,\lambda)$ a random variable having the pdf Eq. (2.1). The survival function, $S(x)$, hazard rate function, $h(x),$, reversed hazard rate function, $r(x)$ and cumulative hazard rate function $H(x)$ of X, are given by

$$S(x:a,b,\lambda)=1-F(x;a,b,\lambda)=e^{-a[e^{\lambda x}-1]^b},x>0, \tag{2.3}$$

$$h(x;a,b,\lambda)=ab\lambda e^{\lambda x}[e^{\lambda x}-1]^{b-1},\ \ x>0. \tag{2.4}$$

$$r(x;a,b,\lambda)=\frac{ab\lambda e^{\lambda x}[e^{\lambda x}-1]^{b-1}e^{-a[e^{\lambda x}-1]^b}}{1-e^{-a[e^{\lambda x}-1]^b}},\ \ x>0. \tag{2.5}$$

and

$$H(x;a,b,\lambda)=\int_0^{\infty}h(x;a,b,\lambda)dx=a[e^{e^{\lambda x}}-1]^b, \tag{2.6}$$

Respectively.

III. Applications

In this section we used the three parameters Weibull-G exponential distribution (WGED) to analyze the plasma growth hormone profiles of Sprague Dawley female rats. The plasma growth hormone profiles are presented as schematic representations of the actual circulating profiles as shown in Fig.3.1. Plasma levels of circulating growth hormone obtained from individual undisturbed catheterized Octreotide–infused female rats is shown in Fig. 3.1. Every rat was fitted was a chronic indwelling right atrial catheter for serial blood sampling (Pampori et al., 1991). Four to 5 days following catheter placement, serial blood samples were collected over 8 consecutive h at 15 min intervals (controls). Four to 5 days later, every rat was injected, iv, with 25 µg octreotide/kg body weight and 5 min later, serial blood samples were again collected. Next, the rats were injected, iv, every 12 h with the same dose of Octreotide for a total of 11 doses. Five minutes following the last injection, serial blood collections were again obtained for 8 h. Similar findings were obtained from 6 additional animals.

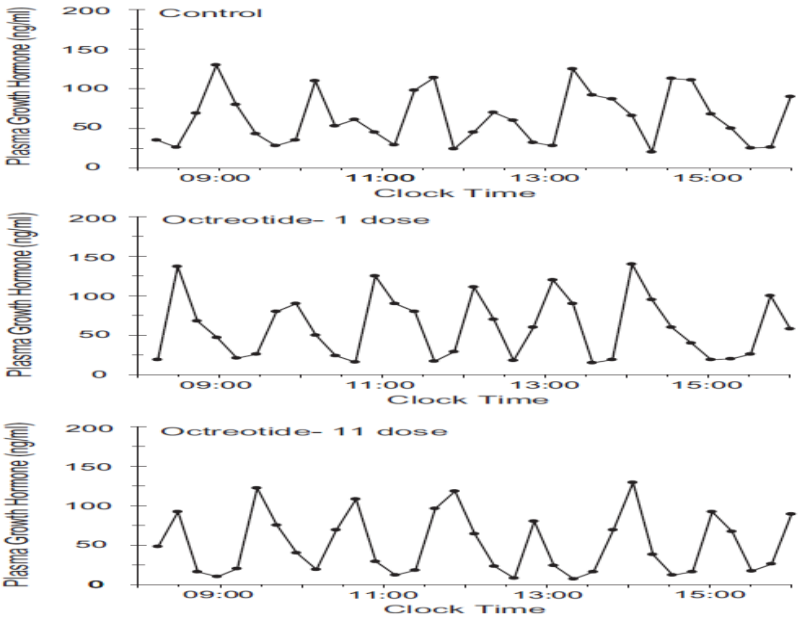
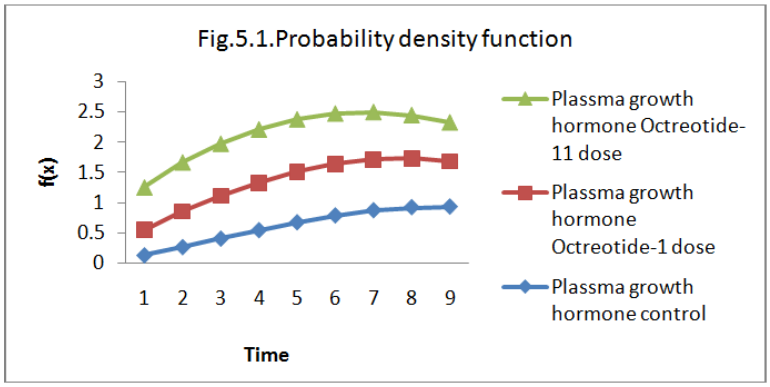
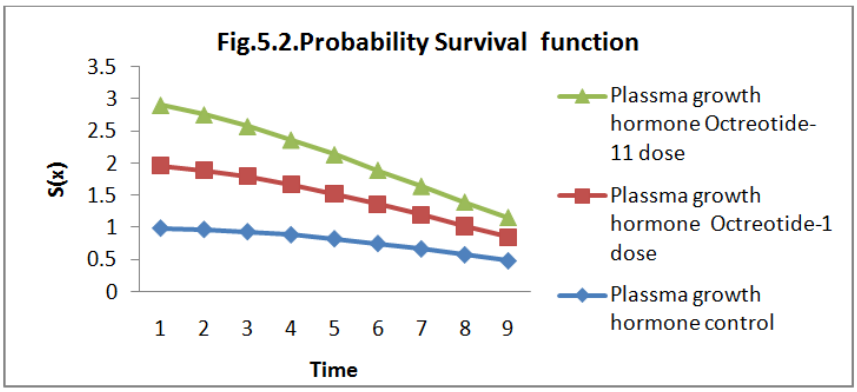


Fig. 3.1. Plasma levels of circulating growth hormone obtained from individual undisturbed catheterized Octreotide –infused female rats

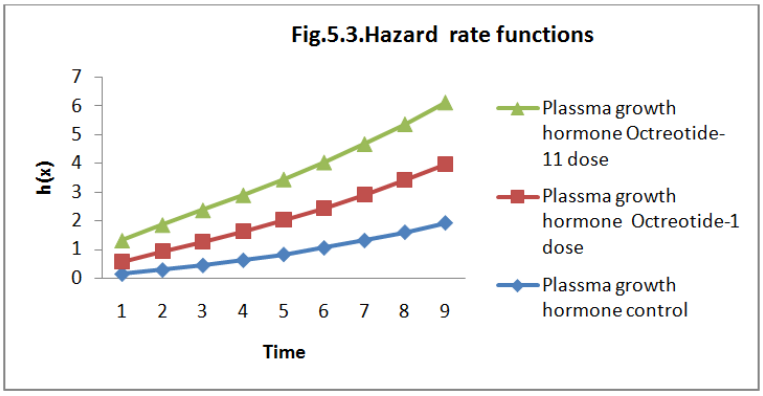
IV. Mathematical Results And Discussion



The plot of probability density function of plasma growth hormone Octreotide-11 dose shows its superiority than the functions plasma growth hormone Octreotide-1 dose and plasma growth hormone control. The plot of plasma growth hormone Octreotide-11 dose function initially monotonically increasing up to t=7 h and then decreasing monotonically. The rate of decreasing is comparatively good than plasma growth hormone Octreotide-1 dose and control functions. After injecting Octreotide-11 dose to female rats, the plasma growth hormone levels are suppressed as time goes on.



The plot of probability survival function of plasma growth hormone Octreotide-11 dose dominates the plasma growth hormone Octreotide-1 dose and control survival functions in the specified range. The probability survival function of plasma growth hormone Octreotide-11 dose decreases rapidly than Octreotide-1 dose and control functions. The probability of suppression of plasma growth hormone levels when injected Octreotide-11 dose beyond any given specified time is higher than the other two cases of Octreotide-1 dose and control.



The hazard rate of plasma growth hormone Octreotide-11 dose function is extremely good than the hazard rates of Octreotide-1 dose and control functions. According to plots the hazard rate functions, the hazard rates of Octreotide-11 dose, Octreotide-1 dose and control functions are 6.5, 4.2, and 1.9 respectively. The hazard rate is also known as failure rate. The failure rate of development of plasma growth hormone levels is high when injecting Octreotide-11 dose comparing with the injecting Octreotide-1 dose and control.

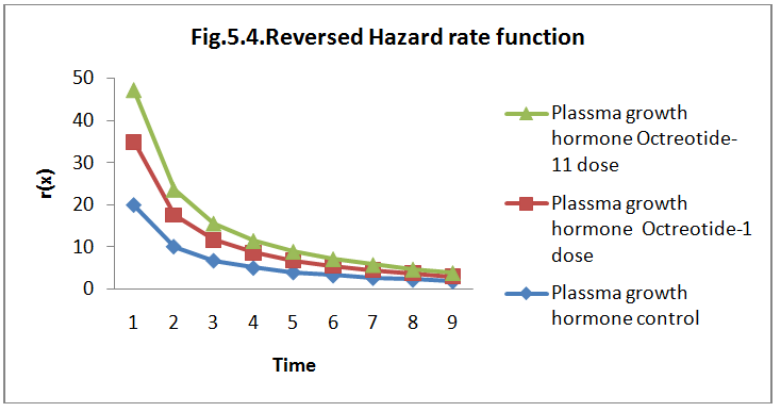


Fig.5.4 represents Reverse hazard rate functions of plasma growth hormone Octreotide-11 dose, Octreotide-1 dose and control. The plots of reverse hazard rate functions are monotonically decreasing. The reverse hazard rate of plasma growth hormone Octreotide-11 dose is higher than that of plasma growth hormone Octreotide-1 dose and control. Which reveal that the suppression levels of growth hormone is higher when injecting the Octreotide-11 dose comparing with Octreotide-1 dose and control.

V. Conclusions

In the present study, we used Weibull-G exponential distribution model to analyze the plasma growth hormone profiles of female rats. Here we have plotted probability density function, probability survival function, hazard rate functions and reverse hazard rate functions for the selected medical data. The suppression levels of plasma growth hormone profiles of female rats when injecting the control, Octreotide-1 dose and Octreotide-11 dose has been observed. All the plots reveal that the growth hormone suppression levels are high in the female rats when injecting Octreotide-11 dose as compare with the Octreotide-1 dose and control. It is concluded that the Weibull-G exponential distribution model is well fitted to analyze medical data mathematically. It is useful for medical professionals.

References

[1] Banerjee, S., Das, R.K., Shapiro, B.H., 2013. Growth hormone- independent suppression of growth hormone- dependent female isoforms of cytochrome P450 by the somatostain analog octreotide. Vol. 715, pp. 256-261.
[2] Gupta, R. D. and Kundu, D. (2001). Exponentiated exponential family; an alternative to gamma and Weibull. Biometrical journal, Vol. 43, pp. 117-130.
[3] Gupta, R. D. and Kundu, D. (2003). Discriminating between the Weibull and the GE distributions. Computational Statistics and Data Analysis, Vol. 43, pp. 179-196.
[4] Marbach, P., Neufeld, M., Pless, J., 1985. Clinical applications of somatostain analogs. Adv. Exp. Med. Biol. 188, 339-353.
[5] Pampori, N.A., Agrawal, A.K., Shapiro, B.H., 1991. Renaturalizing the sexually dimorphic profiles of circulating growth hormone in hypophysectiomized rats. Acta Endocrinol. 124, 283-289.
[6] Turner, J.p., Tannenbaum, G.S., 1995. In vivo evidence of a positive role for somatostain to optimize pulsatile growth hormone secretion. Am. J. Physiol. Endocrinol. Metab. 269, E683-E690.
[7] Weibull, W. (1951). Wide applicability. Journal of applied mechanics, Vol. 40, pp. 203-210.
[8] Yang, L.P.H., Keating, G.M., 2010. Octreotide long-acting release (LAR): a review of its use in the management of acromegaly. Drugs 70, 1745-1769.

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