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A MATHEMATICAL MODEL FOR THE EFFECTS OF GHRELIN DURING FASTING

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Abstract:

In this paper, we designed a mathematical model using Fuzzy Frechet distribution for the effect of Ghrelin during fasting. Ghrelin is an endogenous ligand of the Growth Hormone (GH) secretagogue receptor and is synthesized in the stomach. As ghrelin administration in man stimulates GH release, while serum ghrelin concentrations are elevated during fasting in man, this increase in ghrelin levels might be another mechanism whereby fasting results in stimulation of GH release. Using this mathematical model, we have shown that mean and variance of ghrelin levels during fasting are followed by similar changes in serum GH concentrations.

Key Words: Fuzzy Frechet Distribution, Weibull Distribution, Ghrelin & Growth Hormone.

1. Introduction:

There are many extensions of the Weibull distribution have been proposed to improve its capability to fit diverse lifetime data. The Frechet distribution has been shown to be useful for modeling and analysis of extreme events like floods, earthquakes, rainfall. Both the Frechet and the Weibull distribution are power transformations of an exponential distributed variate. A detailed discussion on constructing life time distribution discussed by Lai [1]. The maximum likelihood and the least squares estimation of the parameters of the inverse weibull distribution have been discussed by Calabria and Pulcini [2]. Keller [3] used the inverse weibull distribution for reliability analysis of commercial vehicle engines. Models involving two inverse weibull distributions was investigated by Jiang [4]. A generalized inverse weibull distribution by adding another parameter to the standard inverse weibull have been proposed by de Gusmao [5]. In humans, fasting enhances growth hormone (GH) secretion and amplifies GH rhythm [6]. Traditionally hypothalamic GH-releasing hormone and somatostatin release are as the mechanisms whereby somatotroph output is regulated [7]. Ghrelin is an endogenous ligand of the GH secretagogue (GHS) receptor (GHS-R) and was recently isolated from rat and human stomach. Where it is synthesized in a distinct endocrine cell type [8]. The gene for ghrelin encodes a 117 amino acid prepro-ghrelin and is expressed not only in the stomach but also in the hypothalamic arcuate nucleus [9]. Ghrelin exits in at least two forms, an octanoylated and a non-octanoylated form. At present only octanoylated ghrelin is thought to be biologically active [10]. I.v. ghrelin administration stimulates GH secretion through the centrally located GHS-R [11]. Besides this effect on GH secretion a metabolic action of ghrelin is also recognized. In animal studies peripheral ghrelin administration also stimulates food intake, gastric secretion, gastric motility and adiposity [12]. As ghrelin administration in man strongly stimulates GH reliease and, at least in animal studies, ghrelin concentrations are elevated during fasting, an increase in ghrelin concentration is another potential mechanism whereby fasting can stimulate GH release [13].

2. Notations:

τ - Scale Parameter of Frechet distribution

δ - Shale Parameter of Frechet distribution

$\bar{\tau}$ - Fuzzy number for the Scale Parameter of Fuzzy Frechet distribution

$\bar{\delta}$ - Fuzzy number for the Scale Parameter of Fuzzy Frechet distribution

$\overline{\tau[\alpha]}$ - α cut of Scale Parameter

$\overline{\delta[\alpha]}$ - α cut of Shape Parameter

3. Materials and Methods:

3.1 Frechet Distribution: The type-II exteme value distribution is a special case of the generalized extreme value distribution and it is also known as Frechet distribution is equivalent to taking the reciprocal of values from a standard Weibull distribution. The probability density function (PDF) and the cumulative distribution function (CDF) for Frechet distribution is

$g(t;\tau,\delta)=\delta\tau^{\delta}t^{-\delta-1}e^{\left[-\left(\frac{\tau}{t}\right)^{\delta}\right]}$ and $G(t;\tau,\delta)=e^{\left[-\left(\frac{\tau}{t}\right)^{\delta}\right]}$ respectively, where $\tau>0$ is a scale parameter and $\delta>0$ is a shape paramenter, respectively.

Let z be a random variable have the Frechet distribution with parameters τ and δ. For $k<\delta$, the k^{th} ordinary and incomplete moments of z are given by $\mu_k^1=\tau^k\Gamma\left(\frac{\delta-k}{\delta}\right)$ *and* $\varphi_k(t)=\delta^k\gamma\left(\frac{\delta-k}{\delta},\left(\frac{\tau}{t}\right)^{\delta}\right)$, where $\Gamma(a)=\int_0^{\infty}t^{a-1}e^{-t}dt$ is the complete function and $\gamma(a,z)=\int_0^{z}t^{a-1}e^{-t}dt$ is the lower incomplete gamma function.

3.2 Fuzzy Frechet Distribution: The value of the scale and shape parameter will provide us flexibility by changing it into fuzzy parameters. The Fuzzy Frechet distribution is defined by changing the scale and shape parameters of Frechet distribution into fuzzy parameter. The PDF and CDF of the Fuzzy Frechet distribution is $\overline{g}\left(t,\overline{\tau},\overline{\delta}\right)=\overline{\tau}\overline{\delta}^{\overline{\tau}}t^{-\overline{\delta}-1}e^{\left[-\left(\frac{\overline{\tau}}{t}\right)^{\overline{\delta}}\right]}$ and $\overline{G}\left(t,\overline{\tau},\overline{\delta}\right)=e^{\left[-\left(\frac{\overline{\tau}}{t}\right)^{\overline{\delta}}\right]}$ respectively, the k^{th} ordinary moment of the Fuzzy Frechet distribution is $\overline{\mu}_k^1=\overline{\tau}^{-k}\Gamma\left(\frac{\overline{\delta}-k}{\overline{\delta}}\right)$.

The mean and variance for the Fuzzy Frechet distribution is

$$\overline{m}=\overline{\tau}\Gamma\left(\frac{\overline{\delta}-1}{\overline{\delta}}\right) \text{ and } \overline{v}=\overline{\tau}^{2}\Gamma\left(\frac{\overline{\delta}-2}{\overline{\delta}}\right)-\left[\overline{\tau}\Gamma\left(\frac{\overline{\delta}-1}{\overline{\delta}}\right)\right]^2.$$

The corresponding alpha cut of the mean and variance for the Fuzzy Frechet distribution is given by

$$m_u[\alpha]=\max\left\{\overline{\tau}\Gamma\left(\frac{\overline{\delta}-1}{\overline{\delta}}\right)\right\},\ m_l[\alpha]=\min\left\{\overline{\tau}\Gamma\left(\frac{\overline{\delta}-1}{\overline{\delta}}\right)\right\} \text{ and}$$

$$v_u[\alpha]=\max\left\{\overline{\tau}^{2}\Gamma\left(\frac{\overline{\delta}-2}{\overline{\delta}}\right)-\left[\overline{\tau}\Gamma\left(\frac{\overline{\delta}-1}{\overline{\delta}}\right)\right]^2\right\},\ v_l[\alpha]=\min\left\{\overline{\tau}^{2}\Gamma\left(\frac{\overline{\delta}-2}{\overline{\delta}}\right)-\left[\overline{\tau}\Gamma\left(\frac{\overline{\delta}-1}{\overline{\delta}}\right)\right]^2\right\}$$

4. Results and Discussion:

In the present study we have taken that the possible role of ghrelin in the mechanism whereby fasting leads to somatotroph hyperactivity, the effects of fasting on GH and ghrelin concentrations which was discussed by Alex F Muller et al[14]. Ten healthy male subjects (mean(S.D.) age, 23.4±2.7 years; range 20-28) with a normal body weight (mean(S.D.) body mass index, 21.8±1.8kg/m^2 ; range 19.7- 25.8)were asked to participate. None of the subjects had a relevant medical history or used medication. The local ethical committee approved the study and all subjects gave written informed consent. It should be noted that the GH values obtained with this method are approximately 50% of those obtained by conventional RIA methods. The inte-assay coefficient of variation values were 4.1% at 4.0µg/I and 3.8% at 20µg/I. The intra-assay coefficient of variation values were 3.4% at 0.25µg/I, 1.9% at 2.5µg/I and 4.5% at 25µg/I. Fasting rapidly induced a diurnal ghrelin and GH rhythm in Fig.1 that was not seen in the fed state(data not shown).

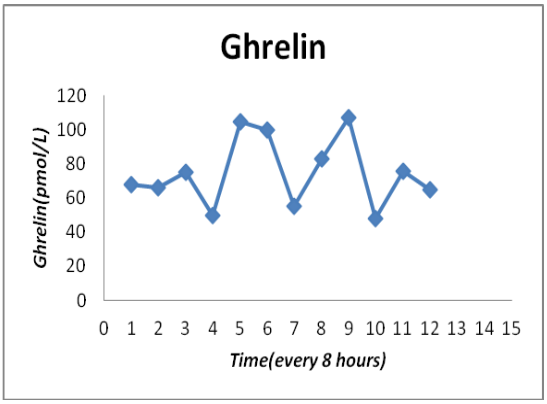

Figure 4.1: Ghrelin Concentration During Fasting

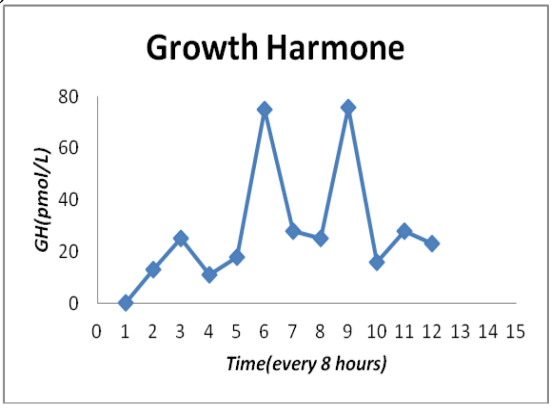

Figure 4.1: GH Concentration During Fasting

The shape and scale parameters for the Ghrelin concentration are 3.8893 and 61.376, their corresponding Fuzzy triangular numbers are given by (3.3893, 3.8893, 4.3893) and (58.376, 61.376, 64.376). The alpha cut for the shape and scale parameters are given by

$$\overline{\tau[\alpha]} = (3.3893 - 0.5\alpha,\ 4.3893 + 0.5\alpha) \text{ and } \overline{\delta[\alpha]} = (58.376 - 3\alpha,\ 64.376 + 3\alpha).$$

The shape and scale parameters for the GH concentration are 2.1319 and 19.183, their corresponding Fuzzy triangular numbers are given by (2.0819, 2.1319, 2.1819) and (16.183, 19.183, 22.183). The alpha cut for the shape and scale parameters are given by

$$\overline{\tau[\alpha]} = (2.0819 - 0.05\alpha,\ 2.1819 + 0.05\alpha) \text{ and } \overline{\delta[\alpha]} = (19.183 - 3\alpha,\ 22.183 + 3\alpha).$$

Table 4.1: Shows the Alpha cut values of Ghrelin concentration using Fuzzy Frechet distribution

α	$m_l[\alpha]$	$m_u[\alpha]$	$v_l[\alpha]$	$v_u[\alpha]$
0	75.321	77.058	1698.833	826.210
0.1	75.337	77.213	1785.368	804.447
0.2	75.367	77.373	1879.954	783.745
0.3	75.412	77.537	1983.677	764.034
0.4	75.474	77.705	2097.813	745.248
0.5	75.555	77.876	2223.878	727.328
0.6	75.654	78.052	2363.682	710.217
0.7	75.775	78.230	2519.404	693.867
0.8	75.918	78.413	2693.687	678.229
0.9	76.085	78.598	2889.767	663.261
1	76.278	78.787	3111.642	648.924

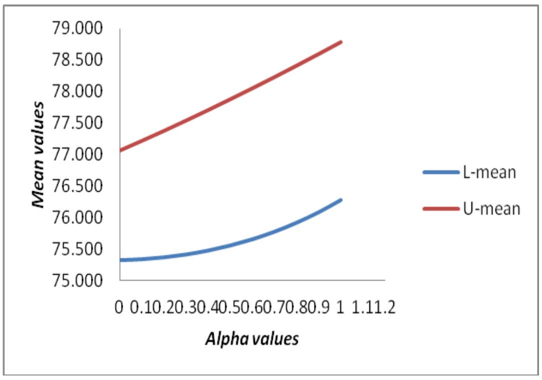

Figure 4.1: Mean alpha cut values of Ghrelin concentration

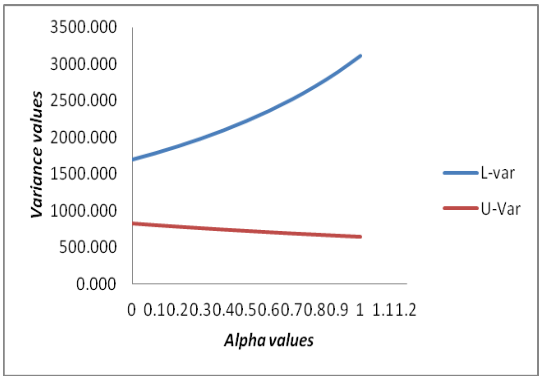

Figure 4.2: Variance alpha cut values of Ghrelin concentration

Table 4.2: Shows the Alpha cut values of GH concentration using Fuzzy Frechet distribution

α	$m_l[\alpha]$	$m_u[\alpha]$	$v_l[\alpha]$	$v_u[\alpha]$
0	27.623	36.377	5752.893	4332.986
0.1	27.169	36.801	5938.396	4308.228
0.2	26.714	37.223	6151.738	4285.277
0.3	26.258	37.645	6399.203	4263.989
0.4	25.799	38.065	6689.106	4244.232
0.5	25.339	38.484	7032.688	4225.887
0.6	24.878	38.901	7445.519	4208.848
0.7	24.414	39.318	7949.815	4193.017
0.8	23.949	39.734	8578.396	4178.306
0.9	23.481	40.148	9381.872	4164.636
1	23.012	40.562	10442.587	4151.931

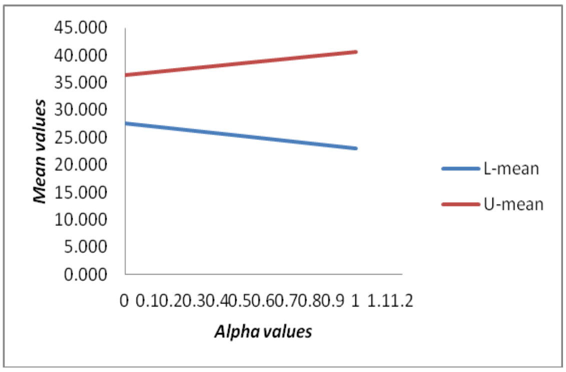

Figure 4.3: Mean alpha cut values of GH Concentration

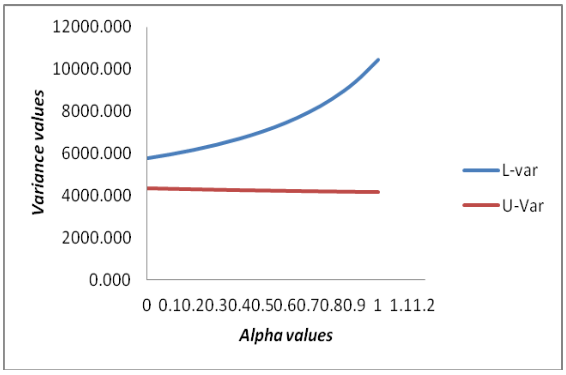

Figure 4.4: Variance alpha cut values of GH Concentration

5. Conclusion:

The changes in serum ghrelin levels during fasting are followed by similar changes in serum GH concentrations, indicating that ghrelin is the driving force of increased GH secretion during fasting is shown by using the alpha cut values of mean and variance of Fuzzy Frechet distribution.

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