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A NEW STOCHASTIC MODEL TO ESTIMATE THE CONCENTRATION OF INSULIN USING WEIBULL DISTRIBUTION

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Abstract:

The present study reveals that more quantitative approach to the measurement of insulin secretion in normal and obese volunteers. This quantitative approach involves the application of a two-compartment model to the analysis of peripheral C-peptide concentrations and the use of individual kinetic parameters of C-peptide, allows the secretion rate of insulin to be accurately quantities even under non-steady state conditions. In this paper, we estimate the concentration of insulin by using stochastic methods with the help of Weibull distribution.

Key Words: Insulin Secretion, Exponential Distribution, Bivariate Distribution & Weibull Distribution

1. Introduction:

The pancreatic insulin secretion rates were derived from peripheral concentrations of C-peptide using a two-compartment model of C-peptide kinetics [1-2], which we have previously validated in human experiments [4]. The use of this technique allowed us to compare insulin secretion in a group of normal weight and obese subjects under basal conditions, during 24-h sampling on a mixed diet and during a hyperglycemic clamp. Basal hepatic insulin extraction was calculated and the relationship between the insulin secretory rate and peripheral insulin concentrations was explored.

Exponential distributions play a central role in analyses of lifetime or survival data, in part because of their convenient statistical theory, their important 'lack of memory' property and their constant hazard rates. In circumstances where the one-parameter family of exponential distributions is not sufficiently broad, a number of wider families such as the Gamma, Weibull and Gompertz Makeham distributions are in common use; these families and their usefulness are described by Cox & Oakes more complete treatments of each distribution are given by [13]. By various methods, new parameters can be introduced to expand families of distributions o for added flexibility or to construct covariate models. Introduction of a scale parameter leads to the accelerated life model, and taking powers of the survival function introduces a parameter that leads to the proportional hazards model. For instance, the family of Weibull distributions contains the exponential distributions and is constructed by taking powers of exponentially distributed random variables. The family of gamma distributions also contains the exponential distributions, and is constructed by taking powers of the Laplace transform [9]. In this paper, another general method of introducing a parameter into a family of distributions is discussed. In particular, starting with a survival function $\bar{F}$, the one-parameter family of survival functions

$$\bar{G}(x;\gamma) = \frac{\gamma \bar{F}(x)}{1-\bar{\gamma}\bar{F}(x)} = \frac{\gamma \bar{F}(x)}{F(x)+\gamma \bar{F}(x)} \quad (0 < x < \infty, 0 < \gamma < \infty) \tag{1}$$

Where $\bar{\gamma} = 1 - \gamma$, is proposed and discussed in section 3. Note that, when $\gamma = 1$, $\bar{G} = \bar{F}$. The particular case that F is an exponential distribution yields a new two-parameter family of distributions which may sometimes be a competitor to the Weibull and gamma families. In this paper, we estimate the concentration of insulin by using stochastic methods with the help of Weibull distribution.

2. Notations:

γ – Scale Parameter
η – Shape Parameter
x – Time
λ – Scale Parameter
r – Hazard Rate
σ^2 – Variance of X
μ – Expectation of X

3. Density and Hazard Rate of the New Family:

Whenever F has a density, the survival function $\bar{G}$ is given by (1) have easily-computed densities. In particular, if F has a density f and hazard rate r_F then G has the density g given by $g(x;\gamma) = \frac{\gamma f(x)}{\{1-\bar{\gamma}\bar{F}(x)\}^2}$ (2)

And hazard rate

$$r(x;\gamma) = \frac{1}{\{1-\bar{\gamma}\bar{F}(x)\}} r_F(x) \quad (0 < x < \infty) \tag{3}$$

Thus

$$\lim_{x\to 0} r(x;\gamma) = \lim_{x\to 0} r_F(x)/\gamma, \quad \lim_{x\to\infty} r(x;\gamma) = \lim_{x\to\infty} r_F(x)$$

It follows from (3) that

$$r_F(x)/\gamma \le r(x;\gamma) \le r_F(x) \quad (0 < x < \infty, \gamma \ge 1) \tag{4}$$

$$r_F(x) \le r(x;\gamma) \le r_F(x)/\gamma \quad (0 < x < \infty, 0 < \gamma \le 1) \tag{5}$$

$$\bar{F}(x) \le \bar{G}(x;\gamma) \le \bar{F}^{1/\gamma}(x) (0 < x < \infty, \gamma \ge 1) \tag{6}$$

$$\bar{F}^{1/\gamma}(x) \le \bar{G}(x;\gamma) \le \bar{F}(x) (0 < x < \infty, 0 < \gamma \le 1) \tag{7}$$

Note also from (3) that $r(x;\gamma)/r_F(x)$ is increasing in x for $\gamma \ge 1$ and decreasing in x for $0 < \gamma \le 1$. When $F(0) = 0$, the hazard rate $r(0;\gamma)$ at the origin behaves quite differently than it does for the Weibull or gamma distributions; for both these families, the distribution can be an exponential distribution, or $r(0) = 0$, or $r(0) = \infty$, so that $r(0)$ is discontinuous in the shape parameter [8]. Such is not the case with the family having hazard rates (3), so the family may be useful to 'fine tune' the distribution F. However, in spite of (4-7), it need not be that F and G are at all similar [7].

4. A New Family Containing the Exponential Distributions:

When $\bar{F}(x) = \exp(-\lambda x)$, the two-parameter family

$$\bar{G}(x;\gamma,\lambda) = \frac{1}{e^{\lambda x} - \bar{\gamma}} \quad (x > 0, \lambda > 0, \gamma > 0) \tag{8}$$

is obtained from (1). The case $\gamma = 1$ is the exponential distribution. For $\gamma \ge 1$, this distribution is the conditional distribution, given $Z > 0$, of a random variable Z with the logistic survival function $P(Z > z) = \gamma/(1 - \bar{\gamma}e^{\lambda z})$ for $0 < z < \infty$. As special cases of (2) and (3), it follows that G has the density g given by

$$g(x;\gamma,\lambda) = \frac{\gamma\,\lambda e^{-\lambda x}}{(1-\bar{\gamma}e^{-\lambda x})^2} = \frac{\gamma\,\lambda e^{\lambda x}}{(e^{\lambda x}-\bar{\gamma})^2} \quad (x > 0, \lambda > 0, \gamma > 0)$$

And hazard rate

$$r(x;\gamma,\lambda) = \frac{\lambda}{1-\bar{\gamma}e^{-\lambda x}} = \frac{\lambda e^{\lambda x}}{e^{\lambda x}-\bar{\gamma}} \quad (x > 0, \lambda > 0, \gamma > 0)\,.$$

Note that $r(x;1,\lambda)=\lambda$, that $r(x;\gamma,\lambda)$ is decreasing in x for $0<\gamma\leq 1$, and that $r(x;\gamma,\lambda)$ is increasing in x for $\gamma\geq 1$. From (4-7) it follows that

$$\lambda/\gamma \leq r(x;\gamma,\lambda)\leq \lambda \quad (0<x<\infty, \gamma\geq 1),$$
$$\lambda \leq r(x;\gamma,\lambda)\leq \lambda/\gamma \ (0<x<\infty,\ 0\leq\gamma\leq 1),$$
$$e^{-\lambda x} \leq \bar{G}(x;\gamma,\lambda)\leq e^{-\lambda x/\gamma} \quad (0<x<\infty, \gamma\geq 1), \qquad (9)$$
$$e^{-\lambda x/\gamma} \leq \bar{G}(x;\gamma,\lambda)\leq e^{-\lambda x} \quad (0<x<\infty, 0\leq\gamma\leq 1) \qquad (10)$$

Since distributions with an increasing (decreasing) hazard rate are 'new better (worse) than used', it follows that, when X has the distribution G, the conditional survival function satisfies

$$\mathrm{pr}(X>x+t/X>x)\begin{cases}\leq \mathrm{pr}(X>t) & (\gamma\geq 1),\\ \geq \mathrm{pr}(X>t) & (0<\gamma\leq 1).\end{cases}$$

Proposition:

The function $\log \mathrm{g}(.;\gamma,\lambda)$ is convex for $0<\gamma\leq 1$ and concave for $\gamma\geq 1$. This result is readily verified by differentiating $\log \mathrm{g}(x;\gamma,\lambda)$ with respect to x. Of course, this means that, for $\gamma\leq 1$, g is decreasing and, for $\gamma\geq 1$, $\mathrm{g}(.;\gamma,\lambda)$ is unimodal, with

$$mode(X)=\begin{cases}0 & (\gamma\leq 2),\\ \lambda^{-1}\log(\gamma-1) & (\gamma\geq 2).\end{cases}$$

It follows from (9-10) that G has finite moments of all positive orders. Direct computation shows that, if X has distribution G, then

$$E(X)=-\frac{\gamma\log\gamma}{\lambda\bar{\gamma}} \qquad (10^*)$$

Note that this quantity is always positive. More generally,

$$E(X^r)=r\int_0^\infty \bar{G}(x;\gamma,\lambda)\,x^{r-1}dx=\frac{r\gamma}{\lambda^r}\int_0^1\left\{\frac{(-\log y)^{r-1}}{1-\bar{\gamma}y}\right\}dy \qquad (11)$$

Which, for $r=1$, yields (10*). The Laplace transform of g is given by

$$E\left(e^{-s\lambda X}\right)=\int_0^1\{\gamma y^s/(1-\bar{\gamma}y)^2\}dy \qquad (12)$$

Both (11) and (12) can be expressed as infinite series when $|\bar{\gamma}|\leq 1$. Then, the integrands of (11) and (12) can be expanded in a power series and the result integrated term by term to yield

$$E(X^r)=\frac{r\gamma}{\lambda^r}\int_0^\infty x^{r-1}e^{-x}\sum_{j=0}^\infty \bar{\gamma}^j e^{-jx}\,dx=\frac{r\gamma}{\lambda^r}\sum_{j=0}^\infty\frac{\bar{\gamma}^j\Gamma(r)}{(j+1)^r}\quad(|\bar{\gamma}|\leq 1),$$
$$E(e^{-sX})=\gamma\int_0^1 y^s\sum_{j=0}^\infty (j+1)y^j\bar{\gamma}^j\,dy=\gamma\sum_{j=0}^\infty\bar{\gamma}^j\,\frac{j+1}{s+j+1}\ (|\bar{\gamma}|\leq 1) \qquad (13)$$

As a consequence of Proposition, total positivity properties yield moment inequalities which are not true in general. In particular, the coefficient of variation σ/μ is less than 1 for $\gamma>1$ and is greater than 1 for $\gamma<1$: here, σ^2 is the variance and μ is the expectation of X. It is straightforward to show that the qth quantile x_q of G is given by

$$x_q=\frac{1}{\lambda}\log\left(\frac{\bar{q}+\alpha q}{\bar{q}}\right).$$

In particular, $\mathrm{med}(X)=\{\log(1+\gamma)\}/\lambda$. It is easy to see that $\mathrm{med}(X)$, $\mathrm{mode}(X)$ and $E(X)$ are all increasing in γ and decreasing in the scale parameter λ. From the monotonicity of $\log x$ and the fact that $\log x\leq x-1$ $(x>0)$, it follows that

$$\mathrm{mode}(X)\leq \mathrm{med}(X)\leq \gamma/\lambda\leq E(X),$$

but notice that $\lim_{\gamma\to\infty}\mathrm{mode}(X)/E(X)=1$.

If $E(X)$ is fixed, say $E(X)=1$, then the weak limit of $\bar{G}$ as γ tends to infinity is degenerate at 1, and the limit as γ tends to 0 is degenerate at 0. Notice also that $\lim_{\gamma\to\infty} r(x;\gamma,\lambda)=\lambda$ is bounded and continuous in the parameters, like the gamma distribution but unlike the Weibull distribution [6].

5. Extended Weibull Distributions:

When $\bar{F}(x)=\exp\{-(\lambda x)^\eta\}\quad(x\geq 0,\eta>0)$ (14)

is a Weibull survival function, the (1) yields the new three-parameter survival function

$$\bar{G}(x;\gamma,\lambda,\eta) = \frac{\gamma \exp\{-(\lambda x)^{\eta}\}}{1-\bar{\gamma}\exp\{-(\lambda x)^{\eta}\}} \quad (15)$$

This geometric-extreme stable extension of the Weibull distribution may sometimes be a competitor to the more usual three-parameter Weibull distribution with survival function

$$\bar{F}(x;\lambda,\eta,\delta) = \exp\{-\lambda(x-\delta)\}^{\eta} \quad (x \geq \delta;\ \lambda,\eta \geq 0, 0 < \delta < \infty).$$

If X has an exponential distribution with parameter 1, then $X^{1/\eta}/\lambda$ has the survival function (14). Similarly, if X has the survival function (8) with $\lambda = 1$, then $X^{1/\eta}/\lambda$ has the survival function (15). As a result, moments of (15) can be obtained from non-integer moments of (8). Thus, from (13), it follows that, if X has the survival function (15), then

$$E(X^s) = \frac{s\gamma}{\eta}\sum_{j=0}^{\infty}\frac{\bar{\gamma}^j}{(j+1)^{\frac{s}{\eta}}}\Gamma(s/\eta)\ (|\bar{\gamma}| \leq 1) \quad (16)$$

When $|\bar{\gamma}| > 1$, the moments can be obtained from (11) **w**ith the same change of variable used above to obtain (16). However, those moments cannot be given in closed form; thus, even the first moment of (15) must be obtained numerically. By writing

$$E(X^s) = \int_0^{\infty} s x^{s-1}\bar{F}(x)\,dx \quad (s > 0),$$

It can be shown that $\lim_{\beta\to\infty} E(X^s) = \lambda^s\ (s > 0)$. Of course, these are just the moments of a random variable degenerate at $1/\lambda$. The density and hazard rate of the distribution given by (15) can be obtained directly from (2) and (3). In particular, the hazard rate is

$$r(x;\gamma,\lambda,\eta) = \lambda\eta(\lambda x)^{\eta-1}/[1-\bar{\gamma}\exp\{-(\lambda x)^{\eta}\}] \quad (17)$$

This function is graphed in Fig. 2. It can be verified using elementary calculus that this hazard is increasing if $\gamma \geq 1, \eta \geq 1$ and decreasing if $\gamma \leq 1, \eta \leq 1$. If $\eta > 1$, then the hazard rate is initially increasing and eventually increasing, but there may be one interval where it decreasing. Similarly, if $\eta < 1$, then the hazard rate is initially decreasing and eventually decreasing, but there may be one interval where it is increasing; here, the slope changes are subtle and hard to see graphically [7].

6. Example:

Studies were performed in 14 normal volunteers and 15 obese subjects who did not have a personal or family history of diabetes. The normal and obese groups were well matched for age (38.5±3.7 vs. 35.8±2.8 yr, P <0.001) and sex (7 male, 7 female vs. 10 female, 5 male) and differed significantly only in parameters of obesity, namely weight (70.1 vs. 105.7±6.6 kg P <0.001) body mass index (23.0±0.5 vs. 37.0±1.9 kg/m^2, P <0.001), and percent ideal body weight (102.6±2.5 vs. 167.5±8.6%, P <0.001) [3], [5] & [10-12].

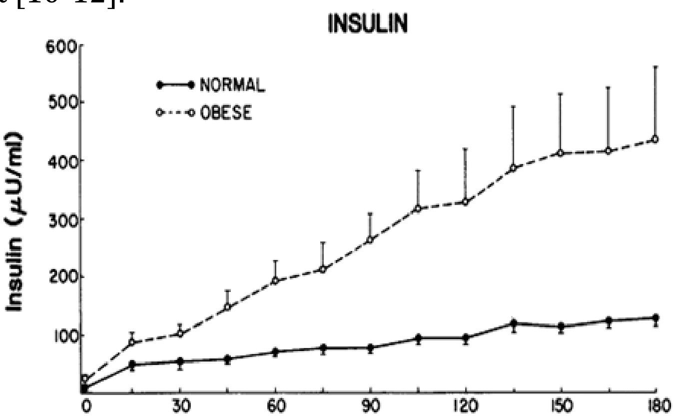

Figure (1): Concentration of insulin secretion rates measured during the hyperglycemic clamp in the normal and obese subjects.

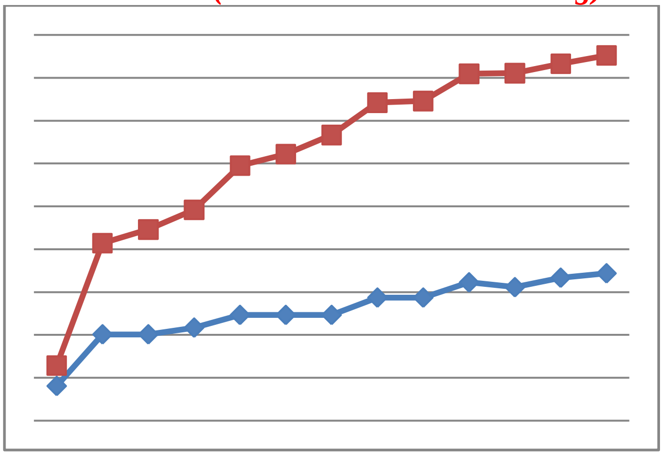

Figure (2): Concentration of insulin secretion rates measured during the hyperglycemic clamp in the normal and obese subjects using weibull distribution.

7. Conclusion:

The study asserts that insulin secretion is increased in obesity under basal conditions, over a 24-h period on a mixed diet and in response to intravenous glucose. A highly significant linear relationship was found between both basal and 24-h insulin secretion and body mass index, which indicated that insulin secretion increases as the degree of obesity increases. There is no significance difference between medical and mathematical reports. The medical reports are beautifully fitted with the mathematical model. Hence the mathematical report {Figure (2)} is coinciding with the medical report {Figure (1)}. At the completion of the reliability growth test, it concludes that from {Figure (2)}, the results coincide with the medical findings.

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