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A FUZZY MATHEMATICAL MODEL FOR THE SECRETION OF THYROID STIMULATING HORMONE

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ABSTRACT

Modelling through mathematics is becoming an increasingly valuable tool for medical field. A mathematical model using fuzzy shock was developed and used this model to calculate the fuzzy expected time and variance of Thyroid stimulating hormone in the given time interval. The theoretical study of the effect of Thyroid stimulating hormone in autoimmune thyroiditis with severe hypothyroidism resistant patients was investigated. The suitable disease of Thyroid stimulating hormone in response to increasing thyroxine level showed that if the intake of thyroxine would be suitable, the patient might attain the thyroid level.

Keywords: *Thyroid stimulating hormone, Rayleigh distribution, shock model.*

2010 Mathematics Subject Classification: *97Mxx, 93A30, 60A86.*

1. INTRODUCTION

Mathematical models are of broad use in physics, operations research, life science, management engineering and other disciplines. Models should be made for particular goals with clear assumptions. Hear we consider systems subject to shocks that occur randomly in time. Shock models have been studied by various authors and provide a realistic and sensible formulation for modeling certain reliability systems in a random environment. Several of the models are physically motivated. Shock models in system reliability are usually defined by the time between two consecutive shocks, the damage caused by a shock, the system failure and the undecided state relationship among the above elements [2, 7 & 10]. Consider a system subjected to shocks occurring randomly in time. Each shock causes damage and the damage accumulates. The system fails when the total accumulated damage exceeds a certain threshold level [3,5 6, & 9].

The pituitary glandis produced Thyroid stimulating hormone (TSH) [1] and its role is to control the production of hormones by the thyroid gland. Thyroid stimulating hormone is produced and released into the bloodstream by the pituitary gland. Thyroxine and triiodothyronine are important to maintaining the body's metabolic rate, heart and digestive functions, muscle control, brain development and maintenance of bones [1, 4]. These hormones have a negative effect on the pituitary gland and stop the production of thyroid stimulating hormone if the levels of thyroxine and tri iodothyronine are too high;

(i) If a person has too much, this may indicate that their thyroid gland is not making enough thyroid hormone.
(ii) If a person has too little thyroid stimulating hormone, it is most likely that their thyroid gland is making too much thyroid hormone.

2. FUZZY MATHEMATICAL MODEL

The two-parameter [4, 9] generalized Rayleigh distribution has the cumulative distribution function

$$F(x; \alpha, \lambda) = [1- e^{-\lambda x^2}]^{\alpha}; \qquad x > 0;$$

and the corresponding probability density function is

$$f(x; \alpha, \lambda) = 2\alpha\lambda x e^{-\lambda x^2}[1 - e^{-\lambda x^2}]^{\alpha-1}; \qquad x > 0;$$

A three-parameter generalized Rayleigh distribution can be obtained from a two-parameter generalized Rayleigh distribution by introducing the location or threshold parameter β. Therefore, for $\alpha > 0$, $\lambda > 0$ and $-\infty < \beta < \infty$, a three-parameter generalized Rayleigh distribution has the cumulative distribution function

$$F(x; \alpha, \lambda, \beta) = [1- e^{-(x-\beta)^2}]^{\alpha} \qquad x > \beta; \alpha, \lambda > 0;$$

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Here $\alpha > 0$ and $\lambda > 0$ are the shape and scale parameters, respectively and the corresponding probability density function is

$$f(x;\alpha,\lambda,\beta) = 2\alpha\lambda\,(x-\beta)e^{-\lambda(x-\beta)^2}[1-e^{-\lambda(x-\beta)^2}]^{\alpha-1};$$

Assume that shocks occur randomly in time in accordance with a three parameter generalized Rayleigh distribution. Taking the shape parameter as $\alpha = 1$ and the corresponding mean and variance becomes

$$E(T) = \frac{\lambda^2+\beta^2+2\beta^2\lambda+2\beta^3+\beta^3\lambda+2\lambda^2\beta^3+\beta^4+2\beta^4\lambda}{c[\beta^2+2\lambda^2\beta^3-2\beta^3+2\beta^3\lambda+\beta^4]}$$

$$V(T) = \frac{[\lambda^2+\beta^2+2\beta^2\lambda+2\beta^3+\beta^3\lambda+2\lambda^2\beta^3+\beta^4+2\beta^4\lambda]^2}{C^2[\beta^2+2\lambda^2\beta^3-2\beta^3+2\beta^3\lambda+\beta^4]^2}$$

The alpha cut of fuzzy mean life time is $\overline{E}(T) = [\overline{E}_l(T), \overline{E}_u(T)]$, where

$$\overline{E}_l(T) = \min\left\{\frac{\overline{\lambda}^2+\overline{\beta}^2+2\overline{\beta}^2\overline{\lambda}+2\overline{\beta}^3+\overline{\beta}^3\overline{\lambda}+2\overline{\lambda}^2\overline{\beta}^3+\overline{\beta}^4+2\overline{\beta}^4\overline{\lambda}}{c[\overline{\beta}^2+2\overline{\lambda}^2\overline{\beta}^3-2\overline{\beta}^3+2\overline{\beta}^3\overline{\lambda}+\overline{\beta}^4]},\ \overline{\lambda}\in\overline{\lambda}[\alpha], \overline{\beta}\in\overline{\beta}[\alpha]\right\}$$

$$\overline{E}_u(T) = \max\left\{\frac{\overline{\lambda}^2+\overline{\beta}^2+2\overline{\beta}^2\overline{\lambda}+2\overline{\beta}^3+\overline{\beta}^3\overline{\lambda}+2\overline{\lambda}^2\overline{\beta}^3+\overline{\beta}^4+2\overline{\beta}^4\overline{\lambda}}{c[\overline{\beta}^2+2\overline{\lambda}^2\overline{\beta}^3-2\overline{\beta}^3+2\overline{\beta}^3\overline{\lambda}+\overline{\beta}^4]},\overline{\lambda}\in\overline{\lambda}[\alpha], \overline{\beta}\in\overline{\beta}[\alpha]\right\}$$

The alpha cut of fuzzy variance is $\overline{V}(T) = [\overline{V}_l(T),\ \overline{V}_u(T)]$

Where $$\overline{V}_l(T) = \min\left\{\frac{[\overline{\lambda}^2+\overline{\beta}^2+2\overline{\beta}^2\overline{\lambda}+2\overline{\beta}^3+\overline{\beta}^3\overline{\lambda}+2\overline{\lambda}^2\overline{\beta}^3+\overline{\beta}^4+2\overline{\beta}^4\overline{\lambda}]^2}{c^2[\overline{\beta}^2+2\overline{\lambda}^2\overline{\beta}^3-2\overline{\beta}^3+2\overline{\beta}^3\overline{\lambda}+\overline{\beta}^4]^2},\overline{\lambda}\in\overline{\lambda}[\alpha], \overline{\beta}\in\overline{\beta}[\alpha]\right\}$$

$$\overline{V}_u(T) = \max\left\{\frac{[\overline{\lambda}^2+\overline{\beta}^2+2\overline{\beta}^2\overline{\lambda}+2\overline{\beta}^3+\overline{\beta}^3\overline{\lambda}+2\overline{\lambda}^2\overline{\beta}^3+\overline{\beta}^4+2\overline{\beta}^4\overline{\lambda}]^2}{c^2[\overline{\beta}^2+2\overline{\lambda}^2\overline{\beta}^3-2\overline{\beta}^3+2\overline{\beta}^3\overline{\lambda}+\overline{\beta}^4]^2},\overline{\lambda}\in\overline{\lambda}[\alpha], \overline{\beta}\in\overline{\beta}[\alpha]\right\}$$

3. APPLICATION

A female patient [4, 8 &11] suffered in 42th year from autoimmune thyroiditis resulting in severe hypothyroidism. She was treated for several years by district physician with the dose of 150 µg L-thyroxine daily. Since the level of TSH was repeatedly very high and no improvement of clinical signs has been observed, she was referred to the Medical Faculty Hospital. Thyroid ultrasound showed remarkable diffuse hypoechogenicity, thyroid scintigraphy showed enlarged thyroid with low ^{99m}Tc uptake, TRH test was normal, thin needle biopsy supported autoimmune thyroiditis. X-ray examination showed normal sellaturcica and no changes in the pituitary were observed with computer tomogram- phy. In spite of increasing the dose of peroral L-thyroxine to 300 µg/d and later to 500 µg/d the clinical status and TSH level did not improve. The patient was originally suspected from malabsorption of thyroxine. However, the test with a large single peroral dose (1000 µg) of L-thyroxine showed a rapid decrease of TSH level (from 126 to 75 mU/l) and increase of total T_4 level (from 18 to 64 nmol/l) within 4 hr. Later the patient has been treated with intravenous L-thyroxine (500 µg every 3-4 days for 4 weeks) which resulted in the decrease of TSH level to 10 mU/l and increase of T_4 level to 80-100 nmol/l.

After that it was concluded that the problem is a poor compliance of the patient who apparently does not actually take the medication, although she always claimed that she is doing so. Referring to some similar cases described in the literature the case was classified as thyroxine pseudomalab- sorption. In spite that this problem has been explained to her and her relatives, she refused to take any medication and is consistently neglecting all invitations to further examinations.

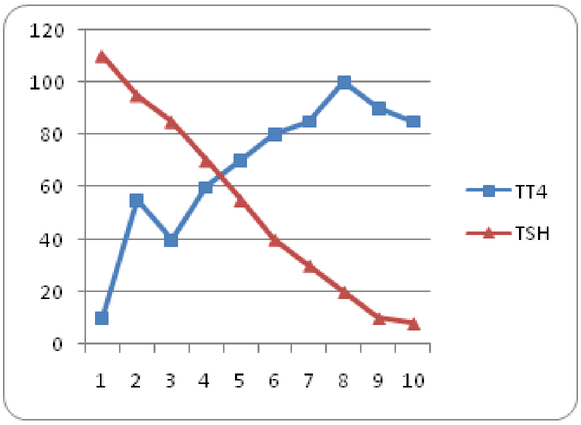

Fig: 3.1. *Serum levels of total thyroxine (TT_4) and TSH level during 24 hours afterperoral administration of powdered tablets containing L-thyroxine.*

The scale parameter of exponential distribution for the TSH response to the higher TT_4 and the triangular fuzzy number is

$$\overline{\lambda}[\alpha]=[59,59.19,60]$$

$$\overline{\beta}[\alpha]=[1,1.21,2]$$

and the corresponding α cuts are

$$\overline{\lambda}[\alpha]=[59+0.19\alpha,\ 60-.0.81\alpha]$$

$$\overline{\beta}[\alpha]=[1+0.21\alpha,\ 2-.0.79\alpha]$$

Under the alpha cut zero, the fuzzy expected value for the autoimmune thyroiditis response to the higher TT_4 doses for various c values are calculated from $\overline{E}(T) = [\overline{E}_l(T),\ \overline{E}_u(T)]$ and shown in Table: 3.1. Also the fuzzy variances are calculated from $\overline{V}(T) = [\overline{V}_l(T),\ \overline{V}_u(T)]$ and shown in Table: 3.2. The mean and variance for the various c values are shown in Fig. 3.2(a), 3.2(b) and Fig. 3.3(a), 3.3(b) respectively.

***Table: 3.1.** Mean of autoimmune thyroiditisat various c values.*

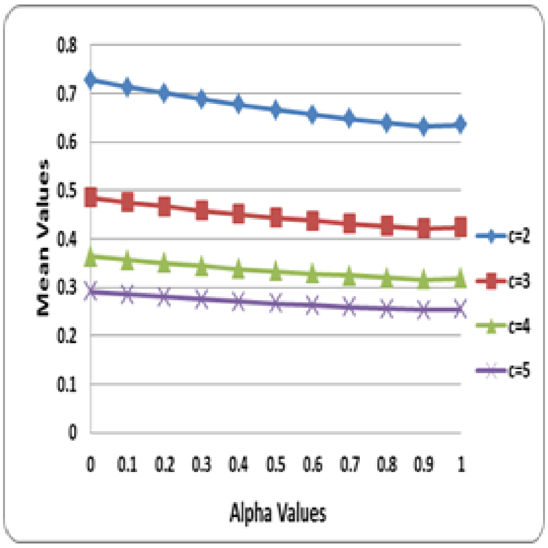

***Fig: 3.2(a).** Lower α cut from the mean*

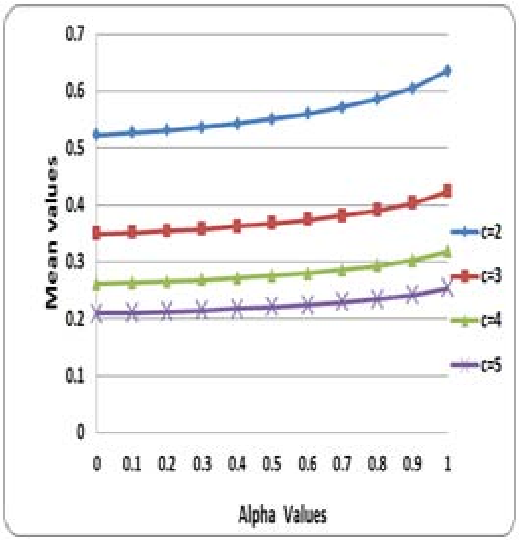

***Fig: 3.2(b).** Upper α cut from the mean*

α	c=2		c=3		c=4		c=5	
	$\overline{V}_L(T)$	$\overline{V}_U(T)$	$\overline{V}_L(T)$	$\overline{V}_U(T)$	$\overline{V}_L(T)$	$\overline{V}_U(T)$	$\overline{V}_L(T)$	$\overline{V}_U(T)$
0	0.363681	0.261275	0.161636	0.116122	0.09092	0.065319	0.058189	0.041804
0.1	0.356568	0.263197	0.158475	0.116976	0.089142	0.065799	0.057051	0.042112
0.2	0.350015	0.265462	0.155562	0.117983	0.087504	0.066366	0.056002	0.042474
0.3	0.343969	0.268151	0.152875	0.119178	0.085992	0.067038	0.055035	0.042904
0.4	0.338381	0.271367	0.150392	0.120608	0.084595	0.067842	0.054141	0.043419
0.5	0.33321	0.275247	0.148093	0.122332	0.083302	0.068812	0.053314	0.04404
0.6	0.328416	0.279971	0.145963	0.124432	0.082104	0.069993	0.052547	0.044795
0.7	0.323967	0.285781	0.143985	0.127014	0.080992	0.071445	0.051835	0.045725
0.8	0.319832	0.293009	0.142147	0.130226	0.079958	0.073252	0.051173	0.046881
0.9	0.315983	0.302115	0.140437	0.134273	0.078996	0.075529	0.050557	0.048338
1	0.317723	0.317794	0.14121	0.141242	0.079431	0.079449	0.050836	0.050847

α	c=2		c=3		c=4		c=5	
	$\bar{V}_L(T)$	$\bar{V}_U(T)$	$\bar{V}_L(T)$	$\bar{V}_U(T)$	$\bar{V}_L(T)$	$\bar{V}_U(T)$	$\bar{V}_L(T)$	$\bar{V}_U(T)$
0	0.363681	0.261275	0.161636	0.116122	0.09092	0.065319	0.058189	0.041804
0.1	0.356568	0.263197	0.158475	0.116976	0.089142	0.065799	0.057051	0.042112
0.2	0.350015	0.265462	0.155562	0.117983	0.087504	0.066366	0.056002	0.042474
0.3	0.343969	0.268151	0.152875	0.119178	0.085992	0.067038	0.055035	0.042904
0.4	0.338381	0.271367	0.150392	0.120608	0.084595	0.067842	0.054141	0.043419
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0.7	0.323967	0.285781	0.143985	0.127014	0.080992	0.071445	0.051835	0.045725
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0.9	0.315983	0.302115	0.140437	0.134273	0.078996	0.075529	0.050557	0.048338
1	0.317723	0.317794	0.14121	0.141242	0.079431	0.079449	0.050836	0.050847

Table: 3.2. *Variance of autoimmune thyroiditis at various c values.*

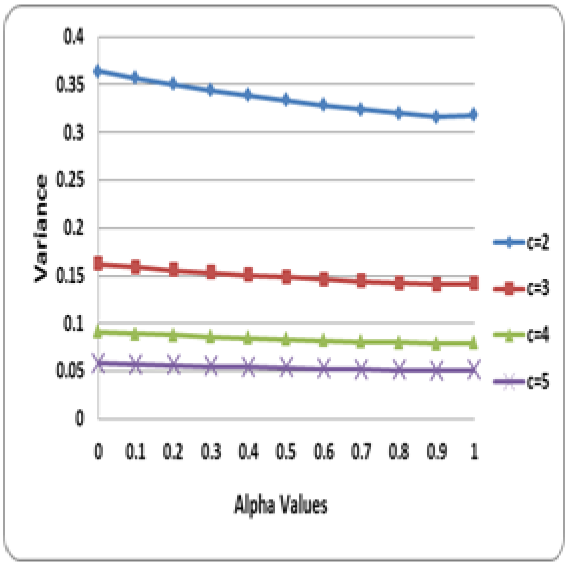

Fig: 3.3 (a). *Lower α cut from the variance*

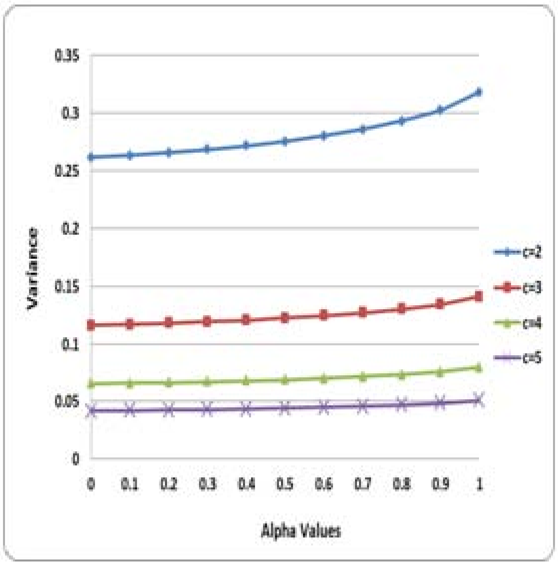

Fig: 3.3 (b). *Upper α cut from the variance*

4. CONCLUSION

In this paper, we showed that the fuzzy mean and variance for the patients with autoimmune thyroiditis with severe hypothyroidism resistant after TSH treatment is decreased in the lower α cuts and they are increased in the upper α cuts by using fuzzy mathematical model. The appropriate decrease of Thyroid stimulating hormone in response to increasing thyroxine level showed that if the intake of thyroxine would be appropriate, the patient might attain the thyroid level.

5. REFERENCE

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