A Mathematical Model for the Effects of Critical Care in Infancy on Cortisol Levels in Subsequent Childhood and Teen Years using Exponential-Exponential Distribution

A Leema Rose[1*], A Manickam[2], C Senthilkumar[3]

[1] Department of Mathematics, Auxilium College of Arts and Science for Women, Pudukkottai-622302, India

[2] Department of Mathematics, SRM Institute of Science and Technology, Trichy-621105, India.

[3] Departments of Mathematics, Government Polytechnic College, Aranthangi -614616, India

*Corresponding author: anto.leema14@gmail.com

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ABSTRACT

Real-world events are typically described using statistical distributions. Their theory is widely studied and used in a variety of practical situations due to the usefulness of these statistical distributions. The Exponential-Exponential distribution is a novel probability distribution that is proposed in this work. This study sought to determine how cortisol levels in children and adolescence were impacted by intensive care treatment and early exposure to stress and pain. Neither the general hospitalization group nor the intensive-care unit subgroups differed significantly from the control group in terms of cortisol waking reaction, diurnal decline, or stress reactivity.

Keywords: Exponential Distribution, Survival function, Hazard function, Exponential-Exponential Distribution, Cortisol, HPA axis.

1 Introduction

Statistical distributions are in general, used in describing real-world occurrences. In line with the usefulness of these statistical distributions, their theory is largely studied and applied to many scenarios in real life. One of the main challenges of statisticians is to find the appropriate and efficient statistical distribution in modelling natural life events in the form of known probability distributions. Probability distributions posed important usefulness in modelling natural life phenomena that are characterized by uncertainty and riskiness. It was noted in [1,2] that the interest in developing and modifying existing distributions to form more flexible statistical distributions remains an arguable topic in the statistics profession; numerous generalized forms and classes of distributions have emerged and applied to describe various phenomena a common feature of these generalized distributions is that they have more parameters. In several fields of studies such as medicine, engineering, and finance, estimating and analyzing lifetime data is fundamental, some lifetime distributions have been employed to model such kinds of data, and the feature of the techniques used in a statistical analysis depends heavily on the assumed probability distributions given this, significant efforts have been used in the development of large classes of typical probability distributions along with pertinent statistical procedures [3,4].

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2 Mathematical Model and Assumptions

2.1 The Derivation of the new model Exponential-Exponential Distribution (EED)

Let x be continuous independent random variables such that x~ E (x , λ) has an exponential distribution. Let f(x) and F(x) be the probability density function and CDF of the exponential distribution, which are as follows:

$$f(x) = \lambda e^{-\lambda x}, \quad x > 0, \ \lambda > 0 \qquad \text{And} \qquad (1)$$

$$F(x) = 1 - e^{-\lambda x}, \quad x > 0, \ \lambda > 0 \qquad (2)$$

Similarly, from [1], let

$$g(x) = \lambda f(x)(1 - F(x))^{\lambda - 1}, \quad x > 0,$$

Assuming that f(x) and 1-F(x) represent the pdf and survival function of the baseline distribution, and that (1) and (2) are inserted into (3) above, the pdf of the Exponential-Exponential distribution is obtained as

$$g(x) = \lambda^2 e^{-\lambda^2 x}, \quad x > 0, \ \lambda > 0 \qquad (3)$$

2.2 Statistical Properties of the Exponential-Exponential Distribution (EED)

This section yields the following statistical characteristics of EED, particularly the first four moments: variance, coefficient of variation, moment generating function, characteristic function, skewness, and kurtosis[5,6].

2.2.1 Moments

If X is a random variable distributed as an EED(x, λ), then the r^{th} non-central moment is given by $\mu_r{}' = \frac{\Gamma(r+1)}{\lambda^{2r}}$

$$\text{Mean} = \mu_1{}^1 = \frac{1}{\lambda^2}$$

$$\mu_2{}^1 = \frac{2}{\lambda^4}$$

$$\text{Variance} = V(x) = \frac{1}{\lambda^4}$$

$$\mu_3{}^1 = \frac{6}{\lambda^6}$$

$$\mu_4{}^1 = \frac{24}{\lambda^8}$$

2.2.2 Moment Generating Function (M.G.F)

If X is a continuous random variable distributed as an EED (x, λ), then the moment generating function is defined as $\mu_x(t) = \frac{\lambda^2}{\lambda^2 - t}$

2.2.3 Characteristic Function (C.F)

If X is a continuous random variable distributed as an EED $(\boldsymbol{x}, \boldsymbol{\lambda})$, then the characteristics function is defined as $$\boldsymbol{\phi_x}(\boldsymbol{it}) = \frac{\boldsymbol{\lambda^2}}{\boldsymbol{\lambda^2 - it}}$$

2.2.4 Cumulative Distribution Function (CDF)

The likelihood that a random variable X will assume a value less than or equal to x is its cumulative distribution function, which is defined as follows:

$$F(x) = P(X \leq x) = \int_0^x f(x)dx$$

2.2.5 Survival Function

S(x)=1-F(x), where F(x) is the cumulative distribution function of x, is the survival function, sometimes referred to as the reliability function, which provides the likelihood that a patient, device, or other items of interest would survive past a particular stated period of time.

$$= 1 - \left(1 - e^{-\lambda^2 x}\right)$$

$$S(x) = e^{-\lambda^2 x}$$

2.2.6 Hazard Function

The instantaneous risk that the event of interest occurs within a very short time period is known as the hazard function, which is also known as the force of mortality, instantaneous failure rate, instantaneous death rate, or age-specific failure rate. It is defined as follows:

$$\mathrm{h}(x) = \lambda^2$$

2.2.7 Cumulative Hazard Function

The integral of the hazard function is the cumulative hazard function. It can be described as follows and understood as the likelihood of failure at time x given survival until time x:

$$\mathrm{H}(x) = \lambda^2 x$$

3 Applications

Painful procedures and conditions are among the many stressors that infants admitted to the critical care unit are subjected to [7]. The stress response and associated brain networks, which mature throughout the first few years of life, may be hampered by this exposure. By causing epigenetic alterations, stress exposure during this delicate time may have long-term impacts on the functioning of the hypothalamic-pituitary-adrenal (HPA) axis. Stress in early life may therefore have a long-term effect on kids' physical and mental well-being [7].

The diurnal cortisol drop was measured using the diurnal cortisol slope (nmol/L/h). Using time as an independent variable, a regression line was fitted to each participant's cortisol levels to determine the slope. The diurnal cortisol drop was calculated using cortisol samples obtained immediately after waking up, prior to bedtime, and at least one other time point.

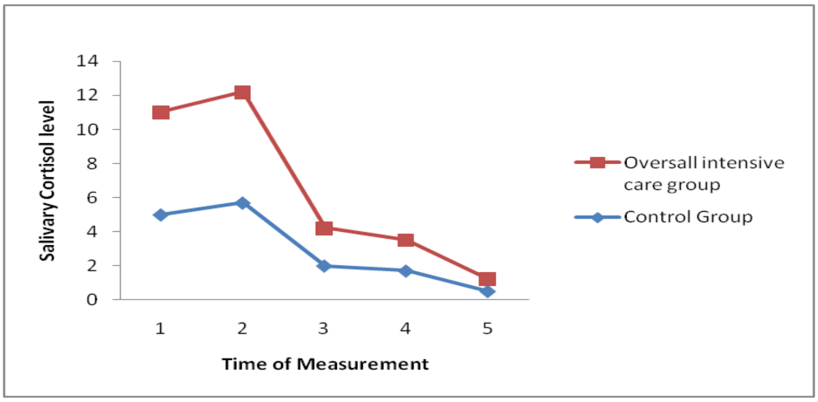


Fig.1 : Line graph showing diurnal cortisol levels in the overall intensive care group and control group

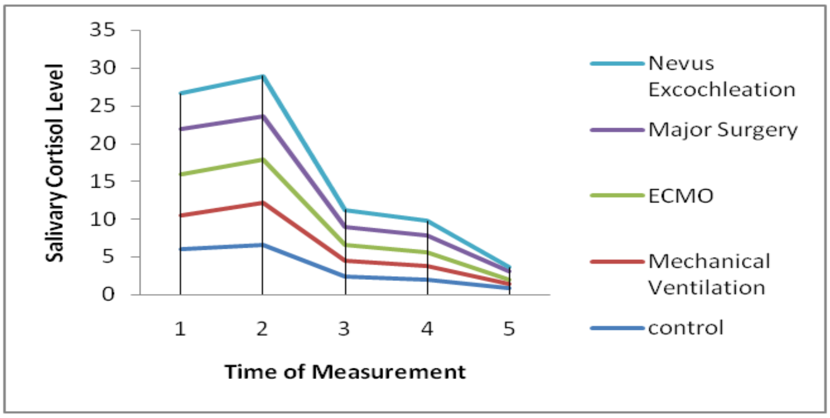
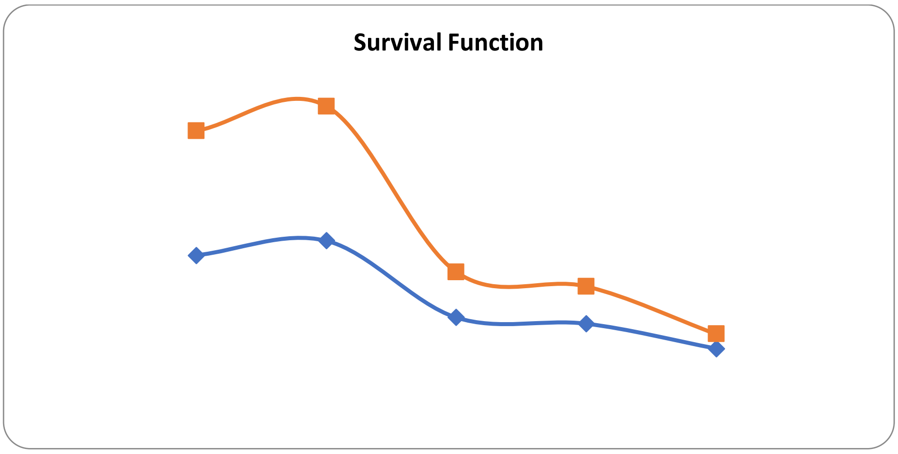


Fig.2 : Line graph showing Salivary cortisol levels in the overall intensive care group and control group

Mann-Whitney tests were used to compare the cortisol levels per measurement between the control group and the intensive care group as a whole, and Kruskal-Wallis tests were used to compare the cortisol levels between the intensive care subgroups and the control group. As illustrated in **Fig. 1& 2,** children and adolescents with a history of critical care treatment appeared to have lower cortisol levels upon awakening, which may have contributed to their reduced diurnal cortisol output compared to the control group. This decrease in morning cortisol levels appeared to be most noticeable in the nevus excochleation cohort, which had likely experienced the most pain during infancy, and the mechanical ventilation subgroup, which mostly consisted of preterm-born children.

Blunted morning cortisol has been seen in very preterm infants with a history of neonatal intensive care therapy [8]. This may be due to the down regulation of the HPA axis in response to chronically elevated cortisol levels caused by stress [9]. Due to altered parenting practices, children and adolescents who have previously had intensive care therapy may have lower morning cortisol levels. Children and adolescents with overprotective parenting had lower cortisol levels when they wake up, according to Chen et al. [10].

4 Mathematical Result



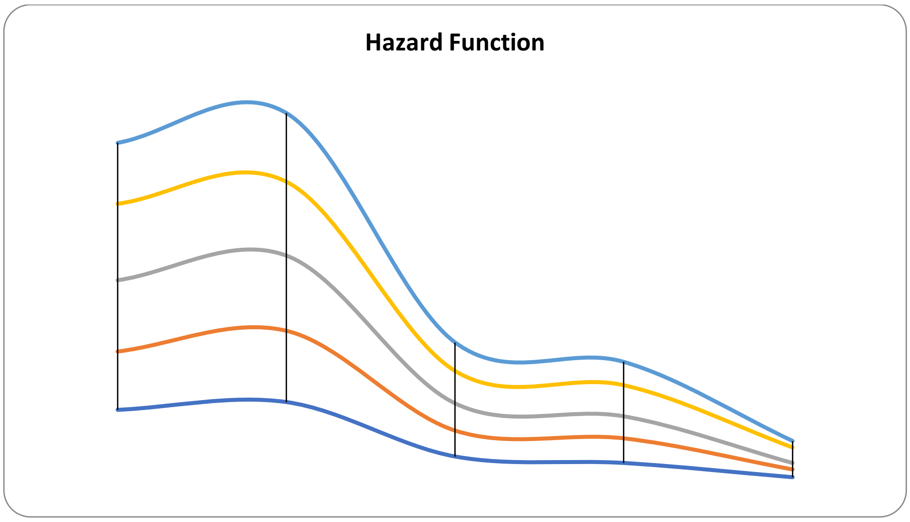


Fig 3: Survival and Hazard Function

5 Conclusion

With the exception of an 18% decrease in diurnal cortisol output, which can be attributed to lower cortisol levels upon awakening, children and adolescents with a history of intensive care treatment during infancy exhibit stress reactivity and diurnal cortisol levels that are comparable to those of age-matched healthy controls. It is currently unknown what the observed decrease in total diurnal cortisol output will mean clinically. In the fields of statistics and probability, several distributions have been created, defined, and shown to be commonly used. A new Exponential-Exponential distribution was defined, examined, and established in this study. Its properties, such as its first four moments, moment generating function, characteristics function, cumulative distribution function, survival, and hazard functions, were derived, and its parameter estimate was obtained using the maximum likelihood estimation method.We came to the conclusion that the mathematical and medical outcomes were equal after comparing them.

6 Declarations

6.1 Competing Interests

The authors declare that there is no conflict of interests.

6.2 Acknowledgements

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