Mathematical Model for lung function measurements in asthmatic children

Saiva Raju, N.*, Kavitha, N.** & Lakshmi, S***

*Prof. & Head of Mathematics, Shri Angalamman College of Engg. & Tech., Siruganoor, Tiruchirappalli.
**Assistant Professor of Mathematics, Anna University of Technology, Tiruchirappalli, Pattukkottai Campus, Rajamadam, Thanjavur district.
***Head & Asso.Prof. of Mathematics, KN Govt arts college, Thanjavur.

Abstract
Hazard rate of the Inverse Gaussian distribution is utilized for finding the critical maximum of the curves which are described in the application part. Here lung function measurements (FEV_1) during the four study days in children with exercise challenge, histamine challenge and on control day were analyzed. The curves are analyzed by using the Mathematical Model and the results have been obtained which gives clear report to the medical professionals.

Keywords : Inverse Gaussian distribution, Hazard rate, Histamine

Introduction
Methods for estimating the critical time of the hazard rate for the Inverse Gaussian distribution are discussed to asthmatic children when the following stresses are given

(i) Histamine challenge
(ii) Exercise1 challenge
(iii) FEV_1 during a control day
(iv) Exercise 2 challenge

In probability theory, the Inverse Gaussian Distribution (also known as the Wald distribution) is a two parameter family of continuous probability distributions with support on (0, ∞) [7]. Its distribution function is

$$F(x) = \phi\left[\sqrt{\frac{\lambda}{x}}\left(\frac{x}{\mu}-1\right)\right] + \exp\left(\frac{2\lambda}{\mu}\right)\phi\left[-\sqrt{\frac{\lambda}{x}}\left(\frac{x}{\mu}+1\right)\right] \qquad x \geq 0,\ \mu,\lambda > 0$$

where λ and μ are parameters. The probability density function is

$$f(x) = \left[\frac{\lambda}{2\pi x^3}\right]^{1/2} \exp\left(\frac{-\lambda(x-\mu)^2}{2\mu^2 x}\right)$$

The mean and the variance are respectively μ and $\frac{\mu^3}{\lambda}$ [3, 8].

Failure (or Hazard) Rate
The failure rate is defined for non-repairable populations as the (instaneous) rate of failure for the survivors to time *t* during the next instant of time [3, 9].

The failure rate is calculated from

$$r(t) = \frac{f(t)}{1-F(t)} = \frac{f(t)}{R(t)} = \text{the instantaneous (conditional) failure rate.}$$

Special case
The probability density function, reliability, and hazard rate of a Inverse Gaussian distribution with mean μ and dispersion $\lambda(\mu > 0, \lambda > 0)$ are:

$$f(x;\mu,\lambda) = \sqrt{\frac{\lambda}{2\pi x^3}} \exp\left(\frac{-\lambda(x-\mu)^2}{2\mu^2 x}\right) x > 0$$

$$R(x;\mu,\lambda)=\phi\left[\sqrt{\frac{\lambda}{x}}\left(1-\frac{x}{\mu}\right)\right]-\exp\left(\frac{2\lambda}{\mu}\right)\phi\left[-\sqrt{\frac{\lambda}{x}}\left(1+\frac{x}{\mu}\right)\right] \qquad x\geq 0$$

$$r(x;\mu,\lambda)=\frac{f(x;\mu,\lambda)}{R(x;\mu,\lambda)}$$

In one dimension the Gaussian function is the probability density function of the Normal distribution

$$f(x)=\frac{1}{\sigma\sqrt{2\pi}}e\left(-\frac{(x-\mu)^2}{2\sigma^2}\right)$$

In two dimensions the circular Gaussian function is the distribution function for uncorrelated variates X and Y having a bivariate Normal distribution and equal standard deviation

$$\sigma=\sigma_x=\sigma_y$$

$$f(x,y)=\frac{1}{2\pi\sigma^2}e\left(-\frac{(x-\mu_x)^2+(y-\mu_y)^2}{2\sigma^2}\right).$$

The differentiable failure rate $\lambda(t)$ has a bath tub shape if

$$\lambda^1(t)<0 \text{ for } t\in[0,t_0),\ \lambda^1(t_0)=0,\ \lambda^1(t)>0 \text{ for } t\in(t_0,\infty)$$

and it has an upside-down bath tub shape if

$$\lambda^1(t)>0 \text{ for } t\in[0,t_0),\ \lambda^1(t_0)=0,\ \lambda^1(t)<0 \text{ for } t\in(t_0,\infty).$$

Application

Since long it has been recognized that exercise can reduce acute bronchoconstriction in patients with asthma the so-called exercise – induced bronchoconstriction E1B. In childhood asthma the prevalence of EIB varies from 70% to 90% [4, 6]. Children suffering from EIB may complain about any of the following symptoms during or after strenuous exercise; wheezing, shortness of breath, cough or chest pain. The bronconstrictor response to exercise is determined by the level of ventilation reached during exercise as well as the temperature and water content of the inspired air. The precise mechanism by which EIB occurs is still a matter of debate. However, studies with mediator antagonists and synthesis inhibitors have provided supportive evidence for the release of mediators such as histamine, prostaglandins and leukotrienes during the early asthmatic response [EAR] after exercise.

Ever since its first description in 1980 [2] there is considerable controversy in the literature on the potential development of a late asthmatic response (LAR) to exercise on asthma. It is known that the occurrence of a LAR after allergen challenge is associated with an influx of inflammatory cells and the development of bronchial hyperresponsiveness. Therefore, if a LAR after exercise does exist, it could have important consequences for our understanding of the pathophysiological mechanisms of EIB, and consequently for the therapy of asthma.

A number of studies have been published ranging from 10% to 89%. However, nearly as many studies have been unable to document a LAR. The experimental design of some of the studies showing a LAR has been criticized because of the lack of 'appropriate' control days, during which lung function is being documented without exercise or following bronchoconstriction induced by inhaled histamine.

In the present study, we have applied an analogous approach, using multiple linear regression analysis per patient, to evaluate the occurrence of LAR after exercise in a group of asthmatic children. To that end we repeatedly measured lung function upto 8 hours after exercise challenge. We also measured lung function during a control day without exercise (negative control), and on a day after histamine challenge inducing a matched level of bronchoconstriction as observed after exercise (positive control).

Lung function measurements were made either using a dry rolling seal spirometer or a pnenmotachograph. Exercise challenge was performed by running a treadmill for 6 minutes [1]. A standardized dosimetric technique was used to perform the histamine challenge [5]. During spontaneous recover from the bronchoconstriction to histamine FEV1 measurements were repeated in triplicate at the same time intervals as used after exercise challenge upto 8 hours.

This allowed the calculation of the EAR to histamine in the same way as used for exercise. To assess bronchial responsiveness to histamine, PD_{20} histamine was determined by linear interpolation between two data points on the non-cumulative log dose – response curve.

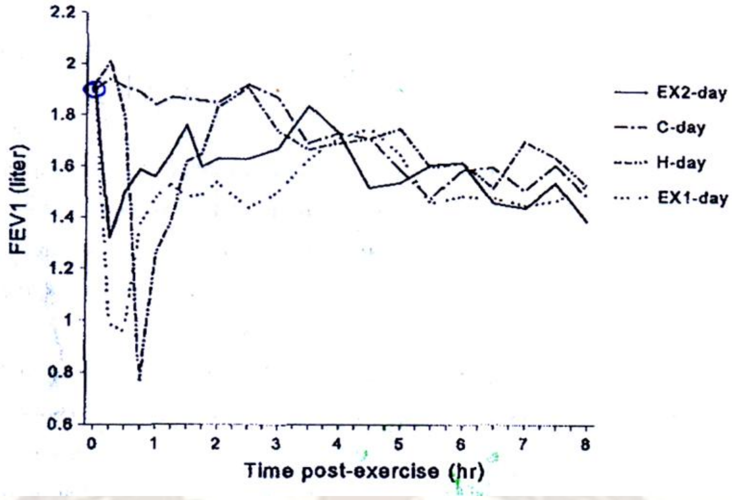
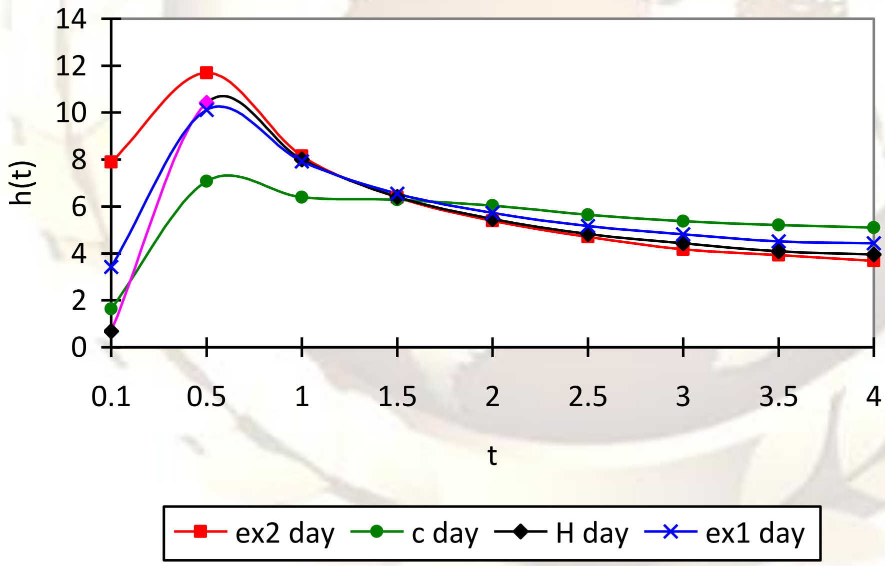


Fig.1. Lung function measurements (FEV1) during the four study days in children nr.13

Here we had taken the children as outpatient of a clinic; the result will give severe effect to other asthmatic children who are admitted in the clinic.

Result

Failure rate of Inverse Gaussian distribution has a upside down bathtub shape.



Conclusion

From the mathematical figure the failure rate suddenly increases and attains a maximum value and decreases in the particular periods. For the control day maximum hazard rate value is small when it is compared with other three cases, but it decreases slowly than other cases. When exercise is given to the asthmatic children the hazard rate attains maximum value. But it decreases suddenly when it is compared to other three cases.

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