

How to Cite:

Kavitha, R., & Durgadevi, N. (2022). A trivariate compound generalized poisson model for corticotropin-releasing hormone effects on human pregnant and nonpregnant. *International Journal of Health Sciences*, 6(S5), 1494–1503. <https://doi.org/10.53730/ijhs.v6nS5.8911>

A trivariate compound generalized poisson model for corticotropin-releasing hormone effects on human pregnant and nonpregnant

Dr. R. Kavitha

Assistant Professor, Department of Mathematics, Chevalier T. Thomas Elizabeth College for Women, Chennai -11, Tamil Nadu, India.
Email: kavi.jash@gmail.com

Dr. N. Durgadevi

Research Scholar, P.G and Research Department of Mathematics, K.N. Govt. Arts College for Women (Autonomous), Thanjavur – Dt (TN), India.
Email: ndurga2013@gmail.com

Abstract---In this paper, we apply a new approach to uterine contractions to a large panel of human pregnant non pregnant myometrial strips, treated or not by corticotropin releasing hormone (CRH). This model is based on a fine analysis of the contraction curves. This analysis yield four mathematical parameters beta, theta, tau1 and tau2 related to excitability, duration of plateau phase, and time constants for relaxation describing respectively, the different portions of the contraction cycle. This leads to specific differences in spontaneous contractile activity between pregnant and nonpregnant states. In the present study, we compare nonpregnant and pregnant women close to the term vitro CRH myometrial responsiveness, to describe uterine contractile activity during a parturition. We have a Trivariate compound generalized Poisson model for uterine contraction to a pregnant and nonpregnant myometrial strips, treated or not treated by corticotrophin- releasing hormone (CRH). Although, the biochemical signification of these results remains to be elucidated, we contribute to emphasize CRH action at the myometrical level. The results reveal highly significant differences between pregnant and nonpregnant myometrium as well as in their response to CRH.

Keywords---corticotropin-releasing hormone, human pregnant, nonpregnant.

Mathematical model

Compound Generalized Poisson Distribution (CGPD)

Many applications for the generalized Poisson distribution can be found in the literature: Scollnik [11] mentions some applications in the analysis of actuarial data; Famoye Singh [5] build a regression model with the generalized Poisson distribution and apply it to domestic violence data; and Sheth [12] uses it as the limit distribution on a clustering model with Poisson initial conditions.

Generalized Poisson Distribution

Consul and Jain (1973) proposed a new (1985) to: A discrete random variable N is said to have a generalized Poisson distribution (GPD) if its probability mass function is given by

$$Pr(N = n) = p_n(\lambda, \theta) = \begin{cases} \lambda(\lambda + n\theta)^{n-1} \frac{\exp(-\lambda - n\theta)}{n!} & \text{for } n = 0, 1, 2, \dots \\ 0 & \text{for } n > m \text{ when } \theta < 0 \end{cases}$$

$\lambda > 0$, $\max(-1, \frac{-\lambda}{m}) \leq \theta < 1$ and $m (\geq 4)$ is the largest positive integer for which $\lambda + \theta m > 0$ probability generating function is given by the Lagrange expansion of any probability generating function under a suitable transformation (Consul and Shenton (1972)).

Let N denote the number of claims produced by a portfolio of policies in a given time period. Let X_i denote the amount of the i^{th} claim. Then,

$$S = X_1 + X_2 + \dots + X_N \quad (1.1.1)$$

represents the aggregate claims generated by the portfolio for the period under study. In order to make the model tractable, two fundamental assumptions are made in risk theory and they are:

1. $X_1, X_2, \dots$ are identically distributed random variables with the distribution function $F(x)$.
2. The random variables $N, X_1, X_2, \dots$ are mutually independent [2,3].

When a GPD is chosen for N , the distribution of S is called a compound generalized Poisson distribution, In terms of the convolution operation, we can write the distribution function of S as:

$$F_S(x) = \sum_{n=0}^{\infty} F^{*n}(x) \lambda(\lambda + n\theta)^{n-1} \frac{\exp(-\lambda - n\theta)}{n!}$$

The moment generating function of S is given by

$$M_S(t) = M_N(\log M_X(t)), \quad (1.1.2)$$

$M_S(t) = M_N(\log M_X(t))$ function (mgf) of the GPD and $M_X(t)$ is the mgf of the claim amount distribution. By using the expression,

$M_N(t) = \exp\left\{-\frac{\lambda}{\theta}[W(-\theta \exp(-\theta + t)) + \theta]\right\}$, we can write the mgf of S as

$$M_S(t) = \exp \left\{ -\frac{\lambda}{\theta} [W(-\theta \exp(-\theta) M_X(t)) + \theta] \right\}. \quad (1.1.3)$$

Similarly, the probability generating function of S, when the distribution of claim severity is arithmetic, can be written as

$$P_S(z) = \exp \left\{ -\frac{\lambda}{\theta} [W(-\theta \exp(-\theta) P_X(z)) + \theta] \right\}. \quad (1.1.4)$$

Where $P_X(z)$ is the pgf of claim amount distribution [1, 4].

Property of CGPD

If the claim sizes are random variables on the positive integers with probability mass function $f(x) = \Pr(X = x), x = 0, 1, 2, \dots$, then the probability mass function $g(\lambda, \theta; x)$ of CGPD satisfies the recurrence equation

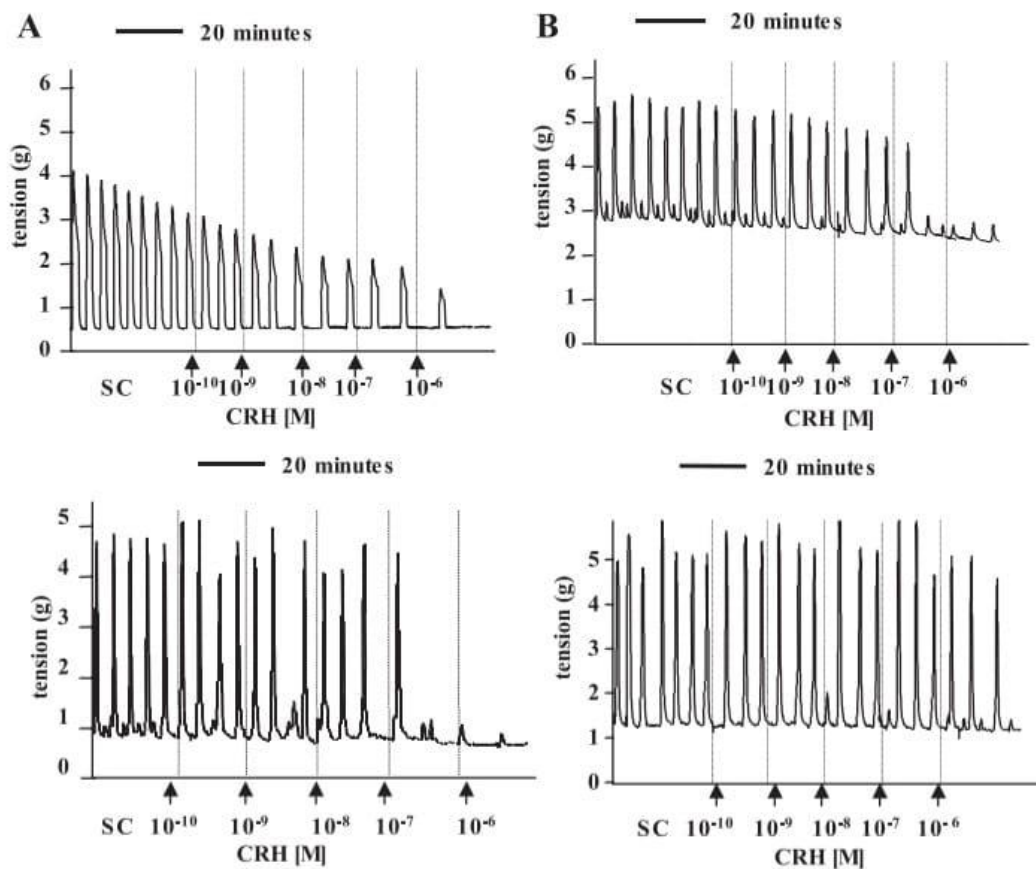
$$g(\lambda, \theta; x) = \frac{\lambda}{\lambda + \theta} \sum_{y=1}^x \left(\theta + \lambda \frac{y}{x} \right) g(\lambda + \theta, \theta; x - y) f(y). \quad (1.1.5)$$

A similar model is developed for our application part.

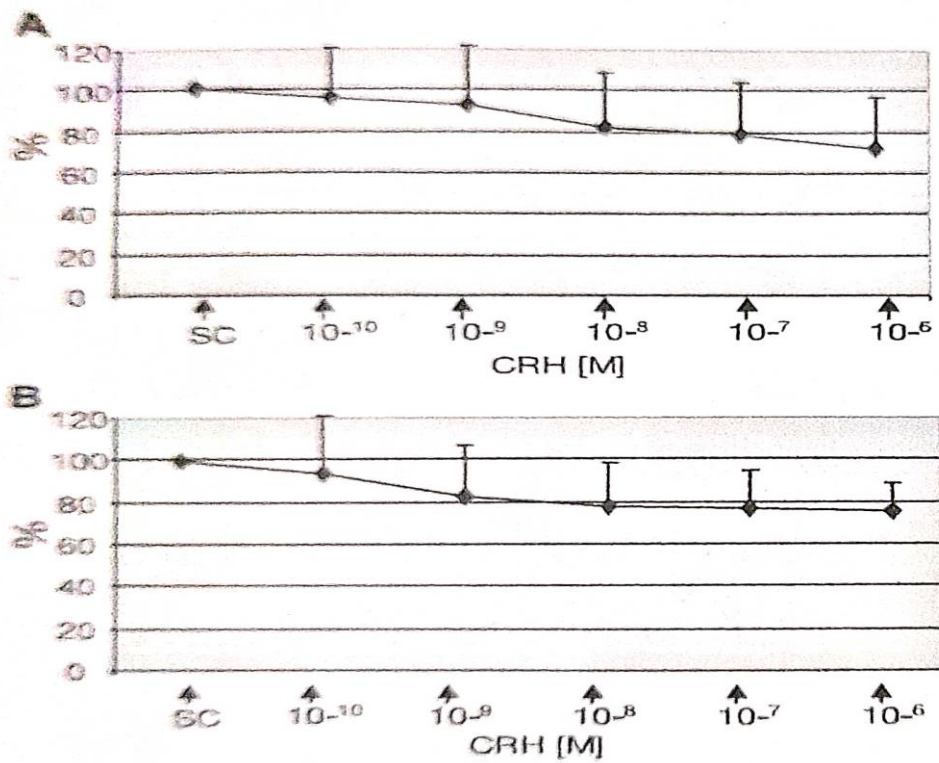
Application

CORTICOTROPIN - RELEASING HORMONE (CRH), a 41 amino acid neuropeptide, was isolated from ovine hypothalamus. In humans, the exponential rise in maternal plasma CRH between the second trimester of pregnancy and term and further increase during labor have been attributed to synthesis by gestational tissues. Human myometrial tissue was obtained from 19 cycling woman undergoing hysterectomy for benign gynecological indications. None of the patients was under hormonal treatment at the time of surgery. Myometrial tissue was also taken from 13 women with normal uncomplicated pregnancies. Consequently, the human myometrium can be viewed as the final target of CRH action on uterine contractile activity. However, the identification of multiple specific CRH receptor isoforms in the myometrium (6,8) raises the question of a direct action of the peptide (7). Because the expression and biological activity of several of these receptor isoforms change during pregnancy and with labor, a physiological, receptor-based switch from relaxation to contractility was hypothesized at the time of parturition (9). In the meantime, other experiments investigated the effects of CRH on contractility of myometrical strips obtained from term pregnant women before the onset of labor. Furthermore, the CRH binding protein play a regulatory action in inhibiting the contractile activity. The effects of cumulative application of CRH are illustrated by four examples of contraction profiles. Clearly, CRH has a dose-dependent relaxing action in nonpregnant and pregnant myometrium (10). Although the specificity of the antagonists like R1 receptor is preferentially involved in the response to CRH. We notice a clear variability between individuals both in pregnant and nonpregnant.

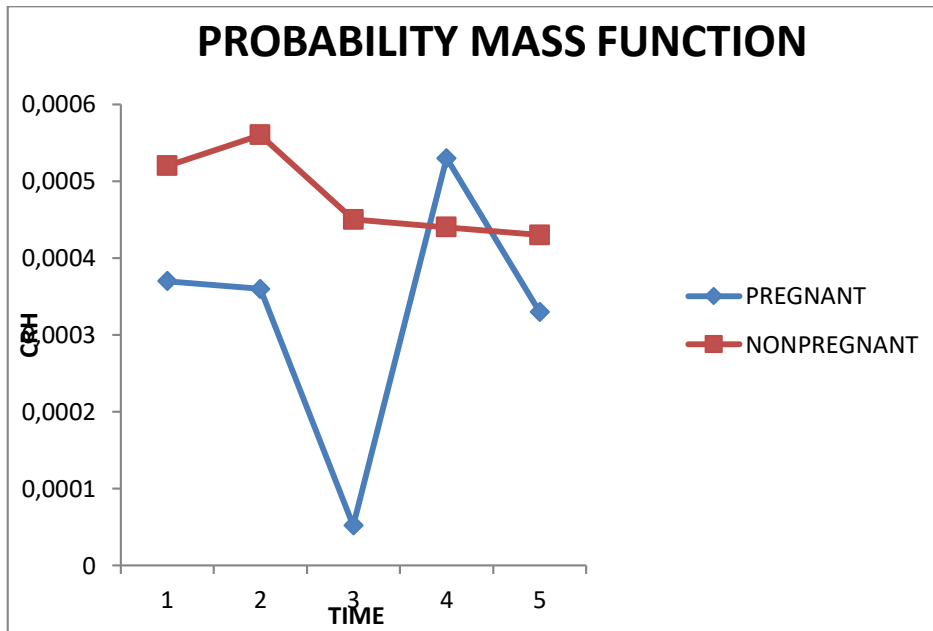
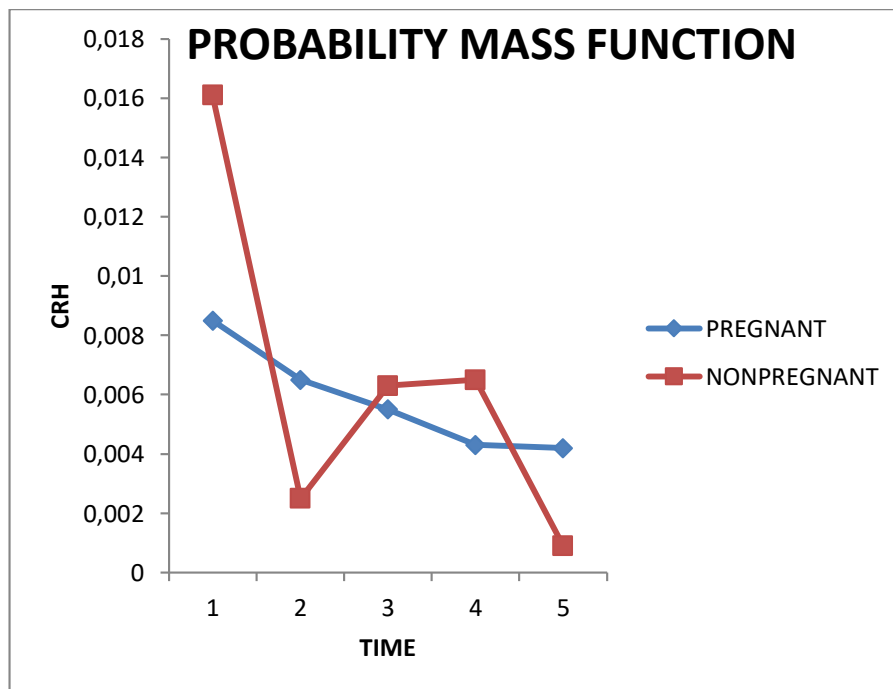
CRH EFFECTS ON UTERINE CONTRACTION

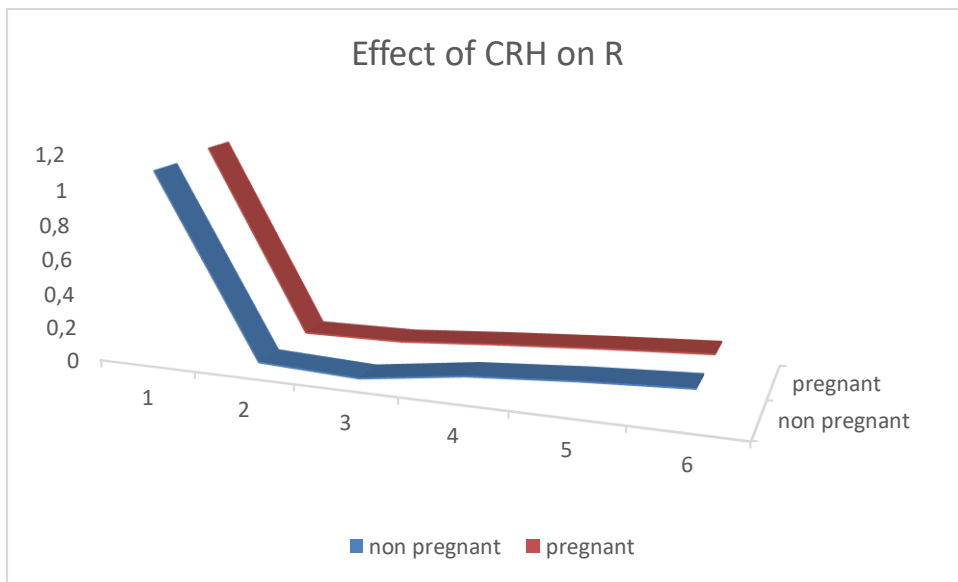
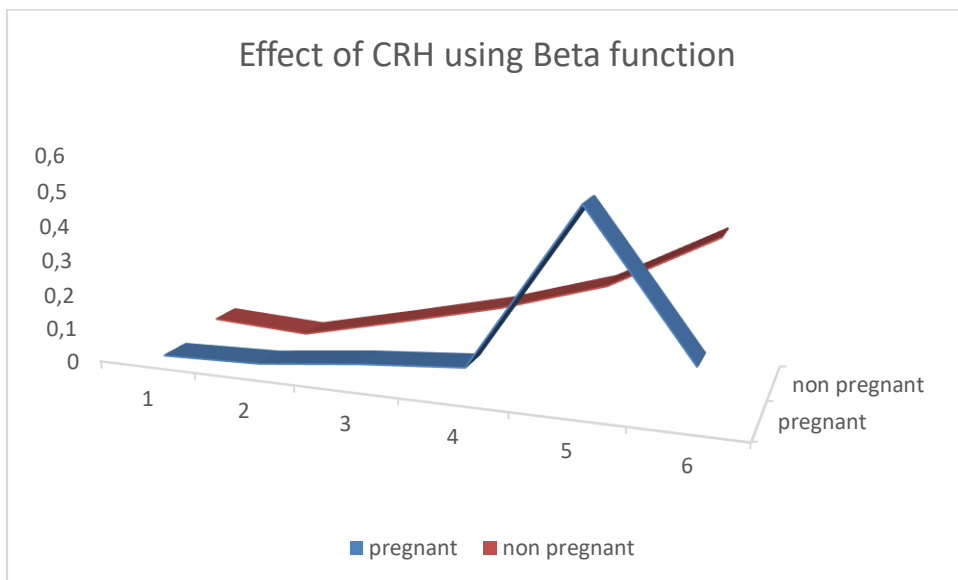


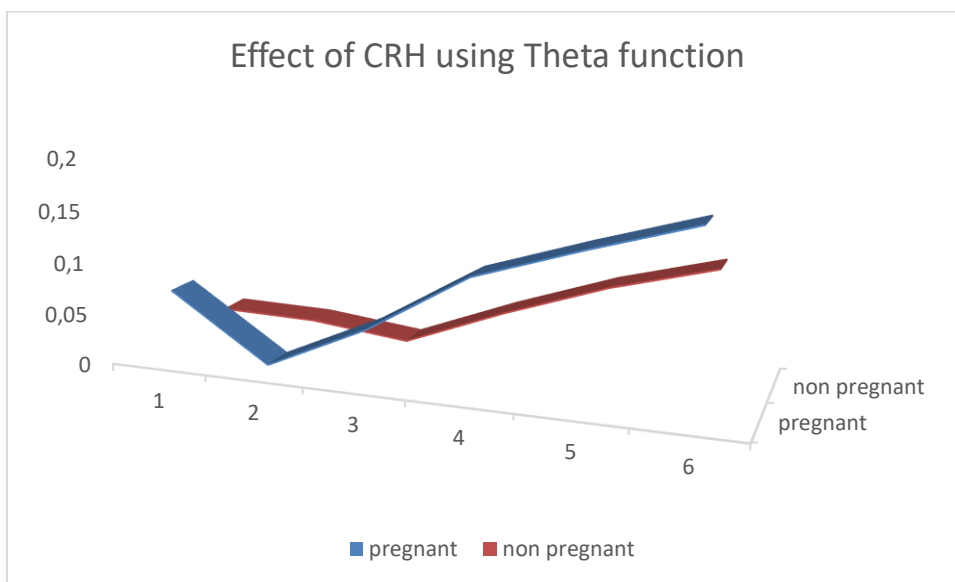
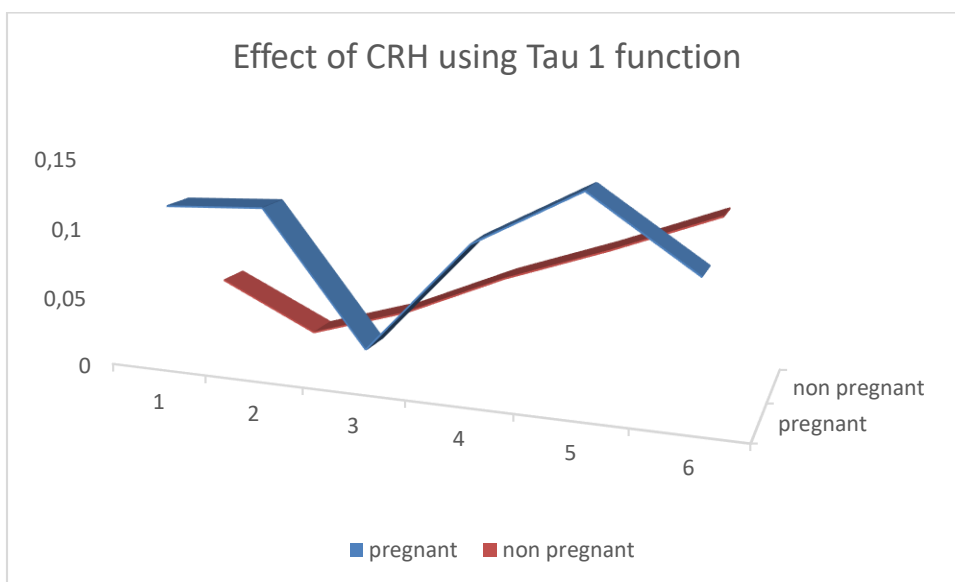
Effects of cumulative addition of corticotrophin releasing hormone (CRH) on spontaneous contractions (SC) in longitudinal myometrial strips from 2 nonpregnant (A) and 2 pregnant).

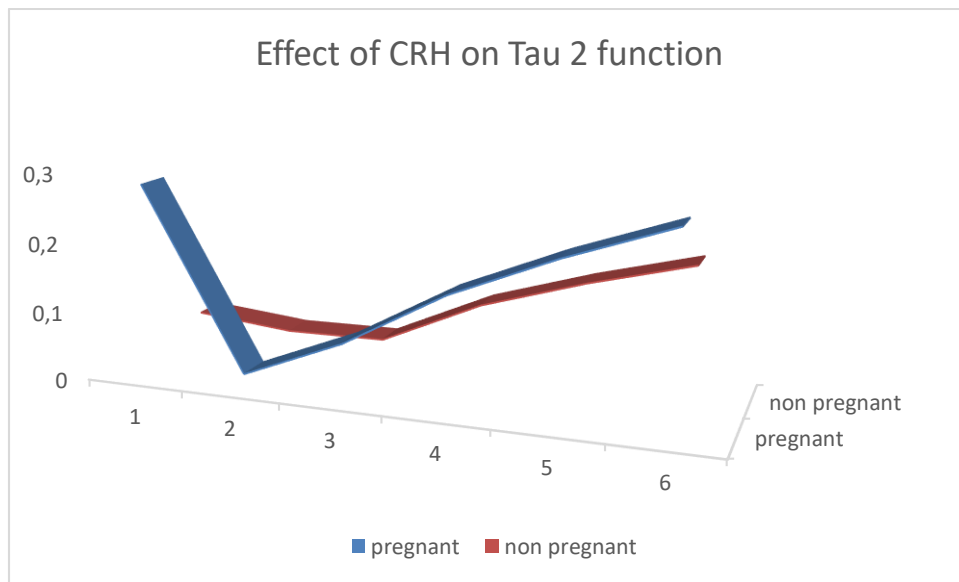


Variations of R according to increasing CRH concentrations in non pregnant (A) and pregnant (B) myometrium.

Mathematical results**Fig 1****Fig 2**

**Fig 3****Fig 4**

**Fig 5****Fig 6**

**Fig 7**

Conclusion

In this paper, we present an enhanced way of analyzing the contractility of the uterus, which relies not merely on the energetic efficiency R of the contraction but also on the specific shape of this contraction. We compared systematically the effects of various CRH concentrations on spontaneous myometrial contractility in both pregnant and nonpregnant uteri. R is significantly higher in nonpregnant women that, in pregnant outside the labor, efficient contractions are prevented. In addition, we demonstrate relaxing effects of CRH in both pregnant and nonpregnant myometrium, albeit higher concentrations are necessary to observe a difference in nonpregnant uteri. This is consistent with the documented higher affinity of myometrial CRH receptors in pregnant women near term. In our study we have pooled the curves obtained from the patients at each CRH concentration used. Although pooling of curves could be less sensitive to detect individual variations in the parameters estimated, it ensures a good robustness of the results obtained. Strikingly, excitability (β) in spontaneous contraction is not less intense in nonpregnant myometrium. The duration of theta is not diminished. In contrary, Tau 1 represents a subsequent phase of the contraction wave, is lower in nonpregnant state, suggesting that the curve drops rapidly. A correlation is observed between theta and tau1 in pregnant myometrium. This shows that efficient contraction will happen near term. In the case of Tau2 parameter the strong variations are seen among CRH contractions. Our results suggest that to evaluate more accurately the modifications of uterine contractions at risk pregnancy such as preterm labor, preeclampsia, and intrauterine growth retardation.

References

- [1] Ambagaspitaya, R.S., and Balakrishnan, N (1993) Some remarks on Lagrangian distributions.
- [2] Consul, P.C., and Jain, G.C., (1973) A generalization of Poisson distribution Technometrics, Vol 15, pp 791-799.
- [3] Consul, P.C., and Shenton, L.R., (1972) Use of Lagrange expansion for generating discrete generalized probability distributions. SIAM Journal of Applied Mathematics, Vol 23, pp 239-248.
- [4] Consul, P.C., and Shoukri, M.M (1985) The generalized Poisson distribution when the sample mean is larger than the sample variance. Communications in Statistics – Simulation and Computation. Vol 14, pp 1533-1547.
- [5] Famoye, F., Singh, K.P., (2006) Zero- inflated generalized Poisson regression model with an application to domestic violence data, Journal of Data Science. Vol 4, pp 117-130.
- [6] Grammatopoulous, D.K and Hillhouse, E.W., (1995) Activation of protein kinase C by oxytocin inhibits the biological activity of the human myometrial corticotropin releasing hormone receptor at term, Journal of endocrinology. Vol 140, pp 585-594.
- [7] Hillhouse, E.W and Grammatopoulous, D.K., (2001) Control of intracellular signaling by corticotropin releasing hormone in human myometrium, Journal of Horm Res. Vol 27, pp 66-74.
- [8] Linton, E.A.W.J., Asboth, G., Glynn, B.P., Plested, C.P and Bernal, A.L (2001) Corticotropin releasing hormone: its potential for a role in human myometrium, Journal of Exp Physiol, Vol 86, pp 273-281.
- [9] McGrath, S., and Smith, R (2001) Corticotropin releasing hormone and parturition, Journal of Clin Endocrinol (Oxf), Vol 55, pp 593-595.
- [10] Rels, F.M., Fadalti, M, Floro, P., and Petraglia, F (1999) Putative role of placental corticotropin releasing factor in the mechanisms of human parturition, Journal of Soc Gynecol Investig, Vol 6, pp 109-119.
- [11] Scollnik, D.P.M., (1998) On the analysis of the truncated generalized Poisson distribution using a Bayesian method. ASTIN Bulletin, Vol 28, pp 135-152.
- [12] Sheth, R.K., (1998) The generalized Poisson distributions and a model of clustering from Poisson initial conditions. Monthly notices, Royal Astronomical Society, Vol 299, pp 207-217.