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A MathematicaL Model For Finding Maximum Likelihood Estimator Functions of Luteinizing Hormone, Follicle Stimulating Hormone, Estradiol and Progesterone.

Dr,S.Lakshmi * and M.Agalya**
*Principal, Govt.Arts and Science College, Peravurani ,Thanjavur Dist.
** Research Scholar, PG& Research Department of Mathematics, K.N. Govt.Arts College for Women,Thanjavur.

ABSTRACT
The Corpus luteum is formed by the action of luteinizing hormone (LH) on the mature preovulatory follicle. Ensuing events, including steroidogenic outpouring, programmed senescence, and capacity for extension by gestation, depend on features characteristic of an adequately developed preovulatory follicle, including, most importantly, the number and LH, Follicle stimulating hormone (FSH) ,Estradiol (E_2), and progesterone (P). The Maximum likelihood functions are obtained for the above medical variables before and after infusion of LH surge ,which are well explained by mathematical figures in the section [3].

Keywords: **MLE, LH , FSH, E_2, P.**
Mathematical Classification: $60G_{XX}$, 60E05

I. Mathematical Model

M/M/1/N queuing model for the secretion of DHEA due to human stress, is developed by Lakshmi.S and Geetharani.B [12].Stochastic Model for endocrine stress responses in chronic fatigue syndrome , is developed by Lakshmi.S and Shanmugapriya.S [13] .A Mathematical model for finding the Association of Thyroid Stimulating hormone with LH and FSH is developed by Lakshmi.S and Agalya.M.[11].Here we have obtained Maximum likelihood Estimator function for the medical variables LH,FSH, Estradiol and Progesterone.

Let x_1 , x_2, x_3, ….. x_n be a random sample from a normal distribution N(μ,σ) [4,9,13,15].
The likelihood function of (μ,σ) is

$$L(\mu,\sigma ;X) = \frac{1}{(2\pi)^{n/2}\sigma^{n}} \exp\left(-\frac{1}{2\sigma^{2}}\sum_{i=1}^{n} (x_i-\mu)^{2}\right)$$

$$= \frac{1}{(2\pi)^{n/2}}\frac{1}{\sigma^{n}} \exp\left(- \frac{1}{2\sigma^{2}}\sum_{i=1}^{n}(x_i - \bar{x})^{2} - \frac{1}{2}\frac{n}{\sigma^{2}}(\bar{x}-\mu)^{2}\right) \quad \text{…….(1)}$$

$-\infty < \mu < \infty$, $0 < \sigma < \infty$. It follows immediately that the likelihood function is maximized, for each value of σ , by $\bar{\mu}_n = \bar{x}_n$

Where $\bar{x}_n$ is the sample mean.

Let $Q_n = \sum_{i=1}^{n} (x_i - \bar{x})^{2}$. Substituting $\bar{\mu}_n$ in (1) ,we obtain

$$L(\bar{\mu}_n,\sigma ; x) = \frac{1}{(2\pi)^{n/2}\sigma^{n}} \exp\left(-\frac{1}{2\sigma^{2}}Q_n\right). \quad \text{…….(2)}$$

Hence ,

$$\frac{\partial}{\partial x} \text{ in } L(\overline{\mu}_n, \sigma ; x) = -\frac{n}{\sigma} + \frac{Q_n}{\sigma^3}.$$

Equating this partial derivative to zero and solving for σ ,we obtain the Maximum likelihood Estimator MLE [10]

$$\overline{\sigma}_n = (\frac{Q_n}{n})^{1/2} = (\frac{1}{n} \sum_{i=1}^{n} (x_i - \bar{x})^2)^{1/2}.$$

Thus ,the MLE of (μ ,σ) is ($\overline{\mu}_n, \overline{\sigma}_n$).

II. Application

The Corpus luteum is a remarkable, transiently functioning organ that provides the endocrine conditions that are necessary and sufficient for the establishment and maintenance of early pregnancy. On a weight basis, it is the most productive steroid-secreting tissue in the body. It is abruptly formed from the remnants of the preovulatory follicle, and it undergoes continuous change thereafter.

The corpus luteum is formed by the action of luteinizing hormone (LH) on the mature preovulatory follicle. Ensuing events, including steroidogenic outpouring, programmed senescence, and capacity for extension by gestation, depend on features characteristic of an adequately developed preovulatory follicle, including, most importantly, the number and LH receptivity of the granulosa cell population, both of which are follicle-stimulating hormone (FSH)–dependent properties. Acquisition of LH receptor (LHR) by preovulatory granulosa cells results from estrogen-stimulated and FSH-stimulated transcription of the LHR gene, the actions of which are mediated largely by intracellullar cyclic adenosine monophosphate (cAMP)[16]. Actions of LH and human chorionic gonadotropin (hCG) define the functional unfolding of luteal events and are thought to be exclusively dependent on activation of this single, G-protein–coupled receptor.

LHR-mediated effects occur primarily via the Gs / adenylyl cyclase / cAMP / PKA signaling pathway, although evidence for activation of other signaling pathways (e.g., inositol phosphate pathway) and possible roles for these is accumulating [2]. The luteotropic action of LH or hCG on follicles that are not mature can produce luteinization of the theca, where LHRs are present, but does not set in motion the distinctive sequence of changes in morphology and function of the granulosa and theca that characterize the corpus luteum.

In ovulatory cycles, there is an increase in progesterone levels that begins before the LH surge, thought possibly to contribute to the positive feedback signal for pituitary release of LH (Fig-1). This harbinger of luteal function is accompanied by a preovulatory increase in circulating 17-hydroxyprogesterone, the levels over time of which differ in pattern from those of progesterone by decreasing after the LH peak, in contrast to the rapid postovulatory increase in progesterone levels. These events may reveal an innate tendency for the granulosa cells of the mature follicle to secrete progestins, as occurs spontaneously when such cells are studied in vitro without an LH signal.

They foretell the remarkable increase in the overall rate of steroidogenesis that soon will be underway: In a few days, the steroidogenic output of the ovary increases from a few hundred micrograms of estrogen to 20 mg or more of progesterone daily—a 100-fold increase. Ovulation marks a shift in inhibin production from the inhibin B dominance of the follicular phase to predominant production of inhibin A, the levels of which roughly parallel steroid secretion by the corpus luteum. Late follicular phase granulosa cells elaborate alpha subunit and beta (B) subunit mRNA in response to FSH and LH.

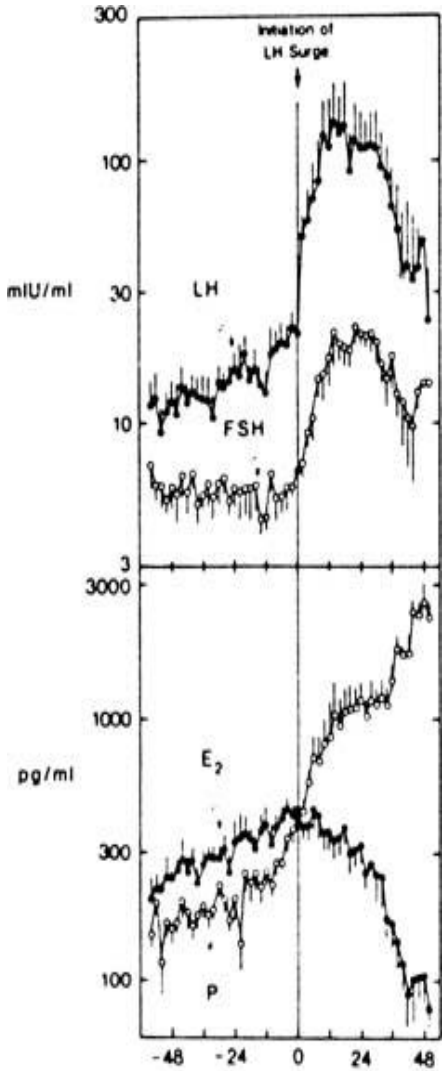
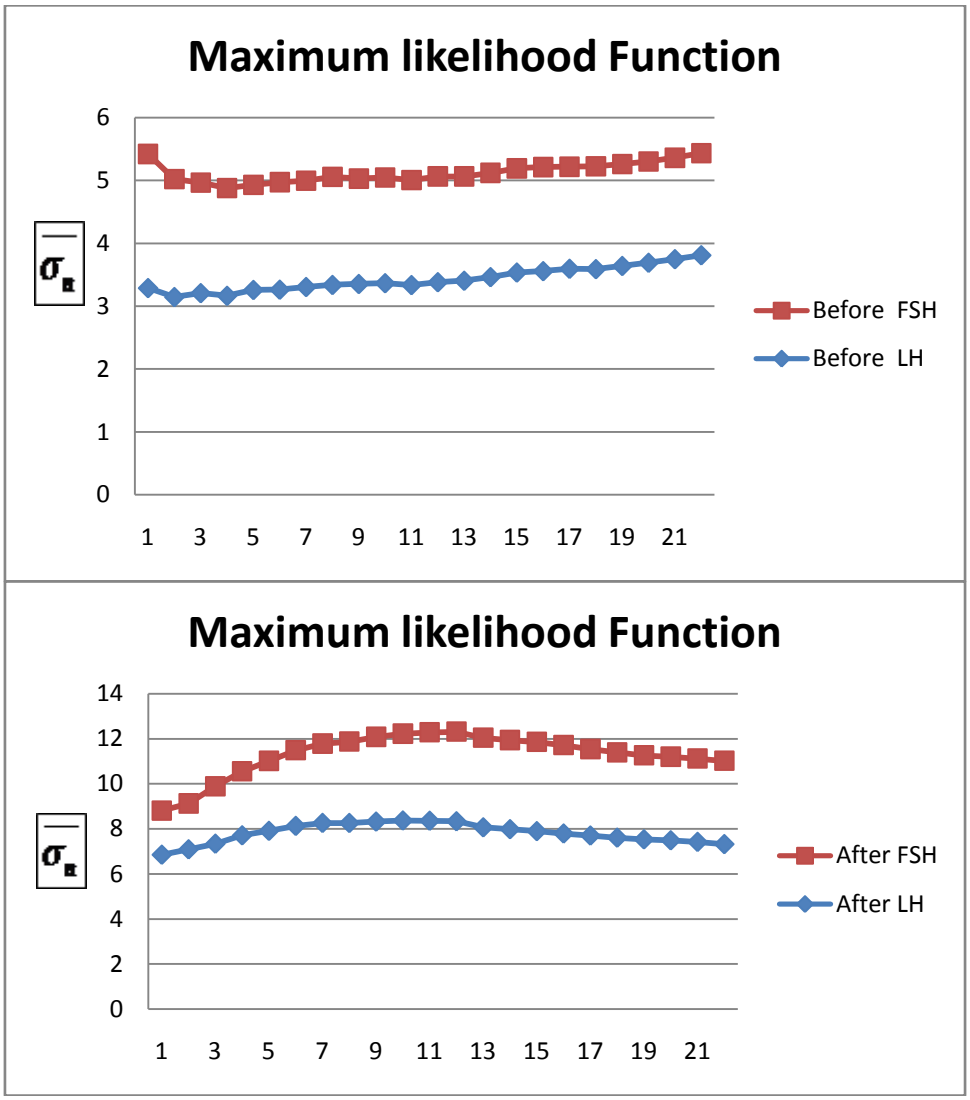
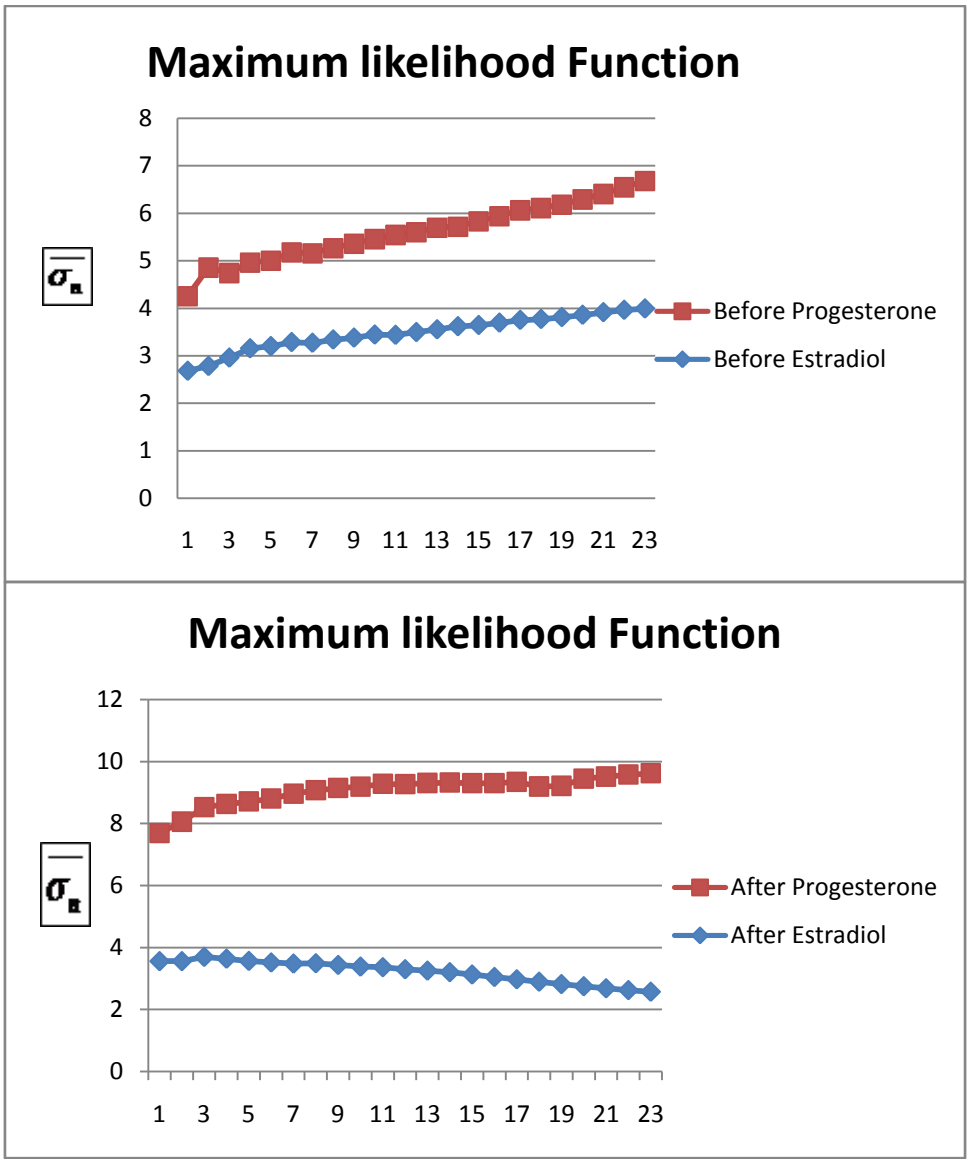


Fig. 1. Mean (± SE) luteinizing hormone, follicle-stimulating hormone, estradiol, and progesterone levels over 5 days at mid cycle in seven studies in five subjects. The data are centered on the luteinizing hormone surge. Progesterone levels rise in several phases—before, during, and after the luteinizing hormone surge.

The increase in steroidogenesis in the periovulatory period is accompanied by granulosa cell proliferation and considerable functional and structural reorganization that eventuate in the distinct morphology of the corpus luteum. Expression of the transcription factor early growth response factor-1, known as a coordinator for multiple transcriptional alterations in circumstances of tissue change, is induced in human granulosa cells by hCG. Expression of this growth factor also is stimulated by cholinergic activation of muscarinic receptors on granulosa cells[7]. Activation of muscarinic receptors also blocks gap junctions via phosphorylation of connexins therein and stimulates cell proliferation via increases in intracellular calcium, together suggesting that cholinergic mechanisms may participate in the rapid reprogramming of granulosa cells in the periovulatory period [8].

III. Mathematical Results:





From the Mathematical results we have obtained the following results:

i) Before infusion of LH surge, LH ,FSH are gradually increasing
ii) Before infusion of LH surge, E2, and P are gradually increasing
ii) After infusion of LH Surge, LH and FSH increasing and then gradually decreasing
iii) After infusion of LH Surge, Progesterone increasing gradually but Estradiol suddenly decreases.

IV. Conclusion

The increase in steroidogenesis in the periovulatory period is accompanied by granulose cell proliferation and considerable functional and structural reorganization that eventuate in the distinct morphology of the corpus luteum. The maximum likelihood functions have been obtained and analysed for all the four variables before and after of LH Surge in the corresponding mathematical figures in section [3].

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