A Fuzzification of Follicle Stimulating Hormone-Computerized Prediction

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ABSTRACT

This study presents a novel computerized fuzzy equation model address the infertility diagnosis regarding reproductive hormone. Follicle Stimulating Hormone, profile during the female menstrual cycle of a non-pregnant, healthy, adult female. We classified standard normal reference range of FSH test value among low, normal and high category to predict FSH current status. This method predicts FSH status and gives computerized prediction. This will give simplicity and more exactness to medical expert's predictions, traditionally these predictions are experience based decisions. This technique results better infertility management by means of more precise, straightforward and accurate analysis, this model effectively assesses FSH varieties all through the menstrual cycle. Fuzzification of this technique is followed by if-then rule and trapezoidal membership function.

KEYWORD

Infertility; FSH-Follicle Stimulating Hormone; μ_L is low fuzzy membership function; μ_N is normal fuzzy membership function; μ_H is high fuzzy membership function; Menstrual Cycle.

1. INTRODUCTION

Infertility, considered as 1 year of endeavored conception without success, is one of the most common health disorders relating young adults. Clinical estimation about infertility specified that if a fertile aged couple has not get pregnant after 1 year of regular unprotected intercourse, meanwhile by that period around 85% couples will get pregnant. [8]. According to bulletin of The World Health Organization (WHO), infertility affects up to 15% of reproductive-aged couples worldwide (<http://www.who.int/bulletin/volumes/88/12/10-011210/en/>). Infertility treatment has been done by treatment of reproductive system in both male and female. Last three decades, are the most frequently upgraded decades of infertility treatment, progressed parallelly with medical sciences. Usually physicians face challenges to predict or estimate success rate of infertility treatment among Assisted Reproductive Treatment (ART) methods. Recently, prediction models for infertility treatment success have been proposed in Europe and America. Therefore, prediction of treatment success is a new field in infertility treatment. There are various methods for predictions based on statistics or neural networks, individual model has their own supportive and risk factors. Herein IVF prediction model have shared more [10].

In 1965, Zadeh introduced Fuzzy sets, define fuzzy set as a class of objects with a continuum of grade of membership. Such a set is characterized by a membership function which assigns to each object a grade of membership ranging between zero and one [4]. Sanchez in 1976 contributed to fuzzy and plans to explore medical aspects of fuzzy relations in future [11]. Holzmann *et.al.* in 1988 developed a fuzzy model for medical diagnosis, this model was a

fuzzy computerized expert system for six cardiopathies [12]. Gradually with respect to time fuzzy used with many more sections of medical science and other disciplines also. Fuzzy Logic is a rule based decision making system. A fuzzy control system is an extended form of fuzzy logic. An architecture of a simple fuzzy control system is consisting of input-process-output corresponding to fuzzification (define membership function), design rules and defuzzification [13]. There are different types of membership functions has been proposed for fuzzy control system like Triangular, Trapezoidal, Gaussian, Two-Sided Gaussian, Bell-Shape etc., among them triangular and trapezoidal are most commonly implemented with fuzzy control system [3]. Kumar *et.al.* in 2015 developed a fuzzy mathematical model to diagnose the level of diabetes using trapezoidal membership and COG technique [7].

In this experiment, author tried to suggest solution for the problem medical expert's do not have common computerized FSH prediction through the female menstrual cycle. Take fuzzy logic as a tool to develop the model because it is one of best and most popular tool to implement a suitable mathematical model against uncertainty and linguistic variables. Linguistic variables are the variables with verbal descriptions and explanations of phenomena. The proposed new fuzzy equation model is an initiative to generate final model to calculate rate of infertility which provide better infertility diagnosis (female infertility) and will help in infertility management; by providing exactness to the medical expert's predictions regarding FSH status throughout the female menstrual cycle. General diagnostic approach is if current test value of a hormone between reference range is considered as normal, current test value below its lower limit is considered as low and above then upper limit is considered as high. The fuzzification process is applied on standard normal reference range of FSH, fuzzified with the help of if-then rule and trapezoidal membership function as μ_L , μ_N and μ_H as low, normal and high respectively. That is why, our model, gives common and more accurate interpretation of FSH current status with respect to medical expert's prediction, because these predictions are based on individual's experience, which may or may not vary.

2. FEMALE REPRODUCTIVE SYSTEM

The female reproductive system is the combination of the internal and external sex organs, responsible for human reproduction. Female fertility study begins with the study of female menstrual cycle. Feminine cycle (menstruation) frames an ordinary part of a typical cyclic process happening in healthy women among puberty and at the end of the reproductive years [1]. Towards the end of puberty, girls begin to release eggs as part of a monthly period called the female reproductive cycle, or menstrual cycle. A typical menstrual cycle is of 28 days, hormones variations takes place at variety of circumstances. Diagnosis of female infertility starts with a medical history, physical examination and details of menstrual cycle. The female reproductive system is principally regulated by following hormones including estradiol, progesterone, follicle stimulating hormone, and luteinizing hormone refer fig.1. It is a complex process there are different scenarios of hormones in a menstrual cycle like level, secretion, stimulate, release etc.

Fig 1: Female Menstrual Cycle [1].

The ovary and uterus two different reproductive organs involved in female menstrual cycle phenomenon. The ovary produces ova or egg, is a location where follicle grows. The uterus also known as the womb is an organ where offspring are conceived and in which they carry before birth. Describe menstrual cycle in Fig.1 and Table 1 describes menstrual cycle phases with corresponding events. The reproductive cycle is divided into an ovarian cycle and a uterine cycle. The ovarian cycle reflects changes in the ovary occur during the menstrual cycle. The uterine cycle describes changes in the endometrial lining of the uterus.

Menstrual cycle is divided into three phase follicular phase, ovulation phase and luteal phase respectively. Number of menstrual day is the key or base of classification. Fundamentally, a typical menstrual cycle is of 28 days. From day 1 to day 13 is follicular phase. Day 14 is considered as ovulation day which is ovulation phase or mid cycle peak. And from day 15 to day 28 is luteal phase (refer Table 1). It is a cyclic process; every new cycle starts from day1 when periods (bleeding) starts. Each new cycle generates new egg or eggs and gives next opportunity to get fertile. Follicular phase is the time period when quantity and quality of follicle is being get define; that is why when medical experts has to plan for pregnancy, they start planning at this phase. To improve the quantity and quality of eggs or follicles medical experts start treating at follicular phase.

Table 1. Ovarian and Uterine Cycles in the Nonpregnant Woman [1].

Ovarian Cycle	Events	Uterine Cycle	Events
Follicular phase - Days 1-13	FSH secretion begins.	Menstruation - Days 2-5	Endometrium breaks down.
....	Follicle maturation occurs	Proliferative phase - Days 6-13.	Endometrium rebuilds
....	Estrogen secretion is prominent.		
Ovulation - Day 14	LH spike occurs.		
Luteal phase - Days 15-28	LH secretion continues.	Secretory phase Days 15-28	Endometrial thickens, and glands are secretory.
....	Corpus luteum forms.		
....	Progesterone secretion is prominent.		

Numerous parameters are sketched out for the cause of infertility like age, weight, lifestyle, environmental, psychological and medical (hormonal and structural) problems etc. The infertility causes due to insufficiency or imbalance hormones [15] are most common, now days. Various endocrine issue, can lead to female infertility by interacting and impairing the normal reproductive ovarian function. These endocrine issues should be terminating in women with ovarian purposes behind infertility, without overlooking interchange explanations behind female infertility, for instance tubal disorders, obstructions of the genital tract and endometriosis [2]. In this manner, we trust that proposed model is helpful in female infertility treatment and recommend another method to predict FSH current status more precisely, will be helpful in infertility management.

2.1 Follicle Stimulating Hormone (FSH)

Follicle Stimulating Hormone is abbreviated as FSH. FSH test values and the gonadotrophin releasing hormone (GnRH) stimulation are the few from among several strategies have been utilized to estimate ovarian reserve. The pituitary gland secretes FSH and luteinizing hormone (LH) in a pulsatile manner in response to GnRH [9]. FSH has a key part in the development and function of the reproductive system is generally used both analytically and remedially in the developmental and reproductive medicine [6] because it indicates the quality of egg produced. FSH is involved in the maturation of ovarian follicles and estrogen secretion in females means FSH excites an undeveloped follicle to grow. Once it is grown, it releases estradiol, which indicate the release of GnRH and LH, encourages ovulation, and when FSH is at its peak level it signals the ovary to release an egg. FSH variates throughout a female menstrual cycle. Their imbalance ratio and a mature growth of a follicle affect fertility rate.

3. METHODOLOGY

This fuzzification method of follicle stimulating hormone is restricted for a non-pregnant, healthy, adult female means only for female gender, pregnancy status must be negative, age must be greater than or equal to 18yrs., and female do not suffer from any kind of health disorder like cancer, tubal disorder, HIV etc. Hormones reference ranges may or may not vary laboratory to laboratory, because ideally, laboratories should either verify these ranges or determine their own reference ranges, based on the populations they serve. However, performing detailed reference range studies can be logistically complex, and are beyond the capabilities of many clinical laboratories. This is especially true for reproductive hormones, for which serum concentrations vary significantly throughout the menstrual cycle, as well as from woman to woman [14]. For this research, Follicle Stimulating Hormone reference ranges of healthy adult females at follicular phase is 2.50 – 10.20, mid cycle peak is 3.40 – 33.40 and luteal phase is 1.50 – 9.10, measuring unit is mIU/mL. For the betterment of membership function, we considered them as 2-11, 3-33 and 1-10 respectively.

The fuzzification method of FSH has categorized in to three sections (Follicular Phase, Mid Cycle Peak or Ovulation Phase and Luteal Phase) of a female menstrual cycle (refer. Table 1.). For each section, we have designed distinct trapezoidal membership function, represented through graph. Graphs are generated in MS- EXCEL 2016 and designed their corresponding fuzzy membership functions also. Every fuzzy membership function further divided into three sub classes as μ_L , μ_N and μ_H where μ_L is a fuzzy membership function belongs to class ‘Low’, μ_N is a fuzzy membership function belongs to class ‘Normal’ and μ_H is a fuzzy membership function belongs to class ‘High’. The current test value of FSH predict

itself corresponding to μ_L , μ_N and μ_H . Suppose if FSH current test value calculate itself equivalent to μ_N then interpretation is Normal. Similarly interpreted Low and High case also.

3.1 FSH Follicular Phase Fuzzification Graph

Fig 2: Fuzzification of FSH Follicular Phase

3.1.1 FSH Follicular Phase Fuzzy Membership Functions

$$\mu_L(x_1) = \begin{cases} 1 & \text{if } x_1 < 3 \\ \frac{(5-x_1)}{2} & 3 \leq x_1 \leq 5 \\ 0 & \text{otherwise } x_1 > 5 \end{cases} \dots (1)$$

$$\mu_N(x_2) = \begin{cases} 1 & \text{if } 5 < x_2 < 7 \\ \frac{(x_2-3)}{2} & 3 \leq x_2 \leq 5 \\ \frac{(9-x_2)}{2} & 7 \leq x_2 \leq 9 \\ 0 & \text{otherwise } x_2 < 3, x_2 > 9 \end{cases} \dots (2)$$

$$\mu_H(x_3) = \begin{cases} 1 & \text{if } x_3 > 9 \\ \frac{(x_3-7)}{2} & 7 \leq x_3 \leq 9 \\ 0 & \text{otherwise } x_3 < 7 \end{cases} \dots (3)$$

3.2 FSH Mid Cycle or Ovulation Phase Fuzzification Graph

Fig 3: Fuzzification of FSH Mid Cycle or Ovulation Phase.

3.2.1 FSH Mid Cycle or Ovulation Phase Fuzzy Membership Functions

$$\mu_L(x_1) = \begin{cases} 1 & \text{if } x_1 < 8 \\ \frac{(13-x_1)}{5} & 8 \leq x_1 \leq 13 \\ 0 & \text{otherwise } x_1 > 13 \end{cases} \dots (4)$$

$$\mu_N(x_2) = \begin{cases} 1 & \text{if } 13 < x_2 < 19 \\ \frac{(x_2-8)}{5} & 8 \leq x_2 \leq 13 \\ \frac{(23-x_2)}{4} & 19 \leq x_2 \leq 23 \\ 0 & \text{otherwise } x_2 < 8, x_2 > 23 \end{cases} \dots (5)$$

$$\mu_H(x_3) = \begin{cases} 1 & \text{if } x_3 > 23 \\ \frac{(x_3-19)}{4} & 19 \leq x_3 \leq 23 \\ 0 & \text{otherwise } x_3 < 19 \end{cases} \dots (6)$$

3.3 FSH Luteal Phase Fuzzification Graph

Fig 4: Fuzzification of FSH Luteal Phase.

3.3.1 FSH Luteal Phase Fuzzy Membership Functions

$$\mu_L(x_1) = \begin{cases} 1 & \text{if } x_1 < 3 \\ \frac{(5-x_1)}{2} & 3 \leq x_1 \leq 5 \\ 0 & \text{otherwise } x_1 > 5 \end{cases} \dots (7)$$

$$\mu_N(x_2) = \begin{cases} 1 & \text{if } 5 < x_2 < 6 \\ \frac{(x_2-3)}{2} & 3 \leq x_2 \leq 5 \\ \frac{(8-x_2)}{2} & 6 \leq x_2 \leq 8 \\ 0 & \text{otherwise } x_2 < 3, x_2 > 8 \end{cases} \dots (8)$$

$$\mu_H(x_3) = \begin{cases} 1 & \text{if } x_3 > 9 \\ \frac{(x_3-6)}{2} & 6 \leq x_3 \leq 8 \\ 0 & \text{otherwise } x_3 < 6 \end{cases} \dots (9)$$

4. COMPUTERIZED INTERPRETATION

To avoid calculation complexity (described above) and provide ease to the end user we have developed a computer program, using PHP. PHP acronym as Hypertext Preprocessor. PHP is an open source, scripting language, can be embedded into HTML, exclusively suitable for web development. This section describes how electronically predict FSH profile during female menstrual cycle. For example, suppose name of patient is ABC, age is 25yrs. By default, her sex is female, present pregnancy status is negative and disorder is also negative. She came for the test name FSH (Follicle Stimulating Hormone), at day 12, and test value in FSH test report is 7.5 (refer fig 5.). Then computerized interpretation or prediction against her current FSH status is Normal. Resultant screen display two more additional details like you are at which phase of menstrual cycle and what is the standard reference of test name (FSH). In this example, additional details are you are at follicular phase and standard reference range of FSH for follicular phase (refer fig 6.).

Follicle Stimulating Hormone		
ENTER NAME :	ENTER AGE :	
ABC	25	
ENTER SEX :	PREGNANCY :	DISORDER :
Female	Negative	Negative
ENTER MENSTRUAL DAY :	ENTER TEST NAME :	ENTER YOUR TEST VALUE :
12	Follicle Stimulating Hormone *	7.5
<input type="button" value="Submit"/>		

Fig 5: Details Entry Form.

Follicle Stimulating Hormone		
Result		
NAME : ABC	AGE : 25	
SEX : FEMALE	PREGNANCY : NEGATIVE	DISORDER : NEGATIVE
MENSTRUAL DAY : 12	TEST NAME : FSH	TEST VALUE : 7.5
<p style="text-align: center;">Interpretation</p> <ul style="list-style-type: none"> ■ You are at follicular phase. ■ Standard Reference Range of FSH for follicular phase is 2 to 11 mIU/mL. ■ Normal 		

Fig 6: Computerized Interpretation Result.

5. CONCLUSION

A new computerized fuzzification technique is introduced in this paper by means of fuzzy equations. The FSH hormonal profile describes all through the typical female menstrual cycle of 28 days in correspondence with standard reference range (traditionally considered as normal reference range). This study is applicable for non-pregnant, healthy and adult female. This methodology will give straightforwardness and more exactness to the medical expert's interpretation. Usually these interpretations depend on individual's experience. This fuzzification methodology enables FSH computerized prediction as low, normal and high. To maintain a strategic distance from presumptions either FSH will increase and how much increase. This is an initiative to generate final model to handle infertility diagnosis and provide better infertility management in terms of linguistic variables for giving more precision to expert's assessment via computerized predictions.

The future perspective of the research is to fuzzify rest of the baseline reproductive hormone's Luteinizing Hormone (LH) and Prolactin. The complexity is persistent hormonal variations under various conditions all through a menstrual cycle.

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