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Algorithm: Fuzzification of Anti-Mullerian Hormone and Thyroid

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ABSTRACT: Presented research work introduces a new fuzzy equation based mathematical methodology using fuzzy logics, fuzzified Anti-Mullerian Hormone (AMH) and Thyroid (TSH), predicts AMH and TSH hormonal profile. Predictions like what is its current status either it is Low, Normal or High. This technique developed using trapezoidal membership function and if-then rule. There are three trapezoidal membership functions μ_L, μ_N and μ_H as Low, Normal and High respectively. Traditionally individual medical expert prediction against hormone variation may or may not vary because these estimations are based on individuals experience. Proposed methodology will give a common prediction more accurately and easily.

Keywords: Infertility; AMH- Anti-Mullerian Hormone; TSH-Thyroid; μ_L is low fuzzy membership function; μ_N is normal fuzzy membership function; μ_H is high fuzzy membership function; Menstrual Cycle.

INTRODUCTION

The Endocrine System comprised of the pituitary gland, thyroid gland, parathyroid glands, adrenal glands, pancreas, ovaries (in females) and testicles (in males). A gland is a collection of cells that expels a chemical substance known as hormones. Hormones are the chemical messengers in the human body. They pass-on the information from one cell to another cell and coordinates the function among different parts of the body. Therefore, if there is hormonal imbalance, communication problem occurs and results improper body function(s). Now a day's hormonal imbalance is manifest as a major topic of concern regarding female infertility. Endocrine disfunction affects oestrogen and progesterone and/or the hypothalamic-hypophysial axes may alter the menstrual cycle, ovulation and fertility (Mark and Wiersinga 2004). Infertility defined, as 1 year of attempted conception without success, is one of the most common health disorders relating young adults. Clinical evaluation of infertility specified that if a pregnancy has not occurred after 1 year of regular unprotected intercourse, because by that time 85% of couples attempting conception will have been successful (Nicolopoulou-Stamati and Pitsos 2001). Infertility get affected by both male and female both. This study concerns with female infertility. There are many factors affects fertility like environmental, social, biological, psychological etc. As per to the statement of The World Health Organization (WHO) (http://www.who.int/bulletin/volumes/88/12/10-011210/en/) "infertility is distress for 15% of reproductive-aged couples worldwide".

While exploring hormonal imbalance medical specialist try to predict either the suspected hormone will increase or decrease and if then how much? Usually they conclude according to their own experience which may or may not vary person to person. Therefore, they need a centralized prediction system to give a common result. The proposed fuzzification technique will enable medical experts to prognosticate AMH and TSH, also proffer a common electronic prediction for a healthy and adult female, also support female infertility diagnosis and endorse better infertility management (Smith *et al.*, 2003).

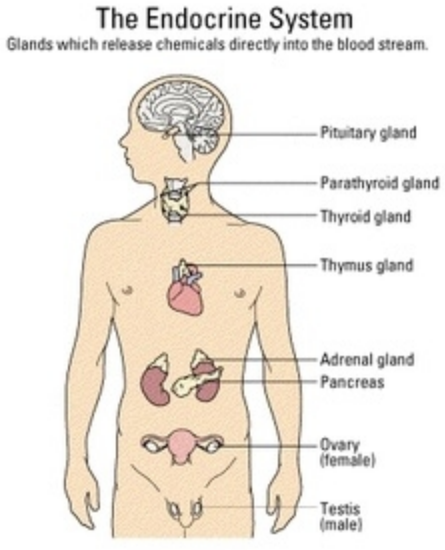

Fig. 1. The Human Endocrine System.

MATERIAL AND METHODS

The objective of the proposed methodology is to predict hormonal status of AMH and TSH. This fuzzification methodology is restricted for female gender who is non-pregnant, healthy (don't suffered from any disorder like HIV, Cancer, tubal and structural disorder) and adult. Defining own hormonal reference range is a complex process because it is based on many factors including the population you are going to serve. This is the reason why laboratories prefer to use predefine reference ranges in respect to define their own, which may or may not vary laboratory to laboratory. This is specifically truth for reproductive hormones because, female reproductive hormones status regularly changes under the different circumstances according the menstrual cycle days (Kris Poppe *et al* 2008). In this study, fuzzification executes using if-then rule and trapezoidal membership function, with three classes μ_L, μ_N and μ_H as Low, Normal and High respectively.

Algorithm: Fuzzification of AMH and TSH.

(AMH=0-7,TSH=0-6,Test_Name, Input_Current_Test_Value, Sex, Age, Disorder and Pregnancy_Status).

Step 1: Start
Step 2: Let Sex= Female, Age>=18, Disorder=None Pregnancy_Status=Negative.
Step 3: Enter test name and current test value.
Step 4: If (Test_Name = AMH) then
Step 5: If (Input_Current_Test_Value = x) then
Execute corresponding fuzzy membership function μL μN and μH and predict accordingly.
Step 6: If (Test_Name = TSH) then
Step 7: if (Input_Current_Test_Value = x) then
Execute corresponding fuzzy membership function μ_L μ_N and μ_H and predict accordingly.
Step 8: End

FUZZIFICATION OF ANTI-MULLERIAN HORMONE (AMH)

Anti-Mullerian Hormone is abbreviated as AMH. AMH level in the body counted by simple blood test. AMH is a key hormone, secreted by the follicles in the ovary. In a typical ovary, AMH attempts to prevent the premature development of the follicles before they are mature – keeping the ovary from developing eggs prematurely. AMH levels did not display a significant variation during the female menstrual cycle.
Because AMH reaches up to its maximum growth at the time of puberty and do not change its status like FSH, LH and PRL during the menstrual cycle. Clinically AMH level serves as a valued applicant marker of ovarian reserve and ovarian ageing. Age is the common and critical factor affects AMH and FSH levels. Abnormal levels of AMH and FSH at specific age may cause infertility (Amara Iverson *et al*., 2011). In this experiment, considerable reference range for AMH is 2-6.80 ng/mL, for betterment of membership function considered as 0-7 ng/mL.

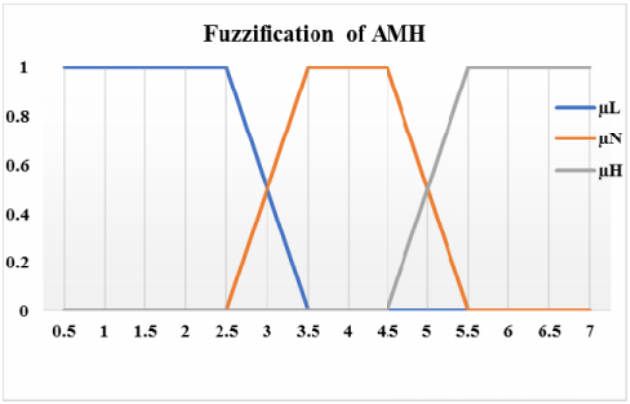

Fig. 2. AMH Fuzzification.

A. Fuzzy Membership Function

$$\mu_L(x_1) = \begin{cases} 1 & if \quad x_1 < 2.5 \\ \frac{(3.5-x_1)}{1} & 2.5 \le x_1 \le 3.5 \\ 0 & otherwise \quad x_1 > 3.5 \end{cases} \quad \dots (1)$$

$$\mu_N(x_2) = \begin{cases} 1 & if \quad 3.5 < x_2 < 4.5 \\ \frac{(x_2-2.5)}{1} & 2.5 \le x_2 \le 3.5 \\ \frac{(5.5-x_2)}{1} & 4.5 \le x_2 \le 5.5 \\ 0 & otherwise \quad x_2 < 2.5, x_2 > 5.5 \end{cases} \quad \dots (2)$$

$$\mu_H(x_3) = \begin{cases} 1 & if \quad x_3 > 5.5 \\ \frac{(x_3-4.5)}{1} & 4.5 \le x_3 \le 5.5 \\ 0 & otherwise \quad x_3 < 4.5 \end{cases} \quad \dots (3)$$

B. AMH and Infertility

Following are the key reasons infertility in contradiction of AMH level.

PCOS. Polycystic Ovary syndrome (PCOS) is a common hormone imbalance that affects fertiled aged female.

PCOS is a "syndrome," or group of symptoms that affects the ovaries and ovulation. The word "polycystic" means "many cysts". Females with PCOS symptoms like

(i) Cysts in the ovaries.
(ii) High levels of male hormones.
(iii) Irregular or skipped periods.

AMH levels appear to be related to the severity of PCOS. Since pregnancy rates decrease as PCOS becomes more severe, it may be theorized that in women with PCOS, pregnancy rates may decrease as the AMH level increases. Therefore, prediction of clinical pregnancy in PCOS is more challenging compared to women without PCOS (Sezai Sahmay *et al*, 2013).

Menopause. Menopause is the condition either just before or after female stops menstruating, marking the end of her reproductive period. There is a direct relationship between age of the female, AMH and menopause. AMH is a promising predictor for the occurrence of the menopause (Ilse *et al.*, 2004). Levels of AMH decrease with advancing age (Timothee Fraisse *et al*, 2008). As the female menstruation starts at age of Puberty or we can say that beginning of reproductive characteristics. Average age of menopause (end of reproductive qualities) is 51 years but varies from 40 to 60 years.

Ovarian Failure. Ovary releases a finite number of follicles during life time. The total number of follicles may vary female to female. Ovarian reserve is the analysed via simple blood test. Ovarian reserve counts the number of follicles produced by ovary. Ovarian ageing shows how many follicles are rest to be produce (approximately). Before menopause (naturally) increase or decrease level of ovarian failure may result infertility (Nadiane *et al*, 2008).

FUZZIFICATION OF THYROID (TSH)

The thyroid gland is a butterfly shaped gland that partially surrounds the wind pipe. The thyroid produces thyroid hormones. The thyroid is part of the endocrine (hormonal) system and is under control of the hypothalamus and the pituitary gland in the brain. There are four terms Thyrotropin Releasing Hormone (TRH), Thyroid Stimulating Hormone (TSH), Triiodiothyronine (T3) and Thyroxine (T4), they sound similar, but they all are independent and interdependent units of endocrine system of human body. Clinically Thyroid level is detected with the help of blood test. For full thyroid assessment you require readings for TSH, T4, T3, rT3 & Thyroid Antibodies. Abnormal functioning of above all or one or more than one can affect reproductive system (female fertility).

In this experiment, considerable reference range for TSH is 0.35-5.50 uIU/mL for improvement of membership function considered as 0-6 uIU/mL.

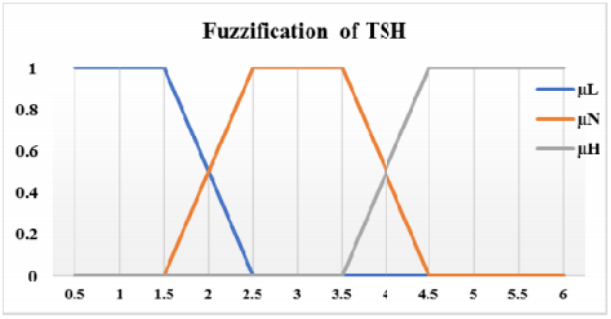

Fig. 3. TSH Fuzzification.

A. Fuzzy Membership Function

$$\mu_L(x_1) = \begin{cases} 1 & if \quad x_1 < 1.5 \\ \frac{(2.5-x_1)}{1} & 1.5 \le x_1 \le 2.5 \\ 0 & otherwise \quad x_1 > 2.5 \end{cases} \quad \dots (4)$$

$$\mu_N(x_2) = \begin{cases} 1 & if \quad 2.5 < x_2 < 3.5 \\ \frac{(x_2-1.5)}{1} & 1.5 \le x_2 \le 2.5 \\ \frac{(4.5-x_2)}{1} & 3.5 \le x_2 \le 4.5 \\ 0 & otherwise \quad x_2 < 1.5, x_2 > 4.5 \end{cases} \quad \dots (5)$$

$$\mu_H(x_3) = \begin{cases} 1 & if \quad x_3 > 4.5 \\ \frac{(x_3-3.5)}{1} & 3.5 \le x_3 \le 4.5 \\ 0 & otherwise \quad x_3 < 3.5 \end{cases} \quad \dots (6)$$

B. TSH and Infertility

There are many factors affects female infertility, among them TSH is one of the major concern because of the following:

Thyroid Autoimmunity (TAI) and Miscarriages. Bad thyroid function equally affects both the conditions, ability to conceive and to maintain a pregnancy. There are complex associations among thyroid autoimmunity (TAI) and hypothyroidism with female infertility, as well as anomalies occurring during pregnancy like miscarriage. Thyroid dysfunction can lead to menstrual irregularities and infertility (Kris *et al.*, 2006). Miscarriage is a common occurrence and higher age is a definite risk factor for miscarriage. **A**n ovulation is the most common gynecoendocrine anomaly in women with primary hypothyroidism, decreased fertility (Abalovich *et al*., 2007).

OUT COME OF THE PROPOSED WORK

The expected outcome of the proposed work is For example,
Suppose if test name is AMH and input current test value is 4.2 then triggering function will be μ_N and interpretation will be "Your PRL current status is **Normal**".

CONCLUSION

This investigation presents an innovative methodology to predict hormonal profile of AMH and TSH like what is its current status either it is Low, Normal or High. This technique fuzzify the normal reference range and gives a common computerized prediction against normal reference range which improve analysis and this will give more accuracy to the female infertility diagnosis and management by avoiding variation in the medical expert's prediction contrary to the same medical situation. Presented fuzzification technique executed with trapezoidal membership function µL, µN and µH based on if-then rule restricted for healthy, adult and non-pregnant female. An algorithm is also designed to give better and easy understanding to the methodology.

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