JOURNAL OF INTERNATIONAL ACADEMIC RESEARCH FOR MULTIDISCIPLINARY
Impact Factor 3.114, ISSN: 2320-5083, Volume 5, Issue 7, August 2017

COMPARISON OF SERUM ANTI MULLERIAN HORMONE (AMH) AND THYROID STIMULATING HORMONE (TSH) IN WOMEN OF REPRODUCTIVE AGE

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Abstract

Anti Mullerian Hormone (AMH), produced by small growing follicles is measureable from birth to approximately near the menopause period and has become a routine test which reflects a decline in the primordial follicle pool during the later reproductive years. AMH can be quite low in amount in cases of women who suffer from diminished ovarian reserve. AMH levels are usually elevated during polycystic ovary syndrome. The best screening test for thyroid disease is Thyroid Stimulating Hormone (TSH) levels. Fertility problems in reproductive age group women lead to abnormal secretion of thyroid hormones. So this study was designed to compare serum TSH and AMH levels in women of reproductive age.

Keywords: AMH, TSH, Ovarian Biomarker, Infertility, Hypothyroidism

Introduction

When a woman fails to achieve pregnancy over a period of 6 months or 1 year in spite of having unprotected sexual intercourse that condition is referred to as infertility. Either of the male or female can be responsible for infertility which can be due to primary or secondary reasons. Thyroid hormonal dysfunction, the most common endocrine disorder is the most common cause of infertility in women disregarding the fact whether the woman is within the reproductive age group. Alteration in the peripheral oestrogen levels, hyperprolactinemia and abnormal secretion of gonadotropin releasing hormone can lead to menstrual disorders and infertility in women suffering from infertility. Infertility due to failure of ovaries to release oocyte during menstrual cycle. Abnormalities in secretion of thyroid hormones leads to dysregulation of the hypothalamus pituitary-gonadal axis in humans. The prevasiveness of subclinical hypothyroidism is characterized by abnormal elevation in TSH levels with normal levels of free thyroxin (T4) in infertile women. The primary reason behind the infertility of every 20 women is subfertility (1). 20% cases of subclinical hypothyroidism have been found which is a primary cause of diminished reproductive capacity (2,3). Overall on an average

levels of TSH in fertile women were less than that of infertile women. An elevation in TSH levels were associated with decreased ovarian reserve in patients with infertility. Hypothyroidism also leads to oligomenorrhoea (4,5). Increase in age decreases female fertility mainly because of diminished ovarian function. AMH, an indicator of functional ovarian reserve is formed in female ovaries. AMH, produced by the granulosa cells from pre-antral and small antral follicles is a dimeric glycoprotein belonging to the transforming growth factor-beta (TGF-B) super family, which act on tissue growth and differentiation. AMH is considered as a suitable biomarker for ovarian reserve in women of reproductive age after oophorectomy showed the association of serum AMH levels with the primordial follicles. Low levels of AMH levels may indicate diminished number of eggs which would be released during each cycle. In older age women, the follicular supply and AMH levels tends to decline attenuating the response of ovary to fertility drugs (6). It is expected that impaired thyroid hormone levels will affect the ovarian function although this is still determined. A dispute has always been there over whether it is thyroid function or thyroid autoimmunity or AMH that affects functional ovarian reserve (2,3). A past study reported disturbances in thyroid hormone levels or TPO-Ab associated with subfertility and early loss of pregnancy. But the exact pathophysiology is not known (6, 7, 8).In this study, we compared the association between TSH and AMH levels in patients ranging from 19-43 age group with healthy individuals.

Materials and Methods

2ml venous blood samples were collected from all the patients visiting Kasturba Hospital Manipal. The blood was then centrifuged and the serum separated from the blood was used to measure both AMH and TSH levels. Both AMH and TSH levels were estimated by Electrochemiluminescence assay (ECLIA). The study protocol was approved by the ethics committee of Kasturba Medical College, Manipal before the commencement of the study. In this retrospective study between time period February to May 2017, 185 consecutive age and sex matched women who visited Kasturba Hospital, Manipal were diagnosed as infertile or fertile according to the diagnostic criteria shown below.95 women of age ranging from 20-42 years considered as cases were recruited for participation in this study. 90 controls of age group 19-43with both AMH and TSH levels normal were taken in order to find the association of AMH and TSH levels. Only ovarian cancer patients were excluded from the study. All women of reproductive age group 19-43 years were included in this study. The

levels of AMH and TSH in the both cases denoted as (Group 1 in Table 1) and controls denoted as (Group 2 in Table 1) were later compared by Independent t test in the above mentioned reproductive age group. Pearson's correlation was used to find the association of AMH with age in women of reproductive age group.

Results

Table 1: Comparison of Serum AMH and TSH levels in Women of Reproductive Age

Name of the groups	**Age (Mean±SEM) (years)**	**AMH Levels (Mean± SEM) (ng/ml)**	**TSH Levels (Mean±SEM) (µIU/ml)**
Cases (Group 1) (n=95)	32.88±.502	2.63±.292	5.951±.145
Controls (Group 2) (n=90)	29.87±.47	5.22±.084	2.21±.098
P- value	<.0001*	<.0001*	<.0001*

P*-Pearson's correlation

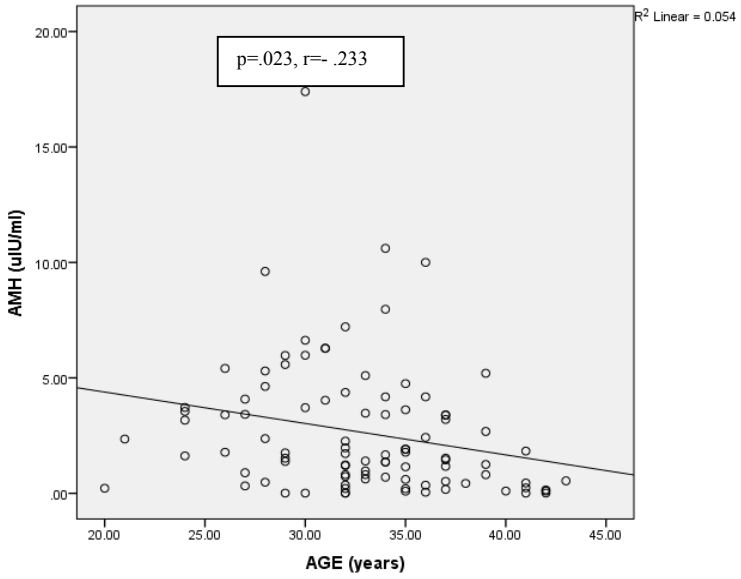

Fig 1: Correlation of AMH levels with ages in cases

Discussion

Study of Hansen et al revealed that serum AMH levels had inverse correlation with patient age and levels of TSH in women with infertility. In the age group of infertile patients TSH levels were shown to affect AMH levels. Strong correlation with infertility was found due to decline in AMH levels according to that study (4). Study of Cramer et al revealed that TSH and AMH levels had inverse correlation in infertile women with diminished ovarian function. The other factors affecting thyroid and ovarian function were included (5). Women who are suffering from subclinical hypothyroidism with high TSH levels are more prone to infertility Michalakis et al. also reported elevation of serum TSH levels is the main cause for widespread of decreases ovarian reserve in infertile women[7]. In in-vitro fertilization Cramer et al also revealed TSH as a significant predictor of fertilization failure in women [3]. Therefore, in infertile patients TSH may be considered as ovarian function influencing factor. Also during early pregnancy thyroid hormone plays a major role for embryo, follicular and placenta development as well as implantation[8,9,10,]. Additionally, follicular development is suppressed by TSH [11] via its interaction in various pathways. To maintain normal reproduction proper functioning of thyroid hormones is important. Many years ago it was reported that changes in sex hormone binding globulin (SHBG) and sex steroids as a consistent feature associated with both hyper- and hypothyroidism in both males and females[12]. In females menstrual disturbances can be a major cause due to thyrotoxicosis and hypothyroidism. Hypomenorrhea and polymenorrhea are basically due to thyrotoxicosis, whereas hypothyroidism is mainly due to oligomenorrhea [13]. According to recent studies, many evidences showed that women who suffered from PCOS is often associated with hypothyroidism or at risk of hypothyroidism in future. Hypothyroidism can also lead to abnormal sexual development whereas severity of it can lead to abnormal monthly release of eggs due to numerous interactions of thyroid hormones with the female reproductive system. Past study revealed increase in TSH concentration leading to increase in the concentration of AMH levels in all infertile women. As per our study we found increase in TSH levels leading to decline in AMH levels which clearly indicates that TSH dysfunction or subclinical hypothyroidism adversely affects functional ovarian reserve in women of reproductive age. On the other hand we found inverse correlation between AMH and age in cases of subclinical hypothyroidism patients which was not observed in cases of euthyroid patients. The results observed in our study clearly indicates that there is a need for aggressive treatment for hypothyroidism in cases of unexplained infertility.

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Acknowledgement

I would like to express my deepest gratitude to my guide and Head of the Department of Biochemistry Department of Kasturba Medical College, Manipal who helped me throughout this study.