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MEAN ANTI-MULLERIAN HORMONE LEVELS;
COMPARISON IN FERTILE AND INFERTILE WOMEN OF REPRODUCTIVE AGE

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ABSTRACT… Objective: To compare the means of Anti-Mullerian hormone levels in both fertile and infertile women. **Study Design:** Case-Control study. **Place and Duration of Study:** This study was conducted at infertility clinic of Gynecology& Obstetrics Unit-II, Civil Hospital, Karachi. The total duration of the study was approximately 1 year from October 2011 to October 2012. **Methods:** A total of 52 infertile women attending the Gynae-Unit-II out-patient clinic at Civil Hospital, Karachi and 48 fertile non-pregnant females of reproductive age group i.e. 20-35 years who met the inclusion criteria were included in the study. The serum Anti-Mullerian hormone levels were measured in both the infertile and fertile groups. Blood samples to determine Anti-Mullerian hormone levels were obtained irrespective of their menstrual cycle days. **Results:** Independent sample t-test showed decreased mean serum Anti-Mullerian hormone levels in infertile group (cases) than the fertile controls. **Conclusions:** Mean concentration of serum Anti-Mullerian hormone in infertile women was sig nificantly lower than that in fertile control women.

Key words: Fertile women, Anti-Mullerian Hormone, infertility.

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INTRODUCTION

In recent decades, infertility has become a major global issue with medical, economic and psychosocial impact on infertile couples. Large number of infertile population is very anxious and eager to be treated. The prevalence of infertility worldwide is approximately 10-15% whereas in Asia it is around 8-12%.Infertility rate in Pakistan is about 21.9%[1,2].

Ovarian reserve is the amount of oocytes present in both ovaries. The conventional tests to determine an individual's ovarian reserve include third day serum follicle-stimulating hormone levels and antral follicle count. Recently, another test has been included as a marker of ovarian reserve i.e. Anti-Mullerian hormone levels (AMH) are measured[3].

Mullerian inhibiting substance is the other name for Anti-Mullerian hormone. It is a dimeric glycoprotein and a 140-kilodalton hormone. It belongs to the super family of transforming growth factor beta[4].

Initially, synthesis of AMH occurs as a large precursor molecule. Later on, it is converted into the pre-prohormone and this forms the homodimers. The homodimer or the mature hormone then undergoes glycosylation and produces two identical 70-kD a monomer subunits. These monomer subunits are bonded by disulphide-linkage by dimerisation, thus producing a 140-kDa dimer. Each monomer subunit contains two domains; an N-terminal domain and C-terminal domain. AMH acquires its full bioactivity by the N-terminal domain which causes the activation of C-terminal domain[5]. It is mainly produced and secreted by the granulosa cells of ovarian follicles. The levels of serum AMH are hardly detectable at birth, but remains stable throughout the reproductive period. With advancing age, AMH levels start declining. According to recent studies, serum AMH levels represent the quantitative aspect of ovarian reserve. Moreover, its levels strongly correlate with the size of the early growing follicle pool, and due to lack of inter-cyclic variability, it can be regarded as a diagnostic marker to assess ovarian reserve. The ovary secretes AMH directly into the blood;

hence it is easy to measure AMH in serum[6].

AMH is involved in the process of folliculogenesis. Physiologically, there are two main functions of AMH i.e.; it inhibits the recruitment of primordial follicle cell and it also inhibits the selection of follicles that are under the influence of FSH for dominance[7].

Female reproductive hormones such as FSH, LH and steroids are involved in late folliculogenesis i.e. during the formation of large antral follicles. Thus, they reflect the peri-ovulatory ovarian activity. On the other hand, AMH is produced by the granulosa cells of early antral follicles and provides information regarding ovarian reserve[8]. Diminished ovarian reserve is regarded as one of the major causes of infertility[9].

AMH is regarded as an excellent marker of the ovarian reserve, a measure of the biological age of the ovaries and a diagnostic marker of ovarian dysfunction[10].

Assessment of ovarian reserve by serum AMH levels can be determined with greater specificity and sensitivity in women of reproductive age rather than by determination of FSH together with other ovarian reserve markers. This is due to the fact that, AMH acts in paracrine fashion and is not under the influence of negative feed-back mechanisms of hypothalamic-pituitary-gonadal axis. It can be measured on any day of the menstrual cycle[11,12].

MATERIAL & METHODS

This study was conducted at Institute of Basic Medical Sciences, Dow University of Health Sciences in collaboration with Gynecology & Obstetrics Unit-II, Civil Hospital, Karachi. Patients were selected from outpatient department and bench work was carried out at the Dow Diagnostic Research and Reference Lab, Ojha Campus.

A total of 100 female subjects were included in this study. Out of this, 48 fertile non-pregnant females (primigravida and second gravid) and 52 infertile females were taken between the age range of 20-35 years. Primary infertile women (no history of previous pregnancy) with normal semen analysis of their husbands and patent fallopian tubes on the basis of hysterosalpingography were included in the study.

Secondary sub-fertile females (history of previous pregnancy), with normal report of husband's semen analysis, patent fallopian tubes and no history of pelvic inflammatory disease or endometriosis were also included in the study.

Fertile and infertile women > 35 years and having the following history were not included in the study:
Blocked fallopian tubes
Ovarian malignancy
Previous pelvic surgeries
Drugs interfering with fertility like estrogen antagonists
Having male infertility factor.

For estimation of serum AMH levels, all selected subject's blood samples were drawn by venipuncture in serum separator tubes. Blood samples were taken from the both the fertile and infertile groups for AMH levels on any day of the menstrual cycle. Approximately, 3ml of blood was collected by venipuncture in separate gel tubes , centrifuged and serum collected and frozen in aliquots at -20^0 C. Samples were stored temporarily at the Dow Collection Point and were then transferred to the Microbiology Lab at the DDRRL for further storage. Serum AMH levels were determined by enzyme linked immunosorbent assay, using Human AMH Elisa kit (CDN-E 1350) at DDRRL.

After data entry, statistical analysis was conducted on SPSS 16.Continuous variables were expressed as mean and standard deviation. Independent sample t-test was done to compare the means of AMH levels between the fertile and infertile groups. A P-value < 0.05 was considered statistically significant.

RESULTS

The age distribution among two groups is

presented in Table-I. The mean age and standard deviation for the infertile subjects was 26 years ± 4.026. The mean age and standard deviation for fertile group was 26.5 years ± 3.655.

Study subjects	Maximum	Minimum	Mean±SD
Fertile group	35	20	26.5±3.96
Infertile group	35	20	26±4.02

Table-I. Age distribution of study groups.
SD: standard deviation 26±4.02

Anti-Mullerian Hormone levels were measured in both the fertile and infertile group. The mean AMH levels in fertile group were calculated as 2.0 ng /ml with mean standard deviation of ± 0.62. Maximum serum AMH levels were 3.2 ng/ml and minimum levels were 1.9 ng/ml.

AMH was measured in infertile subjects and their mean was calculated as 1.6ng/ml with minimum levels of 0.05ng/ml and maximum as 2.9 ng/ml as mentioned in Table-II.

Anti-Mullerian hormone (ng/ml)	Fertile group	Infertile group
Mean±SD Range	2.0±0.61 1.9-3.2	1.6±0.62 0.05-2.9

Table-II. Descriptive statistics of AMH in fertile & infertile subjects

Independent sample t-test was done to compare the means of the serum AMH levels in fertile and infertile groups. AMH levels showed significant difference (P< 0.05) between both the groups as in Table-III.

Groups	Mean Anti-Mullerian hormone	P-value
Infertile (n=52)	1.64±0.62	0.005*
Fertile (n=48)	2.00±0.61	

Table-III. Comparison of means of AMH by independent sample t-test in fertile and infertile groups
** P-value is significant at the 0.05 level*

DISCUSSION

Infertility is a global issue and needs to be assessed at an earlier stage for better options of fertility treatments. There are various conventional tests available for ovarian reserve assessment which includes the basal third day FSH levels and early antral follicle count by transvaginal ultrasound. Apart from these tests, AMH has also been proved as most reliable marker for ovarian reserve assessment[13].

This study was designed to compare mean AMH levels in both fertile and infertile females. In the present study, hundred female subjects were selected in their reproductive age group and mean age was 26 years. Mean serum AMH was 1.6 ng/ml in infertile group and 2.0 ng./ml in fertile group. These findings were consistent with the Gleicher N study in which mean AMH was 1.59 ± 0.12 ng/ml[14].

The means of serum AMH levels in both infertile cases and fertile controls were compared and significant difference (P < 0.05) was found between these two groups. Same results were obtained by a case-control study conducted by Mossa M et al 2012.who found that mean concentration of serum AMH in infertile women was significantly lower than that in fertile control women[15].

CONCLUSIONS

The present study concluded that infertile females have reduced levels of Anti-Mullerian hormone compared to fertile women in their reproductive age group.

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A ship is safe in harbor,
but that's not what ships are for.

William G.T. Shedd