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RESEARCH ARTICLE

Is there a difference in FSH levels between different age groups of infertile patients with poor ovarian reserve?

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ABSTRACT

Aim: The aim of this study is to compare the diagnostic accuracy of follicular stimulating hormone (FSH) in different age groups of poor ovarian reserve (POR) infertile patients.

Material and Methods: The records of infertile patients who presented to a tertiary center hospital infertility outpatient clinic were retrospectively analysed. The patients were divided into two groups: those between the ages of 20-29 were considered as group 1, and those between the ages of 30-39 were considered as group 2. FSH specificity and sensitivity were compared in patients with (POR) with antimullerian hormone (AMH) values below <1 ng/mLThe specificity, sensitivity, and accuracy of the FSH assay as a diagnostic tool for determining reduced OR in females with POR were compared and predicted using ROC curve analysis.

Results: A total of 102 infertile patients were assessed. Those between the ages of 20-29 were considered as group 1, and those between the ages of 30-39 were considered as group 2. The avarages FSH levels for each group were 9.73 ± 3.17 and 10.06 ± 8.74, respectively (p value = 0.85). The sensitivity, accuracy, and specificity of the FSH assay were, 85%, 78%, and 68%, respectively (p=0,001). In group 2, FSH values may be more meaningful for evaluating the ovarian reserve.

Conclusion: FSH was not correlated with AMH and antral follicule count (AFC). In the age-specific FSH assessment showed that FSH is still not a specific marker in POR. This study concluded that FSH and age have a weak correlation with the number of follicles restored and the number of oocytes retrieved.

Keywords: age, antimullerian hormone, follicular stimulating hormone, infertility, ovarian reserve

INTRODUCTION

Primordial follicle granulosa cells generate the glycoprotein-structured antimüllerian hormone (AMH). Follicle growth is inhibited in response to follicular stimulating hormone (FSH). The number of antral follicles and the size of the primordial follicle pool are known to positively correlate with AMH (1-3). One of the endocrine tests used to assess ovarian reserve (OR) is the basal FSH measurement. The

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pituitary secretes the glycoprotein FSH, which binds to receptors on the granulose cells of the ovaries. FSH levels and activity vary throughout a woman's menstrual cycle. A woman's menstrual cycle is often determined by measuring FSH serum levels on days 2-3 of menstruation. It is examined every day. At this stage of the menstrual cycle, low FSH levels are normal, but when follicles become smaller, FSH levels climb. Consequently, low OR is indicated by elevated FSH levels. While FSH has been employed as a marker to estimate OR, there are a number of intra- and inter-cycle variables that make it inconsistent to utilize FSH as a reliable indicator of OR. AMH levels that are more constant over the course of the menstrual cycle make it a more useful tool for OR prediction (4).

The aim of this study is to compare the diagnostic accuracy of FSH in different age groups of poor ovarian response (POR) infertile patients.

MATERIAL AND METHODS

The records of infertile patients who presented to a tertiary center hospital infertility outpatient clinic were retrospectively analysed. The study protocol was approved by the regional ethics committee (2020-459). FSH specificity and sensitivity were compared in patients with POR with AMH values below <1 ng/mL. One hundred two infertile patients were divided into two groups. Those between the ages of 20-29 were considered as group 1, those between the ages of 30-39 were considered as group 2. The evaluation of AMH tests and the cut-off values were difficult to determine because the AMH analysis varies. The cut-off values used for the evaluation of POR vary between 0.10-1.66 ng / mL (5-8). In this study, we evaluated patients with AMH less than 1 ng/mL. ROC curve analysis was used to compare and estimate the specificity, sensitivity, and accuracy of FSH testing as a diagnostic test to identify reduced OR in women suffering from POR Blood was collected (AMH, FSH, LH, E2) on days 2–4 of the menstrual cycle. Antral follicle count (AFC) was evaluated by transvaginal ultrasonography (TV-USG). The total of 2-10 mm follicles in the ovaries was defined as AFC (9). Those who had previous ovarian surgery, had endometrioma and ovarian cysts, have been exposed to pelvic radiation, have been on the contraceptive pill for the past 3 months, and patients older than 40 have been excluded from the study. Statistical analysis Descriptive statistics and (mean ± SD) SPSS were used to analyze statistical data. To evaluate quantitative data, the Student's t-test was used for normally distributed variables and Mann-Whitney U test was used for non- normally distributed variables. The chi-square test and Fisher's exact test were used to compare qualitative data. Statistical significance was determined as $p < 0.05$. ROC curve showing the balance between specificity (what is the false positive rate) and sensitivity (what is the true positivity rate) for FSH testing between the (20-29 years) and (30-39 years) range groups. We estimated the area under the ROC curve (AUC) using empirical methods. The ROC curve, which shows the balance between specificity (what is the false positivity rate) and sensitivity (what is the true positivity rate) for the FSH test, covers the age groups between (20-29 years) and (30-39 years).We estimated the area under the ROC curve (AUC) with the use of empirical methods.

RESULTS

Table 1 shows FSH levels evaluated in the 20-30 age group and 30-40 age group. The averages for each group were 9.73 ± 3.17 and 10.06 ± 8.74, respectively.

There was no significant difference in FSH levels between the groups (p value = 0 .85). The sensitivity, accuracy, and specificity of the FSH assay were, Sensitivity, accuracy and specificity of the FSH indicator 85%, 78% and, 68%, respectively ($p<0.01$) (Table 2).

The sensitivity, accuracy, and specificity of the FSH test were demonstrated by the ROC curve. In group 2, FSH values may be more meaningful to evaluate the ovarian reserve (Figure 1).

Table 1. Demographic and laboratory results and comparison of the two groups

	Group 1 (Age 20-29) n=22	Group 2 (Age 30-39) n=80	P value
Age (years)	26.45 ± 2.79	35.73 ± 2.33	0.43
AMH (ng/mL)	0.42 ± 0.33	0.47 ± 0.33	0.52
LH (mU/mL)	5.13 ± 1.14	7.58 ± 7.39	0.5
FSH (mU/mL)	9.73 ± 3.17	10 .06 ± 8.74	0.85
Antral follicle count (n)	4.32 ± 1.84	3.99 ± 1.86	0.45
Estradiol (pg/mL)	56.68 ± 47.53	66.79 ± 71.34	0.53

Study data (mean ± SD). Student's t-test was used for normally distributed variables, and the Mann-Whitney U test was used for non-normally distributed variables. A chi-square test and fisher exact test was used to compare qualitative data. Statistical significance was set at $p < 0.05$.

Table 2. ROC curve analysis for FSH assays comparing the two groups

Variable	AUC	P value	Sensitiviy	Accuracy	Specificiy
FSH	0.67	0.001	85%	78%	68%

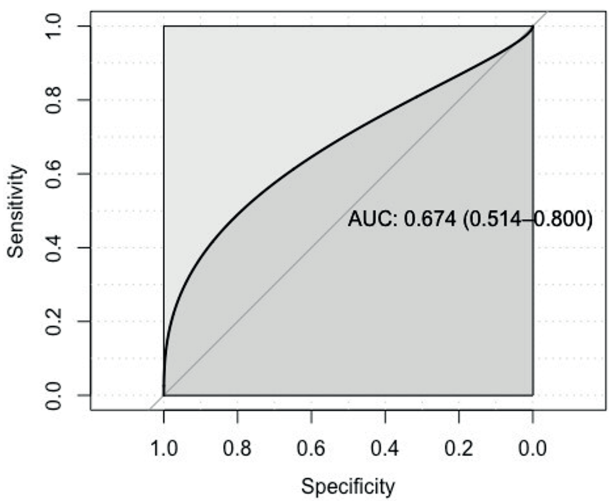

Figure 1. ROC curve analysis for FSH assays comparing the two groups.

DISCUSSION

Early diagnosis still remains an important issue in order to implement effective treatment protocols in infertility. Many tests for OR evaluation, including TV-USG, early antral follicle count, and second-day basal FSH levels, still maintain their current place. The main aim of this study was to determine the correlation between AMH values below 1 ng/mL and specific age ranges in patients. In this study, age-specific FSH evaluation suggests that FSH is still not a specific marker for POR. However, FSH values may be more meaningful for evaluating ovarian reserve in the older age group. AMH, FSH, and AFC are widely used as tests of the ovarian reserve. The AMH test shows better activity in POR estimation than AFC and FSH. These markers have their advantages and limitations. FSH has been reported to have high specificity and low sensitivity in POR estimation (5). FSH does not have a prediction for ovarian hyperstimulation syndrome and is known to have inter-cyclical variability. You cycle 2-4. Considered on the day, AFC has the advantage of generating urgent results and is useful for POR 's estimation and OHSS risk (10). However, AFC requires experienced sonographic experience by experienced specialists. Conversely, blood can be drawn for AMH even when TV-USG is not readily available (11). In this study, AFC was observed to be low in proportion to AMH values. However, it is seen that AFC is more valuable than FSH in POR patients. Abed et al. (12) predicting and comparing the specificity, sensitivity, and accuracy of AMH testing with FSH testing demonstrates the application of ROC curve analysis as a diagnostic test to determine OR in infertile women. When comparing the detection of premature ovarian failure (POF) using FSH or AMH tests between fertile female patients and POF patients, the AMH test remains a more sensitive and specific test than the commonly used FSH biomarkers in detecting POF. When comparing the POF group with the nonfertile control group, the sensitivity of FSH and AMH tests was the same.

However, the FSH test was more specific and accurate than the AMH test. On the other hand, in this study, two of our patients were evaluated as infertile POR, individuals with AMH levels below 1 ng/mL were included in the groups, and it was observed that FSH was not associated with AMH and AFC in both groups. Jamil et al. and Siddiqui et al. showed that FSH had a weak correlation between the number of follicles repaired and the number of oocytes retrieved (13,14). This creates negative differences with AMH, which has a strong relationship with the retrieval of oocytes.

AMH was reported to be more sensitive in detecting ovarian reserve when Parveen et al. (15) compared the diagnostic accuracy of AMH with FSH in the evaluation of ovarian reserve. When comparing individuals with poor ovarian reserve to those with normal to high response, the mean AMH was 0.74 ng/mL. According to Baker et al. (16), the receiver operating characteristic (ROC) curve's AMH cutoff point for determining POR was 0.93 ng/mL with 74.1% sensitivity and 90% specificity. AMH (area under the ROC curve [AUC] = 0.929) performed substantially better in POR prediction than FSH (AUC = 0.615; P<.0001), according to ROC analysis.

In this study, the sensitivity , accuracy, and specificity of the FSH test were demonstrated by the ROC curve.

The FSH test has a sensitivity, accuracy, and specificity of 85%, 78%, and 68%, in that order. It seems that FSH is still not a specific indication in POR based on age-specific FSH examination. For assessing ovarian reserve in the older age range, FSH readings might have greater significance. There has been no research done on the assessment of FSH based on age range. The primary limitation of our study is its retrospective nature. Another limitation is that the study was conducted at a single institute with a small sample size. AMH and AFC had no correlation with FSH. FSH is still not a specific sign in POR, according to the age-specific FSH assessment. This study demonstrates that oocyte number is a poor indicator of FSH and age.

Ethical approval

This study has been approved by the ethics committee of Health Science University Gazi Yasargil Education and Research Hospital (approval date 28/04/2020, number 459). Written informed consent was obtained from the participants.

Author contribution

Surgical and Medical Practices: NP, SE; Concept: NP, SE; Design: NP, SE; Data Collection or Processing: NP, SE; Analysis or Interpretation: NP, SE; Literature Search: NP, SE; Writing: NP, SE. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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