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Serum anti-Müllerian hormone levels are lower in reproductive-age women with Crohn's disease compared to healthy control women

Ebubekir Şenateş [a,*], Yaşar Çolak [b], Emrullah Düzgün Erdem [a], Atakan Yeşil [a], Ender Coşkunpınar [c], Önder Şahin [c], Mustafa Erhan Altunöz [d], Ilyas Tuncer [e], Ayşe O. Kurdaş Övünç [a]

[a] *Haydarpaşa Numune Education and Research Hospital, Department of Gastroenterology, Turkey*
[b] *Mardin State Hospital, Department of Gastroenterology, Turkey*
[c] *Department of Molecular Medicine, Institute of Experimental Medicine Research, Istanbul University, Turkey*
[d] *Sakarya Education and Research Hospital, Department of Gastroenterology, Turkey*
[e] *Göztepe Education and Research Hospital, Department of Gastroenterology, Turkey*

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Abstract

Background and aim: Crohn's disease (CD) decreases fertility both directly, by inducing inflammation in the fallopian tubes and ovaries, and indirectly, through the surgical interventions and tubal adhesions associated with disease treatment. Anti-müllerian hormone (AMH) is a reliable indicator of ovarian reserve in women. We aimed to compare serum AMH levels between reproductive-age women with CD and healthy controls.
Methods: Serum AMH levels were measured by ELISA in 35 women with CD and 35 age-matched healthy women controls.
Results: CD patients and controls were similar in terms of age, height, weight and BMI. Mean CD duration was 60 months. CRP, ESR and leukocyte counts were significantly higher in CD patients compared to the controls ($p<0.001$, $p=0.004$ and $p=0.04$, respectively). AMH levels in CD patients (1.02 ± 0.72) were significantly lower compared to the controls (1.89 ± 1.80) ($p=0.009$). Serum AMH levels in CD patients with active disease (0.33 ± 0.25) were significantly lower compared to CD patients who were in remission (1.53 ± 0.49) ($p=0.001$). Serum AMH levels were similar in CD patients with a disease duration of less than 5 years (17 patients) and CD patients with a disease duration of greater than 5 years (18 patients) ($p=0.8$). In CD patients, a negative

* Corresponding author at: Haydarpaşa Numune Education and Research Hospital, Department of Gastroenterology, Tibbiye Cad. No:40 34668 Uskudar, Istanbul, Turkey. Tel.: +90 216 542 32 32-1623, +90 506 688 38 13 (Mobile); fax: +90 216 346 74 63.
E-mail address: ebubekirsenates@yahoo.com (E. Şenateş).

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correlation between CDAI and serum AMH levels was found ($r=-0.718$, $p<0.001$). Serum AMH levels were similar in CD patients who had (6 patients) and had not undergone (29 patients) surgical treatment ($p=0.2$).
Conclusion: Serum AMH levels of reproductive-age women with CD were significantly lower compared to the controls. CDAI and AMH are inversely correlated.

1. Introduction

Crohn's disease (CD) is a recurrent, chronic inflammatory disease of idiopathic origin that is characterized by periods of remission and flare-ups.

CD is associated with various extraintestinal pathologies in addition to numerous intestinal pathologies. These extraintestinal symptoms often affect the eyes, skin, musculoskeletal, renal, hepatobiliary and hematologic systems.

Women with CD have fewer children compared to healthy women.[1] The underlying reason for this difference is hypothesized to be related to a decreased desire to have children by women with CD rather than being caused by the disease itself.[2] However, the most recent consensus report, published by the European Crohn's and Colitis Organisation (ECCO), documents decreased fertility in women with CD, especially in patients with active disease.[2] CD is a chronic inflammatory disease that decreases fertility both directly, through the induction of inflammation in the fallopian tubes and ovaries, and indirectly, through the surgical interventions and tubal adhesions that are associated with disease treatment.[3–15]

Objective indicators that reflect ovarian reserve, an indicator of fertility in reproductive-age women, include estradiol, follicle-stimulating hormone (FSH) and anti-Müllerian hormone (AMH); additionally, the clomiphene citrate challenge test (CCCT), the exogenous FSH ovarian reserve test (EFORT) or an ultrasound assessment of the antral follicle count or ovarian volume can be performed to assess fertility.[16] Tests involving estradiol and FSH require sample collection on a particular day of the menstrual cycle (day 3), and the collection of more than one sample is often needed.[16] The CCCT, EFORT and ultrasound assessment of antral follicle count or ovarian volume have limitations in their methodologies and value for predicting fertility. However, because AMH levels vary only slightly during the menstrual cycle, an analysis can be conducted on a single sample collected at any point during the patient's menstrual cycle. Therefore, AMH testing has replaced these other fertility tests over time, especially in the context of in vitro fertilization (IVF) studies.[17–19]

In recent studies,[16,20–22] AMH levels have been reported to be a good indicator of ovarian reserve in women. AMH is a member of the transforming growth factor-β (TGF-β) family and is secreted by small (<8 mm) preantral and early antral follicles.[16] AMH levels reflect the size of the primordial follicle pool. In mature women, AMH levels decrease over time due to the reduction in the primordial follicle pool that occurs with advancing age.[23] Consistent with this phenomenon, AMH levels decrease during menopause and eventually become undetectable.[24] AMH levels appear to be an early, reliable, direct indicator of reduced ovarian function. Serum AMH levels exceeding 0.5 ng/mL are indicative of a good ovarian reserve, whereas serum levels below 0.5 ng/mL are indicative of a reduced ovarian pool. Serum AMH levels below 0.15 ng/mL indicate that the patient will respond poorly to IVF.[25,26] Thus, AMH measurements can play an important role in the diagnosis of patients with low ovarian reserve.[27]

The aim of this study was to compare serum AMH levels between female reproductive-age patients with CD and healthy, age-matched women.

2. Materials and methods

In total, 35 reproductive-age female patients who had a definitive clinical CD diagnosis that was confirmed through endoscopic, radiologic and histopathologic findings were included in the study. The women were treated and subsequently followed at the Haydarpasa Numune Education and Research Hospital between 2004 and 2010. Additionally, 35 healthy, age-matched women were included in the study as controls.

Exclusion criteria for CD patients were as follows: age greater than 40 years, having a previous ovarian resection, renal failure (serum creatinine levels >1.2 mg/dL), a diagnosis or suspicion of malignancy, the presence of hereditary or acquired hematologic disease, pregnancy, current lactation, the presence of a serious comorbid chronic illness, chronic liver disease-induced cirrhosis, abnormal thyroid function tests, the presence of a known serious psychological problem, alcoholism and male gender. The control group was selected from women with no known diseases and who had never received any drug or transfusion treatment. In addition, women must have had no inflammatory bowel disease diagnoses in any of their first-degree relatives, no surgical history and not be taking any current medications.

At the beginning of the study, demographic data such as age, height, weight and body mass index (BMI) were recorded for all study participants. Additionally, serum levels of acute phase reactants (CRP, ESR, platelet count and albumin) were determined, and complete blood work analyses were performed for all subjects. For CD patients, the CD activity index (CDAI), sites of intestinal disease involvement and any medications used were recorded. CD patients with a CDAI below 150 were considered to be in remission, whereas CD patients with a CDAI over 150 were considered to have active CD.

Patients and healthy controls were compared in terms of demographics, serum biochemical parameters and serum AMH levels. Next, CD patients were divided into patients with active disease and patients in remission, and the groups were compared in terms of their serum AMH levels. In CD patients, the existence of a correlation between CDAI and serum AMH levels was investigated using a Pearson correlation analysis. Finally, serum AMH levels in CD patients who had