

# Comparison of Presence of Autoimmune Activity in Patients with Premature Ovarian Failure and Menopause

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**Objective:** To assess and compare autoimmune activity in patients with premature ovarian failure (POF) and menopause.

**Method:** Thirteen women with premature ovarian failure but with no history of autoimmune disease were recruited into the study group and 15 women with natural menopause into control group between January 1999 and November 2000. The mean FSH levels of patients with premature ovarian failure were  $73.95 \pm 29.11$  (range: 41-130.7 U/L). Nuclear (antinuclear antibody=ANA, double-stranded DNA antibody=anti-dsDNA) and cardiolipin antibodies (IgM, IgG), immunoglobulins (IgM, IgG, IgA) and complement ( $C_3$ ,  $C_4$ ) levels were determined. Student's t test was used to compare the groups.

**Results:** Antinuclear antibody was positive in 30.7% of patients with premature ovarian failure and in 13.3% of controls. There was no significant difference in anticardiolipin antibodies, immunoglobulins and complement levels between the groups ( $p > 0.05$ ).

**Conclusion:** In our study, no autoimmune deficiency was found in patients with POF.

**Key words:** Premature ovarian failure, autoimmunity and menopause.

Premature ovarian failure (POF) is a clinical entity characterized with amenorrhea lasting 4-6 months, symptoms of hypoenestrogenism and gonadotropin levels above 40U/L before the age of 40. The incidence is 1:100 before the age of 40 and 1:1000 before the age of 30 (1). Chromosomal, infectious and iatrogenic and autoimmune factors may be involved in development of POF. In fact, POF was observed to be associated with autoimmune deficiency (2-5) and the incidence of POF with a concurrent autoimmune disease was reported to be 17% (3).

The aim of this study was to evaluate autoimmune activity in patients suffering from POF and compare autoimmune activity of these patients with that of patients with naturally occurring menopause.

## Material and Method

This study included 13 patients with no history of known autoimmune disease who were diagnosed with POF in the Department of Obstetrics and Gynecology at Ankara University between January 1999 and November 2000. POF was defined as secondary amenorrhea and associated FSH serum concentration over 40mIU/ml occurring before the age of 40 (6). The patients who had undergone an ovarian operation, chemotherapy or radiotherapy were excluded from the study. The average FSH level was  $73.95 \pm 29.11$  mIU/ml (range: 41-130.7mIU/ml) in POF group. Three of 13 patients diagnosed with POF expressed their desire to have a child. Control group consisted of 15 women found to be on natural menopause and, they were not on estrogen replacement therapy (FSH: $58.33 \pm 16.27$ mIU/ml).

To establish a search of autoimmune profile, nuclear (antinuclear antibody=ANA, double stranded DNA antibody=anti-dsDNA) and cardiolipin antibodies (IgM, IgG), serum immunoglobulin (IgM, IgG, IgA) and complement ( $C_3$ ,  $C_4$ ) levels were measured. ANA and cardiolipin antibodies were assessed using enzyme immunoassay and serum immunoglobulin levels with nephelometric tests.

Student's t test was used to compare the groups.  $P < 0.05$  was considered significant.

## Results

The mean age of POF group (n=13) was  $35.38 \pm 5.00$  years, while it was  $46.93 \pm 4.20$  in natural menopause group ( $p < 0.001$ ). ANA was positive in 30.7% of POF group, whereas it was so in 13.3% of natural menopause group. Anti-dsDNA was  $2.08 \pm 1.30$  IU/ml in POF group and  $1.63 \pm 1.40$  in the natural menopause group ( $p = 0.4$ ). Anticardiolipin antibody IgM and IgG levels were similar in both groups. There were no significant differences in serum immunoglobulin (IgA, IgM, IgG) levels between the groups ( $p = 0.14$ ,  $p = 0.21$ ,  $p = 0.52$ ). The mean  $C_3$  level was  $1.19 \pm 0.18$ g/l in POF group and  $1.10 \pm 0.16$ g/l in the

Table I. Autoimmune activity in the POF and natural menopause group.

		Group I (POF, n=13)	Group II (menopause, n=15)	P *
Age**	Years	35.38 ± 5.00	46.93 ± 4.20	< 0.0001
Anti dsDNA**	IU/mL	2.08 ± 1.30	1.63 ± 1.40	0.40
Anticardiolipin IgM**	U/mL	11.6 ± 10.7	17.9 ± 17.9	0.28
Anticardiolipin IgG**	U/mL	19.83 ± 17.9	24.67 ± 21.43	0.53
IgG**	g/L	11.96 ± 3.91	12.73 ± 2.37	0.52
IgM**	g/dL	1.08 ± 0.51	1.34 ± 0.53	0.21
IgA**	g/L	2.10 ± 0.65	1.76 ± 0.55	0.14
C <sub>3</sub> **	g/L	1.19 ± 0.18	1.10 ± 0.16	0.19
C <sub>4</sub> **	g/L	0.24 ± 0.13	0.22 ± 0.07	0.65

\* Student's t test

\*\* Mean ± Standard deviation

natural menopause group (p=0.19). The mean C<sub>4</sub> level was 0.24±0.13g/l in POF group and 0.22±0.07g/l in the natural menopause group (Table I).

## Discussion

Endocrine and immune systems work in conformity in the regulation of ovarian functions. POF is associated with autoimmune diseases such as diabetes type I and polyendocrine autoimmunity (7). POF associated with an autoimmune disease suggests that an immune system pathology may play a role in about 40% of these patients. It is difficult to make a differential diagnosis in autoimmune based ovarian failure. Currently, there is no definitive diagnostic serum test to diagnose autoimmune related POF. The only definitive diagnosis of POF remains to be wedge resection of the ovary (8).

In this study, ANA was positive in 30.7% of POF group and in 13.3% of the natural menopause group. In some studies, ANA positivity was investigated in patients with POF and accompanying chromosomal abnormality and those with POF but without chromosomal abnormality. Although ANA was not positive in patients with chromosomal abnormality, it was positive in 77% of patients without chromosomal abnormality who were aged below 30 years (9).

In this study, no significant differences were found in anticardiolipin antibodies, immunoglobulins and complement levels between patients with POF and women in the natural menopause group. Ovarian autoantibodies have not been tested in this study. Blumenfeld et al observed increases in thyroglobulin, nuclear antigen, heart and gluten antibodies and IgM level and decreases in C<sub>3</sub> and C<sub>4</sub> levels in POF group compared to control group (3). Luborsky et al evaluated ovarian, thyroid, nuclear and cardiolipin antibodies in cases of premature menopause and unexplained infertility. Organ-specific antibodies (ovarian and thyroid antibodies) were seen in 60% of patients, while antibodies not specific to organ were seen

in 13% of patients (10). Ho et al evaluated lymphocyte subgroups and immunoglobulin levels before and after estrogen replacement therapy and they observed significant decrease in CD8+ T cells and increase in serum IgG level (11).

In this study, we found no change in autoimmune activity (anticardiolipin antibody, immunoglobulin and complement levels) in patients with POF. This may be explained by small sample size. ANA was positive in both POF and the natural menopause groups. Estrogen insufficiency is likely to be responsible for the etiology of POF.

In this study, although autoimmune activity did not change in patients with POF, if these patients want to have a child, autoimmune activity should be investigated.

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