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Letter to the Editor

Post-menopausal status in primary antiphospholipid syndrome is associated with low HDL-C levels

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To the Editor,

Antiphospholipid syndrome (APS) is an acquired thrombophilic disorder characterized by recurrent thrombosis, fetal losses, and/or thrombocytopenia [1]. In addition, some APS patients may have cardiovascular events associated with traditional risk factors [2]. One important risk factor for cardiovascular disease (CVD) is the presence of menopause. An increased chance of CVD has been observed during the climacteric phase [3]. However, we were unable to find any previous study that has specifically evaluated the effects of menopause in women with primary APS. Therefore, the objective of this work was to assess the clinical and laboratory associations of women with primary APS patients at pre-menopause and post-menopause.

Patients with primary APS (pAPS) were studied to analyze the clinical and serological differences between individuals at menopause (M) and pre-menopause (PM). Forty-nine female pAPS (Sidney criteria) [4] were included in this observational analysis, which excluded men and patients with other connective tissue diseases. Data were obtained using chart review and also clinical examination. IgG and IgM anticardiolipin antibodies (ACL) were measured at least twice using ELISA (Inova Diagnostics, Inc., San Diego, USA). Moreover, lupus anticoagulant (LAC) was detected following international hematological guidelines [5]. An informed consent was obtained from each participant.

In this sample, 13/49 (26.5%) were post-menopause (group 1), and 36/49 (73.5%) were pre-menopause (group 2). We detected the following significant differences: group 1 had greater mean age (53.2±4.5 vs. 34.6±7.9 years old, p<0.0001), thiazide use (30.8% vs. 8.3%, p=0.049), statin use (53.9% vs. 16.7%, p=0.009), arterial events (84.6% vs. 50%, p=0.03), Sneddon's syndrome (46.2% vs. 16.7%, p=0.033), dyslipidemia (61.5% vs. 13.9%, p=0.014), family history of coronary disease (30.8% vs. 2.8%, p=0.006), and lipoprotein(a) levels (72.9±51.5 vs. 38.4±34.5 mg/dL, p=0.039) than group 2. Concerning lipid levels, HDL-C levels (52.1±13.4 vs. 62.8±13.3 mg/dL, p<0.001) were lower in group 1 compared to group 2. Although mean levels of total cholesterol (183±40 vs. 189 41 mg/dl, p=0.18), LDL-c (108±34 vs. 110±41 mg/dL, p=0.87) and VLDL-c (20.2±10.5 vs. 19.7±9.8 mg/dL, p=0.21) and triglycerides (20.2±10.5 vs. 19.7±9.8 mg/dL p=0.217) were alike between the groups. On the other hand, group 1 had less frequent pulmonary thromboembolism (7.7% vs. 38.9%, p=0.037). No other variable, including disease duration, stroke, thrombocytopenia, lupus anticoagulant, sedentarism, smoking, and others, were significantly different between groups 1 and 2 (p>0.05). We proceeded with a multiple logistic regression analysis, and the independent variable associated with the presence of menopause was only dyslipidemia (p=0.01) and low HDL-C (p=0.01).

The present study found for the first time that females post-menopausal with pAPS have different disease spectra in comparison to women pre-menopausal. More specifically, menopause is associated with the presence of dyslipidemia with low HLDL-c.

Previous studies of the literature, including our group, have shown that pAPS is linked to dyslipidemia, specifically with low HDL-C levels [6]. However, this is the first study to evaluate specifically female pAPS subjects pre- and post-menopausal and found these aspects. In the literature, low HDL is commonly described during the aging process. The literature shows a positive association between HDL-C levels and atherosclerosis-related conditions in PM women [7, 8]. Elevated levels of LDL-C, triglyceride, and total cholesterol are related to CVD, with substantial links to HDL-C levels. An improved understanding of the changes in the levels of HDL-C and other lipids in response to meno-

pause status will ensure more consistent strategies objecting to reduce CVD risk.

Advantages of this work were: inclusion of only patients with primary APS; therefore, we excluded associated diseases linked to APS, such as lupus, that may cause dyslipidemia. Regarding study limitations, some possible ones were the relatively low number of participants and the absence of a healthy control group. Therefore, future studies including a large number of participants and a healthy control group are desired.

It is essential to be aware that the coexistence of these three conditions (APS, menopause, and dyslipidemia), may be associated with amplified cardiovascular morbidity that could be even bigger than the risks associated with each separated element.

In conclusion, post-menopausal women with PAPS have an increased risk of low HDL-C in comparison to pre-menopause ones. It alerts to the fact of being aware of this dyslipoproteinemia, and suggests measuring lipid levels in patients with pAPS. Future studies with a larger number of subjects are needed to confirm the present data.

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REFERENCES

1. Cervera R, Piette JC, Font J, Khamashta MA, Shoenfeld Y, Camps MT, et al; Euro-Phospholipid Project Group. Antiphospholipid syndrome: clinical and immunological manifestations and patterns of disease expression in a cohort of 1,000 patients. Arthritis Rheum 2002;46:1019–27. [CrossRef]
2. Mazidi M, Katsiki N, Mikhailidis DP, Banach M; Lipid and Blood Pressure Meta-Analysis Collaboration (LBPMC) Group. Associations of serum uric acid with total and cause-specific mortality: findings from individuals and pooling prospective studies. Atherosclerosis 2020;296:49–58. [CrossRef]
3. Li H, Sun R, Chen Q, Guo Q, Wang J, Lu L, et al. association between HDL-C levels and menopause: a meta-analysis. Hormones (Athens) 2021;20:49–59. [CrossRef]
4. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006;4:295–306. [CrossRef]
5. Wisløff F, Jacobsen EM, Liestøl S. Laboratory diagnosis of the antiphospholipid syndrome. Thromb Res 2002;108:263–71. [CrossRef]
6. Rodrigues CE, Bonfá E, Caleiro MT, Vendramini MB, Bueno C, Lopes JB, et al. Association of arterial events with the coexistence of metabolic syndrome and primary antiphospholipid syndrome. Arthritis Care Res (Hoboken) 2012;64:1576–83. [CrossRef]
7. Fan AZ, Dwyer JH. Sex differences in the relation of HDL cholesterol to progression of carotid intima-media thickness: the Los Angeles atherosclerosis study. Atherosclerosis 2007;195:e191–6. [CrossRef]
8. El Khoudary SR, Wang L, Brooks MM, Thurston RC, Derby CA, Matthews KA. Increase HDL-C level over the menopausal transition is associated with greater atherosclerotic progression. J Clin Lipidol 2016;10:962–9. [CrossRef]

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