The Risk of Obstetric Complications and the Effects of Treatment in Women with Low Titer and Medium-High Titer Anti-Phospholipid Antibodies

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Background/Purpose: The association of low titer anti-phospholipid antibodies (aPL) with obstetric anti-phospholipid syndrome (APS) is increasingly acknowledged, even though some studies have showed conflicting results. To raise further evidence on the relevance of low titer aPL in pregnancy morbidity (PM), we retrospectively reviewed the clinical records of pregnant women attending a joint obstetric/rheumatology clinic over the years 2009-2016.

Methods: Patients were included when positive in at least one criteria aPL assay, at any titer, in two occasions minimum 12 weeks apart. Statistical analysis was performed using R package.

Results: 111 women (338 pregnancies) were identified. 51 women displayed low-titer aPL, with 160 pregnancies. 60 patients carried aPL at medium-high titers, with 178 pregnancies. 4 patients (4%) had thrombotic APS, 27 (24%) obstetric APS, 7 (6%) thrombotic and obstetric APS, 15 (14%) medium-high titer aPL and non criteria PM, 7 (6%) medium-high titer aPL and no PM, 18 (16%) low titer aPL and non criteria PM and 15 (14%) low titer aPL and no PM. Low-titer aPL were significantly associated with pregnancy complications (c²=8.82, p=0.003). Considering 245 untreated pregnancies, a significant difference in PM distribution was noted for low titer and medium-high titer aPL (p=0.003, **Table 1**). Among patients with low titer aPL, treatment with low molecular weight heparin [LMWH] + low-dose aspirin [LDASA] significantly improved pregnancy outcomes (p<<0.001, odds ratio [OR]=0.07, 95% CI=0.007–0.300), leading to a 14.3-fold reduction of obstetric complications. Hydroxychloroquine [HCQ] was not associated with a significant improvement in

live birth rate (p=0.079). Among women with medium-high titer aPL, the standard therapeutic approach with LMWH+LDASA resulted in a significant improvement of obstetric outcome (p<<0.001, OR=0.20, 95% CI=0.100–0.400). HCQ treatment significantly improved obstetric outcome, carrying a 3-fold increase in the live birth rate (p=0.025, OR=0.34, 95% CI=0.117–0.894).

Conclusion: According to our data, low titer aPL are significantly associated with aPL-associated obstetric complications, with a lower prevalence of premature birth compared to medium-high titer aPL. Treatment with LDASA+LMWH led to a higher increase of live birth rate in women with low titer aPL compared to those with medium-high titer aPL. Additional treatment such as HCQ were effective in women with medium-high titer aPL but not those with low titer aPL. **Table 1. Obstetric outcomes (defined according to Miyakis et al, 2006) in 245 untreated pregnancies in women with low titer and medium-high titer anti-phospholipid antibodies.**

	Live birth	Early loss	Late loss	Premature birth	Total
Low titer aPL	57 (42%)	60 (45%)	16 (12%)	1 (1%)	134
Medium-high titer aPL	31 (28%)	59 (53%)	13 (12%)	8 (7%)	111

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