3 Epidemiology of Antiphospholipid Syndrome

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This chapter will review classification criteria of the antiphospholipid syndrome (APS), the prevalence of antiphospholipid antibodies [aPL; anticardiolipin (aCL); lupus anticoagulant (LA)] in normals and in systemic lupus erythematosus (SLE), the prevalence of aPL in venous thrombosis, arterial thrombosis, and pregnancy loss, and longitudinal studies.

Classification Criteria for APS

Classification criteria for APS (Table 3.1) were developed by consensus at the Sapporo antiphospholipid meeting [1]. These criteria, for the first time, emphasized that vasculopathy (and not just thrombosis) was part of APS and broadened the pregnancy criterion to include severe pre-eclampsia. The Sapporo criteria were validated in an exercise by Lockshin et al [2]. The sensitivity was 0.71.

The Sapporo criteria were not evidence based. As part of the Taormina antiphospholipid meeting, evidenced-based criteria were prepared. These criteria required that the criterion be valid in both primary (non-SLE) and secondary (SLE) APS and be proven by more than one study (and more than one study design). The evidence-based criteria do not include pregnancy morbidity, but do include cardiac valve disease (valvular thickening and/or vegetations; Table 3.2) [3].

Table 3.1. Sapporo classification criteria for antiphospholipid syndrome.

Clinical	Laboratory*
Vascular thrombosis	IgG anticardiolipin – moderate or high IgM anticardiolipin – moderate or high
Pregnancy morbidity 3 or more concurrent spontaneous abortions 1 or more unexplained deaths of a normal fetus at or beyond 10th week of gestation 1 or more premature births before 34 weeks because of severe preeclampsia or placental insufficiency	Lupus anticoagulant

*Present at least twice 6 weeks apart.

Table 3.2. Taormina evidence-based classification criteria for antiphospholipid syndrome.

Clinical	Laboratory
Vascular thrombosis	IgG anticardiolipin – moderate or high IgM anticardiolipin – moderate or high
Pregnancy 3 or more early fetal losses 1 intrauterine fetal demise	Lupus anticoagulant
Cardiac Valve thickening and/or vegetations	

Table 3.3. Prevalence of antiphospholipid antibodies in normals.

Study, year	Number of Controls	Type of controls	aCL-IgG	aCL-IgM	LA	Anti-β_2 GPI
Harris et al, 1991 [4]	1449	Pregnant women	1.8	4.3		
Infante-Rivard et al, 1991 [5]	993	Pregnant women	1.5		3.8	
Perez et al, 1991 [6]	1200	Pregnant women	1.25			
Rix et al, 1992 [7]	2856	Pregnant women			0.07	
Pattison et al, 1993 [8]	933	Pregnant women	1		1.2	
Phadke et al, 1993 [9]	504	Healthy, age-matched	4.2	5		
Juby et al, 1998 [10]	250	Healthy, young	1.2			
Bruce et al, 2000 [11]	129	Healthy				3%

Prevalence of aPL Antibodies in Normals

The prevalence of aCL in most large studies of normals has been 1% to 5%. The prevalence of the LA has been in the range of 0% to 4% (Table 3.3).

Prevalence of aPL in SLE

Representative recent studies of the prevalence of aCL, LA, and anti–β_2-glycoprotein I (anti-β_2 GPI) in SLE are compiled in Table 3.4. In general, aCL is more fre-

Table 3.4. Prevalence of antiphospholipid antibodies in systemic lupus erythematosus.

Study, year	Number of SLE	Assay	LA	aCL	Anti-β_2 GPI
Padmakumar et al, 1990 [12]	55	KCT	13%		
Mayumi et al, 1991 [13]	106	aPTT	16%		
McHugh et al, 1991 [14]	58	KCT, RVVT, TTI	22%	29%	
Wong et al, 1991 [15]	91	aPTT, RVVT, PNP, TTI	11%	44%	
Cervera et al, 1993 [16]	1000	Multiple	15%	24%	
Jones et al, 1991 [17]	200			17%	
Kutteh et al, 1993 [18]	125			25%	
Axtens et al, 1994 [19]	127			24%	
Tsutsumi et al, 1996 [20]	308			12.3%	10.1%
Bruce et al, 2000 [11]	133			13.5%	15.8%
Tubach et al, 2000 [21]	102			23.5%	18.6%