Among antiphospholipid antibodies, Lupus Anticoagulant (LAC) is recognized as the strongest risk factor for thromboembolic events or pregnancy morbidity. The presence of LAC in a subject with previously documented thromboembolism or a significant history of pregnancy loss defines the Antiphospholipid Syndrome (APS). Some patients, however, are diagnosed with LAC without ever having experienced previous vascular thrombosis or pregnancy morbidity. The antiphospholipid antibody profiles of LAC positive patients with or without associated clinical features of APS have been evaluated by us in a multicenter study.

Centers affiliated with Italian Federation of Thrombosis Centers (FCSA) were invited to identify consecutive LAC positive patients diagnosed over a 1-year period. Three hundred twenty-one recruited patients were contacted and after giving informed consent they underwent testing for LAC after at least 12 weeks from the first one using routine laboratory procedures. LAC was not confirmed by Thrombosis Centers in 19 patients (6 were children with previous acute infections). The plasma samples of 302 patients were sent to a central reference laboratory for final LAC confirmation and measurement of anticardiolipin (aCL) and anti-human β2-Glycoprotein I (β2GPI) antibodies by ELISA, as previously described.

On the basis of the results obtained, these patients were classified as category I when either IgG/IgM aCL or IgG/IgM β2GPI were also positive and as category IIa when LAC alone was positive. Fisher exact test (using Woolf approximation) was performed for the comparisons of categorical variables. dRVVT ratios were compared by the unpaired student test. aCL and β2GPI antibody values were compared by the nonparametric Mann–Whitney U test.

Of the 231 patients whose positivity to LAC was confirmed by a central reference laboratory, 152 reported clinical events and were classified as category I. The rate of patients in category I in the LAC/APS group was significantly higher than that in the LAC/noAPS one (63% versus 30%); OR = 3.3, 95%CI 2.2 to 7.0, P < 0.001). On the other hand, the frequency of LAC positivity alone (classification category IIa) was significantly higher in the LAC/noAPS group (51% versus 28%, OR = 2.7, 95%CI 1.5 to 4.7, P < 0.001).

With reference to a large number of patients with LAC, the LAC/APS group was found to have a stronger LAC potency and higher titers of IgG aCL and IgG β2GPI. This is in accordance with the hypothesis that the quantity of IgG β2GPI might be an important determinant of thromboembolic events and pregnancy morbidity. In addition, a clear association with clinical events was confirmed in the patients positive to LAC as well as to IgG aCL and/or IgG β2GPI (classification category I). Conversely, LAC positivity alone is associated with the LAC/no APS group. Although the criterion of single test positivity was maintained at the recent Sydney consensus conference, the association of a single positive test with clinical events appears weaker. Further studies will clarify the nature of the differences observed in the laboratory profiles of LAC positive subjects with or without relevant clinical events.

The subjects in the LAC/APS group were slightly younger, and two-thirds in both groups were female. The ratio between the coagulation times of mixing to control plasma was used to compare LAC potency. Patients in the LAC/APS group had a 1.75 ± 0.55 dRVVT ratio whereas those in the LAC/noAPS group had a 1.59 ± 0.43 dRVVT ratio (P = 0.02).

As shown in the Figure, the median (interquartile) IgG aCL was 41.5 GPL (17 to 98.5) in the LAC/APS group and 17.50 GPL (8 to 39.5) in the LAC/noAPS one (P < 0.001). In the same way, the IgG β2GPI antibody median values (27 U [10 to 81] versus 12.5 U [5 to 23.5], P < 0.001) were significantly different in the 2 groups. No difference instead was found in the IgM aCL and IgM β2GPI median values.

Of the 152 patients in LAC/APS group, 96 were also positive for IgG aCL or IgG β2GPI (71 had triple positivity) and were classified as category I. The rate of patients in category I in the LAC/APS group was significantly higher than that in the LAC/noAPS one (63% versus 30%, OR = 3.3, 95%CI 2.2 to 7.0, P < 0.001). On the other hand, the frequency of LAC positivity alone (classification category IIa) was significantly higher in the LAC/noAPS group (51% versus 28%, OR = 2.7, 95%CI 1.5 to 4.7, P < 0.001).

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None.

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