

determined the association of these antibody isotypes with clinical and laboratory features. The prevalence of elevated IgG ACA in 20 (55.6%) and 2 (5.6%) for IgM ACA is in accordance with that observed in other studies^{18,19}. However our study population was more selective, comprising of patients with a relatively more active disease as opposed to a non-selective SLE group studied earlier¹⁶. McHugh et al²⁰ suggested that IgG ACA was associated with renal disease, while another study found an increased association with renal disease probably due to a possible decrease in the antiphospholipid titres as a result of treatment²¹.

The prevalence of ACAs from the University Hospital Kuala Lumpur study group was 16.5%, with 13% having raised IgG ACA and 2.5% with raised IgM isotype¹⁶. The ACA in this study group was low with rare association with thrombosis. A study among the Indian SLE population in India²² also reported this finding which was thought to be related to genetic and environmental factors. The circulating ACA may not be a serological marker but only appear as a part of the immune process. It may also not be an independent risk factor for thrombosis or recurrent abortions^{6,2,23}.

Discrepancies in results have been due to a number of factors. The sensitivity of various assay techniques have undoubtedly contributed to the wide range of reported frequencies. Investigators have used different techniques of interpreting positive cases. Cut-off points have been analysed differently. The definition of a cut-off point for seropositivity is yet to be determined. The ELISA technique has been widely used but the specificity for different clinical associations appear to be different^{5,9,10,14,15}. Recent efforts were directed at introducing standardized assays for ACA detection. An international workshop was held with the aim of

minimizing the problem of discrepancies in results obtained.

In this study we found no association between the ACA positivity and thrombosis but numbers are too small to draw further conclusions especially since lupus nephritis has not been reported to be associated with thrombosis²⁴. We had three cases who experienced cerebro-vascular accident, where two of them had raised IgG ACA with one having associated raised level of IgM ACA. It has been observed that IgM ACA have a low damaging capacity while IgG ACA have high damaging potential²⁵. Thus ACA predominantly of the IgG isotypes may be of pathogenetic relevance.

Changes in ACA concentrations are a common phenomenon in patients with SLE^{26,27} where variability and fluctuation in ACA titres occur in the course of the disease²⁸. We did not classify our patients according to their disease activity. Blood samples are taken only once. A prospective study would be more accurate to determine the relationship between ACA levels and disease activity as IgG ACA have been reported to be significantly associated with disease activity whereas IgM ACA was much less influenced²⁸. In conclusion, this study shows that the rate of 55.6% ACA positivity is in accordance with those found by investigators elsewhere and that the IgG ACA is the predominant isotype.

Acknowledgement

The authors would like to thank the Director of the Institute for Medical Research for permission to publish this paper.

References

1. Love P E, Santor S A. Antiphospholipid antibodies: anticardiolipin and the lupus anticoagulant in systemic lupus erythematosus (SLE) and in non-SLE disorders. *Ann Intern Med* 1990;112: 682-98.
2. Sammaritano L R, Gharavi A E, Lockshin M D. Antiphospholipid antibody syndrome: immunologic and clinical aspects. *Semin Arthritis Rheum* 1990; 20: 81-96.
3. Asherson R A, Khamashta M A, Ordi-Ros J, Derksen R H, Maching S J, Borgquiner J, et al. The "primary" antiphospholipid syndrome: major clinical and serological features. *Medicine* 1989; 68: 366-74.
4. Lockshin M D, Druzin M L, Goci S, Qamar T, Magid M S, Jovanovic L, Ference M. Antibody to cardiolipin as a predictor of fetal distress or death in patients with systemic lupus erythematosus. *N Engl J Med* 1985; 313: 152-6.
5. Sturfelt G, Nived O, Norverg R M, Thorstensson R M, Krook K. Anticardiolipin antibodies in patients with systemic lupus erythematosus. *Arthritis Rheum* 1987; 30: 382-8.
6. Harris E N, Gharavi A E, Hughes G R V. Anti-phospholipid antibodies. *Clin Rheum Dis* 1985; 11: 591-609.
7. Koike T, Sueishi M, Funaki H, Tomioka H, Yoshida S. Anticardiolipin antibodies and biological false positive serological test for syphilis in patients with systemic lupus erythematosus. *Clin Exp Immunol* 1984; 56: 193-9.
8. Cococo C B, Male D K. Anti-phospholipid antibodies in syphilis and a thrombotic subset of SLE: distinct profiles of epitope specificity. *Clin Exp Immunol* 1985; 59: 449-56.
9. Loizou S, McCrea J D, Rudge A C, Reynolds R, Boyle C C, Harris E N. Measurement of anti-cardiolipin antibodies by an enzyme-linked immunosorbent assay (ELISA): standardization and quantitation of results. *Clin Exp Immunol* 1985; 62: 738-45.
10. Fort J G, Cowchock F S, Abruzzo J L, Smith J B. Anticardiolipin antibodies in patients with rheumatic diseases. *Arthritis Rheum* 1987; 30: 752-60.
11. Harris E N, Hughes G R, Gharavi A E. Anticardiolipin antibodies and the lupus anticoagulant. *Clin Exp Rheumatol* 1986; 4: 187-90.
12. Harris En, Asherson R A, Hughes G R. Antiphospholipid antibodies - autoantibodies with a difference. *Ann Rev Med* 1988; 39: 261-71.
13. Harris En, Gharavi A E, Boey M L, Patel B M, Mackworth Young C G, Luizou S, et al. Anticardiolipin antibodies: detection by radioimmunoassay and association with thrombosis in systemic lupus erythematosus. *Lancet* 1983; ii: 1211-4.
14. Harris En, Asherson R A, Gharavi A E, Morgan S H, Derue G, Hughes G R. Thrombocytopenia in SLE and related autoimmune disorders: association with anticardiolipin antibodies. *Br J Hematol* 1985; 59: 227-30.
15. Altomonte L, Zoli A, Accili D, Mangia A, Bianco A, Magaro M. Thrombosis, recurrent abortions and intrauterine foetal death in a patient with lupus anticoagulant. *Clin Rheumatol* 1985; 4: 455-7.
16. Jones H W, Ireland R, Senaldi G, Wang F, Ksamashta M, Bellingham A J, et al. Anticardiolipin antibodies in patients from Malaysia with systemic lupus erythematosus. *Ann Rheum Dis* 1991; 50: 173-75.
17. Tan E M, Cohen A S, Fries J F, Masi A T, McShane D J, Rothfield N F, et al. The 1982 revised criteria for the classification of SLE. *Arthritis Rheum* 1982; 25: 1271-7.
18. Tincani A, Meroni P L, Brucato A, Zanussi C, Allegro F, Mantelli P, et al. Antiphospholipid and antimitochondrial type M-5 antibodies in systemic lupus erythematosus. *Clin Exp Rheumatol* 1985; 3: 321-26.
19. Abu Shakra M, Urowitz M B, Gladman D D, Ritchie S. The significance of anticardiolipin antibodies in patients with lupus nephritis. *Lupus* 1996; 5: 70-3.
20. McHugh N J, Maymo J, Skinner R O P, James I, Maddison P J. Anticardiolipin antibodies, livedo reticularis, and major cerebrovascular and renal disease in systemic lupus erythematosus. *Ann Rheum Dis* 1988; 47: 110-15.

ORIGINAL ARTICLE

21. Weidmann C E, Wallace D J, Peter J B, Knight P J, Bear M B, Klinenberg J R. Studies of IgD, IgM and IgA antiphospholipid antibody isotypes in systemic lupus erythematosus. *J Rheumatol* 1988; 15: 74-9.
22. Saluja S, Kumar A, Kamashta M, Hughes G R V, Malaviya A N. Prevalence and clinical association of anticardiolipin antibodies in patients with systemic lupus erythematosus in India. *Indian J Med Res* 1990; 92: 224-7.
23. Cowchock S, Smith J B, Gocial B. Antibodies to phospholipids and nuclear antigens in patients with repeated abortions. *Am J Obstet Gynecol* 1986; 155: 1002-10.
24. Massengill S F, Hedrick C, Ayoub E M, Sleasman J W, Kao K J. Antiphospholipid antibodies in pediatric lupus nephritis. *Am J Kidney Dis* 1997; 29: 355-61.
25. Casali P, Notkins A L. CD5+B lymphocytes, polyreactive antibodies and the human B-cell repertoire. *Immunology Today* 1989; 10: 364-68.
26. Shergy W J, Kredich D W, Posetsky D S. The relationship of anticardiolipin antibodies to disease manifestations in pediatric systemic lupus erythematosus. *J Rheumatol* 1988; 15: 1389-94.
27. Kalunian K C, Peter J B, Middlekauff H R, Sayre J, Ando D G, Mangotich M, et al. Clinical significance of a single test for anticardiolipin antibodies in patients with systemic lupus erythematosus. *Am J Med* 1988; 85: 602-8.
28. Henk J O, Philip G D R, Paula H, Marja V V, Derksen R H. Fluctuations of anticardiolipin antibody levels in patients with systemic lupus erythematosus: a prespective study. *Ann Rheum Dis* 1989; 48: 1023-8.