obtained by ELISAs, in order to determine their true significance.

In conclusion, the present study has revealed that some ELISA preparations can be more sensitive, and as specific as the CCIE method for the detection of anti-ENA antibodies. Laboratories that are still using the later method should consider switching to ELISA. However, it is important that laboratories evaluate a range of different ELISA preparations before selecting the most optimal one. In addition, it is recommended that laboratories then audit results in order to determine the true significance of such results. Finally, until the true significance of ELISA-generated results is known, positive ENA-results should be interpreted in conjunction with the clinical picture and this would require close liaison between the clinical Immunology Laboratory and clinicians.

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# Antiphospholipid syndrome among Bahraini patients

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Antiphospholipid syndrome (APS) is defined as the presence of antiphospholipid (APL) antibodies, arterial or venous thrombosis, recurrent spontaneous abortions, and thrombocytopenia. However, not all patients develop such complications. The risk of thrombotic event in patients with APS is 0.5-30%. The syndrome can occur within the context of several diseases, mainly autoimmune, or it may be present without any recognizable disease, the so-called primary APS.[1]

Systemic manifestations of APS are multisymptomatic and can affect most of the systems. The symptoms are secondary to thrombosis that can be located in the vessels of each caliber. Most commonly, APS is associated with systemic lupus erythematosus (SLE). Approximately 35% of SLE patients have elevated levels of APL antibodies.[2] The diagnosis of APS is based on the presence of any clinical manifestation associated with the syndrome in addition to the presence of anticardiolipin (ACL) antibodies or lupus anticoagulant (LAC).[1]

A retrospective study was performed on 22 patients with APS who where treated in Salmaniya Medical Complex (Ministry of Health), largest hospital in Bahrain (1000 bed), over 16 year period from 1988 - 2002. Anticardiolipin immunoglobulin G (IgG) and immunoglobulin (IgM) were tested by enzyme link immunoabsorbent assay (ELISA) technique.

Primary APS was 45.8% while the secondary 54.5%. History of thrombosis was present in 50% of primary APS, while 33.3% of the secondary APS patients. The female to male ratio was 10:1. Among our female patients, 90.5% were married and percentage of pregnancies was 71.4% and number of miscarriages was 57.1%. In the primary APS, history of miscarriage was 80% while 50% in secondary APS group. All secondary APS were SLE patients. Percentage of ACL IgG was higher in primary APS (80%) compared to secondary APS 66.7%. On the contrary ACL, IgM was higher in secondary (75%) compared to primary APS (60%). Venereal Disease Research Laboratory (VDRL) was reactive in 90% of the primary group while 50% in secondary group. Antinuclear antibodies were much common in secondary APS (100%) than in primary APS as expected (20%). Regarding anti double stranded DNA it was positive in 83.3% of the secondary APS while absent in the primary form. Prolonged partial thromboplastin time (PTT) was present in 90% of the primary APS versus 66.7% of the secondary form. Treatment was given to 95.2% after diagnosis: 33.3% received aspirin, 76.2% received steroid, 28.6% received heparin and 28.6% received warfarin.

The present study on Bahraini patients showed that Hughes syndrome is not a common problem among hospitalized patients in Bahrain. Neurological, ophthalmological and cardiac manifestations known to be among the manifestations of APS were uncommon in the present study.

All studied patients in the present study are Bahrainis, results of laboratory and clinical findings in primary versus secondary APS are summarized in **Table 1**, comparison with other ethnic groups namely Saudi and Argentini patients was carried out. The mechanism of action of APL antibodies is not known. It has been shown, that the antibodies bind to the anionic phospholipids of platelet membranes, endothelial cells and clotting components such as prothrombin, protein C and protein S.[1] There is a discrepancy between prolongation of clotting time *in vitro* and thrombosis *in vivo*. No satisfactory explanation of this phenomenon has yet been established, but several theories are proposed. *In vitro* lupus anticoagulant is thought to prolong clotting times by binding with phospholipids and thereby, limiting the phospholipid surface necessary for binding of the prothrombinase complex. The mechanism of paradoxical thrombosis observed *in vivo* is not known. The simplest theory is that, there is an antibody directed against the patient's own platelet and endothelial cell phospholipids that cause platelet aggregation and subsequent vascular occlusion. This also accounts for thrombocytopenia seen in these patients. However, the mechanism of action seems to be more complex and probably not all participating components are known yet.[3]

Lupus anticoagulant and ACL antibodies can both cause a false-positive result of VDRL assay, although it is another phospholipid responsible for true-positive result of this assay in syphilis. Anticardiolipin antibodies are also directed against plasma proteins such as beta-2-glycoprotein I and prothrombin, cofactors, the absence of which can decrease the binding of antibodies to phospholipids. The recently proven cross reaction between beta-2-glycoprotein I and lipoproteins could explain the pathogenesis of both thrombosis and atherosclerosis in patients with primary APS.[4] Familial occurrence of elevated levels of APL antibodies as well as an association with certain human leukocyte antigen, DR4, DR7, DQ7, and DR53 types were reported.[1]

Approximately 4% of the normal population have elevated levels of ACL antibodies.[1] Frequency in the United States of APL antibodies can be found in as many as 50% of individuals with SLE and in 1-5% of the healthy population.[2] On the other hand, ACL antibody tends to occur more frequently in elderly individuals. It is noteworthy, that relatively decreased titers of APL antibodies were also observed in patients with an ongoing thrombotic event. This could be explained by the consumption of antibodies during the event.

Recent literature suggests that the occurrence rate of APS in patients with SLE is 34-42%.[1] Study conducted on a large group of SLE patients in Canada concluded that the presence of ACL antibodies in patients with SLE is associated with prolonged activated PTT (aPTT), thrombocytopenia and positive Coombs' test result, but not with APS.[2] Another study concluded that there is a significant correlation between presence of antibodies and both thrombotic events and recurrent spontaneous abortions in SLE patients and that occurrence of thrombotic complications is in direct correlation with the level of APL antibodies.[5] In a study conducted on Saudi patients with a positive LAC there was a clear association between the presence of LAC and an abnormal aPTT, which was much less obvious with the PT.[3] Regarding the association of isotypes of ACL antibodies and LAC with the clinical outcome, a study on that aspect concluded that in patients with primary APS, the presence of the 3 ACL isotypes plus LAC was associated with a higher number of recurrent spontaneous abortions compared to other possible combinations of ACL antibody isotypes.[5] On the contrary, a study in Israel reported no correlation between APL antibody titers and manifestations of APS.[4] In the present study, there was no correlation between clinical

**Table 1** - Laboratory and clinical findings in Bahrainis versus other ethnic groups.

| Findings | Bahraini population (%) | Saudi population (%) | Argentini population (%) |
|---|---|---|---|
| Total number | N=22* | N=77† | N=92‡ |
| ***Gender*** | | | |
| Male | (9.1) | (27) | (20.7) |
| Female | (90.9) | (73) | (79.3) |
| ***Clinical findings*** | | | |
| Primary APL | (45.5) | (52) | (78.3) |
| Thrombosis | (50) | (49) | (43.1) |
| Abortion | (80) | (51) | (56.9) |
| Secondary APL | (54.5) | (48) | (21.7) |
| Thrombosis | (33.3) | | |
| Abortion | (50) | | |
| ***Laboratory findings*** | | | |
| ACL antibodies | (100) | (87) | (100) |
| Primary APL | | | |
| ACL IgG | (80) | ND | (41) |
| ACL IgM | (60) | ND | (21) |
| ACL IgG and IgM | (40) | ND | (15) |
| LAC | ND | (100) | (51) |
| Secondary APL | | | |
| ACL G | (66.7) | ND | (35) |
| ACL M | (75) | ND | (10) |
| ACL G and M | (50) | ND | (45) |
| LAC | ND | (100) | (80) |

APL -antiphospholipid, ACL - anticardiolipin , IgG - immunoglobulin G, IgM - Immunoglobulin M, LAC - lupus anticoagulant, ND - not done.
*present study, †Owaidah et al[4], ‡Guglielmone et al[5]

presentation and ACL antibody isotype; yet we noticed that percentage of ACL IgG was higher in primary APS compared to secondary APS, on the contrary ACL IgM was higher in secondary compared to primary APS.

Patients with IgG ACL antibodies are at higher risk than those with IgM or IgA antibodies. The probability of thrombosis is higher if both ACL antibodies and lupus anticoagulant are present simultaneously. Significantly higher incidence of thrombosis was also described in patients who had elevated levels of IgG anti beta-2-glycoprotein I antibodies. [1]

Anticoagulation and immunosuppression seem to be the most effective treatment. Long-term therapy with aspirin, warfarin or heparin was suggested, but duration of the treatment and the point at which it should be discontinued are not clear. Life-long anticoagulation is necessary in some patients. Laser photocoagulation is an additional treatment of non-perfused retinal areas. [6]

Antiphospholipid syndrome is a life threatening and vision threatening multisymptomatic disorder. Laboratory tests are essential for the diagnosis and should be considered in patients with unexplained vascular occlusion. Long-term anticoagulation and immunosuppression seem to be the most effective treatment. The patients have to be monitored on regular basis.

The present study on Bahraini patients showed that Hughes syndrome is not a common problem among hospitalized patients in Bahrain.

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# Contribution study of visceral leishmaniasis in Syria

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Leishmaniasis is a parasitic disease, endemic in many countries around the world in approximately 88 countries. An estimated 350 million people are at the risk of contracting the disease, with approximately 100000 new cases annually.[1]

Visceral leishmaniasis (VL) caused by *Leishmania infantum* and *Leishmania donovani* is prevalent in the Middle East. The major features of this disease are intermittent fever, enlargement of spleen and liver, anemia and weight loss. High mortality rate is expected if the disease is left untreated. Diagnosis of VL can be achieved either by demonstrating the parasite microscopically in Giemsa stained smears of spleen, lymph node and bone marrow aspirates, or *in vitro* cultivation. The last method was found to be more sensitive than microscopic examination and allows further characterization of the isolates by isoenzyme analysis.[2] However, *in vitro* cultivation is time consuming, expensive and difficult.[2] Due to limitations of the direct diagnostic methods mentioned above, a number of direct immunological methods have been applied, such as indirect immunoflourescent test, enzyme-linked immunosorbent assay test, with either whole parasite or purified antigen, the western blot analysis and the direct agglutination test with aqueous suspension and *Leishmania donovani* promastigotes.[3] In recent years, the amplification of parasite kinetoplast DNA (kDNA) by polymerase chain reaction (PCR) has proved to be rapid, sensitive and a specific method for detection of *Leishmania* parasites in a number of different clinical materials: blood, bone marrow, lymph node and spleen.[3,4] In this study, we reported the following: 1. the distribution of VL in Syria according to data collected between 1993 and 2003, due to little was known on the epidemiology and prevalence of VL in Syria; 2. the presence of VL was confirmed using PCR technique, as a new diagnostic test instead of the traditional methods