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IMMUNOLOGICAL PROFILE OF SLE PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODY SYNDROME

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ABSTRACT

Studies Associate with APS and SLE are very scanty from our part of country. So the present study was conducted to find out the relation of APS with special reference to SLE in this region. Prospective study was carried out in 103 patients after approval by the Institute Ethical Committee and informed consent was taken from the patients who are attending Kamineni Hospitals. Estimation of different auto-antibodies was done by using standard immunological tests. 103 patients having SLE in the age group 21 to 30 years with female predominance. 22 patients had APS 13 male patients having SLE with APS. The most common clinical manifestation in SLE patients was musculoskeletal involvement (85.18%) followed by fever (74.07%), the patients having SLE with APS musculoskeletal involvement was the most common manifestation (77.27%) followed by fever and mucocutaneous involvement (72.72% and 59.09% respectively). The results are tabulated. APS syndrome is a major cause of morbidity and mortality in patients of SLE. The prevalence of secondary APS syndrome in SLE varies in different geographical regions. The associated complications and its incidence are also variable in different parts of the world because of genetic susceptibility related to aPL and APS. Screening for the presence of aPL antibody and timely initiation of prophylactic treatment can prevent many of complications.

KEY WORDS: Antiphospholipid antibody syndrome (APS), Antiphospholipid antibodies (aPL), anti-double stranded DNA (Anti-dsDNA)

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INTRODUCTION

Antiphospholipid antibody syndrome (APS) is a systemic autoimmune disease characterised by thrombophilic state and obstetrical complications. Autoimmune disorders occur if the body's immune system makes antibodies that attack and damage tissues or cells. Antibodies are a type of protein. They usually help defend the body against infections. In APS, however, the body makes antibodies that mistakenly attack phospholipids. Phospholipids are found in all living cells and cell membranes, including blood cells and the lining of blood vessels. When antibodies attack phospholipids, cells are damaged. This damage causes blood clots to form in the body's arteries and veins. Usually, blood clotting is a normal bodily process. Blood clots help seal small cuts or breaks on blood vessel walls. This prevents you from losing too much blood. In APS, however, too much blood clotting can block blood flow and damage the body's organs. So the present study was conducted to find out the relation of APS with special reference to SLE especially in this region.

MATERIALS AND METHODS

This prospective, longitudinal study was carried out on the patients attending Departments of Medicine, Rheumatology, Nephrology and Obstetrics and Gynaecology at Kamineni Hospitals, L.B.Nagar, Hyderabad from December 2011 to June 2014. During this study period after a detail history, clinical examination and laboratory testing, patients who fulfilled the American College of Rheumatology (ACR) criteria[1] for the diagnosis of SLE were taken up for the study. Then they were subjected to find out for the presence of APS based on Sapporo's Criteria[2]. Estimation of different auto-antibodies were done by using standard immunological tests. Serological profile of the patients included antinuclear antibody (ANA), anti-double stranded DNA (Anti-dsDNA), rheumatoid factor (RF), IgG and IgM anticardiolipin antibodies (IgGaCL and IgMaCL), lupus anticoagulant (LA) and anti U1RNP antibodies (wherever indicated). In addition to these serological tests other routine investigations were also carried out. Patients were called for follow-up regularly during the study period (mild to moderate SLE with APS). Duration of follow-up of the patients varied depending upon their recruitment in study. It varied from < 1 year to 4 years, as per details given in Table 2. Pregnant females were advised to follow up as per antenatal check-up protocol if there were no anticipatory risk factors which warrant any extra visits. Patients were monitored for the development of APS and data were analysed for different characteristics of APS patients using appropriate statistical methods. Study was approved by the Institute Ethical Committee and informed consent was taken from the patients.

Table 1
Period of follow-up in different categories

Period of follow-up	Total SLE patients (%)	SLE without APS (%)	SLE with APS (%)
< 1 year	3 (3%)	6 (7%)	1 (5%)
1-2 year	14 (14%)	14 (17%)	2 (9%)
2-3 year	30 (29%)	22 (27%)	6 (27%)
3-4 year	56 (54%)	39 (48%)	13 (59%)

Table-2
Age & Sex Distribution of 103 SLE Patients

Age Groups	Male (%)	Female (%)	Total (%)
10-20	4 (3.83)	20 (19.41)	24 (23.30)
21-30	5 (4.85)	41 (39.80)	46 (44.66)
31-40	2 (1.94)	15 (14.56)	17 (16.50)
41-50	1 (0.97)	10 (9.70)	11 (10.67)
>50	1 (0.97)	4 (3.88)	5 (4.85)
Total	13 (12.62)	90 (87.37)	103 (100)

Table-3
Age & Sex Distribution of 22 patients of SLE having APS

Age Group (in years)	Male (%)	Female (%)	Total (%)
10-20	0 (0)	3 (13.63)	3 (13.63)
21-30	1 (4.54)	11 (50.00)	12 (54.54)
31-40	1 (4.54)	2 (9.09)	3 (13.63)
41-50	0 (0)	2 (9.09)	2 (9.09)
>50	0 (0)	2 (9.09)	2 (9.09)
Total	2 (9.09)	20 (90.90)	22 (100)

Table-4

Clinical manifestations of patients of SLE with APS and SLE without APS		
Manifestation	**SLE with APS (no =22) (%)**	**SLE without APS (n=81) (%)**
1.Fever	16(72.72)	60(74.07)
2.Mucocutaneous	13(59.09)	56(69.13)
a. Malar Rash	7(31.81)	26(32.09)
b.Skin Rash	3(13.63)	22(27.16)
c.Photosensitivity	10(45.45)	41(50.61)
d.Oral Ulcers	13(59.09)	35(43.20)
e.Alopecia	8(36.36)	33(40.74)
3.Musculoskeletal	17(77.27)	69(85.18)
a.Arthralgia/Myalgia	11(50.00)	41(50.61)
b.Arthritis	6(27.27)	28(34.56)
4.Pleuropulmonary	3(13.63)	19(23.45)
5.Neuropsychiatric involvement	2(9.09)	12(14.81)
a.Psychosis	1(4.54)	5(6.17)
b.Convulsion	2(9.09)	7(8.64)
6.Renal involvement	7(31.81)	41(50.61)
7.Haematological involvement	16(72.72)	65(80.24)
a.Anaemia	11(50)	41(50.61)
b.Thrombocytopenia	5(22.72)	15(18.51)
8.Obstetrics manifeststions		
a.Early fetal loss (< 10 weeks)	2(9.09)	0(0)
b.Late fetal loss	6 (27.27)	0(0)
c.Prematurity	3(13.63)	0(0)
Thrombotic manifestsation		
a.DVT	4(18.18)	0(0)
b.Stroke	3(13.63)	0(0)
c.Cortical Sinus Thrombosis	2(9.09)	0(0)

Table-5
Immunological findings in 22 patients of SLE having APS

Parametres	Number of patients	Percentage (%)
ANA	21	95.45
Anti-ds DNA	15	68.18
IgM aCL	7	31.81
IgG aCL	18	81.81
IgM aCL + IgG aCL	9	40.9
Lupus Anticoagulant	15	68.18
Alone	3	13.63
With aCL	12	54.54

RESULTS

During the study period there were a total of 103 patients having SLE (Table 2). The mean age at study entry was 21 ± 6 years and majority of patients were in the age group 21 to 30 years (n=46; 44.66%) with female predominance (n=90; 87.37%). Duration of illness prior to presentation varied from 2months to 2 years with a mean 3 ± 1 month. Maximum number of patients presented with duration of illness of more than 2 months. Among the 103 patients of SLE, 22 patients had APS giving a prevalence of 21.35%. The

most common age group affected with APS was 21-30 years with an incidence of 44.66% of the total SLE patients having APS (Table 3). We also found 13 male patients having SLE with APS. The most common clinical manifestation in SLE patients was musculoskeletal involvement (85.18%) followed by fever (74.07%) (Table4). And also in those patients having SLE with APS musculoskeletal involvement was the most common manifestation (77.27%) followed by fever and mucocutaneous involvement (72.72% and 59.09% respectively). Arthritis was present in 6 (27.27%) and arthralgia in 11 (50%) patients of SLE having APS. Among the 22 patients of SLE having APS, multisystem involvement was seen in 12 patients and 9 had life threatening complications. Late foetal loss was noted in 6 (27.27%) of 22 patients, recurrent early foetal losses (< 10 weeks gestation) were seen in 2 (9.09%) patients whereas preterm labour (< 34 weeks gestation) was seen in 3 (13.63%). Out of 2 patients having early foetal losses, 2 patients had 3 consecutive pregnancy losses. Deep vein thrombosis was noted in 4 (18.18%) of which one patient had thrombosis of inferior vena cava just proximal to bifurcation of IVC, 1 patients had thrombosis of right common iliac and popliteal vein and 2 patients had DVT of left lower limb from femoral to calf veins. 3 patients had stroke in whom CT scan revealed infarct with haemorrhagic conversion and 2 patients showed cortical sinus thrombosis. 1 patients had Budd-Chiari Syndrome and 1 patient had splenic vein thrombosis. ANA and Anti-dsDNA were positive in 95.45% and 68.18% respectively (Table 5). IgMaCL and IgGaCL was present in 31.81% (n=7) and 81.81% (n=18) respectively. LA was present in 15 (68.18%) patients out of which 12 (54.54%) had anticardiolipin antibody as well. 4 patients of SLE with APS (18.18%) and 16 patients of SLE without APS (19.75%) were lost to follow-up after variable period.

DISCUSSION

Several studies have been conducted to establish the prevalence of aPL in cohorts of healthy subjects and most of the studies reported a frequency of elevated aPL between 1% and 5%[3]. Most of the aPL in apparently healthy individuals are present in low titre and transient. The antiphospholipid antibody syndrome (APS), which may also occur in a primary form, is increasingly found in association with systemic lupus erythematosus[4].The prevalence of APS among SLE patients is variable in different geographical regions and ranges from 22% to 61%[4-7] However one study in South India found that the incidence in adult SLE was only 13.7%[8] in this study we found that 22 patients were having APS out of 103 SLE patients, giving a prevalence of 21.35%. The prevalence is slightly lower than other studies.[4-7]This difference in disease pattern may be because of different environmental or genetic factors, or both. In our study the most commonly affected age group was 21-30 years and females were more affected than males.[7] The overwhelming female population in the present study may be due to the fact that majority of patients who formed the subject matter of the present study were pregnant females having one or the other pregnancy related morbidity. In contrast to other studies which showed a male dominance during the childhood[8], our study males are not affected in the age group of 10-20 years. Prevalence of different antiphospholipid antibodies in SLE varies in different studies. Afro- Caribbean patients found that prevalence of IgG (2%) and IgM (2%) aCL with SLE was low[9]. Cervera et al[5] found that 87% of patients have aCL whereas LA was present in 53%. However Wong et al[10] found 46% aCL and 11% LA. Shrivastava et al (2001) found IgM aCL in 51%, IgG aCL in 7%, IgA aCL in 5% and any type of aCL in 51%.[6] in our study LA and IgGaCL were present in 68.18% and 81.81% respectively while 54.54% of the patients of SLE with APS had both LA and aCL. IgM + IgG aCL was positive in 40.90% of SLE patients having APS. In addition to aPL, Cervera et al[5] found that some patients with APS had ANA (59.7%), anti-dsDNA (29.2%), anti-Ro (14.0%), and rheumatoid factor (7.8%). In our study we found that ANA and anti-dsDNA were positive in 95.43% and 68.18% of cases. The most common clinical manifestation in our study was the musculoskeletal (77.27%), of which arthralgia was the most common (50%). This is in contrast to other study where arthralgia (38.7%) and arthritis (27.1%) are less

common among the major clinical manifestations[11]. Haematological manifestations in our study were the second most common manifestation, among which anaemia was the most common (50.%). This is in contrast to other studies[5, 8] where thrombocytopenia was the most common manifestation (25-29.6%). In our study 22.72% of the patients had thrombocytopenia. In patients of APS, autoimmune haemolytic anaemia is seen in 14-23% cases[12]. The difference may be a reflection of the fact that our population is undernourished because of poverty and nutritional anaemia contribute a large percent in addition to haemolytic anaemia of APS.Third most common clinical manifestation in our study was muco-cutaneous involvement (59.09%) in the form of malar rash (31.81%) and oral ulcer (59.09%). Dermatologic manifestations are extremely common in secondary APS. Almost 40-50% of patients exhibit various skin lesions including levido reticularis, ulceration and splinter haemorrhages[11, 13], and our finding were not different. Antiphospholipid antibodies occur in up to 20% of women with recurrent pregnancy loss and are strongly associated with pregnancy complications, such as first- and second-trimester miscarriages, preeclampsia, eclampsia, intrauterine growth retardation (IUGR) and preterm labour[14]. On the other hand, patients with aPL have approximately a 22–75% chance of foetal loss[15, 16]. In this study, 36.36% had foetal loss, of which late fetal loss was most common (27.27%), Out of which 2 patients had early foetal losses, 2 patients had 3 consecutive losses. In addition to foetal loss, APS patients may have other obstetrical complications including pre-eclampsia (10%), eclampsia (4%) and abruptio placenta (2%) [5]. However, in our case these were rare. Both thrombotic neurological events and non- thrombotic CNS symptoms are associated with SLE and APS, in our study we found psychosis in 4.54% and seizures in 9.09% of SLE patients having APS. Stroke was present in 13.63% which was similar to other study [5]. One Indian study showed neurological events in 18.18% of patients with APS.[17] Cross-sectional studies reveal 30% incidence of thrombosis in patients with aPL antibody which is slightly lower than our finding (46.93%) [18]. In our study there were 31.81% renal involvements in the form of thrombotic microangiopathy. This is similar to other study from Asia[19].

CONCLUSION

APS syndrome is a major cause of morbidity and mortality in patients of SLE. Severity of disease varied from mild mucocutaneous involvement to severe and life threatening multisystem involvement. The prevalence of secondary APS syndrome in SLE varies in different geographical regions. The associated complications and its incidence is also variable in different parts of the world because of genetic susceptibility related to aPL and APS. Screening for the presence of aPL antibody and timely initiation of prophylactic treatment can prevent many of complications. However, it has been difficult to determine genetic risk factors for aPL antibody and APS because of the heterogenecity in the antigen specificity, and pathogenesis of the clinical manifestations of APS.

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