ORIGINAL RESEARCH

Clinical Profile Of Patients With Antiphospholipid Syndrome In A Tertiary Care Hospital In North India

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ABSTRACT

Background: Antiphospholipid syndrome (APS) is an autoimmune multisystem disorder characterized by arterial, venous, or small vessel thromboembolic events and/or pregnancy morbidity in the presence of persistent antiphospholipid antibodies

Objectives: To study the clinical and immunological profile of APS patients at a tertiary care centre

Participants: All the APS patients attending rheumatology OPD clinic as well as CTD patients admitted under different divisions of Internal Medicine and department of obstetrics and gynecology and diagnosed as having APS.

Study design: It was a hospital based observational study

Methods: The diagnosis of APS was on the basis of characteristic clinical features and autoantibodies. Patients were classified as APS if they fulfilled international consensus statement update of the classification criteria for definite APS, and ACR/EULAR Criteria for associated Rheumatic disease in Secondary APS.

R**ESULTS:** Our study was an observational study of 124 patients. Most common clinical features were early fetal loss in 48(38.7%),late fetal loss in 57(45.6%),thrombocytopenia in 33(26.6%), DVT in 28(22.6%).Most common antibody was lupus anticoagulant 66(53.2%),anticardiolipin antibody 44(35.5%) and β2 glycoprotein antibody 33(26.6%).

Conclusion: APS is a disorder characterized by a wide variety of clinical manifestations. There is a broad spectrum of disease among individuals with aPL, from asymptomatic to imminently life-threatening CAPS. Patients may exhibit clinical features suggesting APS but not fulfill the International Criteria for a ‘‘definite’’ diagnosis. SNAPS patients demonstrate typical idiopathic thromboses but aPL are not initially detected. Microangiopathic APS may present with isolated tissue and organ injury or as the overwhelming ‘‘thrombotic storm’’ observed in CAPS.

Abbreviations: APS: Antiphospholipid Syndrome**,**aPL: Antiphopholipid Antibodies**,**SNAPS: Seronegative Antiphospholipid Syndrome**,**CAPS: Catastropic Antiphospholipid Syndrome**,**SLE: Systemic Lupus Erythematosus**,**MCTD: Mixed connective tissue disorders**,**UCTD: Undifferntiated connective tissue disorders**,**aCL: Anticardiolipin Antibody**,**LA: Lupus Anticoagulant**,**ANA: Anti-nuclear Antibodies**,**CRP: C-Reactive Protein**,**ESR: Erythocyte Sedimentation Rate**,**CBC: Complete Blood Count **,**CTD: Connective Tissue Disorders **,**ELISA: Enzyme-Linked Immunosorbent Assay

Keywords: Lipid levels, Triglycerides, Tinnitus.

INTRODUCTION

Antiphospholipid syndrome (APS) is an autoimmune multisystem disorder characterized by arterial, venous, or small vessel thromboembolic events and/or pregnancy morbidity in the presence of persistent antiphospholipid antibodies (aPL).aPLs are a heterogenous group of autoantibodies which are directed against phospholipid binding proteins.The APS can be found in patients having neither clinical nor laboratory evidence of another definable condition (primary APS) or it may be associated with other diseases, mainly systemic lupus erythematosus (SLE), but occasionally with other autoimmune conditions [(1)], infections [(2)], drugs [(1)], and malignancies [(3)]. The three major antiphospholipid antibody (aPL) tests that are recognized by international classification criteria for antiphos pholipid syndrome (APS) are as follows:1.Anticardiolipin antibodies (aCL) IgG and/or IgM ELISA 2. Anti-beta2-glycoprotein-I (anti-beta2GPI) antibodies IgG and/or IgM ELISA 3.Lupus anticoagulant (LA) test Estimates in the United States suggest that aPL are associated with approximately 50,000 pregnancy losses, 110,000 strokes, 100,000 MIs, and 30,000 DVTs annually[(4-10)]. The pathogenesis of APS-associated clinical manifestations appears to result from a variety of

antiphospholipid antibody effects upon pathways of coagulation, including the procoagulant actions of these antibodies upon protein C, annexin V, platelets, serum proteases, toll-like receptors, tissuefactor, and via impaired fibrinolysis.

CLINICAL MANIFESTATIONS: In addition to venous, arterial, and/or small vessel thrombosis as well as specific pregnancy complications, other more common clinical features of antiphospholipid syndrome (APS) include livedo reticularis,thrombocytopenia,or transient ischemic attack. In rare cases, APS results in multiorgan failure due to small-vessel thromboses, a condition referred to as "catastrophic antiphospholipid syndrome"

	MANIFESTATIONS	PERCENTAGE(%)
1	Venous Thrombosis and Related Consequences	
	a)Deep vein thrombosis	39
	b)Livedo reticularis	24
	c)Pulmonary embolism	14
	d)Superficial thrombophlebitis	12
	e)Thrombosis in various other sites	11
2	Arterial Thrombosis and Related Consequences	
	a)Stroke	20
	b)Cardiac valve thickening/dysfunction and/or Libman-Sacks Vegetations	14
	c)Transient ischemic attack	11
	d)Myocardial ischemia (infarction or angina) and coronary bypass thrombosis	10
	e)Leg ulcers and/or digital gangrene	9
	f)Arterial thrombosis in the extremities	7
	g)Retinal artery thrombosis/amaurosis fugax	7
	h)Ischemia of visceral organs or avascular necrosis of bone	6
	i)Multi-infarct dementia	3
3	Neurologic Manifestations of Uncertain Etiology	
	a)Migraine	20
	b)Epilepsy	7
	c)Chorea	1
	d)Cerebellar ataxia	1
	e)Transverse myelopathy	0.5
4	Renal Manifestations Due to Various Reasons (RenalArtery/Renal vein/Glomerular thrombosis,Fibrosis intima hyperplasia	3
5	Osteoarticular Manifestations	
	a)Arthralgia	39
	b)Arthritis	27
6	Obstetric Manifestations (Referred to the Number of Pregnancies)	
	a)Preeclampsia	10
	b)Eclampsia	4
7	Fetal Manifestations (Referred to the Number of Pregnancies)	
	a)Early fetal loss (<10 weeks)	35
	b)Late fetal loss (≥10 weeks)	17
	c)Premature birth among the live births	11
8	Hematologic Manifestations	
	a)Thrombocytopenia	30
	b)Autoimmune hemolytic anemia	10

CATASTROPHIC APS: A small subset of patients with antiphospholipid syndrome (APS)has widespread thrombotic disease with multiorgan failure, which is called "catastrophic APS." Thromboses in this setting typically involve multiple small blood vessels in various organs rather than a large vessel deep vein thrombosis or stroke, although the latter can occur. Catastrophic APS is frequently fatal, with a reported mortality rate approaching 50 % despite anticoagulant and immunosuppressive treatment[14].

CLASSIFICATION CRITERIA: According to the revised Sapporo APS Classification Criteria[15] (also called the Sydney criteria), APS is present in patients who meet at least one of the following clinical criteria **and** at least one of the following laboratory criteria: The revised Sapporo criteria also indicate that the presence or absence of additional risk factors for thrombosis should be recognized among patients.

DIAGNOSIS: The diagnosis of APS is based on a combination of clinical features and laboratory findings.

Clinical criteria - One or more of the following is present:

Vascular thrombosis - One or more episodes of venous, arterial, or small vessel thrombosis in any tissue or organ, with unequivocal imaging or histologic evidence of thrombosis. Superficial venous thrombosis does **not** satisfy the criteria for thrombosis for APS.

Pregnancy morbidity - One or more unexplained deaths of a morphologically normal fetus at ≥10 weeks gestation, **or** one or more premature births of a morphologically normal neonate before 34 weeks gestation because of eclampsia, preeclampsia, or placental insufficiency, **or** three or more consecutive spontaneous pregnancy losses at <10 weeks gestation, unexplained by chromosomal abnormalities or by maternal anatomic or hormonal causes.

Laboratory criteria - The presence of one or more of the following antiphospholipid antibodies on two or more occasions at least 12 weeks apart: IgG and/or IgM anticardiolipin antibodies (aCL) in moderate or high titer (>40 GPL or MPL units, respectively, or a titer >99 percentile for the testing laboratory),measured by a standardized enzyme-linked immunosorbent assay (ELISA).IgG and/or IgM anti-beta2-glycoprotein (GP) I >40 GPL or MPL units, respectively,or a titer >99 percentile for the testing laboratory, measured by a standardized ELISA .Lupus anticoagulant (LA) activity detected.

MORTALITY – Antiphos pholipid syndrome (APS) is associated with increased morbidity and mortality.

AIMS AND OBJECTIVES

To study the clinical and immunological profile of APS patients at a tertiary care centre.

MATERIALS AND METHODS

The study on the clinical profile of patients of antiphospholipid antibody syndrome at tertiary care center was conducted in the Department of internal medicine, division of rheumatology at Sher-I-Kashmir Institute of Medical Science Soura(SKIMS) Srinagar J&K India. SKIMS soura, a multi speciality, 1015 bedded, teaching hospital and the only tertiary level healthcare facility in the state with the most of the modern medical facilities. SKIMS Soura has a separate department of medical records which is entrusted to keep records of all hospital registration indoor as well as outdoor patients, discharges of patients and other information of the patients pertaining to medical records. In our study we analysed the data both retrospectively from march 2012 to 2018 for the all cases of antiphospholipid syndrome and prospectively from 2018 onwards to the period of one and a half year for the same patients under different divisions of Department of Internal Medicine, SKIMS soura Srinagar. The diagnosis of APS was on the bases of characteristic clinical features and autoantibodies. Patients were classified as APS if they fulfilled international consensus statement update of the classification criteria for definite APS, and ACR/EULAR Criteria for associated Rheumatic disease in Secondary APS. For the retrospective part we collected data from the department of medical records regarding the APS patients which contains detailed investigations which include baseline i.e CBC, Chemistry, Routine urine examinations, 24 hours urinary protein etc. plus Special investigations like Anti cardiolipin, lupus anticoagulant, anti-beta2-glycoprotein (GP), ANA, Anti ds DNA,Anti-Sm, Antiphospholipid antibodies, RF, Complement levels like C3, C4 etc. depending on the history and examination. For prospective part we collected data about the clinical profile of each patient diagnosed as a case of APS after proper history, meticulous physical examination and investigations. No major ethical issues were involved as the study does not involve any interventional experimentation, since it is purely an observational study. However, informed consent for confidentiality and permission for publishing the data was taken.

INCLUSION CRITERIA

Included all the APS patients attending rheumatology OPD clinic as well as CTD patients admitted under different divisions of Internal Medicine and department of obstetrics and gynecology and diagnosed as having APS on the basis classification criteria for definite APS(revised sappora criteria), and ACR/EULAR Criteria for associated Rheumatic disease in Secondary APS **.**

STATISTICAL ANALYSIS

The recorded data was compiled and entered in a spread sheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar diagrams. Student's independent t-test and analysis of variance (ANOVA) were employed for comparing continuous variables.

RESULTS

Our study was an observational study of 124 patients. The data was collected both prospectively 80(64.5%) and retrospectively 44(34.5%).Primary APS was present in 46(37.1%),secondary APS in

73(58.9%),SNAPS in (3.2%) and CAPS in 1(0.8%) patients[Table 13].Mean age of study patients was 31.8±9.78 years[Table 2].Our study consisted of 122(98.4%) females and 2(1.6%) males[Table 3].Our study cohort included 59(48.36%) pregnant females and 63(51.63%) non pregnant females[Table 4].

Table 1: Distribution of study population		
Study population	**Number**	**Percentage**
Prospective cases	80	64.5
Retrospective cases	44	35.5
Total	124	100

Table 1 shows distribution of study patients out of 124 patients 80(64.5%) were prospective and 44(35.5%) were retrospective patients

Table 2: Age distribution of study patients		
Age (Years)	**Number**	**Percentage**
18-25	24	19.4
25-29	31	25.0
30-34	32	25.8
35-39	18	14.5
≥ 40	19	15.3
Total	124	100
Mean±SD (Range)=31.8±9.78 (14-66)		

Table 2 shows age distribution of study patients with 32(25.8%) in the age group of 30-34 followed by25-29 age group which constituted 31(25%) patients.

Table 3: Gender distribution of study patients		
Gender	**Number**	**Percentage**
Male	2	1.6
Female	122	98.4
Total	124	100

Table 3 shows gender distribution of study patients .Of the 124 patients 122(98.4%) comprised females and males comprised only 2(1.6%) patients.

Table 4: Pregnancy status of study patients		
Pregnancy status	**Number**	**Percentage**
Pregnant	59	48.36
Non pregnant	63	51.63
Total	122	100

Table 4 shows pregnancy status of the study patients.

Table 5: Clinical profile of study patients		
Clinical manifestations	**Number**	**Percentage**
Venous thrombosis	33	26.6
Arterial thrombosis	16	12.9
Pregnancy morbidity	77	62.1
Non thrombotic neurological symptoms	3	2.4
Nephropathy	11	8.9
Hematologic manifestations	45	36.3
Skin manifestations	76	61.3
Oral ulcers	57	46.0
Alopecia	40	32.3
Synovitis	14	11.3
Sicca symptoms	7	5.6
Renal manifestations	10	8.1

Table: 5 shows clinical profile of the study patients. Most common clinical manifestation was pregnancy morbidity 77(62.1%) followed by hematological 45(36.3%), venous thrombosis was found in 33(26.9%) and arterial thrombosis in 16(12.9%) patients.

Table 6: Clinical profile of study patients			
		Number	**Percentage**
Venous thrombosis	DVT	28	22.6
	Pulmonary embolism	7	5.6
	Superficial thrombophlebitis	1	0.8
	Budd Chiari syndrome	2	1.6
	Cerebral venous thrombosis	3	2.4
Arterial thrombosis	Stroke	9	7.3
	Leg ulcers/digital gangrene	5	4.0
	Arterial thrombosis in extremities	1	0.8
	Splenic infarct	1	0.8
Pregnancy morbidity	Early fetal loss	48	38.7
	Late fetal loss	57	45.6
	Premature birth among live births	2	1.6
Non thrombotic neurological symptoms	Migraine	1	0.8
	Epilepsy	2	1.6
Hematologic manifestations	Thrombocytopenia	33	26.6
	AIHA	4	3.2
	Leucopenia	8	6.5
	Lymphopenia	22	17.7
Skin manifestations	Malar rash	70	56.5
	Photosensitivity	69	55.6
Renal manifestations	Urinary proteinuria	5	4.0
	Positive renal biopsy	5	4.0

Table: 6 shows detailed clinical features of APS patients. Early fetal loss was present in 48(38.7%),late fetal loss in 57(45.6%), thrombocytopenia in 33(26.6%), DVT in 28(22.6%).Other features included stroke in 9(7.3%), PTE in 7(5.6%),leg ulcers and digital gangrene in 5(4%), AIHA in 4(3.2%), cerebral venous thrombosis in 3(2.4%), Budd chiari syndrome ,epilepsy and premature births in 2(1.6%), superficial thrombophlebitis, migraine and splenic infarct in 1(0.8%) patients. Mucocutaneous manifestations which included malar rash 70(56.5%), photosensitivity 69(55.6) and oral ulcers 57(46%) were found mainly in secondary aps patients.

Table 7: Comparison of clinical profile of patients with primary APS and secondary APS						
Clinical Parameters		**Primary APLA [n=46]**		**Secondary APLA [n=73]**		**P-value**
		No.	**%age**	**No.**	**%age**	
Venous thrombosis	DVT	8	17.4	19	26.0	0.273
	Pulmonary embolism	2	4.3	5	6.8	0.869
	Superficial thrombophlebitis	1	2.2	0	0.0	0.387
	Budd Chairi syndrome	0	0.0	2	2.7	0.521
	Cerebral venous thrombosis	0	0.0	1	1.4	1.000
Arterial thrombosis	Stroke	3	6.5	6	8.2	0.733
	Leg ulcers/digital gangrene	1	2.2	4	5.5	0.648
	Arterial thrombosis in extremeties	0	0.0	1	1.4	1.000
	Splenic infarct	0	0.0	0	0.0	-
Pregnancy morbidity	Early fetal loss	31	67.4	14	19.2	<0.001*
	Late fetal loss	24	52.2	29	39.7	0.183
	Premature birth among live births	2	4.3	0	0.0	0.147
Nonthrombotic neurological	Migraine	0	0.0	1	1.4	1.000
	Epilepsy	0	0.0	2	2.7	0.521

symptoms						
Hematologic manifestations	Thrombocytopenia	9	19.6	24	32.9	0.143
	AIHA	0	0.0	4	5.5	0.158
	Leucopenia	0	0.0	7	9.6	0.042*
	Lymphopenia	2	4.3	20	27.4	0.004*
Skin manifestations	Malar rash	3	6.5	63	86.3	<0.001*
	Photosensitivity	4	8.7	61	83.6	<0.001*
Renal manifestations	Urinary proteinuria	0	0.0	5	6.8	0.155
	Positive renal biopsy	0	0.0	5	6.8	0.155

Statistically Significant Difference (P-value<0.05)
P-value by Chi-square test or Fisher's exact test, whichever appropriate

Table7: shows comparison of clinical profile of primary APS and secondary APS patients. There is statistically no difference in most of the clinical features except hematological (leucopenia and lymphopenia) and skin manifestations (malar rash and photosensitivity) which are more common in secondary APS group while as early fetal loss was more common in primary APS group.

Table 8: Hematological manifestations of study patients

Hematological manifestations		Number	Percentage
Hb (gm%)	< 7	3	2.4
	7-9.9	25	20.2
	≥ 10	96	77.4
TLC ($x10^9$/L)	< 1	0	0.0
	1-2	0	0.0
	2-3	3	2.4
	3-4	4	3.2
	≥ 4	117	94.4
ALC ($x10^9$/L)	≤ 500	10	8.1
	501-1000	12	9.7
	1001-1500	60	48.4
	> 1500	42	33.9
Platelets ($x10^3/mm^3$)	≤ 20	3	2.4
	21-50	0	0.0
	51-100	28	22.6
	> 100	93	75.0
ESR(mm/hr) (Wintrobe method)	≤ 20	27	21.8
	21-40	49	39.5
	41-60	31	25.0
	61-80	14	11.3
	81-100	2	1.6
	> 100	1	0.8

Table: 8 shows cumulative distribution of hematological manifestations of our study patients.31(25%) had thrombocytopenia , out of them 28(22.6%) had 51-100 thousand platelets and 3(2.4%) had <20 thousand platelets.7(5.6%) had leucopenia(<4000) while as lymphopenia(<1000) was present in 22(17.8%) patients. All patients who had anemia (Hb< 10) constituted 28(22.6%) of our study cohort. Among patients with anemia

Table 9: Immunological profile of study patients

Immunological profile		Number	Percentage
Lupus Anticoagulant	Positive	66	53.2
	Negative	58	46.8
β2 glycoprotein	Positive	33	26.6
	Negative	91	73.4
Anti cardiolipin antibody	Positive	44	35.5
	Negative	80	64.5

AIHA was present in 4(3.2%).ESR was positive (>20mm/hr) was positive in 97(78.2%) patients.

Table 9: shows immunological profile of study patients .Most common antibody was lupus anticoagulant 66(53.2%) followed by anticardiolipin antibody 44(35.5%) and β2 glycoproteinantibody 33(26.6%).Double antibody positivity was 39(31.2%) patients of which lupus anticoagulantantibody and β2 glycoproteinantibody was positive in 10(8%) patients , β2 glycoprotein antibody and anticardiolipin antibody was present in

16(12.8%) patients , anticardiolipin antibody and lupus anticoagulant antibody was present in 13 (10.4%) patients .Triple positive antibody was present in 5(4%) patients.

Table 10: Immunological profile of study patients

		Number	Percentage
β2 glycoprotein	IgM	16	12.9
	IgG	18	14.5
	Both IgM and IgG	12	9.7
Anti cardiolipin antibody	IgM	6	4.8
	IgG	14	11.3
	Both IgM and IgG	8	6.5

Table 11 : Comparison of Immunological profile of primary APS and secondary APS patients

Immunological profile		Primary APLA [n=46]		Secondary APLA [n=73]		P-value
		No.	%age	No.	%age	
Lupus Anticoagulant	Positive	25	54.3	40	52.6	0.962
	Negative	21	45.7	33	43.4	
β2 glycoprotein	Positive	16	34.8	17	22.4	0.173
	Negative	30	65.2	56	73.7	
Anti cardiolipin antibody	Positive	11	23.9	33	43.4	0.019*
	Negative	35	76.1	40	52.6	

Table 11: shows comparison of immunological profile in primary APS and secondary APS patients. Statistically there is no significant difference in the pattern of distribution of immune antibodies between primary APS and secondary APS group.

Table 12: Other immune antibodies of study patients		
Antibody	**Number**	**Percentage**
ANA	78	62.9
Anti dsDNA	33	26.6
Anti RO	8	6.5
Anti LA	8	6.5
Anti Sm	1	0.8
DCT	6	4.8
Anti CCP	3	2.4
Low C3	16	12.9
Low C4	13	10.5

Table 12 Shows other antibodies present in the study patient which includes ANA in 78(62.9%), Anti dsDNA in 33(26.6%), Anti RO 8(6.5), Anti LA in 8(6.5%), Anti Smith in 1(0.8%), DCT in 6(4.8%), Anti CCP in 3(2.4). Low C3 and C4 was present in 16(12.9) and 13(10.5%) patients respectively.

Table 13: Antiphospholipid syndrome presentation in study patients		
Antiphospholipid syndrome	**Number**	**Percentage**
Primary APS	46	37.1
Secondary APS	73	58.9
SNAPS	4	3.2
CAPS	1	0.8
Total	124	100

Table 13 shows cumulative distribution of the study patients. Out of 124 patients primary APS was present in 46(37.1%), secondary APS in 73(58.9%), APS with SNAPS IN 4(3.2%) and APS with CAPS IN 1(0.8%).

Table 14: Overlapping autoimmune diseases in study patients		
Autoimmune diseases	**Number**	**Percentage**
SLE	72	85.7
Rheumatoid arthritis	3	3.6
Sjogren's syndrome	3	3.6
UCTD	6	7.1
MCTD	0	0.0
Systemic vasculitis	0	0.0
Total	84	100

Table 14 shows the presence of overlapping autoimmune diseases in our study patients. SLE was present in 72(85.7%), Rheumatoid arthritis in 3(3.6%), Sjogren's syndrome in 3(3.6%) and UCTD in 6(7.1%).

DISCUSSION

Our study was an observational study of 124 patients. The data was collected both prospectively 80(64.5%) and retrospectively 44(34.5%).Mean age of study patients was 31.8±9.78 years[Table 2] which is consistent with the study conducted by Cervera et al[12] in which mean age was 34+-13 years(range 0-81;median 31) and Eleftheria P. Grika[16]. Although APS is being recognised with increased frequency in medical practice ,the diversity of its clinical and labortary features makes precise diagnosis challenging and this has been reflected in our study .The

prevelance of major clinical features[table8] in our study was as following .Venous thrombosis was present in 33(26.6%) patients which included DVT in 28(22.6%),pulmonary thromboembolism in 7(5.6%),cerebral venous thrombosis in 3(2.4%),budd chiari syndrome in 2(1.6%) and superficial thrombophlebitis in 1(0.8%) patients. Arterial thrombosis was present in 16(12.9%) patients which included stroke in 9(7.3%), leg ulcers in 5(4%), digital gangrene in 5(4%) and splenic infart in 1(0.8%) patients. Most of these findings are in agreement with the study conducted by Cervera et al[12,13] and Eleftheria p. grika et al[16].In the report by Cervera et al , the most common clinical features were DVT (31.7%), thrombocytopenia (21.9%), stroke (13.1%), superficial thrombophlebitis (9.1%), Pulmonary embolism (9.0%), fetal loss (8.3%) and hemolytic anemia (6.6%) . Other clinical features which are not the part of classification criteria for definite antiphospholipid syndrome that were present in our study included thrombocytopenia 33(26.6%), lymphopenia 22(17.7%), leucopenia in 8(6.5%),AIHA in 4(3.2%),epilepsy in 2(1.6%) and migraine in 1(0.8%) patients which are in agreement with the study conducted by Cervera et al[12,13] and Eleftheria p et al[16]. Interestingly one of the most common clinical manifestation of the APS in our study is pregnancy morbidity[Table 5 & 6] ,including abortions both early and late,intrauterine deaths,intrauterine growth retardation and premature births.Early fetal loss was present in 48(38.7%),late fetal loss in 47(37.9%),intrauterine death in 15(12%),intra uterine growth retardation in 2(1.6%) and premature births in 2(1.6%) patients. Other features which include malar rash, photosensitivity, alopecia, sicca symptoms and renal involvement were mostly associated with secondary APS patients. Also, when we compared the clinical features of primary APS with secondary APS[table 7], we found that both the groups have almost similar clinical features except hematological (leucopenia and lymphopenia) , skin manifestations (malar rash and photosensitivity),alopecia ,arthritis and glomerulonephritis which are more common in secondary APS group while as early fetal loss was more common in primary APS group.This observation is supported by the study conducted by JL. Vianna et al[11] and Cervera et al[12,13] who found almost similar results. The immunological profile of the study patients was compared with previous studies. Most common major antibodies[Table 9] present in study patient were lupus anticoagulant 66(53.2%),anticardiolipin in 44(35.5%) and β2 glycoprotein in 33(26.6%) patients which are in agreement with the study conducted by Cervera et al[12,13].other antibodies included[Table 12] ANA in 78(62.9%), anti dsDNA in 33(26.6%),anti RO and anti LA in 8(6.5%),anti CCP in 3(2.4%) and anti Sm in 1(0.8%) patients.APS is associated with various autoimmnune diseases.In our study primary APS was present in 46(37.1%) and secondary APS in 73(58.9%) patients, which included patients of SNAPS 4(3.2%) and catastrophic APS 1(0.8%)[Table 13]. The overlapping autoimmune diseases in our study were SLE 72(85.7%),Rheumatoid arthritis and Sjogren's syndrome in 3(3.6%) and UCTD in 6(7.1%) patients[Table14].

CONCLUSION

APS is a disorder characterized by a wide variety of clinical manifestations. Virtually any organ system or tissue may be affected by the consequences of large- or small-vessel thrombosis. There is a broad spectrum of disease among individuals with aPL, from asymptomatic to imminently life-threatening CAPS. Patients may exhibit clinical features suggesting APS but not fulfill the International Criteria for a ''definite'' diagnosis. SNAPS patients demonstrate typical idiopathic thromboses but aPL are not initially detected. Patients defined with definite APS demonstrate nearly identical sites of venous and arterial thrombosis, regardless of the presence or absence of SLE. Microangiopathic APS may present with isolated tissue and organ injury or as the overwhelming ''thrombotic storm'' observed in CAPS.

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