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ORIGINAL ARTICLE

Study of clinical utility of antibodies to phosphatidylserine/prothrombin complex in Asian-Indian patients with suspected APS

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Abstract

Antiphospholipid syndrome (APS) is the most common acquired pro-thrombotic disorder, also associated with obstetric complications. Phosphatidylserine/Prothrombin complex antibody (aPSPT) though associated with various APS manifestations, is not included in the revised Sapporo Criteria. To study the prevalence of aPSPT in Asian-Indian patients with suspected APS and compare its performance with the criteria anti-phospholipid antibodies (APLs). Electronic charts of 372 individuals whose sera was tested for aPSPT in suspected APS between June 2014 and May 2016 were retrieved and analyzed. aPSPT was assayed by ELISA. aPSPT tested individuals were categorized into cases—seropositive and seronegative APS (SNAPS) and controls. aPSPT was positive in 24/58 (41.3%) cases and 17/314 (5.4%) controls ($p < 0.001$). aPSPT positivity was seen in 44.5%, 38.7%, and 58.4% in primary, secondary and SNAPS patients respectively. aPSPT had the best performance among all APLs, in obstetric APS with 31% sensitivity, 97.7% specificity, and an odds ratio of 18.8. It showed 41.4% sensitivity, 94.6% specificity for the classification/diagnosis of primary APS and 38.7% sensitivity, 91.5% specificity for secondary APS. Addition of aPSPT to current APS criteria to SNAPS patients led to reclassification of additional 12.1% patients as APS overall and 42.8% in obstetric APS category. In Asian-Indian patients with suspected APS, aPSPT outperformed all classical APLs in diagnosis/classification of obstetric APS and both isotypes of beta 2-glycoprotein-I antibodies in diagnosis/classification of APS. aPSPT could reclassify additional 12.1 and 42.8% patients as APS overall and obstetric APS respectively, over and above the cases satisfying revised Sapporo criteria.

Keywords Antiphosphatidylserine prothrombin complex antibody · APS · aPSPT · Obstetric APS · Seronegative APS

Introduction

Antiphospholipid syndrome (APS) is an autoimmune disease characterized by thromboses (arterial/venous/both) and/or obstetric complications, along with a positive antiphospholipid antibody (APL) status [1–3]. Classical APLs included in the revised Sapporo criteria [1] for APS are either detected by coagulation tests, such as lupus anticoagulant activity (LA) or by an enzyme-linked immunosorbent assay (ELISA) as in cases of anti-cardiolipin antibodies (ACL) and antibodies

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against β2-glycoprotein I (anti-β2GPI). However, several other antibodies, not a part of the revised Sapporo criteria, are often seen in association with seropositive as well as seronegative APS. These antibodies have been described to be associated with various manifestations of APS.

Antibodies against prothrombin (aPT) can be detected by ELISA targeting prothrombin alone, coated onto the plates, or by targeting the phosphatidylserine/prothrombin complex. Antibodies to phosphatidylserine/prothrombin complex (aPSPT) have considerable appeal as a biomarker for diagnosis of APS, especially in cases of seronegative APS (SNAPS) and as a predictor of clinical manifestations of APS.

There have been contradictory reports regarding aPT antibodies in relation to manifestations of APS, where some studies showed no relation at all while a few reports mention good correlation [4–7]. aPSPT has been described to correlate with arterial/venous thrombosis and recurrent pregnancy loss (RPL) in various studies. aPSPT has also been considered to be a better surrogate marker of LA activity in some studies [8–11], as compared to aPT. Some studies have also reported PS/PT complex and not PT alone, as the target of LA activity [12]; therefore, assays involving PS/PT, rather than PT alone for LA activity may be ideal in patients on oral anticoagulation, in whom testing for LA activity is a challenge. Recently, it was shown that aPSPT could also be pathogenic by inducing thrombosis, when Wistar rats were injected intravenously with aPSPT [13].

The idea of SNAPS as an entity was originally mooted in patients with classical clinical manifestations of APS, in absence of classical APLs [14]. aPSPT has been described to be detected in almost half of these SNAPS patients recently, thus serving as a reasonable lab biomarker for identification of APS patients who are negative for classical APLs [15].

Objectives

Using a commercial ELISA kit, we aimed:

a) To study the prevalence of aPSPT in Asian-Indian patients with suspected APS
b) To compare its performance with the three classical APLs currently included in the APS criteria, namely, LA, ACL, and IgG/IgM anti-β2GPI antibodies.

Methods

The study was approved by the institutional review board (IRB) and performed in accordance with the guidelines prescribed by the ethics committee of Christian Medical College, Vellore with Approval no IRB no 11001(retro) dated 22/11/2017. A special waiver of consent was duly obtained from the IRB in view of this study being of a retrospective design. Electronic medical records (EMR) of 372 individuals with suspected APS, who were tested for aPSPT between June 2014 and May 2016 in the Department of Clinical Immunology and Rheumatology, Christian Medical College Hospital, Vellore, were reviewed retrospectively. EMRs were browsed for arterial events like peripheral gangrene, stroke, non-healing ulcers, adrenal insufficiency, cardiac thromboses, and mesenteric thromboses. Venous thromboembolism like deep venous thromboses of lower limbs, cortical venous thromboses, Budd-chiari syndrome, inferior vena-caval thromboses, renal vein thromboses, pulmonary thromboembolism, and central retinal vein occlusion was also searched for and noted. Non-criteria manifestations of APS like thrombocytopenia, autoimmune hemolytic anemia, livedo reticularis, cardiac valvular abnormalities, chorea, migraine, and Pseudo multiple sclerosis (MS) like presentation on neuroimaging, seizures, and Raynaud's phenomenon were also recorded from the EMRs whenever present. Obstetric events were categorized into late pregnancy losses (> 10 weeks of gestation), early pregnancy losses (< 10 weeks of gestation), and premature births (< 34 weeks of gestation) and their frequencies were collected from the EMRs along with their most probable cause documented by the obstetricians.

aPSPT testing

Combined IgG/IgM aPSPT were tested by commercial ELISA (Aesuku, Germany) platform. In accordance with the manufacturer's instructions, cut-off values for IgG/IgM aPSPT were > 24 U/ml.

LA testing at our center was done as per International Society of Thrombosis and Haemostasis guidelines [16, 17]. IgG ACL, IgG, and IgM β2GP1 antibodies were tested using commercial ELISA (Euro-immune) and interpretation was done as per 2006 revised Sapporo criteria definition.

Case definition

Patients were classified as APS on the basis of Revised 2006 Sapporo criteria. Patients satisfying only clinical arm of the revised Sapporo criteria without fulfilling laboratory arm who were managed with anticoagulation, were classified as SNAPS.

Control definition

Patients with systemic autoimmune diseases, with or without the three classical APLs, but not satisfying the clinical arm of Sapporo criteria were categorized as connective tissue disease (CTD) controls. Obstetric controls were patients with recurrent pregnancy loss (RPL) due to other causes and not satisfying the definition of revised Sapporo criteria for APS.

Thrombotic controls were patients with pro-coagulant states, other than APS. Non-CTD and non-RPL controls were individuals attending rheumatology clinic for rheumatic symptoms other than CTD or RPL.

Statistical analysis

Statistical analysis was performed using SAS version 9.2. The measurement data is expressed as mean (± standard deviation) or median (with inter-quartile range) based on the normality of distribution of values. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratios (LR), and odds ratios (OR) were calculated for the classical APL tests as well as for aPSPT. The chi-square (χ^2) test was performed for the comparison of categorical variables between two groups whenever needed. Logistic regression was performed to identify in the patients, the independent risk factors for clinical events like thromboses or RPL. $p < 0.05$ was considered statistically significant.

Results

Description of cases, controls, and clinical manifestations

A total of 58 cases with definite APS and 314 controls were studied. The mean age of the subjects was 32 ± 9.25 years, with a female predominant ratio of 8:1. The sub-classification of cases is described in Table 1.

Majority (53, 91.4%) of patients with APS had thrombotic events, 34 (58.6%) with venous thrombosis, and 24 (41.3%) of them being arterial. Seventeen (29.31%) patients had obstetric events. Venous thromboembolism included deep vein thromboses in 29 (50%) and pulmonary thromboembolism in 6 (10.3%). Arterial events included stroke in 10 (17.2%), gangrene in 7 (12%), acute coronary syndrome, adrenal infarction and non-healing ulcers in 2 (3.4%) each, intra-cardiac thrombosis and mesenteric artery thrombosis in 1 (1.7%) patient each. Among the patients with obstetric events, 14 (24.1%) had late pregnancy loss, 7(12%) had early pregnancy loss, and 2 (3.4%) had premature births after 34 weeks of gestation. Non-criteria manifestations noted in the cohort were thrombocytopenia in 5 (8.6%) patients; autoimmune hemolytic anemia in 4 (6.9%) patients; cardiac valvular abnormalities, livedo reticularis, chorea, and seizures in 2 (3.4%) patients each; and Pseudo MS like presentation and migraine in 1 (1.7%) patient each.

Among the 314 controls, 56% were obstetric controls, 40.8% were CTD controls, 0.9% were thrombotic controls while 4.1% were non-CTD, non-RPL disease controls (Table 2).

Frequency of aPSPT in cases and controls

Forty-one of 372 (11.02%) individuals tested positive for the antibody. The frequency of aPSPT was higher in APS cases ($n = 24$, 41.3%) as compared to all controls together ($n = 17$, 5.4%) ($p < 0.001$). Sub-group analysis showed presence of aPSPT in 12/27(44.5%) patients with primary APS, 12/31(38.7%) cases with secondary APS and in 7/12 (58.4%) of patients with SNAPS.

Comparison of aPSPT with classical APLs

Among definite APS patients, LA was positive in 38/58 (65.5%) cases, followed by aPSPT in 24/58 (58.5%), ACL in 19/58 (32.75%), IgG anti-β2GPI antibodies in 13/58 (22.41%), and IgM anti-β2GPI antibodies in 7/58 (12.06%) patients. Triple positivity (all criteria APLs) was seen in 11/58 (19%) patients, of which 9 patients had quadruple positivity (criteria APLs+ aPSPT). Addition of aPSPT to the current APS criteria led to re-classification/diagnosis of additional 7 (12.1%) patients as APS with sensitivity of 88.3%, specificity of 83.8%, PPV of 50.9%, NPV of 97.4% with OR of 39 (Fig. 1). Addition of aPSPT to current APS criteria in sero-negative obstetric APS sub-group led to re-classification of 3/7 (42.8%) patients as sero-positive obstetric APS with a sensitivity of 100%, specificity of 85.8%, PPV of 21.9%, and NPV of 100% with an OR of 89.1.

Logistic regression (Fig. 2, Table 3) was done to assess independent association of all antibodies with different sub-categories of APS. Among all the antibodies, LA had the best association with diagnosis of APS (sensitivity 65.5%, specificity 92.3%, OR 8.46) followed by aPSPT (sensitivity 41.4%, specificity 94.6%, OR 12.3). LA again was the best performing antibody in diagnosis of APS in the setting of CTD (sensitivity 74.2%, specificity 87.9%, OR 20.9) followed by ACL IgG (sensitivity 38.7%, specificity 97.1%, OR 20.8) and aPSPT (sensitivity 38.7%, specificity 91.5%, OR 6.78). aPSPT had the best performance in the setting of obstetric APS in comparison to classical APLs (sensitivity 31%, specificity 97.7%, OR 18.8), followed by LA (sensitivity 27.6%, specificity 96.9%, OR 11.7).

Clinical associations of aPSPT

Regression analysis (Supplementary Table 1) found aPSPT to have an independent association with occurrence of arterial, obstetric and non-criteria manifestations as well as with recurrence of arterial and venous events ($p < 0.05$). aPSPT was however, positive in only 41.46% patients who were positive for lupus anticoagulant.

Table 1 Clinical characteristics and sub-categorization of APS cases in the study

Definite APS cases ($n = 58$)	Parameter value
Age (mean ± SD in years)	34.4 ± 8.3
Sex (female: male)	49:9
Primary APS	27 (46.5%)
Secondary APS	31 (53.5%)
SLE	24 (41.3%)
Undifferentiated CTD	5 (8.6%)
Sjogren's syndrome	1 (1.7%)
Scleroderma	1 (1.7%)
Seronegative APS	12 (20.6%)
Thrombotic APS	53 (91.4%)
Obstetric APS	17 (29.3%)
Antiphospholipid antibody (APL) positivity	53 (91.4%)
Single positivity (classical APLs)	29 (50%)
Double positivity (classical APLs)	6 (10.3%)
Triple positivity (classical APLs)	11 (19%)
Quadruple positivity (classical APLs + aPSPT)	9 (15.5%)
Time since last APS related event (median with interquartile range) in days	165 (30–600)
Venous thromboembolism	34 (58.6%)
Deep venous thrombosis	29 (50%)
Pulmonary thromboembolism	6 (10.3%)
Arterial thromboses	24 (41.3%)
Stroke	10 (17.2%)
Peripheral gangrene	7 (12.0%)
Acute coronary syndrome	2 (3.4%)
Adrenal infarction	2 (3.4%)
Non-healing arterial ulcers	2 (3.4%)
Intra-cardiac thrombosis	1 (1.7%)
Mesenteric gangrene	1 (1.7%)
Obstetric events	17 (29.3%)
Late pregnancy loss (> 10 weeks of gestation)	14 (24.1%)
Early pregnancy loss ≥ 3 consecutive (< 10 weeks of gestation)	7 (12.0%)
Premature births due to placental insufficiency (< 34 weeks of gestation)	2 (3.4%)
Non-criteria manifestations	12 (20.7%)
Thrombocytopenia	5 (8.6%)
Auto-immune hemolytic anemia	4 (6.9%)
Livedo reticularis	2 (3.4%)
Cardiac valvular abnormalities	2 (3.4%)
Chorea	2 (3.4%)
Seizures	2 (3.4%)
Pseudo multiple sclerosis like presentation	1 (1.7%)
Migraine	1 (1.7%)

APS, anti-phospholipid syndrome; *APL*, antiphospholipid antibody; *CTD*, connective tissue disease; *SD*, standard deviation; *aPSPT*, antiphosphatidylserine/prothrombin antibody

Discussion

There is a need for newer biomarkers in APS which could pick up SNAPS and improve the management of thrombotic or obstetric manifestations of these patients. Missing the diagnosis of SNAPS could prove costly in certain scenarios like life-threatening thrombosis and recurrent pregnancy loss. aPSPT has generated enough interest in this regard, and clinicians and researchers alike have raised the point in favor of including aPSPT in the classification criteria of APS, based on

Table 2 Distribution of controls under each sub-category in the study

CTD controls (n = 176/314; 40.8%)	Obstetric controls (n = 128/314; 56%)
SLE 100 (56.8%)	Structural abnormalities-female genital tract 8 (6.25%)
Sjogren's syndrome 2 (1.1%)	Chromosomal anomalies 4 (3.13%)
MCTD 7 (3.9%)	Clinically suspected of obstetric APS, but not proven 89 (69.5%)
UCTD 27 (15.34%)	TORCH complex infections 3 (2.3%)
Scleroderma 2(1.1%)	Gestational diabetes 1 (0.7%)
Rheumatoid arthritis 4 (2.3%)	Ectopic pregnancy 1 (0.7%)
Vasculitis 27(15.34%)	Blighted ovum 8 (6.25%)
CTD related PAH 7(3.9%)	Gestational trophoblastic disease 2 (1.5%)
	Fetal structural abnormalities 4 (3.1%)
	Pregnancy-induced hypertension 4 (3.1%)
Non-CTD, non-RPL disease controls (n = 13/314; 4.1%)	Thrombotic controls (n = 3/314; 0.9%)

APS, anti-phospholipid syndrome; *CTD*, connective tissue disease; *UCTD*, undifferentiated connective disease; *MCTD*, mixed connective tissue disease; *PAH*, pulmonary artery hypertension; *TORCH complex*, toxoplasma gondii, rubella virus, cytomegalovirus, and herpes simplex infections; *RPL*, recurrent pregnancy loss

data-driven evidences. aPSPT was present 41.4% of APS patients in our cohort. The prevalence of aPSPT in APS reported in literature was 43.3% in Polish cohort [18], 51% in a Spanish Cohort [19], 65% in an Italian cohort [20], 68.6% in a Japanese cohort [21], and 63.0% and 86% in two Chinese studies [15, 22], whereas two American studies reported this frequency as 54.6% and 83% respectively [23, 24]. Table 4 shows comparison of aPSPT in the present study with the studies mentioned above belonging to different geo-ethnicities. The lower prevalence in our cohort needs to be confirmed by future studies in this geo-ethnic population. However, we feel that the lower prevalence could have been due to delay in performing this test following the preceding thrombotic event (median 165 days); effect of immunosuppression in majority of our patients with secondary APS could also be a contributing factor.

In our evaluation of aPSPT in patients with suspected APS, it was the second best performing antibody after LA, in diagnosis/classification of APS (sensitivity 41.4%, specificity 94.6%, OR 12.3). LA was the best performing APL in all clinical scenarios of seropositive APS, except in obstetric APS. aPSPT also displayed sensitivity of 38.7%, specificity of 91.5% with OR of 6.78 in the diagnosis of APS in the setting of CTD. LA again was the best performing antibody in this setting (sensitivity 74.2%, specificity 87.9%, OR 20.9) followed by IgG ACL (sensitivity 38.7%, specificity 97.1%, OR 20.8). In obstetric APS, aPSPT had the best sensitivity (31%) with equivalent specificity (97.7%) comparable to that of classical APLs.

aPSPT could diagnose/re-classify an additional 12.1% cases as seropositive APS overall; however, among the obstetric APS cases, this test yielded 42.8% higher pick up rate, over and above the cases satisfying revised Sapporo criteria. The frequency of aPSPT in SNAPS reported from our study adds to the growing evidence of reported frequency of aPSPT in SNAPS in recent studies, and we could document this by including SNAPS patients as cases in the study population. In a recently published Chinese study, aPSPT was detectable

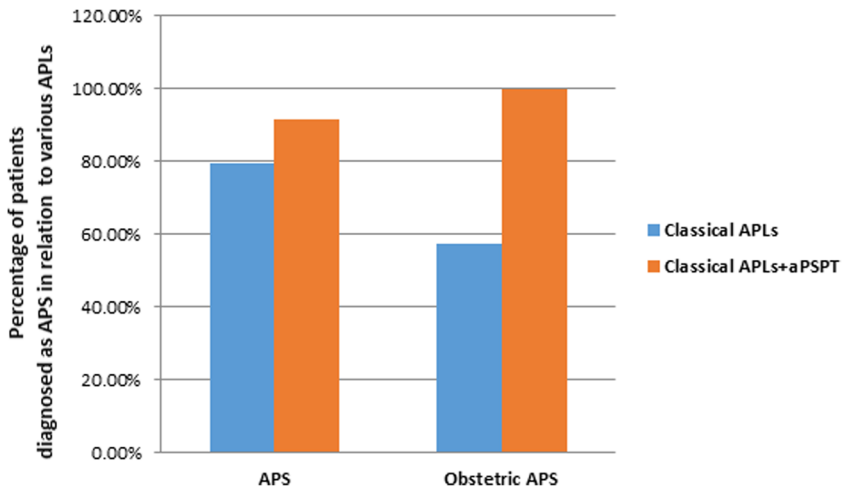

Fig. 1 Showing the additional pick up rate of APS including aPSPT in the APS classification criteria for SNAPS (overall) and seronegative obstetric APS patients. APS, antiphospholipid syndrome; APL, Antiphospholipid antibody; aPSPT, Anti phosphatidylserine-prothrombin antibody; Seronegative APS (SNAPS)

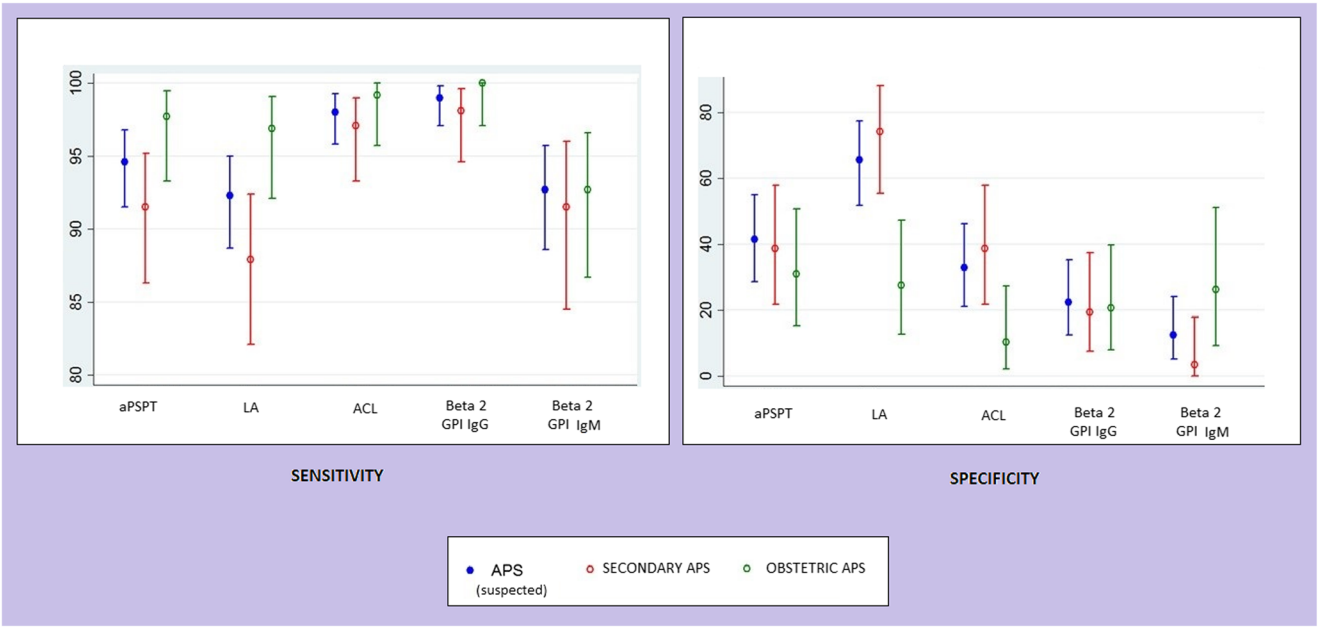

Fig. 2 **a**, **b** showing sensitivity and specificity of aPSPT and classical APLs in the setting of suspected APS, obstetric APS and APS in the setting of CTD. APS, antiphospholipid syndrome; APL, antiphospholipid antibody; aPSPT, antiphosphatidylserine-prothrombin antibody; LA, lupus anticoagulant; ACL, anti-cardiolipin; GPI, glycoprotein I; CTD, connective tissue disease

Table 3 Performance of aPSPT in comparison to other criteria APLs in all patients who were evaluated for suspected APS in the study

Category of APS		aPSPT	LA	ACL IgG	anti-β2GPI IgG	anti-β2GPI IgM
Suspected APS	Sensitivity	41.4%	65.5%	32.8%	22.4%	12.5%
	Specificity	94.6%	92.3%	98%	99%	92.7%
	PPV	58.5%	61.3%	76%	81.3%	29.2%
	NPV	89.7%	93.5%	88.5%	86.7%	81.6%
	LR (+) (95%CI)	7.64 (4.39–13.3)	8.46 (5.52–13)	16.7 (6.97–40)	22.1 (6.51–75.2)	1.72 (0.75–3.95)
	LR (−) (95%CI)	0.62 (0.49–0.77)	0.37 (0.26–0.53)	0.68 (0.57–0.82)	0.78 (0.68–0.90)	0.94 (0.84–1.05)
	OR (95%CI)	12.3 (6.07–25.1)	22.6 (11.5–44.7)	24.4 (9.4–62.8)	28.2 (8.25–95.7)	1.82 (0.73–4.54)
APS in the setting of CTD	Sensitivity	38.7%	74.2%	38.7%	19.4%	3.45%
	Specificity	91.5%	87.9%	97.1%	98.1%	91.5%
	PPV	44.4%	52.3%	70.6%	66.7%	10%
	NPV	89.4%	95%	89.7%	86.3%	77.6%
	LR (+) (95%CI)	4.54 (2.36–8.75)	6.15 (3.91–9.66)	13.2 (4.99–34.7)	10.3 (2.73–39.1)	0.4 (0.05–3.08)
	LR (−) (95%CI)	0.67 (0.5–0.89)	0.29 (0.16–0.53)	0.63 (0.47–0.83)	0.82 (0.69–0.97)	1.0 (0.96–1.15)
	OR (95%CI)	6.78 (2.81–16.4)	20.9 (8.42–51.9)	20.8 (6.84–63.1)	12.6 (3.2–48.8)	0.3 (0–2.49)
Obstetric APS	Sensitivity	31%	27.6%	10.3%	20.7%	26.3%
	Specificity	97.7%	96.9%	99.2%	100%	92.7%
	PPV	75%	66.7%	75%	100%	35.7%
	NPV	86.2%	85.4%	82.9%	84.6%	89.1%
	LR (+) (95%CI)	13.2 (3.82–45.9)	8.76 (2.83–27.1)	13.1 (1.42–122)	–	3.63 (1.36–9.67)
	LR (−) (95%CI)	0.7 (0.55–0.9)	0.74 (0.59–0.93)	0.9 (0.79–1.02)	–	0.79 (0.6–1.04)
	OR (95%CI)	18.8 (4.99–69.5)	11.7 (3.41–40)	14.5 (1.98–119.6)	–	4.56 (1.41–15)

APS, anti-phospholipid syndrome; *APL*, antiphospholipid antibody; *CTD*, connective tissue disease; *aPSPT*, antiphosphatidylserine/prothrombin antibody; *LA*, lupus anticoagulant; *ACL*, anti-cardiolipin; *β2GPI*, beta 2 glycoprotein I; *CTD*, connective tissue disease; *OR*, odds ratio; *LR*, likelihood ratio; *PPV*, positive predictive value; *NPV*, negative predictive value; *CI*, confidence interval

Table 4 Geo-ethnic comparison of data on aPSPT in APS: present study vs existing literature

Study	Geographic region of the study	Study design	Number of APS patients	Number of controls	Sensitivity of aPSPT for APS	Specificity of aPSPT	Clinical associations of aPSPT
Present study	India	Cross sectional with retrospective chart review	58	314	41.4%	94.6%	1) Arterial thrombosis, obstetric events, non-criteria manifestations 2) Recurrent venous/ arterial thrombosis 3) 12.1 and 42.8% better pick up of seronegative patients 4) No LA correlation
Vlagea et al. 2013 [19]	Spain	Cross sectional	295	150	51.7%	85.5%	1) Venous thromboses and obstetric abnormalities 2) LA correlation
Hui Shi et al. 2018 [15]	China	Cross sectional	186	176	53%	97.7%	1) LA 2) Venous Thrombosis and pregnancy loss 2) 50% of SNAPS patients were positive for aPSPT
Lei Zhu et al. 2017 [22]	China	Cross sectional	108	191	63%	92.8%	1) Arterial and Venous Thrombosis 2) LA correlation
Pregnolato et al. 2013 [24]	American	Cross sectional	80	179	81.6% (APS	92% (APS)	1) Thrombotic manifestations 2) LA correlation
NM Heikal et al. [23]	American	Cross sectional	104	–	45.5–54.6%	–	LA correlation

APS, antiphospholipid syndrome; *aPSPT*, antiphosphatidylserine-prothrombin antibody; *LA*, lupus anticoagulant

in about 20% of patients in SNAPS category, where as in our cohort aPSPT was seen in 58.4% of our SNAPS patients [22]. However, another recent publication from China reported a prevalence of 50% aPSPT positivity in their SNAPS patients [15]. In a Slovenian cohort of APS with adverse pregnancy outcomes, aPSPT testing along with classical APLs could guide treatment of additional 7% patients belonging to the SNAPS subset [25].

Similar to various studies, aPSPT in our study also correlated significantly ($p < 0.05$) with occurrence of arterial, obstetric and recurrent arterial/venous thrombotic events [15, 19, 20, 22]. Furthermore, in our study, aPSPT correlated significantly ($p < 0.05$) with occurrence of non-criteria manifestations; similar association with two non-criteria manifestations, namely, Raynaud's phenomenon and migraine, has been reported only in another recent study [18]. Contrary to the previously reported studies, aPSPT was positive in only 41.46% of LA positive patients; hence, it did not correlate with LA activity in our study unlike earlier studies reporting aPSPT as a clinical surrogate of LA activity [15, 22–24].

The present study was a retrospective review of data of all patients/subjects who underwent aPSPT assay at our center. Ideally, a prospective case control design would be a preferred study design. However, the results of our study reflect the inclination of clinicians to look for newer antibodies to increase their pick-up rate of seropositive APS cases, in real world clinical practice where in only three markers for APS exist. aPSPT could be a very useful biomarker for pure obstetric APS in absence of thrombotic events, as well as in the absence of classical APLs. Rate of classical APL positivity and sensitivity in our study is lower than the reported rate in the literature, possibly due to bias of ordering aPSPT only in the setting of suspected seronegative APS. Our study is a novel one as this is the maiden study on aPSPT in Asian-Indian sub-population. Moreover, our study reflected "real life" scenarios in clinical practice, where in clinicians order aPSPT testing for pro-thrombotic situations and RPL; thus, prevalence rates of aPSPT in APS and SNAPS in our study may reflect its true frequency while dealing with suspected APS patients.

Conclusion

The present study is the first collected data on aPSPT in Asian-Indian patients with suspected APS. aPSPT performance was

comparable to that of ACL for diagnosis of primary and secondary APS; however, it outperformed all classical APLs in diagnosis of Obstetric APS. aPSPT also outperformed IgG and IgM anti-β2GPI antibodies in the diagnosis of primary, secondary and obstetric APS. aPSPT could also diagnose an additional 12.1% patients as APS in overall and 42.8% more cases of obstetric APS, over and above the cases satisfying revised Sapporo criteria. aPSPT correlated with occurrence of arterial, obstetric and non-criteria manifestations and also with recurrent arterial/venous thromboses.

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Compliance with ethical standards

The study was approved by the institutional review board (IRB) and performed in accordance with the guidelines prescribed by the ethics committee of Christian Medical College, Vellore with approval no: IRB no. 11001(retro) dated 22/11/2017. A special waiver of consent was duly obtained from the IRB in view of this study being of a retrospective design.

Disclosures None.

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